Welcome to BioMag 2012, the 18th international Conference on BioMagnetism. The program this year, thanks to your excellent and numerous contributions, is particularly exciting, with 5 satellite events, almost 600 posters, 90 oral presentations organized in 21 symposia, and 5 keynote lectures by Maurizio Corbetta, Krish Singh, Anne-Lise Giraud, Christopher Moore, and Karl Friston.

A growing multidisciplinary community. BioMag history is rooted in lively exchanges crossing disciplinary borders, from physics and sensor developments to sophisticated methodological advances to make the best out of the high dimensionality of the signals we acquire, applied to various organs, from heart and enteric system to brain, in both basic and clinical research. The field is quickly expanding, with the emergence of new sensors and instruments (ultra-low field MRI, atomic magnetometer, magnetic nanoparticles), the explosion of new methods to apprehend all aspects of biological dynamics and interactions (connectivity, causality), and the growing interplay between SQUID-based measurements and other techniques such as EEG or fMRI.

Express your opinion at the Business Meeting on Wednesday August 29 at 17:30 in Hall A: Where should BioMag 2016 take place? What would be the contours of our community in the future?

In memoriam. Line Garnero, who took an active part in initiating BioMag2012, would have been profoundly happy to see you here. For those of you who knew her, symposium S-Th-A1 "The neural dynamics underlying the brains default-mode and resting-state networks" (Thursday August 30, 9:00, Hall A) is dedicated to her memory.

Share the latest scientific results, have a great meeting, enjoy your stay in Paris, and mark your calendars for the next BioMag Conference in Halifax, Canada, August 23-29, 2014.

Paris, June 2012

Catherine Tallon-Baudry, Olivier Bertrand
Ecole Normale Supérieure, Paris Lyon Neuroscience Research Center
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28bis, rue Saint-Dominique - Paris
web: http://www.maisondelachimie.com

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Métro:
line 8, stop: Invalides
line 12, stops: Assemblée Nationale or Solférino
line 13, stop: Invalides

Bus: lines 63, 69, 83, 93 and 94
RER: Line C, stop: Invalides

Important telephone numbers

International country code for France: +33
The countrywide number for all emergency situations: 112
from mobile phone and 15 otherwise (17 for police)

Lost credit card

Master Card 08 99 23 31 54
Visa 08 99 23 31 53
Visa Premier 08 99 23 87 60

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www.paris.fr

Taxis

Fares: 50 to 60 from CDG Airport to Downtown Paris
(+15% at night or during week-end)

- Taxi Bleu: 08 91 70 10 10
- Taxi G7: 01 47 39 47 39
- Aéro-Taxi: 01 47 39 01 47
- Artaxi: 01 42 03 50 50 or 08 91 70 25 50
- Alpha Taxi: 01 45 85 85 85
- Taxis Sept Mille: 01 42 70 00 42 or 01 42 70 95 50

Weather forecast

http://www.meteo-paris.com/ile-de-france/previsions.php

Road condition

http://www.sytafrin.fr/

Currency and Exchange Facilities

Official currency of France is the Euro. Foreign currencies
can be exchanged at bank exchange counters and exchange
offices, hotels, and airports. Hotels, stores, and restaurants
in France accept major credit cards. Cash can be with-
drawn at ATMs in all cities and tourist centers.

Internet connexion

Internet connection at Maison de La Chimie: A free WIFI
access will be available during BioMag 2012.
REGISTRATION INFORMATION

Registration desk is open from 8:00 to 19:30.

Individual REGISTRATION is mandatory for all Biomag2012 participants.

WARNING: ON SITE REGISTRATIONS ARE PAYABLE BY CREDIT CARDS ONLY!

Registration package includes:

• Scientific sessions
• Conference material
• BIOMAG 2012 Program booklet
• Welcome reception
• Refreshment breaks

The participants will receive attendance certificates.

The BIOMAG 2012 registration fee does not include any insurance coverage. Participants are responsible for arranging an appropriate insurance on their own. Health and accident insurance is recommended and should be arranged in your country of origin.

Registration package for accompanying persons includes the Welcome reception.

Registration terms and conditions
It is agreed that the Local Organizing Committee, its officers, volunteers, contracted staff, contracted companies and agents shall not be held liable or responsible for:

1. Any loss or damages, however caused by any person engaged by, participating in, or attending the Biomag2012 and its satellite events for any reason whatsoever;
2. Refusal of admission, any changes in program dates, content, speakers, location, or cancellation of any programs or functions.

Cancellation Policy
Cancellations (sent to congres@spat.fr), made prior to May 30th, 2012 will be charged a processing fee of EURO 80. Cancellations, received after May 30th, 2012 will not be honored. All refunds will be made after Biomag 2012.
BIOMAG 2014

Chairs: Margot Taylor & Ryan D’Arcy

Web site: www.biomag2014.org
**SA TELLITE EVENTS**

### Emerging MEG applications in TBI, stroke, AD, autism and pain: Advances in networks and connectivity

**Chairs:** Ryan C.N. D’Arcy (Halifax, Canada) & Margot Taylor (Toronto, Canada)

**Sponsor:** Elekta Neuromag and Elekta Atlantic

**Location:** The satellite event will take place at the new Brain Institute at Hôpital Pitié-Salpêtrière (ICM) in Paris, on Saturday the 25th, August 2012, from 9 am to 6 pm.

**Description:** This Biomag 2012 Satellite Event is planned for a full day. There are five key disease themes: traumatic brain injury (TBI), stroke, Alzheimer’s disease (AD), autism spectrum disorder (ASD), and pain. The two cross-cutting themes relate to MEG strengths and advances in imaging of neural networks and functional connectivity.

**Instructors:** Dr. Ryan D’Arcy, Halifax, Canada, Dr. Margot Taylor, Toronto Canada, Dr. Tim Bardouille, Halifax, Canada, Dr. Bruce Dick, Edmonton, Alberta, Dr. Jyrki Makela, Helsinki, Finland, Dr. Mingxiong Huang, San Diego, USA, Dr. Timothy Roberts, Philadelphia, USA, Dr. Bob van Dijk, Amsterdam, Netherlands

**Workshop Objectives:**

- to highlight emerging clinical applications beyond traditional ones (e.g., epilepsy and presurgical mapping);
- to foster the utilization and development of network and connectivity approaches as a MEG technology advantage; and
- to identify common challenges to overcome in order to integrate emerging applications into best clinical practices. These challenges include:
  - diagnostic biomarkers,
  - clinical evaluation, and
  - therapeutic monitoring for recovery/rehabilitation.

### Studying the brain as a network using MEG: practical considerations

**Chairs:** Ole Jensen (Nijmegen, The Netherlands), Sarang Dalal, (Konstanz, Germany) & Johanna Zumer, (Nijmegen, The Netherlands)

**Location:** The satellite event will take place at the new Brain Institute at Hôpital Pitié-Salpêtrière (ICM) in Paris, on Saturday the 25th, August 2012, from 9 am to 6 pm.

**Description:** It is becoming increasingly important to study the working brain as network both in cognitive and clinical neuroscience. MEG provides an excellent opportunity to study the functional interactions between various brain regions. There are now multiple approaches and tools available for doing this. The aim of the proposed workshop is to elucidate practical approaches for studying brain connectivity using MEG. This will be done by a set of presentations in which basics of connectivity and source space analysis are introduced. Then follows presentations by various toolbox developers. The toolbox presenters will be asked to 1) outline conceptually the types of connectivity approaches their toolboxes allow for and 2) describe how it practically can be done. Finally we will discuss how various connectivity measures can be tested using standardized data sets.
Advances in Source Space Functional Analysis of MEG/EEG data
Chairs: Srikantan S. Nagarajan (San Francisco, USA) & Kensuke Sekihara (Tokyo, Japan)

Location: The satellite event will take place at the new Brain Institute at Hôpital Pitié-Salpêtrière (ICM) in Paris, on Sunday the 26th, August 2012, from 9 am to 3 pm.

Description: Estimating the functional connectivity between activated brain regions continues to remain a significant problem in field of electromagnetic brain imaging. Many new methods are constantly being developed to reconstruct the functional coupling between activity patterns across brain regions from MEG and EEG data. Some of these advances include novel bivariate and multivariate metrics of non-directional and directional coupling, model-free versus model-based estimates, non-parametric versus Bayesian methods etc. The aim of this satellite workshop is to provide MEG researchers an opportunity to exchange ideas and discuss their preliminary results/work-in-progress investigations about novel analytical methods for functional connectivity analysis in a very friendly informal atmosphere.

Brainstorm Community Workshop Clinic
Chairs: Sylvain Baillet & Francois Tadel (Montreal, Canada)

Location: The satellite event will take place at SupTelecoms in Paris, on friday the 31st, August 2012, from 9 am to 6 pm.

Description: Academic software applications for MEG and EEG data analysis have grown considerably over the past decade, reaching an increasing number of users and achieving higher degrees of sophistication (Baillet et al., 2011). Brainstorm is a software project that is entering its second decade of development and distribution, with an open-source and free-of-charge policy (Tadel et al., 2011, and neuroimage.usc.edu/brainstorm). Brainstorm’s website statistics indicate than more 4000 users have downloaded the software code or executable packages (which does not require a Matlab license), with 500 registered active users, accessing the software updates on a regular basis. Brainstorm’s user community is growing rapidly and features a great variety of research areas in MEG and EEG. We believe Brainstorm is serving well its users, in terms of facility and convenience of utilization and improvements in productivity and reproducibility of their research output. More than 90 journal articles feature results obtained using Brainstorm. The software is now featuring new elements for scripting large batches of data workflows (automated analysis pipelines, group analyses, etc.) and which let users plug in their own processes for data analysis. As the user community is growing in size and diversity, and as its contributions to the application are facilitated, it is timely to gather some of Brainstorm’s users to feature their most exciting and cutting-edge usage of the software and communicate the essential elements of the application to other researchers. This workshop and clinic will feature both oral communications from Brainstorm users and a hands-on training course. We anticipate it will be a unique opportunity for the Biomag community to provide feedback on the software, to help its developers improve and provide new features, and to carry in-depth insight about current and future developments to new users.

Educational course on DCM for fMRI and EEG/MEG data
Chairs: Jean Daunizeau (Paris, France) & Jérémie Mattout (Lyon, France)

Location: The satellite event will take place at the new Brain Institute at Hôpital Pitié-Salpêtrière (ICM) in Paris, on thursday the 30th, from 3 to 6 pm and on friday the 31st, August 2012, from 9 am to 6 pm.

Description: During the past decade, human brain mapping research has undergone a paradigm switch. In addition to localizing brain regions that encode specific sensory, motor or cognitive processes, neuroimaging data is nowadays further exploited to understand how information is transmitted through brain networks. The ambition here is to ask questions such as: “what is the nature of the information that region A passes on to region B”? Such analysis of brain imaging data relies on advanced mathematical techniques that allow researchers to characterize brain organization. This involves creating models of how the brain is wired and how it responds in different situations. These models are used to interpret measured brain responses using e.g., functional Magnetic Resonance Imaging (fMRI) or magnetoencephalography (MEG). These ideas are at the core of Dynamic Causal Modelling (DCM), which allows for the formal (Bayesian) statistical analysis of large-scale network connectivity based upon realistic biophysical models of brain responses. DCM is part
of the academic freeware called Statistical Parametric Mapping (SPM: http://www.fil.ion.ucl.ac.uk/spm/), which is now being developed since more than two decades under the direction of Prof. K. Friston (UCL, London, UK). No other existing software package is endowed with such functionalities so far.

The DCM course will touch on virtually all aspects of brain connectivity analysis, from experimental design issues to the probabilistic comparison of models of brain dynamics through preprocessing and statistical testing of experimental effects. In brief, workshop attendees will acquire both theoretical knowledge and practical knowhow required to address the experimental identification of functional integration among brain regions from fMRI or EEG/MEG data.
Spontaneous brain activity: a key for understanding the mind and the pathophysiology of brain diseases.

Traditional accounts of brain function (Hubel and Wiesel 1968) emphasize the role of feedforward information processing in generating from the 'ground up' sensory, cognitive, and motor representations that implement behavior. Such feedforward 'sensory-motor' models have been successful in linking activity recorded from single neurons to perceptual decisions. However, a different class of models suggests that the brain is not a passive analyzer driven by sensory information, but that it actively generates and maintains predictions (priors) about forthcoming sensory stimuli, cognitive states and actions. This class of models emphasizes the role of spontaneous activity in maintaining active representations that are modulated rather than determined by sensory information. Accordingly, spontaneous activity should not be random (as often implied by its dismissal as mere 'noise'), but organized into structured spatiotemporal profiles that reflect the functional architecture of the brain, possibly encode traces of previous behavior, or even predict future decisions. Experimental and theoretical evidences reveal that the spontaneous ongoing activity of local cortical circuits result from a global balance between excitatory and inhibitory synaptic currents. At the level of large-scale cortical circuits, organized spatiotemporal patterns of spontaneous or intrinsic activity have been recently described in the resting state, hence Resting State Networks (RSNs). In my lecture I will describe the topography and functional organization of RSNs in the human brain, their neurophysiological basis, and their potential functional significance. Finally, the importance of RSNs for clinical neurology as a bioassay of brain function will be illustrated in the case of stroke, in whom we observe that abnormality of interhemispheric communication, even in the absence of structural damage, seems to correlate with behavioral deficits of movement and attention.

Multimodal neuroimaging of the human visual system: Linking cortical oscillatory dynamics to haemodynamics, neurotransmitters, genetics and behaviour in health and disease.

MEG allows the non-invasive localisation and characterisation of a range of cortical oscillatory phenomena. These are increasingly thought to reflect both local and network properties of the neural populations underpinning various perceptual and cognitive functions. Studies reveal complex, task-specific and spatially localised effects, some of which appear to be co-localised with the BOLD-fMRI response to the same task. In this talk I shall explain some of the methodology behind these studies and how these human MEG signals compare with invasive recordings in both animals and humans.

My main focus will be on how individual differences in oscillatory parameters, such as amplitude and frequency, can be related to variations in perceptual/behavioural task performance and to individual differences in neurotransmitter concentrations. For example, recent work by ourselves and others have demonstrated that visual gamma frequency appears to be a stable trait-marker in healthy controls and is correlated with individual variability in bulk measures of GABAergic inhibition. However, peak frequency is also sensitive to age-related effects and has recently been shown to correlate with structural parameters within the visual system, such as the area and thickness of V1.

I will also talk about the relevance of these studies to clinical conditions such as epilepsy and schizophrenia. If it is indeed true that individual variability in oscillatory dynamics is a sensitive biomarker of synaptic properties within the cortex, then these robust measures have much to offer in terms of endophenotyping and links to both behavioural and genetic markers of disease state, particularly as peak gamma frequency has recently been shown to be highly heritable. Finally, given that low-level oscillatory measures appear sensitive to variability in cortical excitation/inhibition parameters, they offer new opportunities for studying the effects of pharmacological agents, both in terms of assessing drug effects on synaptic function, but also in helping to understand individual variability in treatment response and pharmacodynamics. Pharmaco-MEG has a key advantage over fMRI in this application, as it is not confounded by drug-related systemic changes in physiology or direct modulation of the haemodynamic response.

Oscillation-based predictive mechanisms in audio-visual speech.

Neuronal oscillations are ubiquitous in the cortex and may contribute to cognition in a number of ways, for example by segregating information and organizing spike timing. Recent data show that delta, theta, and gamma oscillations are specifically engaged by the multi-timescale, quasi-rhythmic properties of speech and can track its dynamics. We argue that they play a foundational role in speech and language processing by ‘packaging’ incoming information into units that have a linguistic value, e.g. syllables. Such stimulus-brain alignment arguably results from auditory and motor tuning throughout the evolution of speech and language and constitutes a natural paradigm allowing auditory research to make a distinct contribution to the role of neural oscillatory activity in human cognition.
KEYNOTE 4: Christopher Moore - Department of Neuroscience and Brown Institute for Brain Sciences, Providence, USA


Searching for Meaningful Human States Using MEG, Psychophysics and Realistic Modeling
My laboratory studies how neocortical dynamics contribute to perception. To ground our studies in human relevance, we conduct human neurophysiological recording (MEG) combined with psychophysical testing. These studies examine how emergence of dynamics (e.g., rhythmic oscillatory states such as alpha) impacts perceptual information processing. To understand the neural underpinnings of these dynamics, we apply biophysically realistic neural modeling that make direct predictions as to the neocortical cell types and patterns of activity underlying oscillations and evoked sensory responses. These human studies are led by our long-term collaborator, Dr. Stephanie Jones.

Testing Specific Mechanisms of Oscillatory Emergence by Precisely Controlling Neural Circuits with Optogenetics in Mouse Neocortex
We then systematically test the mechanisms and meaning of these dynamics in mouse models, which allow us to leverage the revolution in genetic engineering in a tractable mammalian model. This preparation allows us to target optogenetic control - the use of light to drive activity--to specific cell types. As one example, we recently demonstrated that selective activation of the thalamic reticular nucleus can generate realistic sleep spindles and shift the mode of thalamic transmission from tonic to burst-firing mode. Similarly, we previously employed this form of selective control to generate realistic gamma oscillations in neocortex by driving fast-spiking interneurons.

Causally Testing the Meaning of Neural Oscillations for Information Processing
In ongoing studies, we are now testing the hypothesis that introduction of gamma enhances sensory processing in mice performing a sensory detection task. We find that optogenetically-induced gamma can enhance detection probability of sinusoidal and naturalistic stimuli. This finding provides direct, causal evidence in support of the long-debated hypothesis that gamma rhythm benefits processes such as attention.

KEYNOTE 5: Karl Friston - Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL, UK

Dynamic causal modelling of electromagnetic responses.

In recent years, dynamic causal modelling has become established in the analysis of invasive and non-invasive electromagnetic signals. In this talk, I will briefly review the basic idea behind dynamic causal modelling - namely to equip a standard electromagnetic forward model, used in source reconstruction, with a neural mass or field model that embodies interactions within and between sources. A key point here is that the resulting forward or generative models can predict a large variety of data features - such as event or induced responses, or indeed their complex cross spectral density - using the same underlying neuronal model. Dynamic causal modelling allows people to compare alternative models or hypotheses based on different networks, using Bayesian model selection. Furthermore, Bayesian model inversion provides posterior estimates of model parameters that have a direct physiological interpretation - such as extrinsic (between-source) connection strengths or synaptic rate constants. This ability to test hypotheses and quantify neuronal parameters at the synaptic level holds great promise for non-invasive studies of health and disease. I hope to illustrate these points using examples from our collaborations, with a special focus on psychopharmacological studies and patient studies.

Dynamic causal modelling brings a new perspective to characterising event and induced responses - empirical response components, previously reified as objects of study in their own right (such as the mismatch negativity or P300) now become data features that have to be explained in terms of neuronal dynamics and changes in distributed connectivity. In other words, dynamic causal modelling emphasises the neurobiological mechanisms that underlie responses - over all channels and peristimulus time - without particular regard for the phenomenology of classical response components. My hope is to incite some discussion of this shift in perspective and its implications.
A large collection of recent studies suggest that the functional role of oscillatory alpha activity has been underappreciated. It is now clear that the 'idling hypothesis' of the alpha activity cannot explain a range of findings suggesting that alpha activity plays a crucial role in cognitive processing. The presentations in this symposium will focus on recent findings based on state-of-the-art approaches designed to understand the functional role of oscillatory brain activity. These approaches include novel types of network analysis, TMS combined with EEG and MEG, and intracranial spike-field recordings in monkeys. From these studies it is clear that the phase of the ongoing alpha activity correlates with the excitability of neuronal activity as assessed by spikes-field data, TMS induced phosphenes and gamma band activity. Further it is also clear that the alpha activity in some regions correlates with oscillatory activity in other regions in a task-dependent manner. In sum these studies point to the alpha band activity playing a crucial role for shaping the functional architecture of the working brain. Not only the amplitude but also the phase of the ongoing oscillations determine the excitability in a given region. These changes in excitability are likely to be involved in how resources are allocated in the brain network. The stage is now set for identifying how the alpha activity is modulated by top-down control and if the functional role generalizes beyond the sensory system.

• About the functional role of alpha oscillations in spatial attention - Joachim Gross (Glasgow, UK)
  A number of studies have shown lateralised modulations of alpha oscillations associated with shifts of spatial attention. I will present three recent studies that further elucidate the functional role of alpha oscillations in spatial attention. The first study provides a detailed characterization of the occipito-parietal generators of alpha modulations during spatial attention and shows that ipsilateral (to the attended hemifield) alpha increases localizes to a dorsal area whereas alpha decreases localizes to a ventral area. The alpha modulation in ventral area (and not the alpha increase in dorsal area) is shown to predict behavioral performance for detecting the subsequent target. The second and third studies explore the possibility of entraining alpha oscillations with the aim of modulating perception. Behavioral performance in a spatial attention task was tested during rhythmic TMS at various frequencies including alpha. TMS was performed over visual and parietal areas in the left and right hemisphere. Target visibility was significantly modulated by alpha stimulation, relative to control conditions. Alpha stimulation selectively impaired visual detection in the visual field opposite to the stimulated hemisphere, while enhancing detection ipsilaterally. This is consistent with a scenario where rhythmic alpha TMS increases alpha oscillations in stimulated areas with behavioral consequences. This hypothesis was directly tested in a MEG, TMS-EEG study. MEG was used to localize generators of alpha modulation during spatial attention in individual subjects and to identify individual alpha frequency. Rhythmic alpha TMS stimulation was performed at this frequency and location while simultaneously recording EEG. Increased alpha amplitudes were observed only during rhythmic TMS and not in control conditions. In summary, these findings suggest a causal role of area-specific alpha oscillations in dynamically shaping perception.

• Network properties assessed by cross-frequency interactions in memory tasks - Hyojin Park (Seoul, South Korea)
  The human memory system recruits various brain regions connected as networks in order to function efficiently. To obtain optimal performance in memory tasks, both enhancement and suppression of task-relevant and task-irrelevant regions are essential. In order to understand this mechanism, oscillatory dynamics could be useful tool since alpha frequency has been reported to reflect active inhibition or disengagement of task-irrelevant areas whereas gamma frequency has been suggested to play information processing. Thus, we investigated how the brain is orchestrated during memory tasks recorded by MEG. We examined network properties by power-to-power correlations within- and cross-frequency at source level. We applied this method to the delay period of a
visuospatial working memory requiring the engagement of both the dorsal and ventral streams. The power correlations within the alpha band showed correlations across posterior-parietal-frontal regions. Importantly gamma power in the right STG was correlated with sources in the alpha band in prefrontal, parietal and posterior regions. From these findings, we suggest that the STG dominated by gamma activity serves as a hub region. In order to further understand the functional role of cross-frequency interactions, we are currently applying the same method to a long-term memory. We have hypothesized that the posterior alpha frequency can serve to suppress the encoding of irrelevant memories by top-down control. We presented to-be-remembered and not-to-be-remembered cues before the memory stimuli. Preliminary results showed that strong posterior alpha power precedes correctly forgotten items suggesting that top-down modulation in filtering incoming information. The present studies demonstrate how oscillatory dynamics can be investigated by means of cross-frequency power correlations in source space. This methodological framework could be of general utility when studying functional network properties of the working brain.

• Perceptual cycles: when perception fluctuates with the phase of ongoing oscillations - Rufin VanRullen (Toulouse, France)

Many theories posit a role for oscillations in sensory perception and attention. An often disregarded consequence of such theories is that perceptual and attentional processes should function periodically, preferentially exerting their effects at certain phases of the oscillatory cycle but not others. Recently, our group started testing this prediction by evaluating whether the precise phase of presentation of a visual stimulus with respect to ongoing oscillations could influence perceptual and attentional performance. We showed that the phase of an EEG oscillation reflecting the rapid waxing and waning of sustained attention can predict the perception of a subsequent visual stimulus at threshold. This phase dependency was also observed for illusory perceptions (phosphenes) that were triggered by direct activation (Transcranial Magnetic Stimulation) rather than external stimulation. Similar ongoing periodicities accounted for a portion of the trial-by-trial variability of saccadic reaction times. All of these phase effects were observed over fronto-central regions (sometimes along with occipital effects), and for oscillation frequencies between 7Hz and 15Hz. Our findings imply that certain perceptual and attentional mechanisms operate periodically or rhythmically, rather than continuously; and further, that ongoing oscillations can be used as a signature of these perceptual and attentional cycles.

• The functional role of alpha oscillations: lessons from animal data applied to interpret MEG findings - Ole Jensen (Nijmegen, The Netherlands)

Optimal cognitive processing is dependent on the engagement but also the disengagement of various brain regions. From electrophysiological investigations it is clear that engagement is reflected by neuronal oscillatory activity in the gamma band (30-100 Hz) whereas disengagement is reflected by oscillatory activity in the alpha band (8-13 Hz). Thus, to understand the working brain as a network it is imperative to investigate how gamma and alpha band activities interact. From laminar neocortical recordings in monkeys we have demonstrated that the phase of alpha oscillations in deep layers modulates the power of gamma activity in superficial layers. Single unit recordings confirm that neuronal spiking decreases as alpha power increases. This suggests that alpha activity in deep layers phasically inhibits neuronal processing. MEG experiments in humans have shown that an increase of alpha activity in task-irrelevant areas is required for optimal task performance. This has been demonstrated using WM, LTM and attention tasks in the visual and sensory-motor modality. The functional inhibition by the alpha oscillations is thought to reflect the allocation of computational resources to task-relevant regions. In conclusion, the interactions between oscillatory activities in various frequency bands and regions provide an opportunity to embrace the working brain as a network from a mechanistic perspective.
Structural and functional connectivity are generally studied with distinct modalities: diffusion MRI (dMRI) on the one hand, and fMRI, EEG or MEG on the other.

DMRI allows to learn about the structural connectivity of individual brains, and, through tractography, reconstruct fibers of the white matter. With MEG, one can reconstruct the electrical activity of the cortex, and observe temporal sequences of activation, as well as phase locked activity between different regions. The goal of this minisymposium is to present the joint analysis of structural and functional connectivity.

We will consider the problem of cortex parcellation, which divides the cortex into subregions that can be considered as relatively homogeneous. Parcellation can be used in MEG and EEG as a ‘regularizing prior’. Such a parcellation can be automatically achieved with a similarity measure between tractographies, and a modified version of Loreta incorporates this new parcellation information. We also present a nested parcellation approach, starting with the MEG lead field matrix to define patches within which sources cannot be distinguished through MEG, and then using dMRI to refine these patches on the basis of tractography similarity. To go further in connectivity analysis, fusion of dMRI and MEG reveals networks better than each modality on its own: it is possible to build an anatomical tractography by using as seeds active sources localized by MEG. This answers whether tractographic paths actually convey functional information and whether the MEG dipole location has an anatomical connection.

In the clinical domain, biomarkers will be presented, that combining MEG-based temporal signatures with the DTI-based structural connectivity signatures to create a multi-parametric spatio-temporal signature of pathology. A clinical study will be presented, in Autism Spectrum Disorders, that jointly analyzes Fractional Anisotropy and M100 latency response in the auditory evoked magnetic field.

- **Diffusion MRI based parcellation as prior knowledge in EEG/MEG source reconstruction - Alfred Anwander (Max Planck Institute, Germany)**

  The human cortex can be subdivided in structural and functional distinct areas. The strong inter-individual differences of functional areas require individual identification of relevant boundaries. For the function of cortical areas, the anatomical connectivity is most relevant and can be used as a criterion for segregation. Diffusion MRI offers the opportunity to compute an estimate of the long range connectivity by probabilistic tractography in the individual living participant. The similarity between different tractograms can be used by an automatic clustering method to parcellate the cortex in homogeneous and mutually distinct function-anatomical areas.

  In this work we present a new method for whole brain individual parcellation of the entire cortex from diffusion tractography. The method is based on a hierarchical clustering of probabilistic tractograms, and encodes the information of the connectivity structure at all granularity levels in a hierarchical tree. The tree can be explored with various levels of details resulting in a hierarchical parcellation of the cortex.

  The inverse problem in EEG/MEG source localization has no unique solution and additional knowledge or assumptions have to be used which can be gained from individual anatomical prior knowledge. In this way, we propose to use the boundaries of functional homogeneous regions as priors into the reconstruction of current distributions from EEG/MEG data. The proposed method incorporates the anatomical patches into the LORETA approach.

  We conclude that diffusion MRI leads to a plausible individual parcellation of the cortex, and improves the localization of EEG/MEG sources.

- **Cortex parcellation by combining MEG and dMRI - Anne-Charlotte Philippe (Sophia-Antipolis, France)**

  Understanding the relationship between structure and function is a major challenge in neuroscience. Diffusion MRI (dMRI) in the only in-vivo and non-invasive imaging modality allowing to have access to the neural structure. Magnetoencephalography (MEG) is also a non-invasive modality and allows a direct access to temporal procedure of cognitive processes. Cortex parcellation being one of the most important ways to understand
structure-fonction relationship, in this work, we propose an innovative method merging MEG and dMRI to parcellate the cortex. Contrarily to what is usually proposed i.e using the result of one modality to inform the other, we propose and develop an approach that really merges these two complementary modalities. The combination of MEG forward problem and connectivity information allows to define cortical areas which can be separated by the MEG inverse problem having a similar magnetic field while having a similar connectivity. Experiments have been performed and promising results show suitable clusters that forecast interesting studies for inter and intra-subjects comparison of the cortex parcellation and a better understanding to differentiate long-range and short-range connectivity in the white matter.

- **DTI and MEG Studies of the Developmental Trajectory Of Auditory System Dysfunction in Autism Spectrum Disorders** - Timothy Roberts (Philadelphia, USA)

  While DTI allows depiction of the white matter architecture of the auditory pathway from sensory input to cortex, MEG allows resolution of the precise timing of evoked responses elicited in auditory cortex, by auditory stimuli. In children with ASD, it has been shown that the 100ms component (M100) of the auditory evoked neuromagnetic field may be 10-20ms delayed compared to that of typically developing controls (Roberts et al., 2010). Furthermore, it has been shown that there is a developmental trajectory of M100 latency in typical development with latency shortening over time. In a concomitant fashion the WM of the acoustic radiations (connecting the medial geniculate nucleus, MGN, of the thalamus with auditory cortex in the superior temporal gyrus, STG) is investigated using DTI and subsequent tract-based quantification of fractional anisotropy, FA, as a surrogate of white matter maturation. A linear trajectory of FA increase is seen in typical development, predicting the shortening of M100 response latency (Roberts et al., 2009). Developmental changes in FA appear slower in children with ASD, perhaps predicting their prolonged M100 latencies. In summary, converging evidence from the developmental trajectories of seemingly independent measures (DTI of the acoustic radiations and MEG assessment of M100 latency) point to a biophysical hypothesis of white matter maturation predicting evoked response latency shortening. Furthermore, this biophysical model can be used to partly account for observed differences in children with ASD.

- **On Creating Multiparametric Spatio-Temporal Signatures of Pathology** - Ragini Verma (Pensylvannia, USA)

  Study of WM integrity and connectivity (structural and functional) is becoming an important part of several clinical studies. WM integrity and structural connectivity is well characterized via diffusion imaging (Diffusion Tensor Imaging (DTI) and High Angular Resolution Diffusion Imaging (HARDI)). Functional connectivity is investigated via MEG, EEG and fMRI. Encouraged by the fact that diffusion and MEG studies have individually been able to characterize different aspects of pathology, in this talk, we will present ways of combining MEG-based temporal signatures with the DTI-based structural connectivity signatures to create a multi-parametric spatio-temporal signature of pathology. The talk will begin with a detailed exploration of different structural measures of WM integrity and connectivity that can be obtained from diffusion imaging, such as scalar maps of WM integrity and complexity, tract-based features such as fiber density maps as well as full-brain inter-regional connectivity features. We will then proceed to identify temporally compatible features from MEG, reflecting functional connectivity, such as numeric dependent variables elicited by specific stimuli, complexity of sensor-level time course signals and full-brain resting state inter-nodal coherence maps. Having identified the issues and challenges of spatio-temporal feature combinations, the talk will proceed to present methods of combining these features into comprehensive multivariate spatio-temporal signatures of pathology using pattern classification techniques. The talk will motivate the methods towards creating markers of pathology that will provide measures of symptom severity and potentially aid in diagnostic and prognostic decisions. Applications to studies in Autism Spectrum Disorder and schizophrenia will be presented.
Time is an inherent property of the (conscious) brain, itself a massive temporal processor. A major challenge in time perception research is to clarify the link between neural dynamics and the awareness of time [1-3] bearing in mind whether time owes to be time in the brain [3]. Timing in neural systems informs on the different anatomical scales of observation: single neurons to cell assemblies to neural populations across different brain regions naturally lend themselves to distinct temporal descriptions such as spike rates, synchronization in particular frequency regimes, inter-areal phase coherence, respectively. Recent neurophysiological findings suggest that low-frequency neural oscillations in the delta range (1-2 Hz) provide a mechanistic framework for the parsing and the (attentional) selection of dynamic stimuli such as speech [4-5]. The ongoing rhythmicities observed in brain functions may lend themselves to temporal predictions and predictive coding at different scales of representation. One richly dynamic and complex class of stimuli in which the temporal structure is fundamental is music; modulations in the beta and gamma ranges have been found to be associated with preparation and anticipation of signal timing in auditory cortex for beat perception [6] and the alpha range (10Hz) has recently been correlated with temporal expectation [7]. The possibility that temporal predictions relate to the encoding of the passage of time is highly relevant to keep track of those features that directly contribute to the subjective construction of the awareness of time.

1 Eagleman et al. (2005) J Neurosci, 25:45
2 Wittmann van Wassenhove (2009), Phil Trans Roy Soc B: Biol Sci, 364: 1525
6 Fujioka et al. (2009), Ann NY Acad Sci, 1169:1

**Neuronal substrates of temporal prediction - Charles E Schroeder (New York, USA)**

Neuronal oscillations reflecting synchronous, rhythmic fluctuation of neuron ensembles between high and low excitability states, dominate ambient activity in the sensory pathways. Because excitability determines the probability that neurons will respond to input, a top-down process like attention can use oscillations as 'instruments' to amplify or suppress the brain’s representation of external events. That is, by tuning the frequency and phase of its rhythms to those of behaviorally and/or cognitively-relevant event streams, the brain can use its rhythms to parse event streams and to form internal representations of them. In doing this, the brain is making temporal predictions. I will discuss findings from parallel experiments in humans and non-human primates that outline specific structural and functional components of this temporal prediction mechanism. I will also discuss its possible generalization across temporal scales. Finally, I will discuss motor system contributions to sensory systems' dynamics.

**Auditory Rhythm and Neural Resonance - Edward Large (Florida, USA)**

This talk will explore the idea that certain classes of rhythms tap into brain dynamics at an appropriate time scale to cause the nervous system to resonate to rhythmic patterns. I will present behavioral and physiological results suggesting that cortical rhythms entrain to temporally structured acoustic signals, and entrainment of neuronal oscillations can function as a mechanism of attentional selection. This response depends upon processes in both sensory and motor systems, and work on sensorimotor synchronization provides a rich source of information about this process. I will present a model intended to encompass rhythm perception, rhythmic attending, and rhythmic coordination. The approach is based on the idea that rhythmic expectancies emerge from nonlinear neural resonance in sensory and motor cortices. I will show how the model predicts certain facts about behavior and neurophysiology.

**Waves of temporal expectation - Anna Christina Nobre (Oxford, UK), Gustavo Rohenkohl (Oxford, UK)**

Temporal expectations play a major role in selective attention, contributing significantly to the selection, integration and prioritization of events according to our current task goals. The brain dynamically extracts temporal regularities between events and uses these in a proactive fashion to enhance the processing of relevant events in
the environment. However, the mechanisms by which temporal expectations are generated and deployed to modulate neuronal excitability remain unresolved. We have demonstrated that temporal expectations can be combined with expectations about the spatial location of relevant events to enhance top-down biasing of visual analysis, and have shown that the timing of oscillatory activity related to anticipatory spatial attention can follow the predicted time course of predicted stimuli. Our current experiments explore in greater depth whether the effects of temporal expectation are mediated by changes in oscillatory power and phase, which in turn enhance visual perceptual analysis of events. We will discuss findings from current work using MEG and EEG, in which we manipulate the degree of temporal regularity of events as well as the perceptual characteristics of stimuli in a systematic way.

- **Temporal predictions and time awareness - Virginie van Wassenhove (Saclay, France)**

Some difficulties in understanding how time is encoded in the brain stem from the existence of distinct temporal resolutions (from milliseconds to day ...), the lack of functionally dissociated timing system(s), the intricacy in distinguishing temporal properties from naturally occurring events (across all senses) and the a priori non-isomorphism between physical and mental time. The distinction between time as an experiential property ('explicit timing' and timing as dynamics of the brain system 'implicit timing') enables a first level at which operational distinctions can be formed but this remains insufficient. Indeed, time perception is a misnomer as the encoding of temporal information encompasses temporal expectation, duration estimation (canonical time estimation), temporal order judgments, etc. A prominent model for time perception is the clock model, consisting of a pacemaker generating discrete events at a fixed frequency and an accumulator counting these events. A switch between the pacemaker and the accumulator regulates the counting mechanism: when it is closed, the units add up in the accumulator, when it is open, accumulation stops. One prominent marker of the accumulation mechanism is the Contingent Negative Variation (CNV) which has recently been questioned as a major index of the accumulator process. Mechanistically however, the phase of neural oscillations in different frequency bands could naturally be used as automatic parser and marker (or temporal flags) of sensory events. I will illustrate this notion with MEG findings relating the phase of oscillatory mechanisms with the encoding of temporal information. The issue of coding efficiency in relation to audiovisual temporal judgment, duration MMN and phase encoding will be discussed.

**Monday, August 27th, 2012, 15:00-17:00**  
**Hall B**  
**S-Mo-B2 MEG in psychiatric and neurologic populations: multimodal imaging**  
**Chair: J. Christopher Edgar (Philadelphia, USA)**

This symposium focuses on the use of MEG to investigate brain function in psychiatric and neurologic populations. With senior as well as more junior speakers representing the US and Europe, the symposium highlights a range of clinical populations: individuals with autism, tumors, schizophrenia, and mild head trauma. A further strength of the symposium is a focus on the use of multimodal imaging - MEG plus another non-invasive neuroimaging method - to better understand brain abnormalities. Thus, the proposed symposium showcases the increasingly sophisticated research in this area and the continued maturation of MEG psychiatry and neurology research.

Dr. Edgar will start the session with a short 5 minute introduction that briefly reviews early papers in this area, examines the number of publications since 1989, and then reviews seminal papers (e.g., studies examining slowing as well as studies examining auditory processes in psychiatric populations). Finally, the future of research in this area is briefly discussed (e.g., the focus on examining younger subjects with psychiatric disorders, and the development of whole-head infant MEG systems).

- **Examining neuronal mechanism of mild traumatic brain injury using an integrated MEG and DTI approach - Mingsxiong Huang (San Diego, USA)**

Traumatic brain injury (TBI) is a leading cause of sustained physical, cognitive, emotional, and behavioral deficits in the civilian population (due to motor vehicle accidents, sports, falls, and assaults) and military personnel (with blast injury as an additional cause). However, mild (and some moderate) TBI can be difficult to diagnose because
the injuries are often not detectable on conventional MRI or CT. The present study integrates resting-state MEG with diffusion tensor imaging (DTI) to detect injured loci and abnormal neuronal networks in patients with mild or moderate TBI caused by blast or non-blast forces. MEG source imaging examines the generation of pathological low-frequency neuronal magnetic signal (delta-band) and altered functional connectivity in the beta band (15-30Hz) in gray matter areas. DTI assesses structural connectivity using diffusion tractography for white matter fiber tracts. Results show that MEG slow-wave source imaging detects abnormalities at rates of 90% for the mild TBI group (blast plus non-blast) and 100% for the moderate TBI group. DTI shows abnormalities in 25% of the mild TBI patients. The relationship between MEG functional connectivity in gray matter areas and DTI structural connectivity in white-matter tracts was examined in mild TBI patients and healthy control subjects. Gray matter areas had reduced functional connectivity when they are connected by the white matter tracts showing reduced DTI connectivity in mild TBI patients. Furthermore, abnormally increased MEG functional connectivity was observed in other gray matter areas indicating altered connectivity patterns in mild TBI patients. This study provides support for an integrated MEG source imaging and DTI approach to assist in the clinical diagnosis of mild TBI.

- **Temporal and frontal cortical thickness associations with M100 auditory activity and attention in healthy controls and individuals with schizophrenia - Yuhan Chen (Albuquerque, USA)**

Although gray matter (GM) abnormalities are frequently observed in schizophrenia (SCZ), the functional consequences of these structural abnormalities are not yet understood. The present study sought to better understand GM abnormalities in SCZ by examining associations between cortical GM and two putative functional SCZ biomarkers - weak M100 ms (M100) auditory responses and impairment on tests of attention. Data was available from 103 subjects (healthy controls = 52, SCZ = 51). Structural MRI provided T1-weighted images and GM cortical thickness measures were obtained for superior temporal gyrus (STG) and prefrontal cortex (PFC). MEG was obtained while subjects were administered the standard paired-click paradigm, and single dipole source localization provided left and right STG 100 ms source strength measures. Subjects were administered the Trail Making Test A and the Continuous Performance Test to assess attention.

Individuals with SCZ had less STG GM cortical thickness than controls bilaterally. Individuals with SCZ had weaker M100 responses than controls bilaterally, and individuals with SCZ performed more poorly than controls on tests of attention. Across groups, left STG was positively associated with left M00 source strength. In SCZ only, less left STG and less bilateral PFC GM predicted poorer performance on tests of attention. Present findings show that in individuals with chronic SCZ, reduced STG and PFC GM is associated with abnormalities in encoding auditory information and also with poorer performance on tests of attention. Thus, reduced GM cortical thickness may serve as a common substrate for multiple functional abnormalities. As suggested by others, functional abnormalities in SCZ may be a consequence of decreased GM dendritic arbors and associated synaptic infrastructure.

- **Cortical morphology and links to resting-state oscillator activity in autism spectrum disorders - Lauren Cornew (Philadelphia, USA)**

Our laboratory recently reported that children with autism spectrum disorders (ASD) exhibit increased resting alpha power in temporal and parietal regions, with alpha activity associated with symptom severity. Other work has shown reduced cortical thickness (CT) in overlapping regions. The present study investigated CT as a potential anatomical correlate of increased alpha power. It was hypothesized that compared to controls, children with ASD would exhibit reduced CT in temporal and parietal regions and that CT would be associated with alpha power.

Participants were medication free 6- to 14-year-old children (20 with ASD, 20 controls). Eyes-closed resting MEG data were processed by projecting each individual’s raw surface activity into source space and applying a FFT. Spectra were averaged and alpha (8-12Hz) power quantified. 3T MRI provided T1-weighted images and CT quantified using Freesurfer.

Analyses revealed reduced CT in ASD than controls in a left frontal region that included the superior and middle frontal gyri (cluster-wise probability=.01), as also in left and right temporal and parietal regions (all cluster-wise probabilities=.0001). Temporal and parietal regions included the superior temporal sulcus, portions of superior, middle, and inferior temporal gyri, and the inferior parietal lobule. CT was also reduced in left fusiform and parahippocampal gyri. Regression analyses revealed associations between increased temporal and parietal alpha and reduced CT in bilateral portions of the superior temporal gyrus, inferior parietal lobule, and precuneus, as well as left superior temporal sulcus and right fusiform gyrus.

Results demonstrated reduced CT in children with ASD, particularly in temporal and parietal regions. CT reduc-
tions were associated with increased alpha power, suggesting a link between atypical brain structure and function in ASD.

- Local protein expression and local neural networks in glioma patients: the hub of the matter - Linda Douw (Boston, USA)

Neuroscience increasingly focuses on the brain as a network. Research in humans, however, is generally limited to global measures. Brain tumor patients often undergo neurosurgical intervention, and thus tissue is available. Two proteins are deemed important: (1) synaptic vesicle protein 2A (SV2A), which is related to neural excitability and epilepsy, and (2) P-glycoprotein (P-gp), which determines the permeability of the blood-brain barrier and is also linked to epilepsy. We hypothesize that expression of SV2A and P-gp in the tumor area is related to local area network characteristics and that alterations in tumor areas affect cognitive functioning and epilepsy. Patients with gliomas were included after tissue collection and underwent MEG and MRI. Time-series from 68 ROIs were filtered into 5 classic frequency bands and divided into local-tumor and non-tumor. Expression of SV2A and P-gp was determined via immunohistochemistry and correlated with local-tumor, non-tumor and global network topology, as well as with epilepsy and cognition. Fifteen patients (mean age 47 years, SD 11 years) were included (12 men). Higher SV2A expression was related to increased delta band connector hubness in the tumor area, and to globally higher clustering in the beta band and lower total number of epileptic seizures. Increased P-gp expression was related to lower local beta band between-module hubness and increased number of seizures. In conclusion, decreasing hub status of the tumor area is related to lower SV2A expression and higher P-gp expression, while clinically rendering the brain more vulnerable to seizures. We speculate that brain-tumor related epilepsy induces microscopic changes in the area surrounding the tumor, thereby changing local network topology in delta and beta frequency bands, which is most severe in regions that play a central role in functional networks.

Monday, August 27th, 2012, 17:30-19:30
Hall A

S-Mo-A3 Perceptual awareness and auditory scene analysis

Chair: Alexander Gutschalk (Heidelberg, Germany)

The mental representation of the acoustic scene formed by the auditory system is generally incomplete and matter of interpretation. One element of auditory scene analysis is to group together the acoustic events belonging to a single source and segregate them from other, co-occurring sound sources. To study how the brain performs this function, auditory scientists have taken advantage of stimuli whose perception can change in the absence of physical stimulus manipulations (e.g. auditory streaming and informational masking). Direct neural correlates of perception have been identified in auditory cortex and elsewhere using such paradigms. However, other activity patterns present in auditory cortex may still reflect physical stimulus properties rather than perception per se, and to some extent this duality is preserved in supramodal areas of frontal and parietal cortex. Finally, attentional modulation of the neural representation of acoustic scenes has been found at several levels of the auditory system, including auditory cortex. While the network that controls auditory perception has not yet been mapped completely, there is evidence for some convergence with visual perception, particularly in prefrontal areas such as the frontal eye fields, which have been shown to be involved in regulating auditory attention. This symposium will spotlight recent efforts to disentangle the neural underpinnings of auditory scene analysis and auditory perceptual awareness. The methodological focus is on studies using MEG, but complementary results from fMRI and intracranial recordings in patients with epilepsy will also be reported.

- Auditory cortex activity associated with awareness and perceptual grouping - Alexander Gutschalk (Heidelberg, Germany)

Many sound sources emit repetitive auditory events that are grouped into auditory streams. A basic example is 'streaming', where two interleaved tone sequences may either form one or two streams. MEG and fMRI studies show that separation of streams by parameters like frequency, pitch or lateralization, selectively reduce neuronal adaptation in the same range where they promote streaming. The earliest activity where this phenomenon is observed in human auditory cortex is the P1m response after 50-70 ms. When streaming is ambiguous, the bistable
perception spontaneously switches back and forth between one and two streams. The P1m is modulated by these different percepts, but the modulation is smaller than the dependence on physical parameters. A more impressive covariation between perceptual awareness and activity in the auditory cortex has been observed with a stream of tones embedded in a multi-tone masker: Although this masker hardly interferes with the targets in the cochlea (and produces no ‘energetic masking’), the target stream may sometimes remain completely unnoticed. This phenomenon is referred to as ‘informational masking’. In trials where listeners are aware of the target stream, each tone evokes a negative wave after 100-200 ms in the auditory cortex, which we refer to as the awareness related negativity (ARN). This wave was not evoked by tones where the listeners had not (yet) detected the target stream. Conversely, the 40-Hz steady-state response and the P1m were evoked by detected and undetected target tones, alike. While MEG cannot distinctively separate primary and secondary auditory areas, fMRI activity is enhanced for detected targets in primary and secondary areas. In fact, the contrast of detected minus undetected events revealed in particular activation in the primary auditory cortex. These results suggest that stimulus-driven and perception-related activity coexist in the auditory cortex, but are dissociated by their timing.

• Auditory figure ground segregation in complex scenes - Maria Chait (London, UK)

In contrast to the rich acoustic environments to which listeners are exposed in the natural world, most studies of auditory scene analysis have used relatively simple signals. To model stochastic variation in frequency-time space, characteristic of many ‘sound scenes’, we recently developed a new stimulus - ‘stochastic figure-ground’ (SFG; Teki et al., 2011). Stimuli consist of a sequence of short (e.g. 50 ms) chords containing a random number of pure-tone components. Occasionally, a subset of tonal components repeat in frequency over several consecutive chords, resulting in a spontaneous percept of a ‘figure’ popping out of a background of varying chords. Figure and background signals overlap in spectrotemporal space, but vary in the statistics of fluctuation. Figures can therefore, only be extracted by integrating the patterns over frequency and time. Our behavioural results demonstrate that human listeners are remarkably sensitive to the emergence of such figures. Here I will present data from MEG experiments further investigating the temporal properties of this figure-ground segregation mechanism and the degree it is susceptible to attentional-load - situations where listeners’ computational resources are engaged by an unrelated, competing task.


• Intracranial recordings in auditory cortex and beyond during bistable auditory perception - Andrew Dykstra (Heidelberg, Germany)

How the brain performs auditory scene analysis (ASA) is not well understood. In particular, what role brain areas outside primary auditory cortex might play in decomposing complex acoustic environments remains vastly understudied, in contrast to the multitude of recent studies examining auditory cortex. For methodological reasons, examining activity outside auditory cortex with both broad coverage and fine resolution is challenging. We sought to circumvent certain limitations of previous work by making electrical recordings directly from the cortical surface of neurosurgical patients with epilepsy while they engaged in two classical ASA paradigms, auditory streaming and multi-tone informational masking. We asked whether neural correlates of auditory streaming and perceptual awareness under informational masking extend into (i) brain areas outside the classically-defined auditory cortex and (ii) frequency regions less observable with non-invasive methods (e.g. gamma-band activity). Most patients were able to perform the tasks and demonstrated behavioral responses similar to those from healthy subjects. In the streaming experiment, evoked responses from widespread brain areas correlated strongly with a physical stimulus parameter known to produce changes in perceptual organization but surprisingly, did not covary with perceptual organization per se. In the informational-masking experiment, correlates of listeners’ perceptual awareness of target tones were found in early activity arising from auditory cortex as well as late activity that spread to ventrolateral prefrontal and anterolateral temporal cortex. Overall, the results demonstrate that in decomposing auditory scenes, humans utilize a network of brain areas that are much more widespread and diverse than previously thought.

• The cortical network controlling auditory spatial attention - Adrian KC Lee (Washington, USA)

Spatial cue plays an important role in segregating objects in a complex auditory scene. Spatial attention is often described as supramodal, e.g., crossmodal spatial cues can enhance the perception of stimuli in another modality when presented in the same location. How similar is the auditory spatial attentional network compared to...
its visual counterpart? In a series of experiments, we studied different aspects of auditory spatial attention by combining magneto- and electro- encephalography, combining anatomical information captured by magnetic resonance imaging. We examined the similarities and the differences in cortical regions recruited for auditory spatial and non-spatial attention. We also investigated what cortical network is involved in switching of auditory attention. Finally, we explored different signal processing strategies that would be best suited to reveal the cortical network involved in auditory spatial attention.

Monday, August 27th, 2012, 17:30-19:30
Hall B
S-Mo-B3 Progress in simultaneous MEG and intracranial recordings in Deep Brain Stimulation patients
Chair: Vladimir Litvak (London, UK)

Deep Brain Stimulation (DBS) has been rapidly developing in the recent years as a method for treatment of a variety of neurological and psychiatric disorders. Presently the most common DBS surgery is for stimulation of the subthalamic nucleus (STN) for advanced Parkinson’s disease (PD), but DBS is also used for other targets in PD and for other indications. For a researcher DBS offers a unique opportunity to record directly from deep brain structures not easily accessible to non-invasive imaging methods in awake humans. Unlike implantation of intracranial electrodes in epilepsy patients, DBS surgery involves precise and consistent placement of electrodes in the same target across patients affording population-level inference. One important way intracranial recordings can be used is to characterize the interactions of DBS targets with the rest of the brain. MEG is the method of choice for this kind of studies as it can access multiple brain areas simultaneously. MEG is well tolerated by patients with fresh surgical wounds and allows for precise source localisation in the presence of burr holes. The early MEG studies in DBS patients were hampered by severe metal artefacts. Recently this problem has been finessed by either using beamforming or special non-ferromagnetic DBS kits. These developments resulted in the first topographical characterisation of coherence patterns between the STN and the cortex. Despite the tremendous potential of simultaneous MEG and intracranial recordings in DBS patients these are only done by a handful of MEG centres worldwide due to clinical and logistic constraints. The proposed symposium will bring together representatives of all these centres (London, Oxford, Berlin and Dusseldorf) to present an up-to-date picture of ongoing research in the field and share their methodological expertise.

- Effects of movement and levodopa on coupling between cortex, STN and muscle in patients with Parkinson’s disease - Jan Hirschmann (Düsseldorf, Germany)

Recent research suggests that oscillatory coupling between cortex, basal ganglia and muscles plays an important role in motor behavior. Impairments of motor function, such as akinesia in Parkinson’s disease (PD), are reflected by an altered pattern of connectivity. In order to characterize this pattern, we investigated connectivity changes in response to movement and pharmacological treatment with levodopa in PD patients undergoing surgery for deep brain stimulation.

We recorded the magnetoencephalogram, local field potentials from the subthalamic nucleus (STN) and the electromyogram (EMG) of forearm muscles simultaneously. Measurements were performed following withdrawal of dopaminergic medication and after administration of levodopa. Coherence and partial directed coherence were calculated for epochs of sustained contraction and continuous hand movement.

Movement led to a reduction of STN-cortical beta coherence compared to sustained contraction. The reduction was significant in a cluster centered on areas in the parietal lobe contralateral to movement. A concurrent reduction in beta coherence with forearm EMG was observed in contralateral motor and somatosensory areas. Administration of levodopa did not significantly modulate coherence. However, it resulted in a reduction of cortical driving of the STN in the beta band, which was not observed for corticomuscular connectivity. Moreover, it led to an increase of gamma band coherence during movement, selectively for STN-cortical coupling.

The data show that while cortex, STN and muscle display similar oscillatory activity, STN-cortical and corticomuscular oscillatory coupling may be modulated independently by pharmacological treatment. Furthermore, the results show clearly that not only motor, but also sensory cortical areas couple to STN and muscle in a task-dependent manner.
**Cortico-subthalamic coupling is modulated during motor planning in patients with Parkinson’s Disease - Ashwani Jha (London, UK)**

Both phenotype and treatment response vary in patients with Parkinson’s Disease. Anatomical and functional imaging studies suggest that individual symptoms may represent malfunction of different segregated networks running in parallel through the basal-ganglia. In previous studies we used simultaneous magnetoencephalographic and intracranial subthalamic recordings, in Parkinsonian patients undergoing surgery for deep brain stimulation, to characterise these cortico-basal ganglia networks electrophysiologically. We have identified a specific role for beta (15-35 Hz) and gamma (¿ 35 Hz) coherence between the subthalamic nucleus and motor and premotor areas both at rest and during self-paced movements. Cortico-subthalamic coherence is also modulated by dopamine and correlates with Parkinsonian symptoms. In this study we use a similar technique to investigate more complex, context-dependent movements in 15 Parkinsonian patients. We found that subthalamic coupling with medial premotor regions is modulated during movement by the context of the visual cue. The results may be useful in understanding the motor planning deficits experienced by Parkinsonian patients.

**Coherence estimates of combined MEG-LFP data from dystonia patients - Tilmann Sander-Thoemmes (Berlin, Germany)**

The treatment of dystonia patients by DBS allows the combined recording of MEG and subcortical LFP. Combined measurements were performed for 9 dystonic patients to study coupling between the internal globus pallidus and cortical MEG during a rest condition.

Data collection extended over a period of two years and novel non-magnetic extension wires connecting the DBS electrodes with the external LFP recording equipment were not yet available. Therefore, data from the left hemisphere are difficult to interpret at the sensor level as the extension wires leave the skull below the left hemisphere MEG sensors. Fortunately, coherences calculated between right side LFPs and right side MEG sensors show in 7 out of 9 patients clear patterns in the alpha-range from 7 to 12 Hz and in the beta-range from 15 to 30 Hz. The patterns are mainly located medially and can be attributed to the motor cortex.

To test significance of coherence patterns surrogate data are often used to estimate a null effect distribution. In our data the physiologically meaningful patterns in the alpha- and beta-ranges are found to be significant. The time shift PCA (TSPCA) can be used to remove signals present both in the LFP and MEG data. Removing the optimally convolved LFP contribution from the MEG data by TSPCA suppresses all significant coherence patterns indicating that these patterns are indeed a signature of signals present in both modalities. As a further test the magnetic wire artifact due to the heart pulsation is removed from the MEG data directly using signal space projection. Right side coherence patterns are essentially preserved indicating their independence from the wire artifact.

In conclusion, reliable subcortical-cortical coupling in the alpha- and beta-range is detected at rest for a group of dystonic patients.

In cooperation with A.A. Kehn and A. Bock of Charité(Berlin), and L. Trahms of PTB (Berlin).

**Using DBS-MEG to understand chronic pain - Hamid Mohseni (Oxford, UK)**

Co-author: Kringelbach ML.

Our group uses MEG to study the effects of DBS on chronic pain (Kringelbach et al., NeuroReport, 8(3):223-228, 2009). This has provided multiple insights into the mechanisms of how DBS alleviates the chronic pain (Kringelbach et al., J. of Pain Management, 3: 301-314, 2007) as well as the principles of how DBS work (Kringelbach et al., Nature Rev. Neurosci., 8:623-635, 2007). Among other things, we will show how we have used MEG to track the changes over a year in chronic pain patients with DBS in the ACC (Mohseni et al, in review). Multiple
challenges remain, however, both in terms of dealing with artefacts from the DBS and in terms of interpreting the data. In order to address some of these important challenges, we have developed a number of theoretical and methodological advances. In particular, we will discuss the results of using the null-beamformer (Mohseni et al, Proc. IEEE Eng. in Medicine and Biology Soc., EMBC-10, 4120-4123, 2010) and our novel fusion method for combining magnetometers and gradiometers as well as other image modalities (Mohseni et al, in review). We will also discuss the results of using our novel non-gaussian beamformer to more precisely localise the effects of DBS stimulation (Mohseni et al, in review). Finally, we will show how our recent findings of a pain signature of 8-12 Hz pain spindles in the local field potential (Green et al., Neurology. 10;72(6):569-71, 2009) can be used in conjunction with MEG to explore the oscillatory networks involved in chronic pain.

Tuesday, August 28th, 2012, 9:00-11:00

S-Tu-A1 Network connectivity measurement: MEG Methodology
Chair: Matt Brookes (Nottingham, UK)

In recent years, a number of studies have begun to show that MEG represents an excellent means to assess functional connectivity between spatially separate but functionally related brain regions. Such studies have shown that MEG elucidates "resting state" brain networks that are spatially similar to those observed using in fMRI. However, the direct nature of MEG offers distinct advantages over the indirect blood oxygenation level dependent fMRI response, in terms of measuring the electrophysiological processes that mediate network connectivity. A number of studies are now showing that neural oscillatory activity is integral to long range network connectivity in the brain.

Despite the promise shown, connectivity measurements using MEG remain difficult with the most significant problems arising due to magnetic field spread and the ill-posed MEG inverse problem: Field spread means that a single source in the brain affects multiple MEG sensors, making sensor space connectivity measurement difficult to interpret. These problems can be alleviated by projection of sensor space data into source space; however the ill posed inverse problem means that voxels at spatially separate locations can exhibit correlated projected timecourses purely due to signal leakage. Such leakage necessarily causes spurious connectivity measurement.

In this symposium, the electrophysiological basis of network connectivity will first be introduced. The symposium will then focus on the latest MEG data processing techniques developed to elucidate functional connectivity between network nodes. Techniques that ameliorate the known problems of MEG network measures and yield unambiguous connectivity measurements without bias due to magnetic field spread or source leakage will be discussed. Attendees will gain a working knowledge of current theories regarding the electrophysiological underpinnings of networks observed in fMRI as well as the latest cutting edge techniques for FC measurement.

- The Squid, the BOLD and the Electrode: hunting down the brain’s intrinsic networks - Karim Jerbi (Lyon, France)

The last decade has witnessed tremendous progress in the understanding of our brain’s intrinsic activity. Our current knowledge of the so-called resting-state networks stems predominantly from neuroimaging studies that examined the activity of our brain while not actively involved in mediating goal-directed behavior. The systematic spatial patterns of correlated network activations - unraeled by BOLD modulations and through functional connectivity measures - have opened exciting and radically new questions about basic brain function and dysfunction. Yet, ironically, functional MRI might not be able to tackle many of the questions it raises because of its relatively sluggish nature, and because the haemodynamic signal remains an indirect measure of neuronal activity. Although still in its early days, electrophysiological investigation of the resting state networks may very well provide the missing links. Thanks to their high temporal resolution, invasive (intracranial EEG) and non-invasive (MEG/EEG) electrophysiological techniques hold the potential to significantly expand our knowledge of the neuronal mechanisms that underlie intrinsic brain networks and, most importantly, their functional role. Nevertheless, a number of limitations still need to be resolved, especially for non-invasive MEG/EEG analysis of resting brain activity. In this talk, I will set the scene by discussing evidence for the putative relationship between
the BOLD signal and oscillatory brain activity and its implications on the quest to unravel the electrophysiological basis of resting state networks. In addition to highlighting recent findings from our group and others in the field I will overview some current methodological challenges that this research faces.

**An atlas-based MEG beamformer solution for the characterisation of frequency-dependent functional connectivity within resting-state networks - Arjan Hillebrand (Amsterdam, The Netherlands)**

Magnetoencephalography (MEG) has the temporal resolution to capture the frequency-dependent interactions between spatially separated brain regions that are thought to underlie cognitive function. However, volume conduction and field spread may lead to spurious measurements when functional connectivity is estimated on the basis of the extra-cranial recordings directly. I will first demonstrate that this problem is not completely solved by going to source-space, and then present a recently developed analysis framework that is based around two main ideas: (i) functional connectivity is computed for a set of atlas-based ROIs in anatomical space that covers almost the entire brain, providing a general framework that allows for a direct anatomical interpretation of MEG data, as well as a direct comparison with (functional) connectivity and network studies based on anatomical and functional MRI (DTI, VBM, fnsensitive to these effects, namely the Phase Lag Index (PLI)). This approach has revealed distinct frequency-dependent patterns of source power and source interactions during an eyes-closed resting-state condition in healthy controls, where alpha and beta band connectivity patterns were confined to posterior and sensorimotor areas respectively, and a generally more dispersed pattern was obtained for the gamma band. Moreover, these connectivity patterns corresponded closely to patterns of relative source power. Finally, I will show how increases in local protein expression affect the characteristics of functional networks in patients with gliomas, and how connectivity patterns in patients with Parkinson’s disease deviate from those in healthy controls.

**Non-stationary analyses of MEG resting state networks and properties of their integration - Francesco de Pasquale (Chieti, Italy)**

In this talk two magneto-encephalography (MEG) studies on the temporal dynamics of band-limited power (BLP) correlation at rest within and across resting state networks are presented. Six Resting State Networks (RSN) showing non-stationary properties are studied with MEG. In particular, epochs of transiently high within-network BLP correlation are identified for these RSNs and correlation of BLP time-series across networks is assessed in these epochs. These analyses demonstrate that functional networks are not equivalent with respect to cross-network interactions. The default-mode network (DMN) and in particular the posterior cingulate cortex (PCC) exhibit the highest degree of transient BLP correlation with other networks especially in the 14-25 Hz (beta band) frequency range. Our results indicate that the previously demonstrated neuro-anatomical centrality of the PCC and DMN has a physiological counterpart in the temporal dynamics of network interaction at behaviorally relevant time scales.

**Detecting Cortical Interactions using Canonical Correlations - Richard Leahy (Los Angeles, USA)**

I will describe our recent work on the problem of detecting large-scale cortical connectivity using MEG. The low resolution of cortical maps not only limits the specificity with which we can localize sources, but also affects our ability to detect connectivity because of the cross-talk or linear-mixing that is invariably present. In practice, even nonlinear methods can produce misleading results as a result of this cross-talk. We are investigating methods that use canonical correlations between feature vectors at each cortical location as the basis for detecting interactions. In this way we can potentially detect more complex interactions, including cross frequency interactions, than we can using direct correlation or coherence measures. A second advantage of the canonical correlation approach is that we can differentiate similarity between sources that is caused by cross-talk from that due to true nonlinear interactions. We have developed a method based on a conjunction analysis of two statistics: one a measure of cross-talk, the other is the canonical correlation value. Through this procedure we are able to detect cortical interactions in low resolution cortical current density maps. I will describe our simulation studies and applications to visuomotor experimental data. As time permits, we will also describe modifications of this approach that use Granger causality to determine directionality in cortical interactions.
How percepts, decisions and actions arise from the orchestrated activity of neuronal populations is probably one of the most fundamental questions in cognitive neuroscience. Great progress has been made over the last decade in characterizing how perceptual decisions are implemented in the non-human primate brain. Neurophysiological studies in monkeys have shown how parietal and frontal areas accumulate evidence during perceptual decisions. These studies have however almost exclusively focused on the spiking activity of individual neurons, measured in one brain region at a time. Therefore, it remains an open question how these local computations are integrated across many brain regions into percepts, decisions and actions. In this symposium, we will discuss new findings, based on EEG/MEG in humans or depth electrodes in monkeys, which illustrate how perceptual decision-making emerges from local and large-scale interactions between neuronal populations. We will show that these interactions are typically oscillatory, and argue that cortical oscillations provide an exquisite window into the cortical computations producing decisions.

Donner will start off making the case of how oscillatory cortical population activity indexes different computational elements of simple perceptual decision processes. Then, Wyart will illustrate the rhythmic nature of evidence accumulation during perceptual categorisation, focusing on slow (2 Hz) fluctuations over parietal cortex. De Lange will show how top-down factors such as prior expectation and prior accumulated evidence influence oscillatory correlates of decision-making, on the basis of MEG data. Finally, Haegens will show novel electrophysiological data illustrating how alpha- and beta-band oscillations contribute to somatosensory decision-making in monkeys.

Together, the symposium will underscore the importance of studying the dynamic cortical network interactions underlying perceptual decisions.

**Two oscillatory signatures of perceptual decisions in the human brain - Tobias Donner (Amsterdam, The Netherlands)**

Perceptual decisions result from temporal integration of sensory information supporting different choices, up to a threshold at which a response is elicited. Using MEG recordings in humans, we find two oscillatory cortical signatures of this process. The first signature is a gradual build-up of ’beta-band’ (12-36 Hz) suppression in the effector-specific part of motor cortex. This local beta-band suppression is the counterpart of a local enhancement of high-frequency (60-100 Hz) activity and, most likely, population firing rate. Functionally, this local beta-signature indexes the ’decision variable’ postulated by computational models of perceptual choice: It (i) depends on the strength of the integrated sensory information; (ii) reliably predicts the upcoming choice; (iii) reflects the subject’s response threshold. The second signature also occurs in the beta range, but it is confined to the lower beta range (12-24 Hz) and expressed in a large-scale frontal-parietal network of association cortices. Beta-band coupling across this large-scale network predicts correct choices. This large-scale beta-signature may index network reverberations underlying the maintenance of past sensory information and/or of the sensory-motor mapping rule. In sum, our results suggest that cortical oscillations index the canonical cortical computations mediating cognition.

**Rhythmic fluctuations in evidence accumulation during decision making in the human brain - Valentin Wyart (Oxford, UK)**

Categorical choices are preceded by the accumulation of sensory evidence in favour of one action or another. Current decision-making models assume that momentary evidence is integrated continuously over hundreds of milliseconds in the form of a decision variable, a quantity that maps the accumulated evidence onto an appropriate action. However, the notion that evidence accumulation occurs at a constant rate is inconsistent with a rich psychological literature describing how human perception is limited by a central bottleneck, giving rise to cognitive blinks of few hundreds of milliseconds during which sensory information is perceived as lagging or even missed. During perceptual categorisation, we found that both the encoding of momentary evidence in human EEG signals and its impact on choice were modulated rhythmically by the phase of ongoing delta oscillations at 2 Hz over the parietal cortex. By contrast, fluctuations in beta-band activity (10-30 Hz) over the motor cortex encoded the accumulated evidence as a response preparation signal. These findings draw a clear distinction between a central stage at which momentary evidence is weighted, and a motor stage at which the accumulated evidence is mapped onto action. They also suggest that the attentional bottleneck identified as responsible for cognitive blinks might impose a cyclic sampling constraint on evidence accumulation, with successive samples competing for limited
processing capacity before being integrated.

- **Pre-stimulus oscillatory activity in motor cortex reflects perceptual expectations** - Floris de Lange (Nijmegen, Netherlands)

  When perceptual decisions are coupled to a specific effector, motor cortical activity provides a window into the dynamics of the perceptual choice. Specifically, previous studies have observed a build-up of activity in motor regions as sensory evidence accumulates over time. Here we ask how this decision-related activity is modified by perceptual expectations. Theoretical models of decision-making have conjectured that expectation could either change the starting point, gain or bound of the decision variable. Using a combination of psychophysics and magneto-encephalography (MEG) in human volunteers, we find that providing probabilistic cues about motion direction strongly biased the starting point of the decision signal towards the expected percept. Moreover, spontaneous fluctuations in the decision signal (in the absence of explicit cues) could also predict perceptual choice. Together, these findings suggest that implicit and explicit perceptual expectations change the initial value of the decision signal prior to the accumulation of sensory evidence.

- **Alpha and beta oscillations in the monkey sensorimotor network contribute to somatosensory decision-making** - Saskia Haegens (New York, USA)

  The neuronal correlate of perceptual decision-making has been extensively studied in the monkey somatosensory system, showing that stimulus encoding, retention, and comparison are reflected by single-unit spikes and widely distributed across cortical areas. However, relatively little work has been done in order to understand what role oscillations play in perceptual decision-making and how they are linked to neuronal firing.

  Here, we simultaneously recorded local field potentials (LFPs) and spikes from diverse cortical areas of the sensorimotor system, while a trained monkey performed a vibrotactile discrimination task. Interestingly, we found that oscillatory activity in the beta band reflected the dynamics of decision-making in the monkey sensorimotor network. During the comparison and decision period, beta activity showed a categorical response that reflected the decision of the monkey and distinguished correct from incorrect responses. In addition, we observed strong activity in the alpha band which decreased in the sensorimotor regions during the discrimination task. This alpha power decrease predicted better discrimination performance. Furthermore, the alpha oscillations demonstrated a rhythmic relation with the spiking, such that firing was highest at the trough of the alpha cycle. Firing rates increased with a decrease in alpha power. These findings suggest that alpha oscillations exercise a strong inhibitory influence on both spike timing and firing rate.

  We conclude that beta band oscillations reflect the temporal and spatial dynamics of the accumulation and processing of evidence in the sensorimotor network leading to the decision outcome, while alpha band activity reflects the state of the system and thereby modulates processing capacities.

**Tuesday, August 28th, 2012, 9:00-11:00**  
**Hall C**  
**S-Tu-C1 Ultra-Low-Field MRI and MEG**  
**Chair: Myriam Pannetier-Lecoeur** (Saclay, France)

Combining functional information given by MEG with structural information given by MRI is an important challenge for the understanding of the brain, its functions and diseases. This can only be addressed under conditions in which both types of signal can be acquired with the same apparatus. Conventional high field MRI cannot be combined with MEG since the SQUID sensors used in MEG systems require a highly magnetically shielded environment. Over the last five years, ultra-low-field-MRI (that is, at fields lower than a few millitesla) has become the preferred technological choice, especially since very sensitive magnetometers such as SQUIDs or mixed sensors offer exquisite sensitivity to detect the magnetic resonant signal under low frequency, low field conditions. This symposium will present the latest advances in ULFMRI systems, specifically highlighting their combination with biomagnetic measurements.
• **Magnetic Resonance Imaging in Microtesla Fields - John Clarke (Berkeley, USA)**

There is growing interest in magnetic resonance imaging (MRI) in magnetic fields of about 0.1 mT i.e. four orders of magnitude lower than in clinical MRI machines with SQUID-based detection of the nuclear magnetic resonance (NMR) signal. Such systems are lower in weight and, potentially, in cost than conventional machines, require only modest homogeneity in the imaging field, are insensitive to variations in the magnetic susceptibility of the specimen being imaged, and have a greater contrast in the longitudinal relaxation time $T_1$ for different tissue types. The decrease in the polarization of the proton spins and hence in the NMR signal amplitude due to the low field is partially compensated by prepolarizing the spins in a higher field. As with high-field MRI, imaging involves switched magnetic field gradients and a spin-echo sequence. Our current MRI machine operates at 0.132 mT, corresponding to a proton frequency of 5.6 kHz, with a 150-mT polarizing field. The noise referred to the lowest loop of a second-derivative, superconducting gradiometer coupled to a flux-locked dc SQUID is $0.6 \frac{fT}{\sqrt{Hz}}$. The system can operate for several hours unattended. The in-plane spatial resolution is about 1mm for phantoms and 2 mm for in vivo images of the arm. The phantom images remain undistorted by the insertion of a titanium bar. Measurements of $T_1$ in phantoms containing different concentrations of agarose gel in water show a much higher contrast than in fields even as low as a few millitesla. Measurements on prostate tissue surgically removed from 35 patients reveal the average values $T_1(100\% \text{tumor}) = (0.70 \pm 0.05) T_1(100\% \text{ normal tissue})$ at 0.132 mT. Provided similar values are found for in vivo tissue, microtesla MRI may have the potential to image prostate cancer. A study of ex vivo healthy and malignant breast tissue is about to begin. Challenges and future prospects are discussed.

• **MRI at 10 mT - Stefania Della Penna (Chieti, Italy)**

Magnetic Resonance Imaging (MRI) at measurement fields of the order of 0.1 mT has been demonstrated thanks to the use of a pre-polarization field of the order of several tens of mT and to the exquisite sensitivity of SQUID based sensors. This MRI set-up might be compatible with MEG, but the time required for recording images is still too large. A possible strategy to speed-up data recording is to avoid the use of the pre-polarization field with the simultaneous increase of the measurement field up to 10 mT. This field strength is still compatible with SQUID sensors used in MEG devices installed in a magnetically shielded room. Compact or open schemes for the magnetizing coils can be adopted. The magnetic resonance (MR) signal at 10 mT can be detected by tuned volume coils at room temperature or by surface channels based on superconducting mixed sensors. The latter ones are hybrid sensors consisting of a superconducting loop (YBCO or Nb) with a constriction above which Giant Magnetic Resistances are placed. These devices are able to detect changes of the local magnetic field as a function of the flux applied to the loop. Mixed sensors are more robust than SQUIDs when operated in a NMR applied field and their sensitivity is suitable for MRI. Different MRI set-ups at 10 mT with compact or open measurement field, using superconducting detection through either mixed sensors or surface coils coupled to mixed sensors or using volume coils at room temperature are discussed and compared.

• **Instruments for Co-registration of Ultra-Low Field Nuclear Magnetic Resonance Images and Magnetoencephalography - Andrei N. Matlachov (Los Alamos, USA)**

Magnetoencephalography (MEG) and magnetic resonance imaging (MRI) were commercialized approximately at the same time, in the mid 1980s, and have coexisted for more than three decades as two technically incompatible methods. Both methods played crucial roles in research and diagnostics of the brain in the last three decades. But for long time they needed two separate expensive machines. The idea of making one machine for both MEG and MRI looked impossible until two key ideas crossed over - the field cycling pre-polarization technique and the use of SQUIDs for signal detection. The first paper with ultra-low field (ULF) MRI of the human brain combined with MEG was published in 2008. MR images were recorded at 46 $\mu$T measurement and 30 mT pre-polarizing fields with $3\times3\times6 \text{ mm}^3$ resolution. A combined MEG and ULF MRI machine is not just an upgraded conventional MEG machine. In addition to pre-polarizing and imaging coils, MRI capability adds new requirements to the SQUID sensors. One of the most difficult is that sensors should work after being immersed in large pre-polarizing field. Another difference between MEG and MRI systems is that the optimization criteria for pick-up coil size are quite different. For MEG pick-up coil diameter can’t be too large to avoid smoothing of spatially sharp field distributions. In the case of MRI the spatial resolution is defined by applied gradients and not by pick-up coil diameter. This is why a ULF MRI system needs a lesser number of pick-up coils of larger size to cover the same area of interest. One approach is a hybrid design of a combined MEG and MRI machine with different kinds of SQUID sensors for separate recording of MEG and MRI signals. In this presentation we discuss our experience in development of such SQUID-based instruments for combined ULF MRI and MEG.
• Challenges in combining MEG and ULF-MRI in a single device - Lauri Parkkonen (Helsinki, Finland)

Ultra-low-field magnetic resonance imaging (ULF-MRI) is a novel structural imaging method that potentially offers unique advantages in the diagnostics of structural brain pathologies such as tumors. Combining ULF-MRI and MEG functions in a single device is attractive since a multi-channel SQUID array excels in picking up both MEG and the low-frequency nuclear magnetic resonance signals of a ULF-MRI setup. Moreover, acquiring MEG and MRI with the same device improves the co-registration of these two modalities. However, even in ULF-MRI the employed magnetic fields are more than ten orders of magnitude larger than those typically encountered in MEG, which renders such a combination challenging.

In ULF-MRI, the sample is typically pre-polarized in fields of 10200 mT to increase the signal. While the SQUIDs do not need to measure during the polarization, they should recover from it in a small fraction of the T1 relaxation time. The SQUIDs should also operate in measurement fields up to 200 µT. A pulsed pre-polarization field may also evoke interference due to eddy currents in the walls of the magnetically shielded room; thus, the polarization coil has to be shielded in addition to producing a reasonably homogeneous field across the helmet-shaped imaging volume. To preserve the MEG function and to allow for high-quality MR imaging, no parts within the dewar should be magnetized by the polarization field.

The European MEGMRI project aimed at realizing a hybrid device capable of both MEG and ULF-MRI. In this project, we constructed a full-scale helmet-shaped prototype system and addressed the above challenges to a sufficient degree to enable ULF-MRI measurements while maintaining the MEG functionality. This full-scale prototype system demonstrates that combining MEG and ULF-MRI in a single device is feasible. Further research is needed to perfect the system and to evaluate its potential as a brain imaging tool.

• MRI capability added to a whole-head MEG: results and promise for the future - Risto Ilmoniemi (Helsinki, Finland)

Modern MEG sensor arrays are highly sensitive, spatially precisely defined, and well-calibrated. However, their ability to locate cerebral sources does not match the instrumental precision. The main reasons are, in addition to fundamental difficulties due to the ill-posedness of the inverse problem, errors in registration of the MEG and MRI coordinate systems as well as poor knowledge of the conductivity distribution of the head. Both of these problems can be alleviated by the measurement of both MEG and MRI with the same set of sensors in the same session. For this end, we have added MRI capability to a commercially-based whole-head MEG system with the result that now the registration error is essentially eliminated. Furthermore, since the MRI is obtained at a very low magnetic field, the distortions of the structural image from signal attenuation or susceptibility artifacts are negligible.

Our initial results using 48 SQUID sensors were obtained at the measurement field of 50 T after prepolarization of the head at 22 mT; with the voxel volume of 0.09 cm³ (3.56 x 3.56 x 3.34 mm³), the scan time was 90 minutes. Comparison with down-sampled 3-tesla MRI indicated that the image was a faithful representation of the head structure. Although we have demonstrated the feasibility of a large-array hybrid MEG-MRI system, the present MRI quality is not yet sufficient. Our aim is to reduce the scan time to about 10 minutes and improve the spatial resolution to 12 mm by using a stronger prepolarization field and by reducing SQUID noise and external disturbances. This would allow us to register the MEG system with the anatomical structures of the brain with millimeter accuracy. The undistorted ultra-low-field MRI can also be used to correct distortions of high-field MRI, with the result of unprecedented MRI quality. The benefits will include improved possibilities to define the conductivity structure of the head and to locate brain sources reliably and with great accuracy.
Electrophysiological studies using MEG, EEG, and ECoG which attempt to probe neurophysiological fundamentals of sensory, motor in the human brain have been progressed as a challenging but robust way to provide in-depth understanding of neural interaction. Main approaches, in particular, cortico-muscular coherence, oscillatory synchronization which characterizes neuronal activities underlying normal physiology or pathological state are now looking for clinical and functional relevance of the phenomenon and will eventually enhance our understanding of the neuropathophysiology of the chronic illness. In this symposium, Dr. Mima will first introduce cortico-muscular coherence measure by MEG, EEG, and ECoG and its generator and physiological mechanisms. Dr. Chung will present the role of descending motor control and ascending sensory feedback to stability of motor output and how each of these components, separately and together contributes, to that event. Dr. Schnitzler will present evidence of disrupted oscillatory synchronization in the basal ganglia and between subcortical and cortical structures which constitute pathophysiological mechanism in Parkinson’s disease and other movement diseases. Lastly, Dr. Jensen will discuss the role of alpha oscillatory activity which serves route processing to task-relevant areas by actively suppressing task-irrelevant areas while performing tactile discrimination task.

- **Cortical control of muscular activity** - Tatsuya Mima (Kyoto, Japan)
  The topic of the talk will be cortico-muscular coherence measures by MEG, EEG and ECoG. Animal experiments using local field potentials are also briefly introduced. Its generator mechanism and application to tremor disorders will be discussed.

- **Directional information flow between human sensorimotor cortex and finger muscles during steady-state contraction** - Chun Kee Chung (Seoul, Korea)
  Converging evidence from both human and non-human primate studies suggests that not only descending corticospinal activity but also afferent feedback pathways were involved in generating corticomuscular coherence. In the previous work, we showed that the magnitudes of beta-band primary motor cortex (M1)-electromyogram (EMG) coherence for thumb muscle were greater than that for little finger muscle. In addition, levels of beta-band coherence were positively associated with EMG stability. These results suggested that strength of beta-band M1-EMG coherence may play an important role in steady-state muscle contraction. However, prior studies including our one have not examined which descending or ascending pathway contributes to stable muscle contraction, thus were not able to discriminate each role. In this regards, we sought to further investigate that how descending motor command or afferent sensory feedback is related to stability of muscle contraction by calculating directed transfer function (DTF) between the sensorimotor cortex and EMG. We recorded magnetoencephalography and EMG simultaneously during steady-state isometric contraction of right thumb muscle (flexor pollicis brevis, FPB) or right little finger muscle (flexor digiti minimi brevis, FDMB). We found that stability of EMG for FPB was higher than that for FDMB. It was also shown that directional information flow appeared not only from sensorimotor cortex to EMG but also back from EMG to sensorimotor cortex in DTF analysis. Strength of beta-band DTF from muscle to sensorimotor cortex for FPB was greater than that for FDMB, suggesting improved sensorimotor integration of descending motor control and sensory feedback in FPB. DTF from sensorimotor to EMG was numerically greater in FPB than FDMB, however not statistically different. Therefore, our findings indicate that afferent sensory feedback to the sensorimotor cortex together with descending motor command to muscle may promote steady-state motor output.

- **Oscillatory communication in the sensorimotor system in movement disorders** - Alfons Schnitzler (Düsseldorf, Germany)
  Growing evidence from invasive and non-invasive electrophysiological recordings in animals and humans indicates that oscillatory synchronization within the basal ganglia and between subcortical and cortical structures is of particular significance in the pathophysiology of Parkinson’s disease (PD) and other movement disorders. Akinesia in PD has been shown to correlate with increased oscillatory beta band power in basal ganglia nuclei and with enhanced cortico-subcortical beta band coherence. Accordingly, clinical improvement due to levodopa replacement or deep brain stimulation (DBS) of the subthalamic nucleus (STN) is associated with a decrease
in beta oscillatory synchronization. Magnetoencephalographic (MEG) studies of PD resting tremor have identified an abnormally synchronized oscillatory network comprising subcortical and cortical areas that are driven at tremor frequency or twice the tremor frequency. The same network is also active during voluntary repetitive movements of healthy subjects imitating PD resting tremor. However, increased thalamocortical and decreased premotor-motor-cortical coherence differentiates PD resting tremor from tremor imitation. Administration of levodopa reduces thalamocortical coherence and results in clinical tremor reduction. These findings provide strong evidence for a pathophysiological role of abnormal oscillatory synchronization. MEG investigations of patients with other tremor syndromes, such as essential tremor and hepatic tremor have also revealed abnormal oscillatory patterns which are, however, distinct from PD tremor. In summary, there is accumulating evidence that distinct abnormal oscillatory synchronization in cortico-subcortical loops constitutes an important pathophysiological mechanism underlying clinical symptoms in movement disorders.

- **Alpha oscillations serve to allocate resources in the sensorimotor system in space and time** - Ole Jensen (Nijmegen, The Netherlands)

Effective processing of sensory input in daily life requires attentional selection and amplification of relevant input and, just as importantly, attenuation of irrelevant information. It has been proposed that top-down modulation of oscillatory alpha band activity (8-14 Hz) serves to allocate resources to various regions depending on task demands. In previous work, we showed that contralateral somatosensory alpha activity decreases in order to facilitate processing of an anticipated target stimulus in a tactile discrimination task. In the current study, we asked whether somatosensory alpha activity is also modulated when expecting incoming distracting stimuli on the non-attended side. We recorded magnetoencephalography (MEG) while subjects performed a tactile stimulus discrimination task where a cue directed attention either to their left or right hand. Distracters were presented simultaneously to the unattended hand. We found that alpha power contralateral to the attended hand decreased while ipsilateral alpha power increased. Importantly, the ipsilateral power increase contributed to discrimination performance. These findings are corporate by recent spike-field recordings from the sensorimotor system of the monkey demonstrating that neuronal spiking is tightly clocked by the phase of the alpha rhythm. Importantly, as alpha power increases, the firing rate decreases. These findings underscore that alpha activity plays an important role for allocation of neuronal processing resources by actively modulating the neuronal firing by ‘pulsed inhibition’.

**Tuesday, August 28th, 2012, 15:00-17:00**

**S-Tu-B2 Scale-free dynamics in neuroscience**

**Chair: Philippe Ciuciu (Saclay, France)**

Starting with the discovery of brain oscillations in EEG and later in MEG, many studies have attempted to explain their mechanism and their possible functional role in behavior and cognition. Some frequency bands were particularly conspicuous and were given names such as (1-3Hz), (4-8Hz), (8-12Hz), (12-30Hz) and (> 40Hz). Besides, very low frequency or ‘infraslow’ activity (< 1Hz) did not attract as much attention due to the power-law distribution of the spectral density in the range of low frequencies. This property is very ubiquitous in dynamic systems (physics, earthquakes, ...) [1]. In brain imaging, several authors have shown that ongoing activity, the major part of brain activity [2], has scale-free dynamics -i.e. a 1/f power spectrum [1-4]. Since then, the study of scale-free properties has emerged as a new research topic in neuroscience. A major finding is that scale-free activity recorded with EEG interacts with ongoing oscillatory activity [5]. Moreover, the surprising correlation between EEG microstates and fMRI resting-state networks (RSN) could be explained by the scale-free properties of these microstates [6]. In this symposium, we will bring into light recent advances in this research avenue by illustrating the modulation of scale-free activity by exogenous (drugs,task) and endogenous (brain state, pathology) factors [1] using different imaging techniques (iEcoG, EEG, MEG, fMRI). We will also discuss how the brain departs from classical self-organized critical systems [8] and the discrepancy between scaling exponent estimates in LFP, EEG and MEG recordings will be finally interpreted in terms of ionic diffusion [9].

• **Scale-free brain activity viewed through electrophysiology and fMRI - Biyu HE (Bethesda, USA)**

Scale-free dynamics are exhibited by many complex processes in nature. Despite long-held interests in fields such as physics and heart physiology, it has so far been largely neglected in mainstream neuroscience research, partly due to its universality. In this talk I will argue that underlying the same power-law distribution, the temporal structures of scale-free dynamics vary from one system to another. Thus, in studying scale-free dynamics, it is important to explore beyond the power-law distribution to uncover fine spatiotemporal patterns and underlying mechanisms. I will further discuss recent findings suggesting the functional significance of scale-free brain activity, such as variation of fMRI signal power-law exponent across brain networks, correlation between fMRI power-law exponent with brain metabolism and modulation of scale-free brain activity by task performance.

• **Infra-slow oscillations in electrophysiological, blood-oxygenation-level dependent (BOLD), and psychophysical signals: enigmatic co-existence of scale-free and quasi-periodic dynamics - J. Matias Palva (Helsinki, Finland)**

'Fast' (1-100 Hz) brain activity is traditionally divided to six frequency bands and although the definitions may be ambiguous and the activities might not show up as a power spectrum peak, there is little question about whether oscillations exist in these frequency bands. The oscillations emerge through distinct time-scale-specific neuronal mechanisms and narrow frequency bands are characterized by distinct functional specializations and phenomenology. A more controversial situation pertains to 'slow' neuronal phenomena with frequencies from 0 to 1 Hz, including the putative infra-slow frequency band (0.01-0.1 Hz). The amplitudes of fast neuronal oscillations exhibit slow fluctuations and similar fluctuations are observable in cortical potentials, BOLD signals, and psychophysical performance. These fluctuations are likely to reflect the same underlying physiological phenomenon and they are scale-free, fractally self-similar, and spatio-temporally correlated across long distances with a power-law decay. In short, many measurable characteristics of (self-organized) critical state dynamics are salient in slow brain dynamics and similar to those of sand piles, earth quakes, and stock markets. The brain, however, is distinct from other critical-state systems in exhibiting fast neuronal oscillations (scale-specific activity) concurrently with slow-scale free dynamics. Based on both existing literature and new electrophysiological data, we add on to this apparently enigmatic situation and posit that also the slow fluctuations may be comprised of quasi-periodic band-limited oscillations rather than being fundamentally arrhythmic. We further argue that these infra-slow oscillations serve essential roles both in large-scale neuronal integration and in sub-system decoupling. The emergence of scale-free dynamics from quasi-periodic 0.01-100 Hz oscillations driven by scale-specific neuronal mechanisms may thus be a universal property of brain activity.

• **Frequency scaling in EEG, MEG and high-density intracranial recordings - Alain Destexhe (Gif sur Yvette, France)**

Scale invariance is a property widely seen in brain dynamics, but it is not clear how scale-free global variables (such as EEG, MEG) relate to local neuronal activity. We have analyzed recordings at multiple scales, such as simultaneous EEG-MEG recordings, simultaneous MEG and intra-cranial (EcoG) recordings, or simultaneous intra-cranial and unit recordings, in both normal subjects and in patients suffering from intractable temporal lobe epilepsy. We compared recordings made in 'desynchronized' EEG states, associated with arousal and active wakefulness and devoid of epileptic activity. The EEG tended to scale between 1/f and 1/f² while MEG showed less frequency dependence, close to 1/f, with sometimes smaller exponents. Interestingly, the frequency scaling of Local Field Potentials (LFPs) were also around 1/f, but the unit activity showed no sign of critical states, confirming our previous observations in cats. We interpret these findings by a frequency-filtering property of electric signals in neuronal tissue, which may be the primary factor responsible for 1/f scaling in LFPs and EEG. We also show results from theoretical models which suggest that ionic diffusion, which is necessarily associated with neuronal membrane currents, can be the factor responsible for such 1/f frequency scaling of brain signals.
• Modulation of scale-free properties of brain activity in MEG - Philippe Ciuciu (Saclay, France)

The analysis of scale-free (i.e., 1/f power spectrum) brain activity has emerged in the last decade since it has been shown that low frequency fluctuations interact with oscillatory activity in electrophysiology, noticeably when exogenous factors (stimuli, task) are delivered to the human brain. However, there are some major difficulties in measuring scale-free activity in neuroimaging data: they are noisy, possibly nonstationary ... Hence, to elucidate the biological meaning of scale-free activity observed in neural systems, new signal processing methods making use of multifractality have become necessary. Here, I will make use of multifractal analysis since it has allowed characterizing scale-free time series that depart from fractal processes and Gaussian processes, namely the multifractal processes. Amongst the existing methods, the Leader-based Multifractal (WLMF) framework has emerged as the most accurate strategy for characterizing univariate scale-free time series. We acquired Magnetoencephalography (MEG) data during i.) Rest (R), and ii.) visualization of Random Dots Kinematograms (RDK) on a cohort of 20 subjects. We demonstrate the presence of self-similarity on all sensors during ongoing and visually evoked activity. Also, we report significant multifractality on the norm of gradiometers. Finally, on the latter signals we study the modulation of multifractal attributes between the R and RFK cognitive states: Although no significant difference could be found when analyzing direction-specific gradio- or magneto-meters, statistical differences are exhibited when analyzing the norm of gradiometers. A criterion is derived to explain this surprising difference and an interpretation is suggested.

Tuesday, August 28th, 2012, 15:00-17:00

S-Tu-C2 Novel Developments in Magnetocardiography
Chair: Matti Stenroos (Helsinki, Finland)

Magnetocardiography (MCG) provides noninvasively information on the normal and pathological electrical activity of the human heart - a kind of information that is difficult to obtain with other methods. The aim of the proposed symposium on MCG is to present the latest developments in this field of research from around the world. We contacted major groups, asking for their recent results. We timely received 11 abstracts, from which 6 were chosen for the symposium based on the novelty. The remaining 5 speakers were kindly asked to submit their valuable contributions as regular abstracts to the Biomag 2012.

The abstracts show that development of MCG signal analysis is focused on spatiotemporal domain. Modern feature-extraction techniques and statistical properties of the data are utilized. In the field of inverse problem, beamformers are now applied in addition to more traditional source models. Since the previous Biomag meeting, new hardware has been developed - in addition to scientific, also clinical.

The pathologies studied with MCG today include atrial fibrillation (AF), coronary artery disease (CAD), arrhythmia risk analysis, and Wolff-Parkinson-Whyte syndrome (WPW). AF is among the most common reasons for hospitalization in industrial countries, and CAD and post-infarction arrhythmias are major causes of death. Based on results presented in these abstracts, MCG may provide efficient tools for screening and treatment-planning in these diseases. Pre-operative localization of accessory pathways in the WPW syndrome is a promising application for the MCG source localization. In conclusion, this symposium proposal shows that magnetocardiography is an advancing field, where novel methods and tools are used in both basic research and in the solving of clinically and economically important questions. Hereby we think that this MCG symposium would make an important contribution to the Biomag 2012 conference.

• Three-dimensional Imaging of Decorrelated Myocardial Electric Activity - Kiwoong Kim (Seoul, Korea)

I introduce a spatially-decorrelated surface potential activation beamformer (SPAB) for magnetocardiographic source localization. Non-invasive localization of reentry activity on the myocardium is clinically useful in many conduction disorders like atrial fibrillation (AF), atrial flutter, and ventricular tachycardia. The solution for the localization problem is basically ill-posed and sensitively depends on mathematical constraints such as a conductor model for the forward problem. Even if we have an exact individual conductor model for the problem, the most problematic matter is the fact that the cardioelectric sources are intrinsically correlated and hence a power leaking interference often shifts the localization result. Especially, MCG-measurable f-waves are originated from
quite spatially-spread sources which have strongly correlated sources. In this presentation, I propose a robust localization method based on source decorrelation for MCG reentry source localization. With linear constraints, the method spatially suppresses all the possible sources other than in a region of interest. In order to demonstrate the performance of the method, we compare the results of three methods, normal SPAB, ICA-preprocessed SPAB, and the proposed spatially-decorrelated SPAB in a clinical AF application.

- **Evaluating cardiac magnetic field maps in patients with coronary artery disease - Peter Van Leeuwen (Bochum, Germany)**

Acute myocardial infarction is associated with structural and functional damage to the heart muscle. Magneto-cardiography (MCG) permits the quantification of electrophysiological characteristics with various measures that describe both spatial and temporal aspects of cardiac de- and repolarization. In this study, we examine structure of magnetic field maps (MFM) on the basis of MFM orientation and coherence as well as spatial QT interval distribution in 112 patients with coronary artery disease (CAD). The results are compared to those of a group of 39 age-matched healthy controls. The results show that patients who have suffered an acute myocardial infarction differ from the healthy controls with respect to all measures, in particular MFM orientation. The values of CAD patients with coronary vessel stenosis but without infarction do not differ substantially from those of the controls. The measures applied here quantifying spatial and temporal aspects of MFM reflect pathological changes in electrophysiological function after myocardial infarction but not necessarily those in stable CAD patients without an acute event.

- **Animation of MCG mapping reveals recurrence and dynamics during atrial fibrillation - Ville Mäntynen (Helsinki, Finland)**

Atrial fibrillation (AF) is the most common arrhythmia requiring medical attention. The disease is diverse and its occurrence is increasing. Better diagnostics are needed to support the management of AF. The degree of organization of atrial activity has been linked to the persistence of AF and predictability of treatment outcome. Spatial properties of MCG mapping can be quantified after applying a well-known visualization method, pseudocurrent density (PCD) transformation (vector arrow map). We define MCG map orientation as the mean orientation of the strongest pseudocurrent vectors. The dispersion of the vector orientations can be quantified and used to assess the statistical significance of the MCG map orientation.

In our earlier studies, we have used the PCD transformation to determine the inter-atrial conduction pathways in AF patients recorded during sinus rhythm. In this study, we report recurrent spatiotemporal patterns in MCG mappings during AF. We confined the analysis to the TQ intervals. The baseline wander was removed using high-pass filtering; to avoid the filter ringing, the QRST complexes were damped down prior the filtering. The results show that the magnetic field pattern of ongoing fibrillation can be visualized and quantified: In PCD animations, frequently appearing cyclical sequence was observed and perceived as rotation of the map. The rotation became even more apparent when the MCG map orientation was plotted versus time. In addition to consistent rotation of several rounds, clockwise as well as counter-clockwise, also abrupt changes in the direction of the consistent rotation were observed. The rotation and its dynamics are likely linked to states of organization of the atrial activation during AF. In conclusion, MCG mapping seems capable to detect sudden fibrillatory phenomena with high temporal accuracy, and, may offer a novel means to study and characterize AF.

- **Automatic classification of Coronary Artery Disease patients based on MCG signal entropy - Silvia Comani (Chieti, Italy)**

Ischemic heart disease is a primary cause of death in industrial countries. Coronary angiography is the gold standard for detecting luminal narrowing of coronary arteries, but is invasive, expensive and time-consuming, whereas other imaging techniques may have a low predictive value. Sensitivity, specificity and accuracy achieved with non-invasive clinical methods to detect Coronary Artery Disease (CAD) generally range from 70 to 85%. Magneto-cardiography (MCG) is non-invasive and able to show the alterations in the electrical myocardial activation due to ischemia on magnetic maps that, however, need to be examined by expert clinicians. We propose an automatic system to classify CAD patients with a lumen narrowing > 50% that is based on the assessment of MCG non-linear features. MCG was recorded with a 61-ch biomagnetometer in 10 patients (56±12 years, 8 male) at rest, during pharmacological stress, and during recovery. After preprocessing with ICA and wavelets, entropy is quantified, and patients are categorized with a Multilayer Perceptron neural network based on Linear Discriminant Analysis. Classification is implemented at a single-beat level, and the system is trained on all data.
sets except data from one patient, later used for testing. This procedure is repeated for all patient data. Sensitivity, specificity and accuracy were assessed, and results validated vs. surrogate data. The sensitivity, specificity and accuracy were (in %): 99, 97, 98 at rest; 86, 60, 70 during stress; 72, 84, 79 during recovery, showing that our system outperforms other methods when MCG at rest is analyzed, which may have a great clinical impact. Comparison between the use of original data at rest and related surrogate data (whose sensitivity, specificity and accuracy were (in %): 79, 76, 77) demonstrated that the high predictive power of our system is not in the fine temporal structure possibly affected by noise, but is related to the general temporal structure of the MCG signal.

- Magnetic field imaging for risk stratification of sudden cardiac death in patients with primary preventive ICD-indication - Tobias Toennis (Trier, Germany)

Noninvasive risk stratification for sudden cardiac death is dominated by left ventricular ejection fraction (EF). However, it has neither a high sensitivity nor a high specificity. QRS-Fragmentation, detected by Magnetic Field Imaging (MFI) has shown promising results in addition to the use of the EF. 153 patients with primary preventive ICD-indication were examined with the MFI-system with 55 SQUID-sensors (Apollo CXS, BMDSys, Magdeburg). In a standard rest protocol the QRS-Fragmentation was determined. In addition to the visual interpretation of the QRS-Fragmentation for quantification we determined the fragmentation index, which derives of several criteria (the difference between extrema, the length of the curve and the derivative). As control 50 healthy volunteers were examined.

The mean follow up time up to now is 14.3 months. 66 % of the patients in the ICD-group had an ischemic, 34 % had a dilative cardiomyopathy. The average left ventricular ejection fraction was 28 ± 8 %, the QRS-width 121 ± 31 ms. 43 pts (28 %) were in atrial fibrillation.

Regarding the fragmentation index the variation range in the ICD-group was markedly increased compared to the control group. There is no correlation with the ejection fraction and only a slight correlation with the QRS-width. In the ICD group 11 pts (7.2%) died, but only 2 in an electrical storm, 5 because of progressive heart failure 4 of other reasons. 17 patients (11.1 %) showed episodes of ventricular tachycardia. One patient with an event had no increased fragmentation but all other showed a medium to high grade QRS-fragmentation.

These preliminary results of a prospective registry show that MFI based QRS-fragmentation in addition to the ejection fraction is able to identify patients who are more likely to get a life-threatening ventricular tachycardia.

- Reconstruction of Current Source Distribution in the Heart with 3D MCG Measurement - Yoshinori Uchikawa (Tokyo, Japan)

One of the important aims in MCG study is to reconstruct the current source of signal generators in the human heart activation using 3D MCG signals. In MCG inverse calculation the magnetic field perpendicular to the surface of the body (normal component) is widely used and an equivalent current dipole (ECD) is applied. However, there are problems of separating multiple sources, which are closely located and overlapped in time, when many distinct areas in the heart are active. In these cases, owing to the lack of a dipole field pattern, ECD method is hard to apply for source localization. To solve these problems, we introduced methods in both signal processing, including inverse calculation with source model, and SQUID instrumentation. First, we developed a 39-channel SQUID system for 3D vector measurement of MCG, which can simultaneously detect magnetic field components perpendicular and tangential to the surface of the body. Second, a method of inverse calculation to reconstruct the current source distribution in the heart activation, using 3D MCG signals measured by a 39-channel SQUID system, was developed. The minimum norm method-based algorithm is used to solve inverse problem. Third, the volume conductor model for estimating current source is a Boundary Element Method (BEM) model including the torso, lungs and heart geometries. The torso and organs, having different conductivities, are triangulated and each surface has 586 triangles. Fourth, two current source model of the heart activation were used. One is the moving dipole and the other is a distributed source model consisting of dipoles, which sets a current dipole to each divided volume element of the heart model. Lastly, with these procedures the reconstruction of current source distribution using 3D MCGs was performed using data of normal subjects and a patient with WPW syndrome. The usefulness of 3D MCG is shown by the improved localizations obtained.
Invasive and noninvasive studies in humans under physiological and pathological conditions converged on the suggestion that neural oscillations implement cognitive processes such as sensory representations, attentional selection, and dynamical routing/gating of information. However, most MEG/EEG studies investigating oscillations analyze temporal modulations of oscillatory amplitude or power differences between experimental conditions while ignoring phase. In contrast, computational models and invasive recordings (mostly in animals) provide compelling evidence about the functional role of phase dynamics in perception and cognition. These studies suggest that temporal phase coding could be advantageous in fundamental operations such as object representation and categorization by implementing efficient winner-takes-all algorithms, by providing robust sensory representations in unreliable environments, by lending themselves to multiplexing and by gating information flow in large-scale brain networks.

Here, we aim to present recent evidence that highlights the functional role of oscillatory phase in coding and communication. The presentations cover a comprehensive range of topics such as the stimulus-specificity of EEG phase and its relation to neural firing (Kayser), phase coding in MEG/EEG signals (Gross), external oscillatory entrainment (Herrmann) and long-range phase synchronization (Siegel).

- **Phase of entrained EEG alpha oscillations determines perception - Christoph Herrmann (Oldenburg, Germany)**

  A number of EEG studies provide evidence that ongoing neural activity prior to the presentation of a stimulus explains a substantial fraction of behavioural and physiological response variability. The phase and amplitude of pre-stimulus alpha oscillations affect event-related, reaction times, stimulus detection and stimulus discrimination. Past results, however, can only account for a correlation of perception with the phase of the ongoing EEG oscillations. Therefore, it is desirable to demonstrate a causal relation between phase and perception. One way to address this question is to entrain spontaneous brain oscillation by applying an external oscillation and then demonstrate behavioral consequences of this oscillation. Recently, we were able to show that transcranial alternating current stimulation (tACS) at individual alpha frequency (IAF) enhances IAF activity in human EEG, suggesting that tACS may be used to alter ongoing oscillations. In the present study, we conducted an auditory detection experiment with concurrent electroencephalography (EEG) and simultaneously applied oscillating transcranial alternating current stimulation at 10 Hz (tACS). Our approach revealed that detection thresholds were dependent on the phase of the oscillation that was elicited by tACS. This behavioral effect was accompanied by an electrophysiological effect: power was enhanced after tACS as compared to a pre-stimulation period. By showing a causal relation between phase and perception, our results extend findings of previous studies that were only able to demonstrate a correlation. We found that manipulation of the phase resulted in different detection thresholds, which supports the notion that perception can be periodically modulated by oscillatory processes. This demonstrates that tACS can serve as a tool in neuroscience to extend the knowledge of the functional significance of brain oscillations.

- **Large-scale cortical phase-coherence during visuomotor processing - Markus Siegel (Tuebingen, Germany)**

  Flexible sensorimotor behavior results from task-dependent neuronal interactions among widely distributed cortical regions. Phase-coherence of neuronal oscillations may be a mechanism to flexibly establish such task-dependent, large-scale interactions. We tested this hypothesis in humans. In a first MEG experiment, we investigated if visuospatial attention modulates phase-coherence between frontal, parietal and visual cortical regions. We found that attention selectively enhanced gamma-band coherence between neuronal populations that process the attended visual space within these processing stages. Enhanced phase-coherence may facilitate the routing of attended visual information through sensorimotor networks. In a second EEG experiment, we investigated brain-wide networks of cortico-cortical coherence during perception of ambiguous visual stimuli. We found a similar network of frontal, parietal and visual cortical regions with enhanced beta-band coherence during stimulus processing. The strength of phase-coherence in this network predicted the different perceptual interpretations of ambiguous stimuli on a single-trial level. Fluctuations of large-scale phase-coherence may underlie fluctuations of attention that in turn bias perceptual disambiguation. In summary, our results suggest that large-scale phase-coherence mediates visuomotor processing by establishing task-dependent interactions between frontal,
parietal and visual cortex.

- **Information-theoretic evidence for the functional role of oscillatory phase in perception - Joachim Gross (Glasgow, UK)**

   Neural oscillations are ubiquitous in neurophysiological measurements of cognitive processes and likely reflect the dynamic routing and gating of information. However, the specific contributions of phase and amplitude for information gating are rarely dissociated. I present two studies where information theoretic measures (mainly mutual information) were used to quantify information coding and communication separately for phase and amplitude. First, in a biologically relevant cognitive task, we instructed six human observers to categorize facial expressions of emotion while we measured the observers’ EEG (Schyns et al, PLoS Biol 2011). We studied how power and phase code the visual information relevant for behavior. We make three points: First, we demonstrate that phase codes considerably more information relating to the cognitive task than power. Second, we show that the conjunction of power and phase coding reflects detailed visual features relevant for behavioral response that is, features of facial expressions predicted by behavior. Third, we demonstrate, in analogy to communication technology, that oscillatory frequencies in the brain multiplex the coding of visual features, increasing coding capacity. In the second study we recorded MEG signals from 22 participants listening to a 7-min long continuous story. Control conditions consisted of the story played backwards and the story scrambled at the word and sentence level. Mutual information analysis was combined with source localization (DICS) to reveal the coupling of brain oscillations to the speech envelope separately for phase and amplitude. The analysis revealed significant phase coupling in the delta and theta frequency band that was significantly higher than amplitude coupling. In summary, both studies add to the increasing evidence that oscillatory phase has functional relevance for perception and cognition.

- **The relation of EEG phase patterns and the selectivity of neural firing - Christoph Kayser (Tuebingen, Germany)**

   Oscillations are pervasive in encephalographic (EEG/MEG) signals and are considered an important marker or even a causal mechanism for cognitive processes and sensory representations. While the relation between oscillation amplitude (power) and sensory-cognitive variables has been extensively studied, recent work revealed that the dynamic oscillation signature (the temporal phase-pattern) can carry information about such processes to a degree greater than the amplitude. To elucidate the direct neural correlates of such oscillatory phase patterns we compared the stimulus selectivity of neural firing rates and of EEG oscillations generated by these. To this end we study the encoding of natural sounds in auditory cortex by employing the same naturalistic sound stimuli in experiments recording scalp EEGs in human subjects and in experiments recording intracortical field potentials and single neurons in macaque auditory cortex. Using stimulus decoding techniques we showed that stimulus selective firing patterns imprint on the phase structure rather than the amplitude of slow (mostly theta band) oscillations. Importantly, we found that stimuli which can be discriminated by firing rates can also be discriminated by oscillatory phase patterns but not by oscillation amplitude, directly demonstrating a neural basis for stimulus selective EEG phase-patterns. This work reveals a level of interrelation between encephalographic signals and neural firing beyond simple amplitude co-variations and enhance the possibilities to interpret EEG-based studies towards understanding the neural dynamics of sensory perception.

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**Tuesday, August 28th, 2012, 17:30-19:30 **

**S-Tu-B3 Magnetic Source Imaging (MSI) in Epilepsy: from clinics to methods**

**Chairs:** Jean-Marc Lina (Montreal, Canada), François Mauguire (Lyon, France)

- **High frequency MEG oscillations and epileptogenesis - Stephan Rampp (Erlangen, Germany)**

   Dr Rampp will report recent works studying the value of high frequency oscillations (HFO) as a marker of epileptogenesis. There has been several studies in the last 10 years suggesting that HFO recorded by intracranial microelectrodes in animals is a robust marker of epileptogenesis. More recently, HFO have been described
in Human using intracranial EEG and it has been confirmed that they are more frequent in the seizure-onset zone. For those reasons, detecting HFO using non-invasive methods such as MEG would be of great value during presurgical evaluation. Dr Rampp has published the first study in that field and will summarize his recent findings.

- **MSI assessment of epileptogenic volumes in focal epilepsies - Julien Jung (Lyon, France)**
  Dr Jung will show that MEG is useful during presurgical evaluation of epilepsy to delineate pathological volumes. While classical dipole modeling is the most established method to determine the source of epileptic spikes, Dr Jung will show that beamformers may be useful to delineate the source volume of epileptic spikes. He will show applications of those methods in lesional epilepsy but also in MRI negative epilepsy which is considered as a challenging situation during presurgical workup.

- **Imaging the seizure onset zone with Stereo-EEG: Effect of frequency - Olivier David (Grenoble, France)**
  Stereo-electroencephalography is used to localize the seizure onset zone and connected neuronal networks in surgical candidates suffering from intractable focal epilepsy. The concept of epileptogenicity index has been proposed recently to represent the likelihood of various regions being part of the seizure onset zone. It quantifies low-voltage fast activity, the electrophysiological signature of seizure onset usually assessed visually by neurologists. We have recently revisited epileptogenicity in light of neuroimaging tools such as those provided in the Statistical Parametric Mapping software (David et al., Brain, 2011). Our goal was to propose a robust approach, allowing easy exploration of patients brains in time and space. The procedure is based upon statistical parametric mapping, which is an established framework for comparing multi-dimensional image data that allows one to correct for inherent multiple comparisons. Statistics can also be performed at the group level, between seizures in the same patient, or between patients suffering from the same type of epilepsy using normalisation of brains to a common anatomic atlas. Most importantly, the proposed approach to the quantification of the seizure onset zone allows one to summarize complex signals in terms of a time-series of statistical parametric maps that can support clinical decisions. In particular, it is possible to obtain, after thresholding of statistical maps, the activation size of the different frequency bands of interest during seizure onset. In this talk, we will thus provide estimates of the size of epileptic networks as a function of frequency, in human patients and in animal models of epilepsy.

- **Time-frequency localization of brain oscillatory activities from simultaneous MEG-EEG recordings - Jean Marc Lina**
  Localization of the generators of transient brain oscillations recorded in MEG and EEG is challenging because such signals are usually of low amplitude. In general, improvement of the signal-to-noise ratio through data averaging is not possible due to the variability of the discharges and the temporal jitter between trials of oscillatory events. The present study aims at describing and evaluating with simulated and clinical data a new method for the localization of sources of oscillatory cortical activity from MEG and EEG data, combining time-frequency representation and entropic regularization techniques. The proposed methodology relies on a sparse representation of the brain activity in time, and also assumes sparsity in space. Spatial sparsity relies on the assumption that the brain activity is organized among few cortical parcels that are endowed with an activation state variable. Sparsity in time is achieved by transposing the inverse problem in the discrete wavelet representation, for both data and sources. We propose an estimator of the wavelet coefficients of the cortical sources based on the Maximum Entropy on the Mean (MEM) principle. The full temporal dynamics of the sources are obtained from the inverse wavelet transform of the solution at each sample of the discrete time-frequency plane. Principal Component Analysis of the reconstructed time course is finally applied to summarize main spatio-temporal characteristics of oscillatory sources. This methodology is evaluated using realistic simulations of single trial signals, combining a source of a fast and sudden discharge (spike) together with a source of bursts of oscillations in the gamma band. The method is finally applied to the localization of bursts of rhythmic activity in different frequency bands in EEG/MEG data from 9 patients with epilepsy and compared with spike source localization.

- **Characterization of seizure onset zones by means of neural propagation patterns of epileptic interictal high-frequency oscillations in iEEG and Magnetoencephalography - Sylvain Baillet (Montreal, Canada)**
  In patients with partial epilepsy, invasive intracranial EEG (iEEG) studies often reveal bursts of high-frequency (> 80 Hz) oscillations (HFOs) in the vicinity of cortical regions giving rise to seizures. There is mounting evidence that HFOs may represent a clinically useful marker of epileptic dysfunction. Recent evidence suggests
important role of interictal HFOs in the determination of the seizure onset zone (SOZ). The HFO bursts recorded from intracranial electroencephalography and MEG in patients with partial epilepsy across different cortical regions show considerable variability in terms of phase, frequency, amplitude, and duration. Consequently, marking and mapping of these oscillatory events visually is subject to error, variability and observer bias. We propose a method for detecting these HFOs and reducing the multidimensional data to 3-D spatiotemporal maps that capture propagation patterns of oscillatory changes during interictal and ictal HFOs. Our method proceeds by first applying a bank of narrow band-passed filters in the 80-300 Hz range to the raw data and determining the propagation patterns of the HFOs events detected based on the magnitude of the analytic representation of the iEEG signals and MEG traces. We applied this method to interictal and ictal iEEG data from three patients with intractable partial epilepsy. We applied the same technique to source currents computed from interictal MEG recordings from these same patients. The cortical regions that were identified as SOZ using the algorithm were concordant with the regions identified by an expert reviewer. Our results also suggested striking similarities between the SOZ obtained using propagation of interictal and ictal data HFOs in the iEEG recordings and MEG sources. Cortical areas from which the leading ictal oscillatory changes began during seizures were also the regions from which interictal HFOs appear to propagate out from.

**S-Tu-C3 Atomic Magnetometers for Biomagnetic Sensing**

Chair: Svenja Knappe (Boulder, USA) and Tilmann Sander-Thoemmes (Berlin, Germany)

Until now, the detection of magnetic fields emitted by the human body has been the unrivaled field of SQUID-based gradiometers or magnetometers. In recent years, laboratory prototypes of atomic or optical magnetometers have been developed with sensitivities comparable to those of SQUIDs and several measurements of MEG and MCG have been demonstrated. In this symposium we would like to review the current state of research, demonstrate their capabilities for biomedical applications without the need for expensive cooling infrastructure, and identify the challenges that still lay ahead in order to make atomic magnetometers a viable technology for this field. The symposium will introduce several different types of atomic magnetometers that differ in their operation principle, fabrication methods, as well as their performance. We will distinguish between scalar and directional magnetometers, the requirement for shielding, their dynamic range, sensitivity, and bandwidth. Due to their properties, the different atomic magnetometers might be tailored to applications ranging from MCG with minimal shielding and less than 100 magnetometers channels to MEG with normal shielding and up to 200 gradiometer channels. Measurements of MCG, fetal MCG, and MEG signals will be presented in comparison to the state of the art results obtained using SQUIDs. Finally, we will try to assess the technology-readiness level of atomic magnetometers for biomedical applications. Manufacturability and the possibility of inexpensive turn-key systems, as well as system specifications and requirements for specific applications will be of interest.

- **Chip-Scale Atomic Magnetometers for Biomedical Imaging - Svenja Knappe (Boulder, USA)**

Atomic magnetometers have demonstrated impressive sensitivities similar to those of the best SQUID devices and these sensors might have the potential of an uncooled alternative to SQUID magnetometers in the future. We develop chip-scale manufacturable versions of atomic magnetometers. The small size and microfabrication processes allow for very small separation between the sensors and the sample of several millimeters and can therefore detect higher magnitudes of the emitted magnetic fields in comparison to most SQUIDs. Furthermore, dense arrays of small fiber-coupled sensor heads could be placed in a flexible geometry around subjects of different size, potentially ranging from small animals to infants and adults. Wafer-level fabrication and assembly of chip-scale sensor heads could enable inexpensive fabrication and high uniformity across sensors in the array. While the fundamental sensitivity of chip-scale sensors is worse than the one of their larger counterparts, it is still below 1 fT/Hz1/2 in a measurement volume of 1 mm3. We will identify experimental limitations of the current sensors and try to make reasonable predictions for future improvements. We will present measurements of MCG and MEG signals in healthy human subjects with a 4-channel chip-scale atomic sensor system. Spontaneous and evoked MEG signals were measured in several subjects at the Physikalisch-Technische Bundesanstalt in Berlin and compared to those simultaneously recorded with an array of SQUID sensors.

**BIOMAG 2012 - August 26-30, 2012 - Paris, France**
Clinical MCG with optical room-temperature sensors - Georg Bison (Jena, Germany)

Optically pumped magnetometers (OPM), which were originally developed in the 1950s and 1960s, have received a renewed interest over the past decade. During that time, many kinds of OPMs have been developed for applications in fundamental and applied science. Especially applications in biomagnetism have been an important driving force for this effort to improve OPMs. In bio-magnetometer systems, OPMs are an interesting alternative for SQUIDs, since the optical sensors do not need to be cooled and can often be used at temperatures close to room temperature. In the past years a steadily growing number of researchers have shown that different kinds of OPMs have the potential for biomagnetic measurements. In our current work we demonstrate that an OPM-based biomagnetometer system can be realized in a clinical environment. At the University Hospital in Jena we have build a biomagnetometer system with 57 primary OPM sensors. The scalar OPMs work at room temperature and allow a simultaneous mapping of the heart magnetic field of adult persons. Compared to earlier designs [1] we realized a twofold increased sensor density. A single frequency-stabilized diode laser supplies all OPM sensors with the pumping light. The magnetometer system and a special coil system which is used to compensate the earth’s magnetic field are integrated into an aluminum-shielding room. We will report about the system performance under laboratory and clinical conditions and discuss planned system optimizations and future clinical studies.


Atomic magnetometers for biomagnetic measurements - from first principles to off-the-shelf sensors - Michael Romalis (Princeton, USA)

Atomic magnetometers have emerged as an alternative to SQUIDs for detection of biomagnetic fields. Magnetocardiography and magnetoencephalography signals have been recorded by atomic magnetometers in several laboratories. The next challenge, currently being addressed by the atomic magnetometry community, is to develop robust deployable sensors suitable for routine biomagnetic recordings. I will review our early work on ultra-sensitive atomic magnetometers operating in the spin-exchange relaxation free (SERF) regime that allowed atomic magnetometers to reach sensitivities below $1 \text{fT}/\text{Hz}^{1/2}$. I will then discuss the development of the first atomic MEG system using a large alkali-metal cell for spatial mapping of the magnetic fields. Our current efforts are focused on development, with our commercial partners, of a mass-produced fiber-coupled SERF magnetometer suitable for MEG recordings. Fiber-coupled atomic sensors allow a new level of flexibility for recording of biomagnetic fields. They are magnetically passive, reduce the sensor-subject distance to less than 1 cm, and require little maintenance. User-configurable sensor arrangement allows optimization of the system for a variety of studies in both adults and children. The sensors can be operated in compact magnetic shields or in the traditional magnetically-shielded rooms. I will present our results with a new 32-channel fiber-coupled sensor system and discuss the main operational differences between SQUID and atomic sensors for routine biomagnetic recordings.

Application of Atomic Magnetometers to fMCG - Thad Walker (Madison, USA)

Atomic magnetometry can have a major impact on fetal MCG, which competes with ultrasound and is a cost sensitive application. Temporal information is of primary interest for clinical diagnosis and management of Fetal Arrhythmia; spatial information is required primarily to reject non-biomagnetic backgrounds and maternal interference. To this end, we have built and tested a four-channel atomic magnetometer array. The modular design potentially allows independent positioning and orientation of each magnetometer, and is suitable for non-planar geometries. As the array time-shares with other projects in a magnetically shielded room, its functional portability has been utilized from the beginning. Single-channel baseline magnetometer sensitivities of 6-11 $\text{fT}/\text{Hz}^{1/2}$ are obtained. In this talk, we will discuss biomagnetic design and performance issues specific to atomic magnetometers, measurements of adult MCG using the array, and our initial investigations of fetal MCG.
Speech and other natural stimuli are highly dynamic, containing complex but systematic spectro-temporal structure on several different time scales. How the brain continuously encodes sensory input from these stimuli and how the information from this input is then decoded constitute key questions for sensory and cognitive neuroscience. MEG recordings offer a unique opportunity to concurrently study the timing and location of sensory/cognitive cortical processing. Recent advances in experimental design and signal processing techniques have enabled the analysis and modeling of ongoing MEG responses to natural stimuli, such as speech and complex audiovisual scenes. These new approaches provide significant insight into, for example, how the brain segments continuous input signals into perceptual units, performs hierarchical integration of information over different time scales/sensory modalities, and how sensory information is selectively processed based on top-down attentional modulation. The use of natural stimuli significantly extends traditional MEG paradigms that have mainly focused on either the transient response to onsets (i.e. evoked responses) or steady state response to stimuli modulated in a simple fixed manner. The new experimental paradigms provide a useful tool to address questions in many fields, including but not limited to speech perception, multi-sensory integration, and social interaction in naturalistic scenarios. The new approaches also raise challenges for the spatial-temporal processing of MEG signals. The study of naturalistic signals is of broad significance for the neurophysiology and imaging communities and highlights some of the compelling advantages of neuromagnetic data. The four presentations in this symposium highlight recent advances.

- **Ongoing temporal segmentation of natural sensory streams: an MEG phase-based perspective - Huan Luo (Beijing, China)**
  Natural streams such as speech, music, and movies convey information at multiple temporal scales, and it is therefore critical for the brain to rely on a temporal segmentation processes to adaptively entrain to and dynamically represent continuously varying external input. Investigating the neural mechanisms underlying temporal structure extraction has become an exciting topic in cognitive neuroscience. We use magnetoencephalography (MEG) to study the temporal chunking process in the human brain in response to natural spoken sentences and movies. Given that the temporal segmentation is inherently an ongoing process in time, we employ a new ‘ongoing’ analysis perspective, by examining the ongoing phase patterns of cortical neuronal oscillations at different frequency bands, and investigating the way they might track the temporal structure of stimulus streams, as well as a possible active role of prediction in time. We previously demonstrated that theta-band (3-7 Hz) phase patterns derived from MEG signals can track natural speech and correlate with manipulated intelligibility (Luo Poeppel, 2007). Moreover, we recently showed that the low-frequency phase responses in both auditory and visual areas to audiovisual movie stimuli reflect information from both modalities, and that temporally congruent audiovisual streams elicited more reliable tracking than incongruent stimuli (Luo et al., 2010). The results indicate that human brain employs phase modulation neural mechanisms to parse the natural speech signals and natural audiovisual streams, at an ecologically-relevant temporal scale. Crucially, the findings also support the active role of phase modulation of neuronal rhythms in building temporal chunks for incoming stream information in a predictive manner.

- **Multisensory integration in speech processing and selective attention - Elana Zion Golumbic (Columbia, USA)**
  Our ability to attend to a particular conversation amidst competing input streams (e.g. other speakers), epitomized by the ‘cocktail party’ problem, is remarkable. One neuronal mechanism proposed for achieving this feat is synchronization of low-frequency neural activity in auditory cortex (1-7Hz) to the temporal envelope of the attended stream ‘selective speech tracking’. Top-down attention may also aid this tracking by predicting upcoming temporal events in the stream. How these two mechanisms are integrated and consequently, how attended speech is selectively tracked, remains unresolved. We investigated whether congruent visual input of the attended speaker contributes to selective speech tracking in auditory cortex. Since lip and head movements during speech are highly correlated with the temporal envelope of speech, but precede them by 150 ms, visual input provides excellent predictive cues for the timing of upcoming acoustics. We presented natural speech to participants while recording neuromagnetic activity. Speech segments were presented alone (single speaker) or concurrently with another speech segment (cocktail party). In addition, audio was either presented alone (A) or accompanied by a
video of the speaker (AV). For the Single Speaker condition, we found similar low-frequency speech tracking in both AV and A conditions, with no apparent advantage for AV stimuli. However, in the Cocktail Party condition selective speech tracking in auditory cortex was found only when congruent video of the speaker was provided, and was significantly reduced when listening to a ‘cocktail party of voices’. These results suggest that under perceptually challenging situations such as the ‘cocktail party’, visual input plays a key role in focusing attention.

- **Mutual Information analyses of Speech using MEG** - Gregory Cogan (New-York, USA)

  Determining what components of speech are salient for the initial parsing of the incoming acoustic speech signal into meaningful units of analysis is a major goal of the study of speech perception. Recent evidence supports the idea that this initial segmentation is heavily dependent on neuronal tracking of the low frequency (<10Hz) slow fluctuations of the modulation spectrum (the envelope) of the speech signal. While there is now a great deal of evidence for corresponding precise temporal responses within this frequency range in the cortex, the relationship between the measured neuronal responses and the information within the signal itself remains unclear. We demonstrate with MEG, using a unique analysis technique, Mutual Information (MI), that neuronal temporal components (phase) within the low frequency range (1-7 Hz) sum linearly, demonstrating that each response is tracking independent information related to the speech signal. We show that there is a preference for natural speech over matched envelope chimeras. Furthermore, when comparing phase responses between these two stimulus classes, information values also sum linearly, suggesting that while the speech envelope is able to drive the neuronal phase response, the tracking that occurs in natural speech is qualitatively different. Taken together, these findings suggest that low frequency phase responses in the cortex track independent components of the speech signal and that the hypothesis that these responses are entirely envelope-driven must be discarded.

- **Cortical Representation of Continuous Speech in Complex Auditory Scenes** - Nai Ding (Maryland, USA)

  We examine the neural encoding of continuous speech in human auditory cortex using magnetoencephalography (MEG). The temporal structure of speech and other natural sounds is rhythmically organized, and the neural encoding of these structures is especially suitable for study by MEG with its millisecond time resolution. To quantitatively characterize how the spectro-temporal acoustic features of speech are represented in the neural activity, we employ a spectro-temporal response function (STRF) approach. The STRF models the relationship between the acoustic stimulus and the MEG response as a cascaded linear-nonlinear model, which has also been widely employed to model the response properties of single neurons. The advantage of this approach is that the linear element extracts how the brain integrates acoustic information over time and frequency, and the nonlinear element characterizes the neural encoding of sound intensity. We demonstrate that this approach effectively captures the MEG response to continuous speech and reveals that the MEG response is driven by the slow temporal modulations of speech (<10Hz) in a broad spectral region. Additionally, we employ this methodology to examine the neural encoding of degraded speech, i.e. masked by either noise or interfering speech. We find that the neural representation is extremely robust against such degradations. Critically, the observed neural representation is mainly driven by the speech itself, and not the acoustic mixture of the speech with its disruptions. Through computational modeling, several neural principles underlying the robust encoding of speech are discerned. Such a stable and precise representation of the slow temporal modulations provides a plausible neural basis for robust recognition of speech.
What kinds of activity can we expect from the cerebellum? Under what conditions can it be measured noninvasively? What methods exist to confirm MEG/EEG results that suggest cerebellar involvement? This symposium will bring together MEG/EEG and cerebellum experts to discuss these questions, and put forward the evidence regarding noninvasive study of cerebellar electrophysiology.

- **Electrophysiology and neuroanatomy of the cerebellum - Yoshio Okada (Boston, USA)**
  The cerebellar cortex consists of different neuron types that cerebral cortex. Purkinje cells are one of the characteristic cell types, and form a highly regular structure, analogous to the parallel apical dendrites of pyramidal cells in cerebral cortex.
  We have shown that the electrically evoked activity of an isolated turtle cerebellum was measurable with a SQUID, suggesting that Purkinje cells do in fact have an open field configuration that allows their external measurement.

- **High-frequency electrical activity of the human cerebellum: recent MEG findings and revisiting the intracranial electrocerebellogram - Sarang Dalal (Konstanz, Germany)**
  It has been commonly speculated that the cerebellum consists of neurons with ‘closed’ electrical fields, meaning that its electrical activity may not be detectable at a distance. However, this claim arose from an era when ongoing low-frequency oscillations and slow evoked potentials were the EEG phenomena commonly investigated; the closed field idea may have arisen simply to explain why neither of these phenomena were commonly observed in scalp recordings over cerebellar regions. Furthermore, Purkinje cells in cerebellar cortex have a parallel geometry that is in fact very analogous to that of pyramidal cells in cerebral cortex, and cerebellar laminar recordings show that signals arising from the Purkinje and granule layers indeed produce characteristic potentials on the cerebellar surface.
  The earliest local field potential recordings from the animal cerebellum remarked on the lower-amplitude, higher-frequency nature of the spontaneous cerebellar signal (Adrian et al., 1934). A few forgotten reports of intracranial EEG recordings in human patients reveal similar patterns.
  In recent years, the analysis of intracranial electrophysiology and scalp EEG/MEG has come to embrace both frequency-dependent connectivity measures and higher-frequency spectral modulations. These measures have only recently been applied to cerebellar LFP data in animals (deZeeuw et al., 2008; de Solages et al., 2008, Middleton et al., 2008), revealing rich information content in the 30-200 Hz regime. Additionally, connectivity measures often reveal coupling of the cerebellum in the alpha and beta bands with motor cortex.

- **Movement-related oscillatory activity in the cerebellum and its alteration in severe psychopathology - Tony Wilson (Omaha, USA)**
  The cerebellum is densely interconnected with cerebral cortical regions serving sensorimotor processing, and has been historically understood as a movement-related brain structure. Lesions here often produce a variant of the so-called cerebellar motor syndrome, which has been characterized for almost two centuries and includes ataxia, instability of gait, disordered eye and/or extremity movements, poor articulation, and other motor signs. Nowadays, the cerebellum is known to be important for both cognitive and motor functions, and has been identified as a crucial brain structure in several neuropsychiatric disorders. This talk will focus on cerebellar activity in a series of MEG experiments that evaluated sensorimotor functioning in healthy children and those with severe mental illnesses. In these experiments, neural oscillatory activity associated with passive stimulation and finger movements were imaged using beamforming, and statistically evaluated for task and group effects. Our results have shown that areas of the cerebellum, like primary sensorimotor cortical areas, exhibit a beta-frequency event-related desynchronization (ERD) slightly before movement onset, a post-movement beta rebound (PMBR) after movement termination, and a movement related gamma synchronization (MRGS) that coincides with movement onset. However, unlike the primary cortical responses, cerebellar responses in healthy children are generally stronger in the hemisphere ipsilateral to the movement, and appear to decrease in amplitude as a function of increasing age. These motor-related cerebellar responses, and similar responses during passive somatosensory stimulation, have also emerged as a sensitive metric for aberrant sensorimotor processing in youth with psychotic disorders. In conclusion, the cerebellum is crucially involved in sensorimotor processes, and advanced MEG approaches are capable of characterizing the structure’s oscillatory dynamics during applicable experiments.
MEG evidence for cerebellar involvement in rhythmic motor control and tremor - Alfons Schnitzler (Düsseldorf, Germany)

Although the cerebellum is known to be involved in simple and complex motor tasks magnetoencephalography (MEG) recordings have typically failed to demonstrate direct cerebellar activation probably because of a very low signal-to-noise ratio of cerebellar evoked responses. However, coherence analysis applied to MEG data recorded during rhythmic motor tasks or tremor has consistently revealed oscillatory networks which include cerebellar activity ipsilateral to the moving limb. I will present several MEG studies which consistently show that ipsilateral cerebellum is involved in normal tapping and slow continuous finger movements as well as in pathological conditions such as Parkinsonian resting tremor, essential tremor, writer’s cramp, and tremor in Wilson’s disease.
Systemic administration of psychoactive compounds can have profound effects on macroscopic brain dynamics. MEG can measure these pharmacologically-induced changes in exquisite spatio-temporal detail. For compounds with known therapeutic applications, pharmacological (pharmaco-) MEG studies may yield important biomarkers of treatment response, and insight into the neurophysiological origins of pathology in specific disorders. In this symposium, four distinct lines of pharmaco-MEG research converge, covering a range of experiments modulating GABAergic, monoaminergic or glutamatergic neurotransmission. To begin, Dr. Muthukumaraswamy will present his work on effects of the anticonvulsant tiagabine, a GABA agonist, on oscillatory phenomena in sensorimotor and visual cortices in healthy subjects, showing that boosting GABAergic inhibitory signaling produces a complex spectral signature with task and regional specificity. Dr. Hall, also studying effects of a GABA agonist (zolpidem, a sedative hypnotic), will present his findings on pharmacological manipulation of abnormal sensorimotor oscillations in movement disorders. A paradoxical finding emerges in which zolpidem, in the context of improved motor function, reduces sensorimotor beta activity. Dr. Wilson will present his work on oscillatory changes following amphetamine treatment in ADHD. As he will show, amphetamines normalize aberrant resting-state functional connectivity and produce many other task-dependent effects in these patients. Dr. Cornwell will conclude with a presentation on effects of the NMDA antagonist ketamine on cortical gamma activity in the context of treatment response in depressed patients. Rapid clinical response will be shown to be marked by increased stimulus-evoked gamma, but not resting gamma, following NMDA blockage. Collectively, these talks will bring into focus a key role pharmaco-MEG can play in understanding the dynamical brain in healthy and neuropsychiatric populations.

- **GABAergic modulation of oscillatory responses in healthy controls - Krish Singh (Cardiff, UK)**

The MEG signal is generated primarily by the summation of the post-synaptic potentials of cortical principal cells. At a microcircuit level these glutamatergic principal cells are reciprocally connected to GABAergic interneurons. It is thought that a number of cortical oscillations are dependent on the balance of excitation and inhibition between these cell types. To investigate the dependence of cortical oscillations on excitation-inhibition balance we pharmacologically manipulated the GABA system in a group of healthy control participants using the GABA agonist tiagabine. Tiagabine blocks GAT, the GABA uptake transporter and causes an increase in both synaptic and extrasynaptic GABA levels. In a crossover repeated-measures design, participants took either a placebo or 15mg of tiagabine and were scanned, prior to, 1 hour post, 3 hours post and 5 hours post intervention. Following tiagabine administration, the resting MEG showed topographically discrete large increases in delta (1-4 Hz), theta (4-8 Hz) and beta (13-30 Hz) power. In a simple movement paradigm reduced motor evoked fields and reduced post movement beta rebound were seen after tiagabine administration. Finally, during visual stimulation with a grating patch an increase in gamma power was seen following tiagabine. The selective modulation of both resting and task-induced oscillatory responses suggests that GABAergic processes are particularly important in the physiological generation of specific cortical oscillations. These data suggest that future investigations using the broad range of selective GABAergic compounds available will allow a more detailed picture of the physiological generation of these population neuronal responses to be built.

- **GABAergic modulation of pathological oscillations: neuronal network correlates of symptomatic relief in movement disorders - Stephen Hall (Aston, UK)**

The sensorimotor cortices (SMC) are electrophysiologically characterized by spontaneous oscillations in the alpha (7-14Hz) and beta (15-30Hz) frequency ranges. These rhythms exhibit characteristic fluctuations in power, temporally coincident with the performance of movement. Spontaneous beta activity in the motor cortex is generated by networks under the control of GABAergic interneurons, reflected by augmentation by GABA-A modulators. Studies of movement disorders demonstrate exaggerated beta power, at various loci in the motor network. Paradoxically, several studies have demonstrated improvements in motor symptoms following administration of a sedative hypnotic, zolpidem, in a range of neurological conditions. Here we used MEG to investigate neuronal network correlates of zolpidem-mediated improvements in motor dysfunction in drug naïve, unilaterally impaired, stroke and Parkinson’s disease patients. Functional localization of SMC was used to identify focal regions of interest. Source level analysis was used to measure change in spontaneous and functional oscillations, before and after administration of zolpidem, in addition to measures of symptomatic severity, such as
the unified Parkinson’s disease ratings scale (UPDRS). Patients exhibit a notable increase in spontaneous beta power in SMC, which is substantially greater in the hemisphere contralateral to impaired limbs. Oscillations are characterized by distinctive beta-bursting phenomena, the power, frequency and temporal variability of which is modulated by the administration of zolpidem. Furthermore, movement related power change appears altered at beta frequency, consistent with improvements in motor performance. Improvement of motor function and attenuation of beta power are somewhat paradoxical of the expected response to a GABA-A modulator. I will discuss these unexpected observations in the context of parallel studies in animals, which offer a mechanistic basis for the electrophysiological findings.

- Widespread and task-dependent neurophysiological changes following amphetamine treatment in attention-deficit/hyperactivity disorder - Tony Wilson (Omaha, USA)

Attention-deficit/hyperactivity disorder (ADHD) is a neurobehavioral disorder that affects approximately 8% of children and persists in 4% of adults. The core symptoms of ADHD include inappropriate levels of hyperactivity-impulsivity and/or pervasive inattention, with the inattention component being the more frequent and critical feature in adults. Regardless of age, stimulant-based drugs including amphetamines are the most common treatment for persons with ADHD. While their clinical efficacy is clear, the mechanisms by which stimulants alleviate ADHD symptoms are only vaguely characterized. Using magnetoencephalography (MEG), we have systematically evaluated the neurophysiological bases of stimulant therapy in adults with ADHD. Participants with ADHD undergo a battery of MEG experiments after at least an 18-hour medication washout period. They are then administered their normal medication dose and, after a standard waiting period, undergo the same series of MEG experiments in a different order. Matched non-ADHD controls undergo the same protocol, but are not administered the stimulant medications. Thus far, these studies have shown hypo- and hyper-connectivity between different regions of the default-mode network in un-medicated persons with ADHD relative to controls, which were almost entirely normalized following amphetamine administration. In addition, we have found reduced broadband activity in medial prefrontal areas during the awake resting-state in un-medicated ADHD persons relative to controls; these reductions were ameliorated after stimulant ingestion in the alpha and beta bands but not in other frequency bands (e.g., gamma). Finally, un-medicated adults with ADHD exhibit reduced auditory steady-state gamma-band responses relative to controls, and amphetamine delivery significantly enhances and normalizes these responses. In conclusion, amphetamines induce a wide array of related neurophysiological changes which are least partially task-dependent.

- NMDA antagonism and cortical gamma activity in depression: Implications for rapid antidepressant action of ketamine - Brian Cornwell (Bethesda, USA)

NMDA receptor antagonists such as ketamine can alleviate depressive symptoms within hours in patients with major depressive disorder (MDD) and bipolar disorder (BD). This rapid antidepressant action, which can be sustained for up to a week after a single dose, suggests that modulation of glutamatergic neurotransmission is a fundamental step to pharmacological treatments of depression. Acutely, ketamine increases extracellular glutamate levels, neuronal excitability and spontaneous gamma oscillations, but it is unknown whether these effects are key to ketamine’s mechanism of antidepressant action. Here we administered a single intravenous infusion of ketamine (.5 mg/kg over 40 m) to drug-free patients with treatment-resistant MDD (N = 20). Whole-head MEG recordings were obtained several days before and 6-7 h after the infusion to compare baseline cortical activity with cortical activity within the antidepressant response window of ketamine. To measure cortical excitability, patients received simple tactile stimulation of the left and right index fingers. We found that stimulus-evoked somatosensory cortical (SS ctx) gamma-band (30-50 Hz) responses increased post-infusion (relative to baseline) in only those patients exhibiting a rapid and robust reduction in depressive symptoms at 230 m post-infusion. Non-responders showed no change. Preliminary analyses in BD patients confirm this result. Resting-state (eyes-closed) scans were also taken to measure spontaneous cortical activity. In contrast to stimulus-evoked responses, spontaneous SS ctx gamma-band activity during rest increased after ketamine regardless of clinical outcome. Drawing from optogenetic studies in animals and cortical network simulations, we will discuss implications that our pattern of results has for the role of NMDA-mediated glutamatergic neurotransmission in rapid onset of antidepressant responses and, more generally, in emergence of cortical gamma oscillations.
Biophysical models describing brain activity measured by M/EEG can be divided into two large classes: neural mass and neural field models. The main difference between these two classes is that field models prescribe how a quantity pertaining to neural activity (such as average depolarization of a neural population) evolves over both space and time as opposed to mass models which characterize the evolution of this quantity over time only and assume that all neurons of a population are located at (approximately) the same point. This symposium will focus on both classes of such models and discuss several of their aspects, including:

1. The main ideas of neural field theories that span from synapses to the whole brain, comparisons of their predictions with EEG and MEG spectra of spontaneous brain activity, evoked responses, seizures, and fitting to data to infer brain states and map physiological parameters (P Robinson).

2. Techniques for relating such models, in particular neural mass models with EEG activity recorded from patients with epilepsy, where it will be shown how to a) model transitions from inter-ictal to ictal dynamics and b) estimate parameters of a model directly from clinical recordings (J Terry).

3. The relation between neural field and mass models, their relative merits and how Bayesian inference can be used to estimate their parameters and test different experimental hypotheses in modelling empirical data (D Pinotsis).

4. In addition to the discussion of these models in the context of M/EEG, this symposium will also consider their relevance to the effects of TMS, the modelling of ECoG data and the analysis of fMRI inferred connectivity. In particular, the last talk of this symposium will focus on how biophysical models can be combined with fMRI data to understand resting state activity, in particular networks that emerge as structured noise fluctuations around an equilibrium state and their relevance to neuroanatomical connectivity (V Jirsa).

- **Neural fields, neural masses and Bayesian inference - Dimitrios Pinotsis (London, UK)**

  Biophysical models describing brain activity measured by M/EEG can be divided into two large classes: neural mass and neural field models. The main difference between these two classes of models is that field models prescribe how a quantity pertaining to neural activity (such as average depolarization of a neural population) evolves over both space and time as opposed to mass models which characterize the evolution of this quantity over time only and assume that all neurons of a population are located at (approximately) the same point. In this talk, we will consider the relation between neural field and mass models, contrast their relative merits and discuss their application in modelling empirical data. Specifically, we consider neural masses as a limiting case of neural fields when conduction times tend to zero and focus on two exemplar mass models and their field counterparts, namely the so-called Jansen and Rit and the Canonical Microcircuit model. Both models incorporate parameters pertaining to important neuroanatomical attributes; we will describe these models and show how Bayesian inference can be used to estimate their parameters and test different experimental hypotheses. We will show that neural field models provide a better explanation for empirical data obtained from sensory cortices. This application (i) allows for recovering spatial parameters from single electrode data and (ii) exploits the information in high density spatially resolved data; such as those offered by eeg arrays. In other words, neural fields are particularly useful both for disclosing the topographic properties of cortical interactions in the absence of explicit spatial information as well as for understanding temporal dynamics of observed responses over different spatial scales.

- **Modeling Brain Dynamics via Neural Fields - Peter Robinson (Sidney, Australia)**

  Neural field theory enables the dynamics of brain activity and resulting measurements to be interrelated in a unified way across multiple phenomena and measurement methodologies. This theory incorporates salient features of brain anatomy, physiology, and measurement processes over multiple scales from microscopic to the whole brain. It thus enables multiscale analyses to be performed to make realistic predictions for comparison with experiment, gives interpretations of data in terms of physiology and anatomy, and provides unified theories of multiple phenomena.

  This talk briefly outlines the main ideas of neural field theories that span from synapses to the whole brain, and are parameterized in terms of measurable physiological quantities. A selection of successful quantitative applications is then reviewed, including comparisons with EEG and MEG spectra of spontaneous brain activity, evoked...
responses, seizures, and fitting NFT to data to infer brain states and map physiological parameters. Ongoing applications to optimizing the effects of TMS, analyzing fMRI-inferred brain connectivity, and predicting the fMRI resting state spectrum will also be outlined.

• Mapping the space-time structure of the human resting state: criticality, multistability and ghost attractors - Viktor Jirsa (Marseille, France)

The ongoing activity of the brain at rest, i.e. under no stimulation and in absence of any task, is astonishingly highly structured into spatio-temporal patterns. These spatio-temporal patterns, called resting state networks, display low-frequency characteristics ($< 0.1 \, \text{Hz}$) observed typically in the blood-oxygenation level-dependent (BOLD) fMRI signal of human subjects. We aim here to understand the origins of resting state activity through modelling via a global spiking attractor network of the brain. This approach offers a realistic mechanistic model at the level of each single brain area based on spiking neurons and realistic AMPA, NMDA and GABA synapses. Integrating the biologically realistic DTI/DSI based neuroanatomical connectivity into the brain model, the resultant emerging resting state functional connectivity of the brain network fits quantitatively best the experimentally observed functional connectivity in humans when the brain network operates at the edge of instability. Under these conditions, the slow fluctuating ($< 0.1 \, \text{Hz}$) resting state networks emerge as structured noise fluctuations around a stable low firing activity equilibrium state in the presence of latent 'ghost' multi-stable attractors. The multistable attractor landscape defines a functionally meaningful dynamic repertoire of the brain network that is inherently present in the neuroanatomical connectivity.

• An electrophysiological validation of stochastic DCM for fMRI - Jean Daunizeau (Paris, France)

In this note, we assess the predictive validity of stochastic dynamic causal modelling (sDCM) of fMRI data, in terms of its ability to explain changes in the frequency spectrum of concurrently acquired EEG signal. We first revisit the heuristic model proposed in Kilner et al. (2005), which suggests that fMRI activation is associated with a frequency modulation of the EEG signal (rather than an amplitude modulation within frequency bands). We propose a quantitative derivation of the underlying idea, based upon a neural field formulation of cortical activity. In brief, dense lateral connections induce a separation of time scales, whereby fast (and high spatial frequency) modes are enslaved by slow (low spatial frequency) modes. This slaving effect is such that the frequency spectrum of fast modes (which dominate EEG signals) is controlled by the amplitude of slow modes (which dominate fMRI signals). We then use conjoint empirical EEG-fMRI data acquired in epilepsy patients to demonstrate the electrophysiological underpinning of neural fluctuations inferred from sDCM for fMRI.

Thursday, August 30th, 2012, 9:00-11:00 Hall A

S-Th-A1 The neural dynamics underlying the brain’s default-mode and resting-state networks

Chairs: Sylvain Baillet (Montreal, Canada), Karim Jerbi (Lyon, France)

Functional MRI and PET have demonstrated the spatial characterization of resting state networks (Gusnard Raichle, 2001; Raichle et al., 2001; Greicius et al., 2003). Yet the neural correlates and thereby the fine-scale temporal dynamics of the brains intrinsic network activity remain elusive. A full understanding of the mechanisms at play cannot be achieved without input from modalities that directly assess the neuronal signature of the involved structures. This symposium will provide a multi-scale overview of the state-of-the-art by highlighting recent findings from human and non-human electrophysiological studies, including invasive recordings and non-invasive neuromagnetic imaging techniques that investigate the dynamics of neural activity in resting-state networks.

Recent findings from invasive recordings in DMN structures in monkeys (Hayden et al. PNAS 2009) and in human subjects (Ossandon et al. J Neurosci. 2011; Dastjerdi et al., PNAS, 2011; Miller et al., PNAS, 2009; Jerbi et al. Front Syst Neurosci. 2010) provide novel insights into the neural correlates of the DMN. In particular, the invasive studies by Hayden et al. (2009), Dastjerdi et al (2011) and Ossandon et al. (2011) that will be presented at this symposium are critical because they bridge the gap between the role of neuronal firing, high-frequency activity (Gamma-band at 40Hz and above) and the fMRI BOLD signal in the brains default-mode network, while also questioning the link between
DMN deactivation and behavior. These invasive insights are crucial to validate the non-invasive identification of intrinsic brain networks using MEG.

A recent milestone in the non-invasive characterization of the electrophysiology of the resting brain was achieved using MEG source imaging to probe the dynamics of the default-mode and dorsal attention networks (de Pasquale et al., 2010). A further significant MEG study by Brookes et al. recently identified multiple resting-state networks using an approach akin to fMRI resting-state data analysis (Brookes et al., 2011). Both studies indicate that alpha and beta oscillatory fluctuations may provide a structural backbone for resting-state network dynamics. Moreover, Florin et al. have recently used MEG source imaging to reveal cross-frequency coupling phenomena that appear to be at the origin of the slow fluctuations captured with fMRI during the resting-state.

Beyond featuring some of the most advanced research in the exciting field of time-resolved resting-state dynamics, the symposium will specifically allocate time to debate and discuss the implications of these findings. In particular the speakers of this symposium will address the critical question of the putative functional role of the DMN and the discussion will tackle the issue of what electrophysiological findings tell us about the DMN that fMRI cannot. The speakers and attendees will also be invited to discuss the putative agreement and discrepancy between findings obtained with invasive and non-invasive recordings of resting-state dynamics.

- The Default Mode Network is a cortical core for dynamic integration of functional networks at rest - Francesco de Pasquale (Chieti, Italy)
  In this talk we present a magneto-encephalography study on the temporal dynamics of band-limited power connectivity at rest of six brain networks. The within and across network interactions are investigated and these analyses demonstrate that the Default-Mode network and the posterior cingulate cortex exhibit the highest degree of transient BLP correlation with other networks. This occurs especially in the 14-25 Hz (beta band) frequency range. The DMN centrality is observed exclusively only during epochs of high internal connectivity. Outside these temporal epochs this property is lost suggesting that a necessary condition to absolve this role is the internal DMN coherence. Additionally, these temporal epochs rarely overlap with the ones of the other RSNs, suggesting that the DMN non-stationarity might be an efficient means of cross-network interaction. These results indicate that the previously demonstrated neuroanatomical centrality of the PCC and DMN has a physiological counterpart in the temporal dynamics of network interaction at behaviorally relevant time scales.

- Transient suppression of broadband gamma power in the default-mode network is correlated with task complexity and subject performance - Jean-Philippe Lachaux (Lyon, France)
  Task performance is associated with increased brain metabolism but also with prominent deactivation in specific brain structures known as the default-mode network (DMN). The role of DMN deactivation remains enigmatic in part because its electrophysiological correlates, temporal dynamics and link to behavior are poorly understood. I will report findings from our recent study (Ossandon et al. J Neurosci. 2011) in which we provide first electrophysiological evidence for a direct correlation between DMN neural deactivation dynamics and individual subject behavior using extensive depth electrode recordings. We found that all DMN areas displayed transient suppressions of broad-band gamma (60-140 Hz) power during performance of a visual search task and, critically, that the millisecond-range duration and extent of the transient gamma suppressions were correlated with task complexity and subject performance. In addition, trial-by-trial correlations revealed that spatially distributed gamma activations and deactivations formed distinct anticorrelated large-scale networks. Beyond unraveling the electrophysiological basis of DMN deactivation and showing its remarkably transient nature, our results suggest that, rather than indicating a mere switch to a global exteroceptive mode, DMN deactivation encodes the extent and efficiency of our engagement with the external world. Furthermore, our findings reveal a pivotal role for broadband gamma modulations in the interplay between activation and deactivation networks mediating efficient goal-directed behavior and facilitate our understanding of the relationship between electrophysiology and neuroimaging studies of intrinsic brain networks.

- MEG resting state networks, time-varying functional connectivity, and network simulations - Mark Woolrich (Oxford, UK)
  In recent work we independently identified resting state brain networks in MEG data by looking at fluctuations in power of the alpha and beta band oscillations (e.g. Hilbert envelope correlation) and using temporal ICA (Brookes et al., PNAS, 2011). Many of these MEG derived networks match those found in fMRI data using spatial ICA. However, the mechanisms underlying resting-state brain activity remain under debate. It is not clear whether or
not there are more specific functional connectivity relationships that underlie these envelope correlations in the alpha and beta bands, or indeed what sort of network structure or dynamics could give rise to these phenomena.

This talk will review the use of envelope correlation methods and ICA to identify resting state networks in MEG, and show how these same techniques can be used to identify task-positive networks. I will then present a two-pronged approach to investigating what underlies the envelope correlations in the resting state. First, the use of time-varying functional connectivity measures of synchrony. Second, the use of computational network models, based on small world networks and using realistic conduction delays, that can simulate MEG data with similar functional connectivity measures to those seen in real data. Put together, these findings demonstrate the potential of MEG as a tool for understanding both the origin of resting state activity, and for measuring brain connectivity.

- **Cross-frequency coupling mechanis in the ongoing resting-state predict BOLD fluctuations - Esther Florin (Montreal, Canada)**

During the past decade, resting-state networks have been identified with fMRI and more recently, using MEG imaging. The exact electrophysiological counterpart of resting-state BOLD signals however, is still not elucidated. In the present study, we propose and demonstrate with MEG source imaging a possible electrophysiological mechanism structuring resting-state BOLD fluctuations.

We investigated the dynamics of cross-frequency coupling between oscillatory fluctuations observed with MEG source imaging, across the cortex, in 4 subjects. We were able to identify that patterns of phase-amplitude couplings between low-frequency bands and high-gamma oscillations reveal the regions connected during resting-state. Based on these results, we synthesized time series at each cortical location, that essentially model the slow fluctuations observed with BOLD. We verified that conventional correlation analysis based on these pseudo-BOLD time series revealed the expected resting-state networks. Overall, our results suggest that the mechanisms that reveal the brain’s resting-state networks with fMRI are based on the cross-frequency coupling between the phase of low-frequency components and the amplitude of high-gamma oscillatory fluctuations.

**Thursday, August 30th, 2012, 9:00-11:00 Hall B**

**S-Th-B1 Frontal lobe functions: MEG tasks to examine inhibition, social cognition and language in typically and atypically developing children**

**Chairs: Margot Taylor, Elizabeth W. Pang (Toronto, Canada)**

Inhibition, social control and expressive language are functions known to follow a prolonged developmental course. They are also known to have widely-distributed neural circuits that rely heavily on the integrity and maturity of the frontal lobes. The frontal lobes show protracted maturation, following a pattern of myelination, growth, and pruning that impacts where and how these cognitive functions are organised in the brain. MEG, with its excellent spatial and temporal resolution, is the ideal modality to track the development of these complex cognitive abilities. However, the challenge for MEG has been two-fold: to develop age-appropriate MEG tasks to capture the neurodevelopmental trajectory of these functions; and, to develop appropriate analysis strategies that can capture the subtle, often short-lasting, frontal lobe activities. In this symposium, we bring together a group of researchers to present examples of MEG research in typically developing children and clinical groups, aimed at examining inhibition, emotional processing, and motor speech and language control - all aspects of cognition that rely on frontal lobe functions and have protracted a developmental course. As well, we address the challenges of testing children in the MEG and the need to develop age-appropriate technologies and paradigms.

- **MEG measures of inhibition in prefrontal cortex - Julie Vidal (Paris, France)**

Inhibition is a core executive function reliant on the frontal lobes that shows maturation through to adulthood. Atypical activation in underlying brain networks subserving inhibition has been reported in fMRI in developmental disorders such as autism spectrum disorders (ASD). We investigated the spatiotemporal characteristics of neural processing associated with inhibition - withholding a prepotent motor response - during a visual go/no-go task in teenagers and adults, with and without ASD using MEG. We used a contrast between two no-go
conditions, that matched visually but induced different inhibitory contexts, to eliminate a common confound in comparing go with no-go trials. Source analyses were performed using an event-related beamformer algorithm with co-registered individual structural MRIs. Performance was controlled and similar across subjects. MEG data revealed prefrontal activity in the inhibitory condition at 200-300ms after stimulus onset. Peak activation in the right inferior frontal gyrus in typical adults was congruent with the extant literature. However, a similar pattern was not found in either typical teenagers or in participants with ASD; adult ASD MEG data were more similar to control teenagers. These findings provide high-resolution temporal and spatial information regarding the maturation of response inhibition in late childhood and the atypical frontal activity in ASD.

• Early neural network activation during emotional face processing in adolescents with and without autism - Rachel Leung (Toronto, Canada)

The development of emotional processing is critical for acquisition of effective social skills. This ability to understand others’ facial expressions matures throughout adolescence and is largely subsumed by the frontal lobes. Autism spectrum disorder (ASD) is associated with frontal lobe dysfunction and difficulty processing emotional faces. We explored the developmental patterns of emotional processing in typical adolescents compared to typical adults and contrasted this with adolescents with ASD using MEG. Participants performed an implicit emotional processing task with happy, angry and neutral faces, presented very rapidly (80ms) left or right of central fixation. Participants responded to a scrambled pattern on the other side of the fixation point. In response to happy faces, beamformer analyses showed early (80-120ms) left anterior cingulate and right middle frontal activations in control teens while ASD teens showed bilateral middle frontal and left amygdala activation. Angry faces elicited early left medial frontal and right amygdala activations in the control adolescents, while the ASD group showed early left middle frontal and right inferior frontal activation. Adults displayed bilateral middle frontal and right superior frontal activation in response to angry faces and bilateral medial frontal and right middle frontal activation in response to happy faces. These preliminary results indicate distinct early neural network activation in adolescents compared to adults, which varied with positive or negative expressions. ASD adolescents showed a divergent pattern, which was more similar to previous results in a younger cohort, suggesting delayed development. Ongoing data collection will facilitate understanding the neural mechanisms underlying emotional processing in ASD and their differing developmental patterns in key brain regions in the emotional cognitive network: medial frontal and ACC activity, linked with limbic system responses in the amygdalae.

• Changes in auditory gamma band oscillations in autism are associated with reductions in auditory cortical GABA - Donald Rojas (Denver, USA)

One theoretical perspective on autism spectrum disorder (ASD) speculates that an increased ratio of neuronal excitation to inhibition can explain some of the key symptoms and associated medical conditions. Evoked oscillatory abnormalities in EEG and MEG have been described in ASD, particularly in the gamma band range (¿ 30 Hz). Failure to entrain higher frequency stimulus information has been proposed to reflect in GABA-mediated inhibition in the cerebral cortex. MEG measures of auditory steady state evoked fields to 40 Hz amplitude modulated noise were obtained in 12 children and adolescents with ASD, 11 siblings (SIB) of ASD children and 12 healthy controls. In addition, proton magnetic resonance spectroscopy (1-h MRS) was obtained in participants to quantify concentration levels of GABA in the left auditory cortex. Auditory steady state evoked power and phase-locking were reduced in the ASD and SIB group compared to HC. The 1-H MRS / GABA creatine ratio was significantly reduced in both ASD and SIB groups compared to HC. GABA / Cr was correlated with auditory steady state MEG measures. In conclusion reduction in GABA concentration is consistent with previous post-mortem research showing reduced expression of glutamate decarboxylase (GAD) in ASD. Changes in GABA, which could lead to increased cortical excitability, may underlie the oscillatory abnormalities observed and are consistent with prior theories of higher-excitation-inhibition ratios in ASD. As the findings are also present in first degree relatives, this indicates heritability of a biological endophenotype in ASD.

• MEG studies of expressive language representation and plasticity in children - Darren Kadi (Toronto, Canada)

Receptive language has been well-studied using magnetoencephalography (MEG), and there are excellent clinically-validated protocols for mapping Wernicke’s area in both children and adults. In contrast, there remains a paucity of expressive language MEG paradigms, particularly those suitable for use with young children or clinical populations. We recently introduced an expressive language MEG protocol that has been successfully used with paediatric patients and children as young as 4 years of age. The paradigm involves covert or overt verb generation
to developmentally-appropriate picture stimuli. Using differential beamformer analyses and a bootstrap thresholding procedure, we observed low-beta event-related desynchrony (ERD) over canonical Broca’s area in young adults participating in the task. In a small group of children undergoing neurosurgery for intractable epilepsy, we were able to compare ERD lateralization and localizations to findings from intracarotid sodium amobarbital procedure and stimulation mapping, and observed excellent concordance among modalities. To characterize developmental changes in the expressive language network, we studied healthy children and adolescents (5-19 yrs). For this group, we computed laterality indices for ERD in each frontal lobe, and observed increasing left lateralization throughout childhood. We have extended our expressive language studies to include a group of children (3-6 yrs) undergoing intensive 8-week therapy for speech-motor deficits. Children were studied before and after the intervention using MEG and high-resolution MRI. We observe both neuromagnetic and structural changes in the speech-language network over the brief training period. We will discuss how MEG and MRI serve as analytic complements in this study.

- **Neuralsynchronization of cortical networks associated with inhibitory control in adolescents and adults** - Kai Hwang (Pittsburgh, USA)

Inhibitory control, or the ability to voluntarily suppress responses to task irrelevant stimuli, has a protracted developmental trajectory and remains immature during adolescence. Past studies have provided initial evidence suggesting that the development of inhibitory control is supported by increasing functional integration of distributed neural systems. The goal of the present study was to test that hypothesis that the development of inhibitory control is associated with age-related increases in beta-band neural synchrony (15-30 Hz), which has been suggested to support top-down cognitive control and long-distance cortical-cortical communication. We collected MEG (Elekta-Neuromag) data from adolescent (age 14-16) and adult participants (age 20-30), where participants performed antisaccade (AS) and control prosaccade (PS) tasks. Subjects were shown a preparatory cue (a red fixation for AS or a green fixation for PS) for 1500 ms, followed by a peripheral target where subjects were instructed to make a saccade toward (PS) or away (AS) from the target. We used cortically constrained minimum-norm estimate (MNE) to estimate cortical activities. MNE estimates from activated regions were then extracted for phase synchrony analyses by calculating phase-locking values (PLV) between regions of interests. Preliminary data (7 adults and 4 adolescents) showed that for AS, adults showed strong phase-locking between the right middle frontal gyrus (MFG) and the right intraparietal sulcus (IPS), and between the right frontal eye field (FEF) and bilateral IPS in the beta frequency range during the preparatory period, while for adolescents weaker beta phase synchrony were observed. These results suggest that the development of inhibitory control is associated with enhanced efficiency of inter-regional communication between frontal and parietal regions known to support top-down cognitive control.
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To be essential to our colleagues & collaborators.

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To ensure that all individuals living in the United States, who have neurological conditions, receive the highest quality health care by promoting the best clinical practice in magnetoencephalography that is accepted by insurance providers.
Mo-114 - Introducing ELAN: a free package for advanced MEG, EEG and intracranial signal analysis

Pierre Emmanuel Aguera¹, Karim Jerbi¹, Anne Caclin¹, Olivier Bertrand¹

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We present a freely available software package called ELAN (Aguera et al., 2011) which provides a wide range of signal analysis tools for electrophysiological data. ELAN can be used to analyze scalp-level electroencephalography (EEG), magnetoencephalography (MEG), intracranial EEG, and local field potentials (LFPs). The toolbox is written in C and is available for multiple Linux distributions but can also be used under Windows or MAC OS using virtualization software. Download options, user manual and an online user community mailing list and forum are available on the ELAN official website (http://elan.lyon.inserm.fr). Although only recently made available for free download to the community, the ELAN toolbox is based on 25 years of methodological developments at the Brain Dynamics and Cognition laboratory (CRNL, Lyon) and was used in many of the early papers exploring evoked and induced oscillatory activities in humans (e.g. Tallon-Baudry et al., 1996, Tallon-Baudry et al., 1997, Tallon-Baudry & Bertrand, 1999). We provide an overview of the concepts and functionalities of ELAN and highlight its complementarity and interoperability with other toolboxes (e.g. FieldTrip, EEGLab, Brainstorm, SPM, etc.). Illustrative examples of both time and frequency domain analysis will be provided and novel functionalities will be reported.

References:
Mo-115 - Efficient processing of MEG data on a multi-core multi computer infrastructure

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Non Invasive medical diagnostic data are usually big in size. Processing these data multiplicatively magnifies the file size and memory requirements as in the case of Magnetoencephalography (MEG) data. Phase lock value (PLV) is a measure of synchronized activity of different brain regions obtained by application of Hilbert Transform.

The data were collected from 151 MEG sensors, which were transformed into virtual channel space (3950 channels) using the Synthetic Aperture Magnetometry method. This virtual space data was filtered and transformed into the Hilbert space to obtain the magnitude and phase information, which is used to derive PLV between any two channels.

Processing this data on MATLAB platform on a standalone implementation of the above steps resulted in out of memory errors on a server (Quad core processor, 128 GB RAM, Network storage). To counter this inability of processing, we proposed a parallel implementation of the complete pipeline to enable the use of cluster infrastructure with multi-core processing power and large memory, which divides the tasks into multiple (>100) work jobs loaded into the cluster. The code was implemented in C++ language with the function calls controlled in UNIX scripting environment.

On a standalone computer system with typical memory sizes to process MEG data, processing time would be impractical, taking weeks per subject. With the parallel implementation providing increased memory and processing power we were able to process the large data set per subject with 15mm spatial, 2Hz spectral, and 1ms temporal resolutions.

Previous literature has reduced the spatial resolution for comparisons or combined freq/time intervals to reduce the processing to a manageable time. With our implementation we have been able to efficiently process the data (< 2 hours per subject) and obtain improved spatial, spectral, and temporal information. This improvement could unveil previously missed interactions in the brain.

Mo-116 - Maintaining fine temporal resolution when visualizing beamforming results

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The main goal of our study was to find ways to visualize functional activity based on beamforming while maintaining fine time resolution. The primary output of beamformers are virtual sensors which reflect the time-course of estimated brain activity for selected grid locations. When virtual sensors are calculated for a grid of points filling the whole volume of the brain, a functional map can be created based on the virtual sensor traces. In order to display smooth images, maps are typically generated by averaging the activity in specific time-windows for every virtual sensor, thus losing the fine temporal resolution. Visualization of every time point usually yields noisy images due to signal to noise variations over grid points and time, as occurs for example in momentary peaks or with deep noisy sources. In order to overcome this problem two strategies were explored: normalization and masking. Different normalization methods were applied on the virtual sensors in search of a reliable strategy. In addition, we attempted to mask channels which did not reach certain criteria such as a threshold of kurtosis or Z-score value. We will show the application of the different methods on data acquired on a verb generation task and discuss the advantages and disadvantages of each method. We will suggest ways to create single-subject movies of brain activity for a single condition or for comparisons between conditions with millisecond resolution.

Mo-117 - A graphic user interface-based automated processing stream for Granger analysis of source space reconstructions of MEG/EEG data

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We describe a highly automated processing stream for performing Granger causality analysis of source space reconstructions of evoked MEG/EEG data. Our processing stream relies on full cortical reconstructions of high temporal resolution MRI-constrained simultaneous MEG and EEG data collected during task performance. Unlike other imaging techniques that have been applied to Granger analyses, this technique provides sufficient temporal resolution to support timeseries modeling of evoked data, sufficient coverage to sample all cortical contributors to processing interactions, and sufficient spatial resolution to align activations with Brodmann areas for functional interpretation. The raw data are transformed using minimum-norm estimates for cortical activity as well as 40 Hz gamma phase locking values calculated using a wavelet technique. The conjunction of the estimated activity and phase locking to a reference brain region is used to identify a comprehensive set of active or interacting regions of interest (ROIs). Region of interest selection is automated, based on locally high activity and wave similarity by standardized Euclidean norms to
exclude redundant signals and define the spatial extent of individual ROIs. Timeseries data are modeled for Granger analysis using a Kalman filter method, which alleviates the need for stationarity and allows for the modeling of realistically large networks. An index of granger causality strength is calculated for all directional potential connections at each timepoint. A bootstrap permutation technique is used to characterize a null distribution, which can be used for significance testing. The output of these analyses can then be visualized using static and dynamic graphs showing time-varying patterns of directed interaction between ROIs as well as node-based measures of evolving causal sink or gain.

**Mo-118 - The MNE package for MEG and EEG data processing**

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MNE is a software package for processing magnetoencephalography (MEG) and electroencephalography (EEG) data. It provides a full workflow for data preprocessing, automatic forward modeling, and source imaging using cortically-constrained distributed source models.

The core of MNE, available for Linux and Mac OSX, consists of command line tools and two graphical user interfaces. The first, mne_browse_raw, is for reviewing raw data, filtering, marking bad channels, and artifact rejection using SSP (Signal Space Projectors). The second, mne_analyze, is used for co-registering anatomical MRI and MEG, topographic plots, and source estimates exploration. MNE works using the Neuromag fif file format and provides data conversion utilities for other systems (e.g. CTF).

In addition to the compiled C code tools, MNE includes a Matlab toolbox which facilitates access to fif data files and enables development of custom analysis tools based on intermediate results computed with the MNE tools. The third and newest component of MNE is MNE-Python, which implements all the functionality of the MNE Matlab tools in Python and extends the capabilities of the MNE Matlab tools to, e.g., time/frequency-domain analysis and non-parametric statistics. MNE-Python includes dozens of examples illustrating its features. We use an open development model for the MNE Matlab toolbox and MNE-Python, the code is available at https://github.com/mne-tools. The Matlab and Python code is provided under the simplified BSD license allowing code reuse, even in commercial products. MNE-Python is presently evolving quickly. Due to the open development, the changes are fully transparent to the users and user contributions can be easily included.

MNE gives also access to a sample dataset, enabling users to get started quickly and methodological contributions to be reproduced by other researchers. MNE is a freely available package that does not depend on any commercial products.

http://www.martinos.org/mne
Mo-119 - Proposal for a new MEG-MRI co-registration: A 3D-camera system

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MEG is a non-invasive tool for the measurement of human brain functions. However, accuracy of source localization cannot leave any ambiguities. One non-negligible factor regarding reliable source localization is the transformation of the visualization method into an anatomical image, based on the co-registration between the head shape extracted from the anatomical image and obtained using a 3D-digitizer. A Polhemus system has been commonly used as the default 3D-digitizer, however, this digitizer requires hand operation resulting in longer times to take measurements and poor reproducibility. For hospital use, a quick measurement is needed to reduce the burden on patients. Here, we suggest a new quick system, a 3D-camera system based on a laser scanning technique. We propose a very simple measurement method which needs only one snapshot and this makes it possible to gain an instant measurement while maintaining high accuracy and reproducibility. To validate our method, we evaluated the reproducibility of the tactile finger representations between the two modalities. Source localization was performed using MNE. The figure shows the 4 MNE results from SI right thumb (D1) tactile stimulation and shows some differences between the two types of 3D digitizer. With focusing core activation, the upper row indicates higher reproducibility of D1 across the two days of experimentation. Using the Polhemus digitizer, the results on the second day were almost identical to those obtained using the 3D-camera, while data on the first day showed somewhat different results. These findings clearly demonstrate that the 3D-camera-based method significantly reduced the session-to-session variability in the estimated localizations. Our study shows a systematic improvement in MEG measurement that will be beneficial for routine clinical use, because of the advantages of quickness, comfort, accuracy and reproducibility associated with the new MEG co-registration method.

![3D-camera and Polhemus results](image)

Obviously distinct results of the right D1 with 3D-camera and magnetic-field digitizer

Mo-120 - BrainWave: A Matlab toolbox for MEG beamformer analysis

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Neuromagnetic source reconstruction based on the minimum-variance beamformer algorithm has become an increasingly popular method for the localization of brain activity from MEG data. We present a Matlab-based toolbox (BrainWave - Beamformer Reconstruction And Interactive Waveform Visualization Environment) that provides a user-friendly graphical user interface (GUI) for the computation of frequency-specific changes in oscillatory brain activity using the synthetic aperture magnetometry beamformer (Robinson & Vrba, 1997) and analysis of evoked brain responses using event-related beamforming (Cheyne et al., 2006, 2007). Differential or event-related images are generated using scalar, vector or surface constrained beamforming algorithms, and image sequences viewed in a 4-dimensional glass-brain viewer, with built-in peak finding and simple point-and-click waveform plotting and time-frequency analyses. Compiled C/C++ libraries allow for rapid computation of high-resolution images with support for Linux, Mac OS X, and Windows operating systems. Tools are included for importing raw (e.g., DICOM) MRI data, co-registration with MEG data, and creation of spherical head models. Spatial normalization is achieved using the SPM toolbox with ability to view images in MNI template space with anatomical labels using the Talairach database. BrainWave works natively with the CTF.
dataset format with conversion programs to import data from other MEG manufacturers. Other features include spatiotemporal movies, batch processing of multiple datasets, and group analyses, including permutation tests and image contrasts, and pairwise analysis of source waveforms (e.g., phase-locking). Examples will be shown comparing the results of beamformer source analyses of MEG data from different MEG manufacturers (CTF, Yokogawa, Neuromag). The BrainWave toolbox can be downloaded at http://cheynelab.utoronto.ca.

Mo-121 - HERMES: a friendly connectivity analysis software

Guioam Niso

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The analysis of the interdependence between time series has become an important field of research in the last years, mainly as a result of advances in the characterization of dynamical systems from the signals they produce, and the introduction of concepts such as Generalized (GS) and Phase synchronization (PS). In neurophysiology, different analytical tools stemming from these two concepts have added to the 'traditional' set of linear methods, which include the cross-correlation function (in the time domain), the coherence function (in the frequency domain) or more elaborated tools such as Granger Causality. This increase in the number of approaches to tackle the existence of the so-called functional connectivity (FC) and the effective connectivity (EC) between two (or many) neural networks, along with the mathematical complexity of the corresponding time series analysis tools, make it desirable to arrange them into a unified-easy-to-use toolbox. The goal is to allow neuroscientists, neurophysiologists and researchers from related fields to easily access and make use of these FC analysis methods.

In this line, we present a Matlab® toolbox termed HERMES, in which we have included several, commonly used indexes of FC, such as cross-correlation, coherence, Phase Locking Value, Phase Lag Index, S,H,M,N-generalized indexes, Synchronization Likelihood, Partial Directed Coherence, Directed Transfer Function and Granger Causality, among others. HERMES has been specially thought (but not necessarily) for the analysis of neurophysiological data from EEG and MEG. It includes, as well, some useful preprocessing and visualization tools.

Mo-122 - Identification of specific signals in magnetic resonance spectroscopy using advanced techniques

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Magnetic Resonance Spectroscopy(MRS) allows to set the molecules that make up body parts, organs and tissues. The main task in the data analysis of this kind of spectra is the development of a method that could find and fit each one of the peaks that appears in the spectra data, either in time or frequency domain. A lot of work has been made on different techniques that identify each peak and its contribution to the spectra, making possible to subtract them and carry on the search of weaker peaks, easily mistaken with noise contributions, in the residual signal. Our aim is to review the most important methods of peak searching in magnetic resonance spectra and show a new technique, widely used by research groups in other physics fields, and highly competitive with the previous ones, both in denoising and identification of weak signals. This advanced method to detect low concentrations of molecules in organs or tissues could be used to establish new biomarkers from standard clinical MRS tests.

Mo-123 - Software suite for MEG, EEG, EcoG/intracranial EEG data analysis

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We present a software suite for processing MEG, EEG and EcoG / Intracranial-EEG data, developed at the Center for NeuroImaging Research, in Pitié-Salpêtrière hospital, Paris (CENIR: http://meg.cenir.org) in collaboration with the Cognitive Neurosciences and Brain Imaging group (Cogimage/LENA: http://cogimage.dsi.cnrs.fr). In order to represent various kinds of MEG/EEG/SEEG raw and/or processed data, we introduce a common formalism, the LENA format (directory containing required and optional files). We also provide routines to import/export LENA data within Matlab and Python environment, Brainstorm and BrainVisa software and commercial formats.

Advanced signal preprocessing is available through single command-line programs (ERP averaging using combinations of markers, measures, automatic detection/correction of artefacts, PCA). Different measures can also be obtained in the time-frequency domain (power, phase-locking, z-score, phase-synchrony, coherence). We also provide tools for statistical analysis of MEG/EEG data based on parametric and non-parametric testing of mean differences among conditions within and/or between subjects. The user is asked to specify his design in a matlab script. The design to be analysed can comprise any number of independent factors, each with multiple levels, and with or without repeated measurements.
The output files (F and p or -logp values for every main effect and interaction) are in lena format. Besides the resulting F, t, and p values in .lena files, the user has the ability to control for multiple comparison using the cluster-based permutation proposed by E. Maris et al. J. Neurosci Methods, 2007 Apr 10 and extended to repeated-measurements ANOVA.

A dedicated user-friendly graphical interface has been developed to flexibly visualize data at each processing step. It offers various modes of representation: curves with very interactive edition of events, trials or sensors, 2D cartography and 3D rendering.

**Mo-52 - Effect of stimulus presentation rate on music syntactic processing**

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Music seems to have a structure based on syntactic rule. Recent event-related potential (ERP) studies reported that rule breaking of chord sequence oddball induce the Early Right Anterior Negativity (ERAN). The ERAN was indicated to be an indirect proof that human listen music with expectation of chord progression based on musical regularity, however, it remains unclear how the neural processing of music expectation is influenced by stimulus infrequency. In the present study, to examine the effect of presentation rate on neural response of irregular detection, we performed the following experiments. First, in contrast to previous studies, we presented irregular chord frequently while present regular chord infrequently. Then we reversed presentation ratio, presented regular chord frequently and irregular chord infrequently. We finally compared the same stimulus set between different presentation ratio (e.g. frequent irregular chord vs infrequent irregular chord). We found the stimulus presentation ratio differently influenced on between regular chord sequence and irregular chord sequence.

**Mo-68 - Cortical oscillatory changes related to violation of cross-sensory prediction and association**

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Prediction and association of information across different sensory cortices is essential for the rapid emergence of an integrated multisensory percept. Little is known, however, about the neural mechanism underlying how the different sensory systems share error information in prediction and association immediately. Here, we show that violation of audiovisual prediction and association causes rapid and extensive changes in magnetoencephalographic oscillations in low-frequency range. A grating motion moving vertically, either upward or downward, was randomly displayed for a constant time and was followed by a tone burst. Higher and lower tones were designed to be associated with the upward and downward motions, respectively, so that participants can associate a tone with a prior motion cue predictively, 10% of tones disrupted this predictive association. The duration of motion was manipulated to be 100, 300, or 500 ms for distinct sessions to control the time for prediction. When visual prediction was disrupted by an incongruent tone, phase-locked activities in the bilateral supratemporal areas and the cuneous initiated at about 100 ms after tone presentation. Concurrently, induced power in the theta band increased relatively with increasing time for prediction, whereas relative decrease in the alpha band power appeared irrespective of the time. These transitions were detected from a wide range of occipitotemporal regions. Increased theta power, correlated with the amount of prediction, indicates reorganization of audiovisual preprocessing violated by unpredictable input. In contrast, prediction-independent alpha power reduction involves an increase in alertness resulting from audiovisual mismatch detection. We thus conclude that these two oscillatory transitions in the occipitotemporal network signal a cross-sensory prediction error and association error, respectively, and mediate rapid reciprocal communication between the early sensory activities.
Relative variations of alpha and theta activities for audiovisual violation after 500-ms prediction. These were obtained by subtracting the variations for audiovisual congruent combinations from those for incongruent combinations.

Mo-69 - An Audio-Visual Investigation of Brain Connectivity Via Correlations of Beta Power Fluctuations During a Search Task

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Audio-visual (AV) integration is a key component of building a unified sensory experience, and a common topic of interest in brain connectivity. Here we explore the possibilities of using correlations of beta band (15-30Hz) power fluctuations measured via magnetoencephalography as a tool for estimating functional connectivity during audiovisual searching. Eighteen subjects performed a task where they were instructed to locate a correct target ball from four distracter balls on a screen. In an active, audiovisual searching condition the target ball was found based off of a sound that was correlated with its position on the screen. In a control, visual searching condition, a tone was still played but it did not correlate to any of the balls’ positions and subjects were instructed to ignore it, instead the target ball was found based off of its color correlating with its position on the screen. The goal was to produce periods over several seconds with a maximal and minimal cortical aud iovisual interaction, while the stimulus remained the same. Results showed global increases in correlations of beta power fluctuations with left middle temporal gyrus, which neighbors auditory cortex, left inferior parietal lobe, and sections of the left temporal-parietal junction during audiovisual searching as compared to visual searching. Furthermore, correlating sub-bands within the beta band as compared to overall beta power improved results, illustrating a fine frequency specific nature of these functional brain connections. We hypothesize that the global nature of these connections reflects the high difficulty of the task resulting in greater levels of attention to the tone, indicating a mechanism for global attention onto a specific stimulus attribute.

Mo-70 - Combining EEG and MEG to Study Auditory Tonotopy

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It is known that human auditory cortex has a tonotopic organization, i.e., different frequencies are processed in different locations in the auditory cortex. In both auditory evoked fields (AEF) and potentials (AEP), the N1 can be observed, a component with latency around 100 ms. Previous studies showed that the N1 response could be used to investigate the tonotopy and the tonotopic distance is rather small (8 mm depth difference between 500 Hz and 4000 Hz stimulus frequencies). This motivates a very accurate source reconstruction and thus in our investigations, we focus on two aspects. The first one is measuring the EEG (74 channel) and MEG (304 channel whole head) simultaneously to benefit from their complementary information. Secondly, taking into account the different sensitivity profiles of both modalities to allow the combined source analysis. We therefore propose to use a calibrated realistic finite element head model consisting of 6 compartments (skin, skull compacta, skull spongiosa, CSF, anisotropic grey and white
matter) for each subject. Geometry and brain conductivity anisotropy is extracted from individual T1-, T2- and diffusion-tensor-
(DT-) weighted magnetic resonance images, while calibration (conductivity fitting) is performed by means of additionally measured
combined somatosensory evoked potential and field data. The N1 responses for pure sinusoidal tones with 3 different frequencies
(250, 1000, 4000 Hz) are then localized and results are discussed. To compare the effects of accurate volume conductor modelling,
isotropic, three compartment head models are constructed as well. We intend to use, for the first time to our knowledge, a fully-
Bayesian inference for hierarchical Bayesian modelling for the localization of the underlying focal activity. Our main aim in this
study is to contribute to the understanding of the tonotopic organization in the auditory cortex using state of the art forward and
inverse approaches and combined EEG-MEG data.

Mo-71 - Context effects in auditory change detection
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An important aspect of understanding the neural computations underlying auditory change-detection, is measuring how the stimu-
lus context before a transition affects subsequent change responses. The present MEG experiment examines the issue of temporal
regularity: a signal can be deemed regular in one context and irregular in another. E.g., interaurally-correlated white noise (CN) is
‘regular’ (‘order’) relative to interaurally-uncorrelated noise (UCN), and ‘irregular’ (‘disorder’) relative to a pseudo-periodic noise
such as iterated ripple noise (IRN). Our stimuli all share the abstract characteristic that they contain a transition from a state of disor-
der to order (DO), or vice-versa (OD). In previous experiments examining such transitions the stimulus set was limited to transitions
in a single order-disorder dimension. I.e. whilst uncertainty existed as to when a transition would occur, its nature (OD or DO)
could be predicted in advance, potentially facilitating processing and resulting in shorter response latencies. We use CN-to-UCN,
UCN-to-CN, CN-to-IRN and IRN-to-CN transitions (as well as no-change controls) presented randomly a) within the same block
(so the nature of the transition is not predictable from the initial segment of the stimulus) or b) within separate blocks. Using the
same stimuli in different contexts allows us to factor out signal-specific effects from pattern-specific effects. Analysis is ongoing.
Preliminary results (N=12) reveal distinct evoked patterns for OD and DO transitions. CN-to-UCN transitions are detected faster
(from ~50ms post-transition) than the opposite UCN-to-CN and CN-to-IRN transition (~ 120ms post-transition) and involve
different source dynamics. Additionally, we find no significant effect of context on the time-domain response, suggesting that the
observed responses reflect the operation of low level, context independent processes. Full results including time-frequency analysis
and source localisation will be presented.

Mo-72 - Modulations of neural activity in auditory streaming induced by spectral and tempo-
ral alternations of the prior stimuli: an MEG study
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Humans are constantly able to organize perceptually meaningful elements from the mixture of sounds in the environment, a phe-
nomenon described as ‘auditory stream segregation’ or ‘streaming’. The aim of the present study was to investigate the context effect
on auditory streaming, when subsequent sound patterns alternate in spectral or temporal cues.
Two consecutive ABA tone-triplet sequences were presented with no gap in between. In the first experiment the frequency separation
between A and B tones (DeltaF) varied by 2, 4 and 10 semitones in two successive conditions but the inter stimulus interval (ISI)
was kept constant. In the second experiment the ISI between A and B tones varied but a constant DeltaF of 6 semitones was main-
tained. By means of magnetoencephalography (MEG) the auditory evoked magnetic fields (AEFs) were recorded. In a subsequent
behavioral study the same design was used to provide information about the subjects’ perception.
The results showed that the magnitude of the P1 component of the AEF to the B tones of the triplet increased significantly with
increasing DeltaF, predominantly in the left hemisphere. A significant increase in the amplitude of the N1 component was only
obtained for the 10 semitones condition, induced by prior sequence of 2 semitones, more pronounced in the right hemisphere. Al-
ternating the ISI of successive sequences at a constant DeltaF, did not result in a significant difference in AEFs. The behavioral data
indicated an increased probability of two-stream perception for DeltaF of 4 and 10 semitones with a prior sequence of 2 semitones,
in line with the MEG data.
In our study, the P1 component showed nonspecific effects, whereas N1 indicated the specific modulations during large DeltaF,
induced by prior sequence of small DeltaF. The reported different alternations and lateralization effects for P1 and N1 AEF components
suggest that both components represent, at least partially different systems during streaming.
Peak amplitudes of N1 and P1 from each hemisphere to all three degrees of frequency separation. Significant increase in the amplitude of the N1 component was only obtained for the 10 semitones condition, induced by prior sequence of 2 semitones.

Mo-73 - Magnetic mismatch negativity to frequency and phonetic changes in aging: An MNE analysis

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Aging has been associated with decline in sensory-perceptual processes. Although an increasing number of literature investigate aging-related alterations in the integrity of auditory sensory memory, it remains controversial whether the mismatch negativity (MMN) or its magnetic counterpart (MMNm) at a short stimulus onset asynchrony (SOA) is modulated by physiological aging. To reconcile the inconsistent results from previous event-related potential studies, we used a whole-head MEG to explore the aging effects on the functional integrity of MMNm at a short SOA. MMNm responses to both frequency and phonetic changes were recorded (Fig. A). The equivalent current dipole modeling showed prominent MMNm signals in both conditions in one young subject (Fig. B). The grand-averaged evoked responses of the elderly group showed a decreased amplitude of MMNm responses to pitch and phonetic changes (Fig. C). Our primary goal was to use the Minimum Norm Estimate (MNE), a distributed model, to assess the group differences at a source level. To objectively define regions of interests (ROIs), an averaged dynamic Statistical parametric Map (dSPM) for all subjects was calculated from 100-250 ms for frequency MMNm and 150-300 ms for phonetic MMNm. The MNE analysis was based on the ROIs from dSPM calculation. The elderly showed reduced MMNm amplitudes in both conditions, particularly in the superior temporal gyrus. However, the activation of inferior frontal gyrus, considered related to the function of involuntary attention switching, was relatively preserved. The MMNm latency of all the ROIs in each condition was significantly prolonged (Fig. D). In conclusion, the amplitudes of MMNm responses to both pitch and phonetic changes at short SOAs were decreased during physiological aging.
Fetal Alcohol Spectrum Disorder (FASD) is a prevalent, preventable epidemic that results in moderate to severe physiological, cognitive and social disabilities. Animal and human research has demonstrated varying degrees of basic sensory deficits associated with exposure to alcohol in utero, which may contribute to the poor life outcomes of those suffering from FASD. In this study, we examined primary sensory deficits in adolescents (12-21 yrs) characterized as having an FASD (N=14) and age-matched healthy controls (N=14) by measuring auditory evoked responses using Magnetoencephalography (Elekta Neuromag). Participants listened to tones (1000 Hz, 75 dB above hearing threshold) presented on the left or right, unilaterally, while they watched a silent cartoon. We first projected noise from the raw data and performed motion correction using Neuromag Maxfilter. Heartbeat and speaker artifact were then projected from the data using signal space projection before averaging and source localization. Source analysis was performed using the Cortical-Start Spatio-Temporal (CSST) multi-dipole analysis method available in MRIVIEW. The MEG data were registered to the individual subject MRIs for source analysis and visualization purposes. In this preliminary analysis we examined the timecourse of activity for cortical sources localized to primary auditory cortex. We found a delay in latency (11-17ms) of the first prominent peak in the evoked source activity for FASD patients relative to healthy controls (p < 0.01). This result is consistent with animal literature as well as previous results from our lab demonstrating a delay in basic auditory processing in preschool children. Further characterization of these deficits in basic sensory processing may be important for diagnostic and treatment strategies geared toward individuals with adverse effects of prenatal alcohol exposure.
Mo-75 - Functional asymmetry in the brain’s response to left and right auditory space

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Auditory space perception is based on the brain’s ability to use phase and energy differences in sound arriving at the right and left ears (Griffiths et al. 1998). While these interaural cues are known to converge as early as in the brain stem (Irvine 1992), functional MRI (Krumbholz 2004) and MEG studies (Kaiser et al. 2000) have shown that perception of auditory space is processed asymmetrically beyond primary auditory cortex with a right hemisphere dominance for both contralateral and ipsilateral hemifield that parallels the asymmetry in visuo-spatial attention (Corbetta & Shulman 2002).

We recorded 64-channel EEG from 10 subjects (mean age 24) while they were presented with an auditory location oddball paradigm. Sinusoidal pure tones had a duration of 75 ms and were presented every 500 ms. Frequent tones were presented in stereo and had 80% probability of occurrence. Rare tones were presented at 20% probability and were randomly interleaved within the sequence of frequent tones. We used an interaural time delay (ITD) of 800 between left and right ear in order to create the perception of an oddball in subjective left (10%) and right auditory space (10%). All other spectral, amplitude and duration parameters were kept constant.

Group-level SPMs of time-averaged responses to both left and right oddballs show a classical mismatch negativity (MMN) peaking at 144 ms for the left and at 128 ms for the right oddballs, \( p < 0.05 \), FWE corrected (Kilner & Friston 2010). We found an asymmetrical distribution over parieto-frontal sensors which may indicate a spatiotemporal asymmetry at the source level. Critically, the comparison between responses to left and right show an early difference over parietal sensors at 68 ms and at 120 ms (temporal range of MMN) over right temporal sensors, \( p < 0.001 \) uncorrected. In short, these results support the notion of a hemispheric asymmetry in auditory perception of space (Griffiths et al. 1998).

Mo-76 - Awareness related auditory scene analysis: A processing cascade enables a tone pair to be segregated from background and enter awareness

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In daily life, our auditory system detects and segregates sounds, derived from complex auditory scenes. Yet, limited processing capacities allow only a small subset of these sounds to enter awareness. This MEG study used informational masking to investigate the neural mechanisms that enable auditory awareness. On each trial, subjects indicated whether they detected a target that was embedded in a multi-tone background in 67% of the trials. Targets were defined as a pair of two 40 Hz amplitude-modulated tones, presented sequentially with a fixed SOA of 1050 ms. Hence, target detection required subjects to perceive both tones within a pair (Fig. 1B).

We compared MEG activity for hits and misses separately for target tone 1 and 2 both in sensor and source space (Fig. 1A). Successful target detection was associated with changes in transient evoked source activity in bilateral auditory cortices at 3 stages:
(1) an enhanced M50 component for tone 1, (2) a negative component at ~150 ms for tone 2 and (3) a later, long-latency negativity for both tone 1 and 2 at ~300 ms (Fig. 1C). Moreover, subjects’ perceptual sensitivity (d) positively correlated with the magnitude of the M150 component. In addition, we investigated whether steady-state activity was modulated by awareness. Indeed, even though all target tones elicited 40 Hz steady-state responses, the amplitude of 40Hz activity was significantly enhanced when subjects became aware of tone 1 and 2.

In conclusion, our results suggest that awareness of a two-tone pair relies on a cascade of processes that segregate this pair from a complex auditory scene. (1) The processing of detected tones is enhanced as indicated by an increased M50 and steady-state response. (2) The sequential integration of the target pair after the 2nd tone then elicits an awareness related negativity at ~150 ms. (3) Finally, aware signals may elicit additional attentional processes, which may be reflected in the enhanced long-latency negativity.

Mo-77 - Brain activity is related to individual memory capacity in auditory short-term memory for pitch: evidence from magnetoencephalography

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INTRODUCTION
Auditory STM (ASTM) is a critical building block for any function that requires the integration of sounds over time, such as the comprehension of spoken sentences, or the appreciation of music.

Previous brain imaging studies have typically explored ASTM in the context of speech, but few studies have specifically investigated non-verbal ASTM for pitch. To this aim, here we used Magnetoencephalography (MEG) to examine brain activity related to the maintenance of non-verbal pitch information in ASTM as a function of increasing memory load.

METHODS
Sixteen university students (6 women), with normal hearing, participated in the present study. Participants were presented with two sound sequences and had to decide whether they were the same or different. We used very simple acoustic material (e.g., pure tones that varied in pitch) that minimized activation of systems other than ASTM. Memory load was manipulated by varying the number of pure tones to be recalled in the sequences. We recorded the participants’ brain activity while they performed this ASTM task using a whole-head MEG system (CTF-VSM 275 sensors). Source localization was performed using the maximum of entropy on the mean method (MEM) on the time-varying MEG signals. This method is a cortically-constrained distributed source-localization approach. We performed covariation analyses using a General Linear Model considering the MEG response (i.e., normalized source localization maps) as a function of memory capacity.

RESULTS AND CONCLUSIONS
MEG revealed brain activity in frontal and temporal regions that were sensitive to increasing memory capacity during maintenance of pitch representations in ASTM. The present results confirm and reinforce the functional role of frontal and temporal cortex in the retention of pitch information in memory. This research contributes to a comprehensive understanding of the mechanisms mediating
the representation and maintenance of low-level auditory information

**Mo-78 - Auditory evoked magnetic fields related to speaking rate of synthetic speech**

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Text to speech systems such as screen readers and e-book readers are more widely adopted. To clarify the optimum speaking rate, we measured neuromagnetic signals from various areas of the brain while changing the speaking rate of synthetic speech. We found a clear correlation between the auditory evoked magnetic fields (AEF) from the left superior temporal gyrus and each syllable structure when the subjects could understand the speech. If the subjects did not understand the speech because it was too fast, the AEF showed no such correlation. It is suggested that the average duration of each syllable should be at least 80ms for good speech clarity. Stimuli: Following JEITA-IT-4001, guidelines for the evaluation for speech synthesis systems, we used the evaluation phonological statement '/kokoniissatunohongaarimasu/' which means 'One book is here.'. The corpus-based speech synthesis engine 'Cralinet' was used to verbalize the statement, and the time stretch method was used to generate eight different speech rates. Subjects: The three subjects were right-handed with normal hearing ability between the ages of 23 and 28 who gave informed consent. As the preliminary step, the three reference points on each subject were calibrated by 3D visual scanning to permit comparison with MRI data. MEG recording: Each subject laid on her/his back on a bed in a magnetically shielded room, and listened to the speech stimuli which were presented randomly. They were instructed to press one of two keys (Yes, No) depending on whether they could or could not understand the speech stimuli. We used 400 channels dc-SQUID gradiometer, PQ1400RM made by Yokogawa, installed in ATR Brain Activity Imaging Center. Measuring conditions are below. Bandwidth filter: 0.05 ∼ 200 Hz, Sampling rate: 1000 Hz, Baseline: -100 ∼ 0 ms, Measuring time: 3000 ms, Averaging number: 100 times, Inter-stimulus intervals: 2500 ∼ 3500 ms random, Average sound pressure level: 57 dBA, Background noise level: 39 dBA.

The AEF corresponding to each syllable at eight speech rates.

**Mo-79 - Auditory steady-state response reflects the auditory continuity illusion**

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The auditory system has the ability to restore missing information which is masked by noise bursts. This 'auditory induction' gives rise to the auditory continuity illusion. Already the primary auditory cortex compensates for occluded sound segments and renders interrupted sounds as ongoing. In this study we used amplitude-modulated (AM) tones interrupted by gaps to study auditory induction. When the gaps were filled with sufficiently loud noise, subjects perceived the interrupted AM tone as a single long continuous tone. We compared the auditory steady-state response (aSSR) in magnetoencephalogram (MEG) between trials where subjects continued to perceive the tone and trials where they perceived interruptions. MEG was recorded with a 275 axial-gradiometer CTF system while N = 13 healthy subjects listened to a stream of repetitive auditory stimuli (4 runs at 8 min duration each). Stimulation consisted of a 300-ms AM tone (carrier frequency: 1kHz, modulation frequency: 40Hz, 100% modulation depth) followed by a 300-
Mo-81 - Phase shifts of low frequency oscillations in visual and auditory cortices predict temporal recalibration

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Temporal recalibration (TR) is a perceptual phenomenon leading to a shift of perceived temporal order between two events: after repeated presentation of desynchronized audiovisual events (adaptation), participants’ threshold of subjective simultaneity is shifted towards the leading stimulus. Recent neurophysiological findings provide strong support for the role of oscillatory entrainment across auditory and visual cortices and argue for low-frequency phase alignment as a support for the binding of audiovisual information. Thus, we asked whether phase realignments of entrained oscillations are indicative of TR. Participants underwent audiovisual TR during MEG recording. Three types of adaptations were tested: synchronized audiovisual events, auditory leading visual and auditory lagging visual. Eight adaptation blocks per condition were recorded, each followed by a short assessment of participant’s temporal order threshold. Stimuli were presented at an average rate of 1Hz leading to a prominent tagging in both sensory cortices. Analyses were carried out in source space (dSPM, cortically constrained orientations) and restricted to auditory and visual areas. Phase and power of 1 Hz oscillations in the first and last 15 trials of the adaptation blocks were compared. The preferential phase of 1 Hz oscillations significantly shifted between the beginning and the end of the adaptation period. Specifically backward phase shifts were observed in the sensory cortex corresponding to the lagging stimulus during adaptation. Consistent with our hypothesis, phase shifts correlated with perceptual shifts in temporal order. Crucially, no significant power changes were observed in 1Hz. All together, our results provide a novel index of subjective simultaneity implemented as phase shift across sensory modalities. These results indicate that the relative phase of oscillations across cortices can serve as automatic ‘temporal markers’ for the structuring of events in time.
Mo-82 - Auditory Steady State Responses Elicited by a Sequence of Amplitude-Modulated Tones

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Most studies of auditory steady state response (ASSR) has been conducted by using auditory stimuli of long-lasting, typically more than ten seconds, periodic sound such as amplitude-modulated (AM) tones. The ASSR is expected to be used as a measure of loudness in fitting the amplification of hearing aid. To shorten the examination time for different testing frequencies, short-time presentation of AM tones is desirable. As an example of such stimuli, a sequence of AM tones in a short duration having wide range of carrier frequencies (fc) is considered. We made an MEG study of ASSR using a sequence of AM tones of 780 ms length at a modulation frequency of 41 Hz. We used narrow frequency range of fc of about one octave to examine effects of sound pressure level (SPL) and fc in detail. The stimulus sequence was composed of six tones, with no intermission, having different fc from 440 to 990 Hz in a randomized order. The SPL of the six tones was set to be highest of 75 dB at 440 Hz and lowest of 63 dB at 990 Hz. The left ear of subjects was stimulated while the signals detected in several MEG sensors at the right side of the head covering the auditory cortex were averaged for 200 sequences. We made wavelet analysis of the measured MEG signals and obtained the amplitude of 41 Hz component as a function of time for each of six tones. The results of the amplitude of ASSR showed a small dip slightly after the time of fc change and a transient period of about 200 ms to the peak of response. The mean amplitude over the 780 ms period of AM tone varied with fc, being larger for lower fc, in proportion to the SPL in dB of the AM tone. A high correlation coefficient of 0.98 with a significance level of p < 0.001 was obtained. These results suggest that the amplitude of ASSR detected by using short duration AM tones could be a measure of objective loudness of sounds, within a low frequency range of about 400-1000 Hz.

Mo-83 - A simultaneous EEG-MEG MMN paradigm : a DCM study

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Recent advances in M-EEG neuroimaging methods put neuronal network dynamics at the center of research on mental processes. Functional integration and network modulation by experimental design can be assessed with effective connectivity methods such as Dynamic Causal Modeling (DCM) (1).

DCM has been recently validated for EEG auditory data with a Mismatch Negativity (MMN) paradigm (2,3). The MMN is evoked by a deviant sound occurring in a regular sequence of standard sounds. Within the predictive coding theory framework (4), a mismatch between the incoming deviant and the prediction delivered by higher levels elicits a bottom-up prediction error reflected in the MMN.

Since MEG provides a better spatial resolution than EEG, we were interested in comparing DCM for EEG and MEG data, with
the hypothesis that MEG network parameters could be estimated more accurately. Therefore, we recorded simultaneous data (275 MEG sensors, 63 EEG sensors) with a passive frequency MMN paradigm. To assess to what extent the MMN reflects a perceptive inference process or a local adaptation in the auditory cortex, we used a random frequency condition (RF) and a predictive frequency condition (PF), with deviant sounds occurring randomly and in a deterministic way respectively. Under the predictive coding hypothesis, the PF MMN should be smaller than the RF MMN and parameters of the corresponding DCM model should differ on forward and backward fronto-temporal connections.

Preliminary results on EEG and MEG evoked responses confirm the enhancement of the MMN amplitude for the RF condition (Fig. 1). MEG sensitivity should allow refining the parameters of the DCM model accounting for the MMN in both conditions, leading to a better characterization of fronto-temporal dynamics in auditory automatic deviance detection.

Mo-84 - Auditory sampling in Dyslexia: a combined EEG/fMRI study

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Recent studies on developmental dyslexia suggest that the phonological deficit characterizing reading difficulties might be due to impaired auditory sampling (Goswami, 2010, Hämäläinen et al, 2011, Lehongre et al, 2011). The underlying assumption is that if speech is sampled at a rate that is not adequate to grasp phonemic units, phonological representations will be of unusual format, which could impair phoneme/grapheme correspondence. According to the asymmetric sampling in time theory (AST, Poeppel 2003), the left auditory cortex is normally dominant for rapid sampling at gamma rate (25-40Hz) and the right one for slow sampling at delta-theta rate (2-6Hz). The first published data comparing fluent readers and dyslexics are in agreement with AST, and show a deficit in the response of the left auditory cortex to sounds modulated around 30Hz (Lehongre et al, 2011) and a right deficit for those modulated around 2Hz (Hämäläinen et al, 2011) in dyslexics adults. The aim of the present study was to further explore auditory cortical oscillation properties in dyslexics during rest and passive viewing of an audiovisual movie. We recorded 17 dyslexic subjects and 15 matched controls using simultaneous EEG and fMRI. After removing artifacts, we performed a time-frequency analysis of the EEG signal for frequencies up to 48 Hz. For each frequency, the power time course was convolved with the hemodynamic response function (HRF) and correlated with the average bold signal extracted from the left and right auditory cortices. We did not find significant differences between dyslexics and controls in Heschl's gyrus (HG) at rest. In both groups there was a higher correlation in the left HG than in the right HG for frequencies ≥ 25 Hz. Yet during the movie, within the same frequency range, functional asymmetry increased in controls but not in dyslexics. These results confirm a lack of phonological specificity of the left auditory cortex in dyslexia during linguistic processing.

Mo-85 - The investigation of the isofrequency band in human auditory cortex by using a magnetoencephalography

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Some investigations on tonotopic organization of human auditory cortex have been noninvasively performed by using a magnetoencephalography (MEG). Although there were still debates about the tonotopic representation determined from the auditory evoked magnetic fields (AEFs), some studies indeed had shown the preliminary results. In this work, the AEFs with different frequencies were recorded by a 128 channels low-Tc SQUID MEG system to investigate the spatiotemporal features of the iso-frequency band in human auditory cortex. A 250 or 2000 Hz monaural pure tone persisting 425 ms with the sound pressure level of 80 dB was randomly applied to the left ear of subject with the inter-stimulus interval of 1.5-2.8 s to prevent fatigue of nerves. The origins of AEFs were successfully calculated from the AEFs obtained from the right hemisphere after source localization processes. The source location of on-response at 100 ms reveals a systemic change, which suggests distinct functional roles in auditory information processing.
Mo-86 - Neuromagnetic responses to auditory deviance in Huntington’s disease

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Background: Cognitive dysfunction is a common problem in patients with Huntington’s disease. Attention capacity is considered essential for higher-order executive operations. However, little is known about the functional integrity of involuntary attention processing, one of the basic attention elements mediated by the frontal cortex, in Huntington’s disease. The present study aimed to investigate whether Huntington’s disease patients exhibit a deficit in automatic deviance detection that can be indexed by magnetic mismatch responses.

Methods: We used whole-head magnetoencephalography and a passive oddball task to examine neural activation during automatic deviance detection in 8 symptomatic Huntington’s disease patients and 8 healthy control subjects. At the sensor level, the mean amplitude and peak latency of magnetic mismatch responses were calculated from the waveforms in each hemisphere. At the source level, minimum current estimate was applied to estimate the source strength underlying magnetic mismatch responses in the bilateral temporal and frontal cortices.

Results: Huntington’s disease patients exhibited a decreased waveform amplitude (p = 0.003) and a prolonged peak latency (p = 0.016) of magnetic mismatch responses in the left hemisphere. The minimum current estimate analysis also revealed lower activation of the bilateral frontal mismatch responses in patients (p = 0.001).

Conclusions: The underactivation of the frontal mismatch responses in Huntington’s disease patients suggests a deficit of involuntary attention shifting to occasional auditory deviance.

(A) Topographic distribution of grand-averaged neuromagnetic responses to standards and deviants in the control (upper panel) and HD (lower panel) groups. The head is viewed from the top, and the nose points upward.

Mo-87 - Time course of motor influences on auditory-cortex responses to speech sounds: combined TMS and MEG experiments

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Whether the human articulatory motor cortex has a functional role in processing of speech sounds is under debate. Transcranial Magnetic Stimulation (TMS) studies have demonstrated that disruptions within the articulatory motor cortex can impair performance in behavioural speech tasks (Mottonen & Watkins, 2009, J Neurosci, see also D’Ausilio et al., 2009, Curr Biol). Importantly, these motor influences are feature-specific: TMS-induced disruptions in the motor lip area impair performance in tasks that involve lip-articulated sounds (e.g., ‘ba’), but have no effect on tasks that involve only sounds that are articulated by the tongue (e.g., ‘da’, ‘ga’). Here, we investigated whether TMS-induced disruptions within the left articulatory motor cortex influence auditory-cortex responses to speech sounds using MEG. We aimed to find out whether these motor influences are feature-specific and sensitive to changes in the focus of attention. We presented ‘ba’, ‘da’ and ‘ga’ sounds in two conditions. In the Ignore condition, the participants focused on
watching a silent film, whereas in the Attend condition they pressed a button when they heard a repeated speech sound and, therefore, had to focus attention on the distinctive features of the speech sounds. We found that TMS-induced disruption of the motor lip area modulated auditory-cortex responses to lip-articulated ‘ba’ sounds about 80 ms after sound onset in the left hemisphere. This early feature-specific modulation was found in the Attend condition only. Furthermore, we found a later TMS-induced modulation of auditory-cortex responses to all speech sounds bilaterally at about 250 ms. This late non-specific effect was found in both Attend and Ignore conditions. These preliminary findings suggest that the articulatory motor cortex influences late processing of both attended and ignored speech sounds and that the early feature-specific influences emerge when the features of the speech sounds are attended.

Mo-88 - Assessment of temporal resolution of bone-conducted ultrasonic hearing using neuromagnetic and psychophysical measurements

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Bone-conducted ultrasound (BCU) is perceived even by the profoundly sensorineural deaf. We have been developing a novel hearing-aid using BCU perception, that transmits a 30-kHz bone-conducted carrier that is amplitude-modulated by speech or environmental sound. In this study, the temporal resolution of the BCU hearing were assessed by psychophysical and neuromagnetic measurements in normal-hearing and profoundly deaf subjects.

To investigate the temporal resolution of BCU hearing psychophysically, the temporal transfer modulation functions (TMTFs) were measured. TMTF shows the threshold of sinusoidal amplitude-modulation (SAM) detection as a function of modulation frequencies. The SAM detection threshold is determined systematically by measuring a detection of modulation depth. TMTF for 10-, 20-, and 30- bone-conducted (BC) sounds were measured. The detection threshold curves for all carriers commonly showed the low-pass characteristics at low modulation frequencies, the thresholds were roughly constant at modulation frequencies from 10 to about 100 Hz and then begin to increase at about 100-150 Hz as the modulation frequency increases. This result indicated that BCUs have nearly equal temporal resolution to that of lower-frequency BC sounds.

Further, mismatch fields (MMFs) for changes of stimulus-duration were recorded. MMFs for 10-, 20-, and 30-kHz bone-conducted tone bursts amplitude-modulated by 1 kHz, and a 1-kHz air-conducted (AC) tone burst were measured in different sessions. Each session consisted of one standard stimulus (75-ms duration, 85%) and three types of deviant stimuli (52.5-, 37.5-, and 22.5-ms durations, 5 % each). Equivalent current dipoles (ECDs) moments were significantly different between three kinds of BC and AC stimuli (10-kHz BC:20-kHz BC:30-kHz BC:1-kHz AC=0.95:0.92:0.91:1.0), however, ECD moments of BC stimuli were close to that of AC stimulus. This result indicated objectively that our BCUHA has a practical temporal resolution.

Mo-89 - Novel method of presenting mismatch responses in MEG and EEG.

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We compared methods for presenting the difference between the responses to standard and deviant stimuli obtained by multi-channel recording of MEG in an oddball experiment and propose a novel method. Specifically, we compared \( R(D) = m^{-1/2}||d - s|| \), the RMS (across the MEG or EEG channels) of the difference between the standard and deviant responses and \( D(R) = m\left((-1/2)||d|| - ||s||\right) \), the difference between the RMS of the standard and of the deviant response. Here \( m \) is the number of channels, \( d \) and \( s \) are the vectors of deviant and standard responses respectively, and \( ||x|| \) stands for RMS across the \( m \) channels. Our proposal is to use their average: \( A(D, R) = (D(R) + R(D))/4 \). In the figure, the three methods are shown. The auditory oddball paradigm used the complete C major (musical) scale as standard and an incomplete one where the tone G was replaced by a repeated presentation of F as deviant stimuli. To evaluate the behaviors of the three statistics, we used a very simple signal model for averaged responses: \( s = \mu + n1 \), \( d = (1 + k)\mu + n2 \) where \( \mu \) is the true standard response and \( n1 \) and \( n2 \) are independent residual noises after averaging. The presence of a mismatch field is indicated by \( k \geq 0 \) where \( r \) is supposed to be sufficiently smaller than 1. \( k = 0 \) is applied for the time periods irrelevant to a mismatch response. The results of the analysis were as follows: When \( k \geq 0 \), \( E[D(R)] = (-1/2)k||\mu||[R(D)] \) meaning that \( D(R) \) tends to underestimate and \( R(D) \) to overestimate the true mismatch response. For \( k = 0 \), the bias of \( D(R) \) is 0 and that of \( A(D, R) \) is shown to be a half of the bias of \( R(D) \). It is particularly noted that when \( k = 0 \), \( D(R) \) and \( R(D) \) are found to be uncorrelated, which leads to the relationship: \( V[A(D, R)] = (V[D(R)] + V[R(D)])/4 \) suggesting that the variance of the proposed \( A(R, D) \) can be smaller than the the other two. The figure shows these features and the proposed method seems to be a better way at least for representation of mismatch responses.

Mo-90 - Exploring the laminar origin of induced auditory gamma-band responses with 3D microelectrode arrays

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The power of the low-gamma oscillations (30-70Hz) in monkey primary visual cortex (V1) has been show to increase with the size of the visual stimulus size, and the instantaneous power of high-gamma activity (70-170Hz) was shown to be highly correlated with multi-unit activity MUA (1). Whether this observation also holds true in primary auditory cortex (A1) is still unclear. Furthermore, the laminar profile of these low and high gamma responses is poorly understood. To address this question we investigated the laminar profile of the gamma rhythm in the A1 of rats during auditory stimulation.

In this study we used extracellular multi-electrode recordings obtained in A1 of five rats to determine the neuronal encoding for sound attributes. The stimulus battery consisted of amplitude-modulation sound (Carrier frequencies:8k, 24k and 40kHz, Modulation frequencies:50, 200 and 800Hz, Amplitude:30, 50, 70 dB). The time-frequency spectral maps and the phase-locking factors were obtained from the current source density in each layer: the supra-granular, granular and infra-granular layer.
Because the 50 Hz condition generated auditory steady-state responses at the same frequency, we focused our analysis on the 200Hz and 800Hz conditions. We identified the neuronal populations that exhibited a statistically significant gamma-power increase with increasing stimulus amplitude. We found that the number of populations that displayed power increases in response to increasing amplitude was more numerous in the high gamma range than in other frequency range in the granular layer. Moreover, the instantaneous power in the high-gamma range had higher temporal correlation with MUA than power at other frequencies. Our findings complement and extend previous findings in V1. In addition, we discuss the implications of our findings on the nature of the neural generators of auditory gamma activity observed non-invasively with EEG or MEG.


Mo-91 - Neural activity elicited by sound changes in human auditory cortex

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In daily life, we are surrounded by many natural sounds. These sounds are characterized by complex spectral components, which are temporally modulated in specific ways. Spectral and temporal sound characteristics seem to be encoded into different neural activity patterns. In the present study, we investigated auditory evoked fields elicited by spectral, temporal, and spectral-temporal sound changes by means of magnetoencephalography.

We performed two experiments using different sound stimuli. In experiment 1, test stimuli (TS) were composed of two parts (each having a duration of 800 ms): 500 Hz (PT500) or 2000 Hz (PT2000) pure tones, and 40 Hz fully amplitude-modulated (AM) tones with a carrier frequency of 500 Hz (AM500) or 2000 Hz (AM2000). Combinations of two of these stimuli resulted in three experimental conditions: spectral change, temporal change, or spectral-temporal change (Figure 1). In experiment 2, the test sounds were prepared from band-pass filtered pulse-trains. We generated 32 and 48 Hz pulse-trains with a duration of 750 ms. These pulse-trains were then filtered either between 2800 and 4000 Hz (TS32_Low and TS48_Low), or between 4000 and 5600 Hz (TS32_High and TS48_High). As in experiment 1, two pulse-train stimuli were combined to form three experimental conditions: spectral change, temporal change, and spectral-temporal change. In both experiments, the auditory evoked fields elicited by the spectral-temporal change were very similar to those elicited by the spectral change, but were significantly different from those elicited by the temporal change.

In the present study, we used sophisticated sound stimuli, which contained spectral, temporal, or spectral and temporal changes at the same time. In addition, sound inputs were balanced between conditions. The results contribute to our understanding of how the human auditory cortex processes complex natural auditory signals containing multiple and correlated spectral and temporal sound changes.

Figure 1: Sound stimuli.
**Mo-92 - Mismatch fields elicited by prosodic change of speech-modulated bone-conducted ultrasound**

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Speech-modulated bone-conducted ultrasound can transmit speech sound for some profoundly deaf. A hearing aid using bone-conducted ultrasound is considered as a new candidate of hearing system for them. However, how much the bone-conducted ultrasonic hearing aid can transmit the speech information such as prosody is insufficiently studied. Mismatch field (MMF) is indexes auditory change detection, which reflects differences in sound discrimination sensitivity. This study investigated whether the MMF would be evoked by BCU modulated by prosodic-changed word using magnetoencephalography (MEG).

Eight Japanese subjects with normal-hearing took part in this study. We compared MMFs evoked by prosodic-changed and segment-changed words between SM-BCU and air-conducted speech. Japanese words based on speech signals recorded by a native female adult were used. Standard stimulus was /itta/ with a flat pitch pattern. Two deviant stimuli /itta/ with a rising pitch pattern and /ittə/ with a flat pitch pattern were used. BCU stimuli were delivered using a custom-made ceramic vibrator for MEG, which was fixed to the right mastoid. air-conducted speech were delivered to the right ear through a plastic tube placed in an inserted earphone (E-A-R TONE 3A). Intensity level of air-conducted speech stimuli was 40dB SL. Intensity level of SM-BCU was the most remarkably discriminable level. MEG recordings were performed with a 122-channel whole-head neuromagnetomater (Neuromag-122TM).

Clear MMFs were elicited by SM-BCU as well as air-conducted speech. The MMF amplitudes for SM-BCU were significantly smaller than those of air-conducted speech. This result suggests that duration-discrimination of modulated BCU is inferior to that of air-conducted speech. However, our result could objectively prove that prosodic changes of SM-BCU were discriminated likewise those of air-conducted speech.

**Mo-93 - Frequency Characteristics of Neuromagnetic Auditory Steady-State Response (ASSR) to sinusoidally amplitude-modulated chirp tones.**

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Auditory steady-state response (ASSR) is a neuronal electrical component recorded as a continuous sinusoidal signal synchronized to a modulation frequency (fm) of sounds. The ASSR reflects neuronal sensitivity to carrier frequency (fc) of sounds, offering an utility value as an objective index to evaluate the hearing ability per frequency. Earlier studies have shown that the amplitude of the ASSR decreases linearly in response to some discrete/fixed fc between 0.25 to 4 kHz. In this study, we aimed at capturing finer and wider frequency characteristics of the ASSR to facilitate its utility for, e.g., finer fitting of hearing aids and language/music cognitive research in which the effect of the frequencies above 4 kHz is not negligible. Sinusoidally amplitude-modulated (SAM) chirp tones, sweeping exponentially from 0.1 to 12.5 kHz, was presented binaurally. The sound intensity level was calibrated at near ear drums of each subject using a probe microphone and equalized throughout the frequency range by an inverse filtering method. Equivalent Current Dipoles (ECDs) of the ASSR for the SAM chirp tones were estimated. The contour of the ECD moment increased after the tone onset, reached to the peak at around 600 Hz, decreased sharply towards 3 kHz and further decreased gradually after 5 to 12.5 kHz. This global characteristics was consistent for several kinds of SAM chirp tones presented in durations of 5, 15 and 45 seconds, in ascending and descending directions, at sound intensity levels of 50, 60 and 70 dB SPL and at fm of 32, 40 and 51 Hz, and notably for the tones of discrete/fixed fc. However, the ECD moment did not fit well with the auditory threshold or the equal loudness curves in the lower frequency range, indicating that not only the loudness but also other neurophysiological factors such as the intensity growth factor advantageous for lower frequency range and the critical band width may contribute to define the frequency characteristics of the ASSR.

**Mo-94 - Using MEG to Investigate Habituation in Musical Contexts**

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Long-term exposure to music allows us to develop an implicit knowledge of musical syntax and this knowledge serves as the foundation of musical expectation. Expectation violations are an important part of musical experience and give music an ‘ebb and flow’ that keeps listeners interested. Regardless of how many times we listen to a song, when we are confronted with a syntax violation
in the song we can still pinpoint that irregularity. The early-right anterior negativity (ERAN) is related to a listener’s response to harmonic-syntax violations and peaks between 150ms and 250ms after stimulus onset. While numerous studies have investigated the ERAN, very few have addressed how it is affected by habituation. These studies rely on complex harmonic stimuli and focus on implicit response. The present study investigates the MEG-equivalent of the ERAN (mERAN) and how habituation modulates the strength of this response to simple melodies that are either syntactically well-formed, conforming to common-practice tonality (M1), or end with an out-of-key pitch (M2). Both musicians and non-musicians explicitly listened to M1/M2 numerous times and neural responses were recorded using MEG. Even with simplified stimuli, our results reliably replicate earlier findings based on more complex stimuli. Whereas previous studies on short-term habituation of the mERAN only look at changes in the violation condition, we comparatively analyze how responses to both M1 and M2 change over time by employing averages of the response over sequential sets of trials for the duration of the experiment. Such method also allows us to study how the relative relationship between M1 and M2 fluctuates, which effectively controls for fatigue and allows us to clearly show how the mERAN changes both independent of and in conjunction with normal responses. Preliminary results show that the difference between M1/M2 conditions sustains, contrasting with previous claims that ERAN response depreciates over time.

Mo-95 - Distributed source analysis of the P300 recorded with combined EEG-MEG and comparison with BOLD fMRI

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The neural generators underlying the P300 response are still being investigated. We tested how closely a distributed (MNE) estimate of the EEG-MEG measured P300 response, matched an fMRI estimate. We used a standard auditory oddball stimulus with frequent (1000Hz) and deviant (900Hz) tones (75ms dur). Subjects (n=12) pressed a button for deviant tones (14% of stimuli, 1274 stimuli/subject, ISI = 2s, jitter = 0.5s) and were studied with parallel whole head 122-channel MEG and 64-channel EEG and later with fMRI (TR=2, 1200 images, fixed-effects surface-based analysis with 10mm smoothing). The EEG-MEG were preprocessed with a bandpass filter (0.1-20Hz) and SSP. Distributed source analysis was performed using MNE (www.martinos.org/mne). Realistic-shaped boundary element head models were constructed using flash-sequence T1-weighted MRI. Noise-normalized MNE (dSPM) activity (deviant - nondeviant) was averaged across subjects (fixed-effects). fMRI results were highly consistent with previous work (1). Group fMRI, EEG and EEG-MEG results in the P300 latency range showed strong midline activity (cingulate). MEG midline activity was minimal, likely due to decreased SNR in this region (2). On the lateral surface, inferior frontal activity was observed with fMRI, MEG and EEG-MEG. The strongest lateral activity in both MEG and combined EEG-MEG was in and around the auditory cortex, whereas this area was less prominent in fMRI, possibly due to scanner noise. Strong MEG activity in and around auditory cortex is consistent with dipole source analyses of MEG data, which have focused on medial and superior temporal as well as parietal regions (3). Activity in cingulate cortex is in good agreement with previous EEG-fMRI findings (4). EEG and MEG show complementary strengths for the mapping of P300.


![Image](image-url)
Mo-96 - Investigation of optimal auditory signal for visually-challenged people using auditory evoked magnetic responses

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Songs of birds are used as an auditory signal for visually-challenged people in public spaces in Japan. The auditory signal informs them where stairs, toilets, and ticket gates are located. More than 40% of the visually-challenged people reported that the auditory signal is hard to identify. We tried to find the auditory signal that is easy to identify based on auditory evoked magnetic responses. Security guidelines for public transportation facility in Japan recommend that songs of birds with fundamental frequency between 100 and 2500 Hz and broader frequency bands should be used as auditory signals. We analyzed 32 different songs of birds and choose eight songs of birds (Halcyon coromanda, Cuculus poliocephalus, Eophona personata, Garrulus glandarius, Cuculus canorus (Cuckoo), Otus scops, Terpsiphone atrocaudata, Caprimulgus indicus) as stimuli for the experiment according to the guideline. The song of birds was presented at SPL of 60 dB in silent and simulated background noise in underground train stations (SPL of 58 dB). The duration of the song of birds was between 500 and 1000 ms. Ten normal-hearing participants took part in the experiment. Auditory-evoked fields were recorded using a 122-channel whole-head magnetometer in a magnetically shielded room. The most prominent response, N1m, which was found around 100 ms after the onset of the stimuli, was analyzed. The results indicated that the amplitudes of N1m showed maximum when the participants listened to the song of Cuckoo in both silent and simulated background noise conditions as shown in the figure. The song of Cuckoo have broader frequency components and the envelope changes dynamically. The findings suggest that the song of Cuckoo is a candidate for an auditory signal that is easy to identify.

![N1m amplitude for each song of bird](image)

Mo-97 - Auditory Processing Delays in Preschool Children with Fetal Alcohol Spectrum Disorders

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It is now recognized that children with prenatal alcohol exposure experience a wide-range of primary and secondary deficits. However, due to the stigma associated with drinking during pregnancy and the lack of biomarkers for children with prenatal alcohol exposure without facial dysmorphic features, it is difficult to identify children with the broader fetal alcohol spectrum disorders (FASD) categorization. Animal studies of prenatal alcohol exposure show deficits in basic sensory processing with greater deficits in younger animals. Therefore, we studied preschool children (3-6 years) with documented maternal alcohol use during pregnancy (N=10) relative to healthy controls (N = 15), to characterize basic auditory processing using MEG. We collected responses to simple auditory stimuli (1000 Hz tones) while the child watched a silent movie using the 306-channel Elekta Neuromag biomagnetometer. Continuous head position monitoring and post-processing movement compensation were employed using the Neuromag Maxfilter program. Source analysis was performed using the Calibrated-Start Spatio-Temporal (CSST) multi-dipole analysis method available.
in MRIVIEW. The MEG data were registered to the individual subject MRIs for source analysis and visualization purposes. The left and right auditory cortex sources (superior temporal gyrus - STG) were identified for each subject and the first two prominent peaks were characterized. We identified a systematic delay in both the 1st and 2nd peaks for both the left and right STG sources in the children with FASD relative to the healthy control children (p = 0.01). This delay is consistent with previous animal literature and also extends auditory brainstem response studies indicating delays in auditory brainstem processing. Auditory deficits are associated with deficits in language acquisition suggesting that basic auditory processing may provide an important marker for atypical brain development in FASD.

Mo-98 - Objective judgment of the noticed sound in mixed sounds using a coherence function between brain signal and sound envelope

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OBJECTIVE: In this study, we proposed a method to know the noticed sound in hearing mixed sounds using brain signals of a human subject. This method is applied to a BCI system to assist selective listening ability, for example, a hearing aid for elderly people with low speech discrimination. We demonstrate the effectiveness of this method by MEG experiments. METHODS: In our previous study, we showed a method to evaluate the listened sound using a coherence function between brain signals and sound envelope. We apply this method for this study. Two different sounds which are slightly different mixing ratio to the original one are used, and we compare the values of the function applying to these sounds. We assume that the sound which shows a higher value means to be near to the sound which the subject wants to hear. EXPERIMENTS: We performed experiments using a 160-channel whole head MEG system to confirm our assumption. We presented mixed sounds (female and male narration voices, 3min, monaural) to both ears of the subject by plastic tubes from outside of MSR. The subject was conducted to hear the one side of the narration. MEG data were recorded during sound presentation with 1000Hz sampling rate. After preprocessing (off-line filtering and down sampling), values of the coherence function were calculated. RESULTS: In 18 trials out of 20 trials, the remixed sounds which were slightly higher ratio of the noticed sounds showed higher evaluation value than the original sounds, the contrary remixed sounds showed lower value conversely (see attached figure). Especially in the left temporal area, the difference was clear. CONCLUSION: The results indicated that our assumption is correct and the proposed method using a coherence function is useful to judge the noticed sound in mixed sounds. We are planning to realize a pilot BCI system for hearing assistance with this method as next stage.

Mo-99 - A network analysis of phonemic perception in aphasic stroke patients using dynamic causal modelling

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We investigated differences in phonemic perception between normals and aphasics with left hemisphere stroke using a vowel mismatch paradigm, magnetoencephalography (MEG) and dynamic causal modeling (DCM). Subjects passively listened to stimuli in a CTF MEG scanner, where the standard was a consonant-vowel-consonant word, (/bart/). Three deviants were created by varying the frequency of the first and second formant of the vowel to produce D1 (/baart/), an acoustically different but within-class deviant, and D2 (/bart/) and D3 (/beat/), which were perceived as being in a different vowel category. The mismatch fields for both groups were fitted with four equivalent-current dipoles with sources in bilateral A1 and posterior STG (Schofield et al., 2009). The mismatch amplitudes for both groups showed a significant effect of deviancy (D3 ≥ D2 ≥ D1) and hemisphere (LH ≥ RH).

To investigate modulation of the connections of this four-source speech network as a function of phonemic deviancy (i.e., D3 and D2 vs. D1), we used DCM to estimate the average Bayesian models for both groups. The controls revealed a significant positive modulation of self-connections of bilateral A1 and STG while the aphasics showed a significant positive modulation of the self-connection of right A1 and the forward connections from A1 to STG bilaterally.

From a predictive coding point of view, self-connections represent sensitivity to (phonemic) input, while forward connections propagate (phonemic) prediction error from the lower to higher levels of a hierarchical system (Friston, 2010). Thus, in contrast to the normal participants, aphasics show:

a) reduced sensitivity to speech input,
b) impaired phonemic processing in left hemisphere,
c) impaired phonemic processing at the higher levels of the hierarchy, i.e. STG
d) an adaptation of phonemic function from left to right hemisphere, and
e) greater (phonemic) prediction error, which may underlie the neural bases of their impaired phonemic perception.

A comparison of average Bayesian models between controls and aphasics. Controls show greater significant modulation of the self-connections of left A1, left and right STG (red) and reduced modulation of the lateral connection from left to right A1.

Mo-100 - Altered alpha-activity related to impaired short-term memory of tone sequences in congenital amusia

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Congenital amusia is a lifelong disorder that prevents individuals from acquiring basic musical skills. The core deficit seems to be related to pitch perception and memory, and to functional and anatomical abnormalities in a fronto-temporal pathway, including auditory regions and inferior frontal cortex. Our study investigated the cerebral correlates of the short-term memory deficit in congenital amusia using behavioral measures and MEG. Amusics and matched controls performed two short-term memory tasks with melodies (a Contour Task (CT), and an easier Transposition Task (TT)). In both tasks, participants had to indicate whether sequences of six tones that were presented in pairs were the same or different. Behavioral data indicated that, in comparison to controls, amusics’ short-term memory was impaired for the CT, but not for the TT. The here presented analyses investigated the mechanisms underlying the maintenance of pitch information in short-term memory, notably by studying oscillatory brain responses.
during the delay period using a multitaper approach and beamforming. Given that alpha-activity (8-12 Hz) has been shown to reflect the disengagement of task-irrelevant regions in working memory tasks, we investigated whether alpha-modulation could be a marker related to the short-term memory deficits of amusics. For control participants, alpha-power was enhanced in left auditory and frontal regions and in bilateral temporo-occipital regions during the CT in comparison to the TT, suggesting a reduced excitability of these areas. This difference was not observed in primary auditory regions and less extended in the frontal regions of the right hemisphere, which are well known to be involved in music perception and memory. However, these task-related modulations were not observed in amusic participants - thus suggesting abnormal neurophysiological mechanisms of memory processing of musical material in amusia, notably in this distributed fronto-temporal network.

A. Stimuli used for different trials of the CT and the TT. B. Cortical meshes showing significant p-values for the comparison CT ≥ TT. C. Behavioral performance (Hits vs FAs): Square: average performance for the TT, Triangle: average performance for the CT

Mo-101 - Auditory evoked on-response and off-response investigated with magnetoencephalography

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Auditory evoked N100m off-response (off-N100m) fields, which emerges around 100 ms after the termination of stimulus, is remarkably similar to N100m on-response (on-N100m) in some characteristics. Whether on-100m and off-N100m fields are generated from the same or different neurons and what is their physiological function are still an arresting topic in the audiology research. In this study, a helmet-shaped magnetoencephalography (MEG) system was used to study the auditory evoked responses of on-100m and off-100m. The measurements were performed with monaural 250 Hz, 500 Hz, 1 kHz and 2 kHz pure tone stimulations of 80 dB sound pressure level persisting for 425 ms to the left or right ears of subjects. It was found that the equivalent current dipole (ECD) location of off-N100m was more interior than that of on-N100m, which suggest different neuron activities responsible for these two signals in the auditory cortex. The experimental data suggest that brain used different neurons in the auditory cortex to process the information for the onset and cessation of a sound. In response to abrupt auditory changes it was suggested that different physiological mechanisms are involved in on-N100m and off-N100m.

Mo-102 - The Transient-Reduction-of-Excitability (TREX) Model Accounts for the Dependence of the Auditory M100-Peak Amplitude on Stimulus Onset Interval, Stimulus Frequency, and Probability of Occurrence

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The peak amplitude of the M100 component of auditory event-related magnetic fields does not only depend on the stimulus onset interval (SOI), but also on the longer-term history of stimulation. It decreases with increasing SOI up to about 0.5 s and then increases with increasing SOI before saturating at long SOIs, but does so differently in different stimulation designs (e.g., block vs. random).

We proposed a parsimonious (TREX) model which can explain these observations (Zacharias et al., 2012, Psychophysiology, in press). It assumes a transient, temporally asymmetric, reduction in the excitability of a fraction of potentially excitable neurons. So far, we successfully applied the model to paradigms using identical tones (common frequency, duration, amplitude). In many studies, however, stimuli with different properties and different probabilities of occurrence have been used and have revealed that the M100-peak amplitude can also depend on these attributes. We conducted several experiments employing tones of either one frequency or two or more different frequencies, different probabilities of occurrence, and different SOIs. To model the M100-peak amplitudes measured in these experiments with our TREX model, we assume a tonotopic organization of the auditory cortex where the degree of overlap of responsive neuronal populations depends on the frequency separation of the tones. We show that with these plausible assumptions, the TREX model accounts well for our experimental findings. We are confident that our model will be more widely applicable.

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Mo-128 - Empirical Mode Decomposition Phase-Locking Analysis of Auditory Mismatch Negativity Data: An MEG study

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The study of functional connectivity between distant brain regions using M/EEG signals is widespread. Many studies have used coherence among sources, using wavelet or Fourier methods that are restrictive to a set of a priori basis functions. Other functional connectivity methods specifically target phase-locking (PL). Recently, Empirical Mode Decomposition Phase-Locking (EMDPL) has been proposed as a data-driven method that avoids the use of a priori basis functions. EMDPL extracts intrinsic, empirical oscillatory modes from the data and computes a PL measure between modes. In this work, we applied EMDPL to MEG auditory mismatch-negativity (MMN) data that had previously been submitted to a classical coherence analysis. Our goals were to prove the feasibility of this analysis and to use this new method to explore disease-related differences in connectivity.

Six adults with frontotemporal dementia (FTD) and 6 controls underwent MEG during a protocol consisting of 1800 standard and deviant tones (deviations by frequency, intensity, duration, location, silent gap) every 500ms. Source reconstruction was applied using BESA 5.2 (ECD analysis, 6 sources seeded within bilateral temporal, frontal and parietal cortex). EMDPL was applied on a trial-by-trial basis. Time-frequency spectra were built for each subject, for each trial type (standard and deviant) and for each relevant source pair.

The results show frequency and trial specific differences between controls and patients around the MMN latency (125-175 ms). For example, patients show higher frontal inter-hemispheric PL in the alpha band, for both standard and deviant tones, controls show higher left frontotemporal PL (alpha-band) for standard tones.

The main overall conclusions are: 1) this method is able to detect time and frequency specific differences between distant sources, 2) clinical pilot data indicate changes in connectivity patterns in subjects with frontotemporal dementia, versus healthy subjects.

Mo-129 - Canonical Granger Causality

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Fast recordings, such as those from magnetoencephalography (MEG) or electroencephalography (EEG), can be used to investigate causal functional relationships between different brain regions of interest (ROIs). Previous work has generally measured causality between pairs of time series rather than pairs of anatomical ROIs, each of which may exhibit more complex spatio-temporal behavior requiring two or more time series.

We describe a new scalar metric, canonical Granger Causality (CGC), between two sets of signals that is designed to elicit causality between the two ROIs represented by these sets. Our general approach is to measure Granger causality (GC) from a linear combination of one set of signals to a linear combination of the other. In a manner analogous to the canonical correlation, we define CGC as the maximum of the GC over all linear combinations within each set, as illustrated in the figure below. Thus, we extract from each
set of signals the component most strongly influencing the causal network between ROIs. Since our metric is invariant to scaling of the weights, we constrain the 2-norms of the weighting coefficients to be unity, equivalently, for each set the applied weights are constrained to the unit sphere.

We solve for the optimal weights using a gradient descent approach on the product of unit spheres, leveraging computational techniques from optimization on similar submanifolds. To compute GC between linear combinations of signals, we use standard autoregressive modeling and estimation techniques that lead to a closed form expression for the gradient of our cost function.

We compare CGC in Monte Carlo simulations to an alternative previously proposed multivariate causality measure, demonstrating that CGC has the potential to more accurately identify causality from short time records. We also demonstrate CGC in applications to MEG and intracranial electroencephalographic (icEEG) recordings from a human subject with epilepsy.

$$G_{z_{-1}} = \max_{\alpha, \beta} \frac{\text{Var}(\alpha^T \gamma_{z_1} [t] \beta^T \gamma_{z_1} [t-1])}{\text{Var}(\alpha^T \gamma_{z_1} [t] \beta^T \gamma_{z_1} [t-1])}$$

Canonical Granger causality between sets of signals.

Mo-130 - The Partial Phase Locking Value for Circular Gaussian Processes

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It is widely believed that large scale synchronization indicates coordination of neuronal assemblies during cognitive tasks. Presently, oscillatory coupling between neuronal sources is typically quantified by the sample phase locking value (PLV). One of the main limitations of PLV is that it cannot distinguish direct coupling from indirect coupling in a multidimensional network. Furthermore, PLV completely ignores any information contained in the amplitude of signals, even though the latter may contain information complementary to phase.

We investigate a partial phase locking value measure derived from the multivariate circular complex Gaussian (MCCG) model. The model has variables whose real and imaginary parts are, respectively, samples of a neurophysiological time series and its Hilbert transform. While amplitude and phase are independent for the univariate circular Gaussian, this is not true for the multivariate case. For this reason, we explore partial phase coupling in which interactions are conditioned on both the amplitude and phase of the other nodes in the network. This partial phase locking value is computed as the expected value of the phase difference between two sources conditioned on the amplitude and phase information within all other sources.

As expected, the MCCG model accurately reveals the phase coupling in simulated multivariate Gaussian data. We also show that the Gaussian model is, in some cases, a good fit to experimental electrophysiological data. Importantly, the model also performs well even when data do not conform to the Gaussian assumption: nonlinear multivariate Roessler simulations indicate that the MCCG model is more robust and requires fewer samples to quantify phase interactions than other multivariate phase modeling approaches. Interactions between depth electrode measurements of local field potentials from a macaque monkey study also shows that the partial PLV from MCCG model has reduced variance compared to other methods.
Mo-131 - Investigating the temporal dynamics of resting state connectivity with MEG

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The characterisation of resting state networks typically employs measures of functional connectivity that assume temporal stationarity, resulting in a temporal average of the underlying functional network configurations. Here we present a method based on the wavelet transform to explore the temporal dynamics of pairwise functional connectivity to investigate the extent to which these RSNs are driven by transient periods of synchronisation.

The time courses of neural activity at nodes of the default mode network, left/right lateral frontoparietal network, and the sensorimotor cortex were estimated using beamforming. Time-frequency representations of this activity were then computed via the wavelet transform. Functional connectivity was estimated by computing the correlation between the absolute value of the wavelet transformed time series within overlapping sliding windows, resulting in a time course of synchrony for each frequency band. A summary measure that describes the degree of transient synchronisation is the standard deviation of this time course, which we term the ‘metastability’.

To test that the observed metastability truly represents transient synchrony, null data that exhibited the same average connectivity as that found in the real data were generated using a Monte Carlo simulation. The 95th percentile from these simulations was then used to provide a threshold for significance.

To further test for the existence of transient synchronisations, a hidden Markov model (HMM) was fitted to the synchrony time course for each frequency band. This allows for the classification of transient synchronisation events and provides a further measure of metastability by comparing the model evidence for the two-state and one-state HMMs.

Figure 1 shows the metastability between four pairs of network nodes for a single subject. The frequencies at which significant metastability is observed are consistent with those found from studies using global connectivity measures.
Mo-132 - Comparison of brain networks during oscillatory and transient epileptic activity

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INTRODUCTION During presurgical evaluation, non-invasive source localization permits to map the generators and dynamics of interictal epileptic discharges. Most non invasive studies were performed on epileptic spikes. However, oscillatory activity is another important marker of epileptic activity, as observed on intracerebral EEG. A major question is whether networks involved in epileptic spikes and in epileptic oscillations differ, in terms of neuronal substrates and clinical relevance. Our goal was therefore to investigate the networks involved in oscillations and spikes, both in MEG and intracerebral EEG.

METHODS We performed a visual detection followed by classification based on morphology for spikes and frequency for oscillations. For MEG signal, we applied source localization (minimum norm followed by dipolar source estimation for time course estimation). We computed the cross correlation across the different regions identified, separately in MEG or SEEG. We identified significant cross-correlation links across regions, as well as leading regions in the network.

RESULTS We observed a high rate of concordance in region for all patients between networks involved in interictal spikes and in oscillations, with a concordance of regions of 70% for SEEG and 40% for MEG. Oscillatory networks were more extended than spike network in MEG, whereas it was the contrary for SEEG. In terms of leaders, there is 66% of concordance between spikes and oscillations in MEG and 100% in SEEG. The MEG networks involved some regions not explored in SEEG which could not be confirmed, but are an indication that MEG can recover large scale networks.

CONCLUSION MEG can recover large scale networks which are difficult to sample with intracerebral EEG. There is high similarity between regions involved in spike and oscillatory discharges. Further investigation will be necessary to assess the clinical relevance of the additional regions observed in MEG for oscillations.

Mo-133 - Variable Bandwidth Filtering of Gamma for Improved Sensitivity of Cross-Frequency Coupling Metrics

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There is increasing interest in examining cross-frequency coupling (CFC) between groups of oscillating neurons. Most CFC studies use a filter to isolate high frequency gamma band activity and examine how its amplitude is modulated by lower frequency brain activity. This study does not focus on the CFC metric, but rather the filtering used to isolate a high frequency oscillation and compute its amplitude envelope. Improper filter design can destroy amplitude modulation and create false negative CFC measures. Amplitude modulation of a signal is mathematically equivalent to adding sideband signals with frequencies fc+fm and fc-fm to the carrier signal,
where \( fc \) is the high frequency gamma oscillation and \( fm \) is the modulation frequency. Many prior publications have used a fixed bandwidth filter to isolate gamma oscillations. This study demonstrates analytically and with simulations that a fixed-bandwidth filter cannot detect CFC if the bandwidth of the filter is less than the modulation frequency. To improve the sensitivity of CFC metrics, a variable bandwidth filter mechanism is proposed. The variable bandwidth filter is designed to have a band-pass of \((fc-fm)\) to \((fc+fm)\), that is, a bandwidth of \(2fm\) which includes the sidebands. Thus, the bandwidth is variable across the modulation frequency dimension of a comodulogram. Simulated time series data were created with theta-gamma, alpha-gamma, and beta-gamma phase-amplitude coupling. Results indicate that a fixed 4Hz bandwidth high-frequency filter can detect theta-gamma CFC, however fails to detect CFC of amplitude modulations above the theta band. The variable bandwidth approach presented in this paper is capable of detecting CFC of modulations above the theta band. This result is demonstrated using two different CFC metrics proposed in the literature. In summary, when measuring CFC, a variable bandwidth method of filtering an amplitude modulated signal is proposed to preserve amplitude modulation and thus CFC.

**Mo-146 - Extent of electrocardiogram related wire artefact in LFP-MEG coherence of dystonia and Parkinson’s patients**

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MEG recordings of dystonia and Parkinson’s patients with externalized deep brain stimulation wires can be severely affected by the weak permanent magnetization of the wires, which leads to the cardiac cycle artefact (CCA) in the MEG data through the pulsation moving the wires. Wires manufactured from truly non-magnetic materials or assessing source space signals through a beamforming approach are possible solutions. Both approaches require advanced procedures and therefore questions related to the adverse effects of the CCA still need attention. In which frequency band is the CCA artefact influencing coherence? What is the mathematical origin for CCA related patterns in the coherence as the electrocardiogram (ECG) is normally not found in local field potential (LFP) signals? Is an efficient removal of the CCA possible in MEG sensor space?

In a first step, a time domain averaged CCA (tCCA) is calculated using a simultaneously recorded ECG as trigger. This is compared to a frequency domain CCA (fCCA) defined as the coherence between ECG and MEG signals. Both are subjected to PCA and the highest variance PCA subspace of order 6 is removed from the MEG data, i.e., a signal space projection (SSP) is performed. Then, LFP-MEG coherence patterns and overall power are compared before and after SSP.

It is found that coherence in the higher alpha-range for dystonic patients and in the beta-range for dystonia and Parkinson’s patients is not severely affected by the CCA. On the downside, coherence below 10 Hz has to be interpreted very carefully and discarded in individual cases. The mathematical origin of strong coherence patterns below 10 Hz is still unknown.
Mo-147 - Resting state brain dynamics and its transients: a combined TMS-EEG study

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Resting state dynamics has been studied primarily with fMRI aiming at understanding the ultraslow coherent fluctuations (<0.1 Hz) of the BOLD signal. Various proposals have been made regarding the underlying mechanisms generating these oscillations (see Deco, Jirsa, McIntosh 2011), but most of them claim that the large scale brain network dynamics operates close to a transition, that is the resting state dynamics is critical. Implications of this claim are in particular remarkable regarding the meaning of the resting state in reference to information processing: criticality means that the brain operates close to a threshold at which new functionally relevant brain states can be easily created.

If the resting state dynamics of the brain is indeed critical, then there will exist certain subnetworks that express themselves stronger and on a slower time scale than other subnetworks. This behavior is at the core of the local center manifold theorem in dynamic system theory. Here, we investigate the resting state brain dynamics by inducing a direct perturbation with Transcranial Magnetic Stimulation (TMS), while simultaneously recording the EEG. We stimulated two brain regions (fig 1a): the medial prefrontal cortex (PF), supposed to be involved in the alpha rhythm generation, and the primary motor cortex (M1), as a control condition. 8 subjects were instructed to think of nothing and let their thoughts flow freely. On-line processing of the EEG triggered TMS only when alpha bursts appeared close to the stimulation site.

As shown in figure 1b, the ERP differed for both stimulation sites, with marked P50, N100 and P200. Moreover, the results indicate that PF stimulations evoke alpha rhythms in PF that are time and phase locked to the stimulus, whereas M1 stimulations induce alpha responses that are not strictly time locked. Indeed it can observed in the trial-averaged ERP profiles around 400 ms with an alpha wave propagating through the concerned resting state network.

Figure 1: a) Superposition of all stimuli applied over PF and M1. Brown colored needles show the coil location and orange dots indicate the sites of the maximum electrical fields in the cortex, whereas and the arrows the direction of the currents. b) Topo

Mo-148 - Beamforming (in)sensitivity to correlated sources as a connectivity diagnostic

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Beamformers have proven successful in MEG source analysis due to their robustness against external noise sources (1,2,3). However, they yield reduced signal when there are multiple correlated sources: we call this beamforming attenuation (BA). As BA is proportional to correlation between sources, we suggest it can be positively interpreted as diagnostic of source coherence. We offer a method to test BA with synthetic aperture magnetometry (SAM).

Sensor weights with respect to a SAM virtual sensor are functions of the lead field L and sensor covariance matrix C, high correlations in C lead to BA. Determining C at high frequencies where sources are unlikely to be in-phase minimizes this influence, thus we estimate BA in a time-window t for a frequency band of interest f by subtracting the total power in $<\mathbf{t},\mathbf{f}\geq$ with weights set using a band-pass at f from power where weights are set using a (less coherent) control frequency band.

We tested this method in a word-listening paradigm (4). Subjects (adults N=16, children with, N=3, and without, N=3, ASD) passively listened to words while neuromagnetic signals were recorded with 275 gradiometers (VSM Systems) with no on-line filters. We focused on event-related desynchronization (ERD) spanning f = 5-15Hz at time t = .4-.8s after word onset in a left auditory cortex voxel. C was determined using baseline data to avoid effects time-locked to stimulation.

Sample time-frequency plots are shown in Fig A. There was notable BA in all three groups (Fig B): power in the interval of interest (black box) where C was based on 5-15Hz data was significantly reduced compared to when C was based on 30-55Hz data, e.g. Adults t(15) = 3.2, p < .01.

Notably, our approach requires no prior hypotheses about what regions may be connected with the target voxel, which may be of use
in testing the role of coherence in neural impairments.


(A) Time-frequency plots for one sample group with the covariance matrix C tuned activity at 30-55Hz (top) or 5-15Hz (bottom).
(B) Average beamformer attenuation (BA) in each group, lines indicate 95% confidence intervals.

Mo-149 - Higher order spectral analysis for cross-frequency connectivity estimation in EEG/MEG

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The aim of functional connectivity is to describe the complex mechanisms through which different brain regions interact to integrate and process information. The detection of linear - i.e. at the same frequency - and cross-frequency coupling between rhythms of neuronal electrical activity plays a crucial role in understanding such mechanisms. Spectral analysis of EEG and MEG signals is a suitable technique for the characterization of brain functional connectivity in the frequency domain.

In this study, we present a novel approach to the higher-order (third) spectral analysis of EEG/MEG signals for the detection of cross-frequency interactions between neuronal oscillations. We identify interactions by evaluating an antisymmetric combination of cross-bispectra between pairs of EEG/MEG recordings that, in analogy with linear interaction estimate based on the imaginary part of coherence (1), exclusively depends on true interacting sources. Hence, this method provides a robust estimator for interaction that rejects signal arising from non interacting sources.

Furthermore, we can project signal interaction onto brain space by using a fit-based procedure with respect to a specific model. Therefore, the interacting system can be localized and different sources can be distinguished according to a minimum overlap component criterion (MOCA) (2).

We also present an application of this method to the detection of alpha-beta interaction in EEG recordings during resting state activity.

References:
Mo-150 - Cortical rhythms and communication associated with perceived exertion during lift execution

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A previous EEG study supported the hypothesis that the perception of effort arises from the central motor system, with a positive correlation between the amplitude of the movement related potential and the effort ratings (de Morree et al., 2012). The present study aims to extend previous findings to cortical rhythms, in particular to the relation between the perception of effort and the cortical power in the alpha and beta bands. In addition, communication across cortical areas was investigated with Granger causality.

Sixteen healthy right-handed men performed unilateral dynamic elbow flexions to lift a light (20\% one repetition maximum 1RM) and a heavier (35\% 1RM) weight with an eccentrically pre-fatigued (FT) and non-fatigued (NFT) arm while rating the perceived effort (RPE). Biceps brachii EMG, and 62-channel EEG were recorded during exercise execution. Participants performed 4 randomized sessions of 50 flexions (Light NFT, Heavy NFT, Light FT, Heavy FT) of about 2 s duration each, with 6 s rest in between. For each session, the onsets of biceps EMG bursts were automatically identified and used to partition the EEG recordings into three 1800 ms segments: before, during, and after lifts execution. Based on the spatial distribution of power in the alpha and beta bands, 10 out of 62 electrodes were selected to represent cerebral activity. For each condition and for each temporal segment, spectral analysis and Granger causality were performed. The values of the parameters for Granger analysis were predetermined with a built-model with the same number of sources and samples.

Power spectral analysis showed an increase in beta band activity during movement in the Heavy FT condition as compared to the other conditions, revealing a relation between perception of effort and cortical rhythms. Granger analysis revealed a change in connectivity patterns across segments before, during, and after movement.

de Morree HM et al. 2012 Psychophysiology (under review)
Mo-151 - Temporal topological transformation in dynamic MEG-derived graph sequences

Mark Daley

The primary research focus in the application of tools from graph theory to neuroimaging-derived graphs has so far been on static graphs, however, it is an obvious extension to begin investigating dynamic networks in which the topology of the network itself reconfigures in time. The temporal resolution of MEG makes MEG-derived data a good candidate for investigating the dynamics of graph topology in the human brain. First steps have already been taken in this direction by, e.g., (Nicol et al. 2012). Here we considered the topological evolution of graphs at a finer scale using differing approaches to graph generation.

Preprocessed MEG data were filtered into frequency bands of interest and analyzed separately. For each trial, a sliding window was moved over the raw data and for each time window the timeseries from each MEG channel, within that window, were pairwise compared with the Phase Locking Index (Stam 2007). The PLI matrices were thresholded using a new technique based on Random Matrix Theory and treated as adjacency matrices for graph construction. The resulting graph sequence was subjected to three types of analysis: whole-graph, per-vertex and a deeper analysis in which we looked for ‘motif dynamics’.

Preliminary results on simple sensory task MEG data suggest that some whole-graph metrics (in particular, mean centrality metrics) are sensitive to MEG dynamics derived from different task states. To resolve topological evolution on a finer scale we considered also the change in per-vertex metrics which proved better able to separate task states. Having established the existence of fine-scale topological dynamics, the more interesting question is one of the details. Our first step towards answering this was to follow the structural evolution of motifs in the graph which we showed to be highly influenced by task particulars.

These temporally-aware topological methods provide new tools for investigating the dynamics of brain functional networks.

Mo-174 - Complexity in the resting state MEG signal: An independent components analysis

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The resting brain exhibits coherent of activity in multiple distinct, reliable networks. In fMRI, ICA is a commonly used tool to decompose resting activity into multiple networks. While ICA has been applied to extract networks from Hilbert envelopes of band-limited power, here we investigate components derived from a time series of a measure of complexity.

Resting (eyes-closed) MEG scans were acquired for 240 seconds in 19 healthy subjects using a CTF 275-channel MEG (1200Hz). A time series was calculated with an LCMV beamformer (SAM), and a complexity time series was calculated using a rank vector entropy (RVE) algorithm as in the submitted abstract ‘Spatiotemporal Source Complexity Imaging.’ Time series data was concatenated across subjects, and ICA was performed using the Infomax algorithm in MELODIC (FMRIB, UK) to extract 25 components. Images
were thresholded using a Gaussian/gamma mixture model approach, which provides a reasonable fit to our data. Dual regression was used to derive individual subject maps for each component. Resting state RVE was characterized by sparse transient decreases in entropy. Group ICA of the data resulted in primarily single-cluster modes, which could be grouped in bilateral pairs, although some modes indicated long-range coupling. Single subject modes frequently exhibited long range coherence. Within-component regions, and between component bilateral regions exhibited a high degree of correlation for most time points, although correlations were transient in nature. In this analysis, discrete regions which were significant sources of complexity emerged. Sources with bilateral clusters and overlapping components may indicate network-like structure in generation of neural complexity. The pattern of distributed activity is not likely to reflect spillover from lead fields. Future work will involve clustering of components into networks based upon degree of transient correlation.

Top: One independent component exhibiting long range correlations, group and individual maps and individual time series and transient correlation. Bottom: Two paired group components and individual maps, individual time series and transient correlation.

Mo-175 - Estimating neural interactions delays using transfer entropy

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Tracking the flow of information within the brain can help to understand the mechanisms and circuitry behind neuronal processing. Transfer entropy (TE) is an information theoretic measure that detects information flow by implementing Wiener notion of observational causality. This states that a time series X is called causal to a second Y, if knowledge about the past of X and Y together allows one to predict the future of Y better than knowledge about the past of Y alone. While TE captures the strength and direction of predictive information flow, it does not readily estimate interaction delays which are essential variables for theories of coordinated neuronal activity. Here, we present an extension of TE that respects Wiener principle of causality and allows for a precise estimation of interaction delays. We validate our approach based on simulated and real data (LFP, MEG). First, we analyzed the detection of interaction delays in non-linearly coupled stochastic systems. The proposed extension of TE was able to correctly estimate the interaction delays in the case of both single and multiple delays. In addition, we studied the coupling in two cases of non-linearly coupled chaotic systems. The new approach was also able to detect the interaction delays associated with bidirectional coupling and feedback loops. We also applied the new approach to estimate the interaction delays between measures of local field potentials (LFP) recorded from the retina and the optic tectum of the turtle (Pseudemys scripta elegans) where a neuronal one-way connection is likely present. Finally, we analyzed the interaction delays between the reconstructed sources of MEG activity during a perceptual closure task (Mooney faces detection). In summary, we present and validate a novel methodology that allows to estimate the interaction delays between brain areas.
Mo-176 - Multivariate Phase-Amplitude Coupling in a Curvilinear Coordinate

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The phase-amplitude coupling (PAC) between low- and high-rhythms has become an effective measure in the analysis of neuronal signal synchrony indicating a mechanism for effective communication between neuronal populations. This phenomenon has been widely reported in animal and human studies. Reports of PAC are also now emerging from human EEG and MEG signals (e.g., (1), (2) and the references therein).

Several various methods have proposed and employed to measure the PAC (1), (2). However, all these methods are inherently bi-variate, that is, these methods investigate the coupling between one signals from one region and one signal from another region. Considering the neuronal data are in reality multivariate (e.g., LFP from multiples sites or multi channel MEG), these approaches may therefore lose some information.

In this study, first we show that the majority of the available methods analyse the data in the polar coordinate in which the location of each point is identified by one phase and one amplitude. We then present a curvilinear coordinate in which the location of each point is identified by n phases and m amplitudes. Thus, we are able to analyse the coupling between n phases and m amplitudes. Special cases of the proposed curvilinear coordinate are polar (n=1, m=1), spherical(n=2, m=1) and cylindrical (n=1, m=2) coordinates.

We show using some simulation experiments that, as we expected, the accuracy of the PAC operating on multivariate signals is superior to that which operates only on bivariate data. As an example of the application of the method, we present the coupling between signals of two nuclei (ventral posterolateral (VPL) and periaqueductal gray (PAG) nucleus), which were recorded from electrodes implanted in chronic pain patients.

(1) W.D. Penny et al., 'Testing for nested oscillation,' J. of Neuroscience Methods, 2008.

Mo-177 - Berger interactions

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It has been known since the first experiments with human EEG recordings that closing the eyes alters the ongoing neuronal activity, most notably by enhancing so-called alpha-band EEG oscillations in the frequencies around 10 Hz in the parieto-occipital regions. These findings gave rise to the idea of relating the increased amplitudes of alpha-band oscillations to ‘idling’, or non-functional cortical states. These oscillations are generated locally and synchronize activity in visual cortices. However, brain activity may not be considered only locally, but extended interactions between cortical regions are an integral part of proper brain function. Yet, despite recent advances in analysing ongoing cortical activities, it is presently unclear what kind of changes in connectivity take place during the shift between eyes closed and eyes open rest.

In this study, we measure resting subjects with MEG. During the measurement, the subjects open and close their eyes with a period of two minutes. We estimate ongoing cortical activity with realistic individual inverse models and compute inter-areal interactions between all pairs of cortical regions. We then apply machine learning methods to assess the changes in cortical interactions that are associated with the shifts between eyes-open and eyes-closed states. These multivariate statistical methods are sensitive to patterns and thus allow inspection of global connectivity changes, instead of focusing on individual inter-areal interactions. Furthermore, this approach removes the problem of multiple statistical comparisons, which otherwise brings considerable uncertainty to the analysis.

Mo-178 - Cross-Frequency Decomposition: A novel technique for studying interactions between neuronal oscillations with different frequencies
Neuronal synchronization has been hypothesized to be a mechanism allowing efficient communication between the neurons. In addition to interactions typically calculated at the same frequency range, phase synchronization between different frequency ranges has been demonstrated recently. Here, we present a novel method for the extraction of neuronal components showing cross-frequency phase synchronization. The method allows a compact representation of the sets of interacting components without the need to perform inverse modeling. It can be applied for the detection of phase interactions between components with frequencies $f_1$ and $f_2$, where $f_2 = rf_1$ and $r$ is some integer. This class of interactions includes alpha:beta and alpha:gamma synchronization frequently observed in EEG and MEG recordings. We refer to this method as Cross-Frequency Decomposition (CFD), which consists of the following steps: a) extraction of $f_1$-oscillations with the spatio-spectral decomposition algorithm (SSD), b) frequency modification of the $f_1$-oscillations obtained with SSD, and c) finding $f_2$-oscillations synchronous with $f_1$-oscillations using least-squares estimation. Our simulations showed that CFD was capable of recovering interacting components even when the signal-to-noise ratio was as low as 0.01. An application of CFD to real EEG data demonstrated that cross-frequency phase synchronization between alpha and beta oscillations can originate from the same or remote neuronal groups. While interactions occurring at the same spatial location can potentially indicate quasi-sinusoidal waveform of neuronal oscillations, synchronization between spatially remote populations is likely to indicate genuine neurophysiological interactions between oscillations with different frequency content.

Mo-179 - Added value of connectivity analysis on brain waveforms in EEG source reconstruction to detect the epileptic driver during seizures.

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During seizures rhythmic epileptic activity is noticed in the EEG. This activity arises from a functionally connected brain network, in which several brain areas generate epileptic activity. EEG source reconstruction followed by connectivity analysis allows us to analyze the network’s dynamics. We simulated 2000, 5s long ictal EEG-epochs of 512Hz using a finite difference method based forward model. The brain tissue in the model was divided into 256 patches. For each simulation, normal brain functioning was modeled as 1/f-noise in all the patches. To mimic the epileptic network, we superimposed 10Hz ictal rhythmic activity with a SNR of 20dB in 3 randomly chosen patches. In 2 patches the rhythmic activity was delayed randomly from 1 up to 10 samples, so one of the patches in the network was the driver. The simulated brain waveforms were reconstructed using the Multiple Sparse Priors algorithm in the Statistical Parametric Mapping toolbox. Each reconstruction led to a high number of active patches. The 20 patches with the highest activity were clustered into 3 groups. Out of each group the patch with the highest activity was selected, leading to 3 patches with their corresponding brain waveforms.

The epileptic driver behind the seizure was selected using (i) energy, the patch with the highest activity and (ii) connectivity, the patch with the highest number of out-going connections based on the full frequency Adaptive Directed Transfer Function. The method is explained in Fig.1A for 1 simulation. The connectivity-based selection clearly outperforms the energy-based selection and can localize the deep brain source as being the driver behind this seizure. In Fig.1B the results of the 2000 simulations are shown. We prove that the estimation of the driver behind seizures benefits from incorporating connectivity analysis into EEG source localization. This method may improve the localization of the ictal onset zone during the presurgical evaluation in epileptic patients.
Panel A describes the method, panel B shows the resulting cumulative distribution of the localization error of the 2000 simulations. The connectivity-based approach clearly outperforms the energy-based approach.

**Mo-180 - Cross-term deprived covariance approach as an extension of DICS for detection of cross-frequency coupling**

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Cross-frequency synchronization in MEG and EEG data has been found in many experimental paradigms and is currently under active study. Unfortunately spatially and temporally precise analysis available only in a limited number of cases corresponding to neurological patients with implanted cortical grids. In order to provide the flexibility in experimental designs and allow for more specific studies tools for analysis of such non-linear synchronizations are to be developed. Instrumentally, MEG is a unique technology that allows for mapping of cortical activations with very high temporal resolution. Solving inverse problem by means of adaptive beamformers and the use of sufficiently accurate forward models allow for reasonable (0.5 cm) spatial resolution. The time-frequency representation of MEG signals is natural and captures the nature of MEG observed cortical activity as consisting of short time narrow-band bursts.

In this work our goal was to combine the above and develop a signal processing method for identification of the cortical spatial structure of cross-frequency coupling between the oscillations in the two time-delayed non-overlapping frequency windows. Our method is a statistical test contrasting the results of adaptive beamformer based inverse mapping obtained using the original and cross-term deprived time-frequency domain data covariance matrices by calculating the ratio of the two inverse values. We use multiple comparison corrected randomization statistical tests for identification of significant source space coupling. Application of the method to an event-related MEG dataset from a single subject (imagined hand rotation) yielded plausible results with interacting pairs falling into physiologically plausible cortical sites. We observed beta-gamma coupling between sensorimotor-frontal and parietal-occipital regions, consistent with published signal space analysis. One of the pairs of non-linearly coupled sites is shown in Figure 1.
Mo-181 - Modulations of cross-frequency phase-amplitude coupling during visuomotor control: a MEG study

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Cross-frequency phase-amplitude coupling (PAC) is hypothesized to play a functional role in information processing in local neuronal populations in a range of cognitive tasks (Jensen & Colgin, TICS, 2007, Canolty & Knight, TICS, 2010, Axmacher et al., PNAS, 2010). Task-related changes in cross-frequency PAC have been reported using invasive and non-invasive recordings and have been applied to test for local as well as long-range cross-frequency interactions (Tort et al., PNAS, 2008). The goal of the current study was to examine the role of PAC in the brain networks involved in visuomotor control. To this end, we estimated source-level current densities from continuous MEG data using a minimum-norm inverse solution and extracted at each cortical node the signal amplitude and phase at the frequencies of interest using Hilbert transforms. Prior to PAC analysis, we first used simulations to compare the performance of six different implementations of PAC estimation methods with an ROC analysis. The Kullback-Leibler (K-L) divergence technique (Tort et al., J. Neurophysiol., 2010) had the best performance in detecting simulated coupling modulations and was the most robust in the presence of various noise conditions. The application of the K-L divergence to the MEG visuomotor data revealed a strong task-related increase (visuomotor control vs. rest) in coupling between the phase of delta (2-5 Hz) and the amplitude of high-gamma (60-90 Hz) in the occipital and parietal lobes as well as in the cerebellum. Interestingly, when comparing PAC in trials recorded in the first sessions to PAC recorded towards the end of the experiment we found a significant increase in delta-high-gamma PAC over time in the superior parietal lobule, possibly reflecting visuomotor adaptation and learning processes. Our results are discussed in the context of the functional role of cross-frequency brain mechanisms and are compared to classical task-related power modulations.

Mo-182 - Estimates of functional connectivity using beamformer techniques: are they reliable?

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In MEG and EEG functional connectivity (FC) can be easily estimated in sensor space using pair wise sensor time series. This represents a simpler scenario than estimates of connectivity in source space as the nodes are well defined. Often sensors are grouped based on the anatomical regions they cover and conclusions are drawn about functional interactions between such regions. While such techniques have been particularly useful in providing some information on FC, particularly in the context of comparing subjects with neurological and pathological disorders to healthy controls, they remain quite limited in their ability to provide detailed information about brain function in general, and about the location of the disorder when patients are considered. Additionally, shallow
sources generally make larger contributions to sensor signals than deeper ones, and hence, such measures carry little information about deeper sources of interest. Although FC in source space avoids this problem, the accuracy of such estimates is highly limited by the ability to reconstruct multiple sources simultaneously. Most inverse models that are widely in use are able to reconstruct a small number of sources, making it difficult to obtain a detailed measure of FC in source space. Here we focus on one such modality, the beamformer, and use simulations and real data to assess its ability to provide information on FC in source space. In particular, we consider two main drawbacks to beamformer techniques and how they influence estimates of FC: susceptibility to temporal correlations and leakage. We conclude that while synchronization measures that are less sensitive to volume conduction, such as phase lag index and the imaginary part of coherence, are able to reduce the influence of leakage on connectivity estimates, the ability of beamformers to provide accurate connectivity information is quite limited.

**Mo-183 - Entropy Imaging Identifies Source Activity Independent of Oscillatory Power Variation**

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Source waveform morphology and complexity can change without an accompanying change in source power. The question arises as to whether one can identify significant patterns of activation that are independent of frequency-based changes indexed by source power. To address this, we compared spatiotemporal images of rank vector entropy (RVE) with that of beta-band power changes in a working memory (N-back) study. RVE is a non-parametric symbolic entropy measuring the time-varying complexity of a waveform (as outlined in the accompanying abstract, 'Spatiotemporal Source Complexity Imaging').

N-back data were acquired using a CTF 275-channel MEG (DC 4 150 Hz, 600 sample rate). Subjects were instructed to respond to the numbers displayed by pressing 1 of 4 buttons. Six blocks of 11 trials each of 0-back, 1-back, and 2-back were presented, with instructions at the start of each block. A scalar LCMV beamformer (SAM) estimated the source time-series on a 5 mm grid within the head, and the complexity time-series computed from that using RVE. Spatiotemporal images were derived by comparing 2-back to 0-back trials using a Mann-Whitney U-test of either the RVE (4 - 150 Hz) or power (14 - 30 Hz) in a window of +/- 250 ms from the response.

We identified several significant sources using RVE imaging (p < 0.01) for which there was no concurrent change in beta power. In the figure, regions where 2-back exceeds 0-back (in RVE or power) are shown in red, and in blue for the opposite comparison. It has been shown that locations showing a reduction in beta-band power (ERD) correlate with BOLD fMRI activation. The significance of the direction of change for RVE is not known for this protocol, although auditory evoked responses show a decrease in RVE corresponding to the N100m. Presumably the entropy change reflects localized involvement of information flow or processing.

Rank vector entropy (top images and time-series) demonstrates dorsolateral prefrontal activation that is independent of changes in beta band source power for comparison of 2-back vs. 0-back condition.
Mo-184 - Effectiveness of sparse Bayesian algorithm for MVAR coefficient estimation in MEG/EEG source-space causality analysis

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Most popular measures in estimating causal relationships among brain activities are Granger-causality-based measures, which rely on accurate modeling of the multivariate vector auto-regressive (MVAR) process of the source time series. Since, in general, the causality analysis is applied to non-averaged data, the estimated source time series inevitably contains large influence of background brain activity, which is often referred to as the brain noise. However, since the MVAR modeling generally does not take such interference into account, the existence of the interference may cause significant amount of errors in the estimated MVAR coefficients, leading to completely wrong false-positive causality relationships. One approach to reduce those errors is to impose a sparsity constraint when estimating the MVAR coefficients. The key assumption here is that true brain interactions cause small number of MVAR coefficients to have non-zero values and most of MVAR coefficients remain to be zero. If this is true, the sparsity constraint should prevent most MVAR coefficients to have erroneous non-zero values due to the background interference. This paper employs computer experiments to show the effectiveness of a sparse Bayesian algorithm for the MVAR coefficient estimation. Results of our computer experiments show that the interference affects the conventional least-squares method in a very severe manner. It produces large false-positive results, unless the signal-to-interference ratio is extremely high. On the other hand, the sparse Bayesian method is relatively insensitive to the existence of interference, although this robustness is attained at the sacrifice of the detectability of true causal relationships.

Mo-185 - Removal of spurious coherence in MEG source-space coherence analysis

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In source-space coherence analysis, a typical procedure involves first setting a reference point, called the seed point, and computing the coherence between the time courses from the seed point and another voxel’s location, referred to as the target location. By scanning through all target locations in a brain, a three-dimensional mapping of source coherence, namely a source coherence image, with respect to the seed location can be obtained. A serious problem in source-coherence imaging arises from the spurious coherence caused by the leakage of an inverse algorithm, and such leakages are more or less inevitable in any inverse algorithm. One representative ramification of this spurious coherence is an artifactual large peak around the seed voxel, called seed blur, in the resulting coherence image. Quite often, the seed blur dominates the resultant coherence images, and obscures important details of the brain interactions. Examples of the seed blur are shown in our computer simulations and experiments using resting-state MEG data. To remove such spurious coherence, this paper proposes the use of the imaginary part of coherence, which is called the imaginary coherence. The use of imaginary coherence was originally proposed by Nolte et al.(1) to remove the spurious coherence caused by the volume conduction in EEG sensor-space coherence analysis. The present paper extends their sensor-space analysis of imaginary coherence to source-space coherence analysis, and presents a detailed theoretical analysis which explains how the use of imaginary coherence leads to the removal of the spurious coherence caused by the leakage of source imaging algorithms. The validity of our analysis is then demonstrated by our computer simulation and by experiments using resting-state MEG data.

Reference

Mo-186 - Detection of large-scale networks in EEG and comparison with fMRI

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Nowadays, spatial independent component analysis (sICA), a blind source separation technique, is commonly used to extract large-scale functional networks in fMRI. Assuming that the power of electroencephalography (EEG) signal in several frequency bands is correlated with the blood oxygen level-dependant (BOLD) signal, a method using sICA has been developed to detect large-scale functional networks in EEG.

We acquired separately EEG and fMRI data from fifteen healthy subjects in resting states conditions. EEG data was preprocessed and reconstructed on the grey-white matter interface (G-WMI) of each subject using a minimum norm method. We computed the power of the reconstructed signal in several frequency band (theta, alpha, beta, gamma) and processed a sICA on the concatenated data. The output gave us about one hundred components for each subject. Each component is a combina-
tion of a spatial map on the G-WMI of the subject and a time course for each frequency band.

We performed a group analysis by interpolating the spatial maps on a common template. As a last step, a hierarchical clustering algorithm, which minimizes the inter-class similarity, regrouped the components and selected the resulting classes according to their representativity and unicity in the population. We assumed that this classes represent the networks of interest.

We compared these results with the functional networks estimated in fMRI from the same subjects using a Voronoï-based interpolation to project them onto the template used in EEG. The networks revealed in EEG showed a much more focal spatial pattern than the fMRI networks. This disparity comes from the very high temporal resolution of the EEG which allows a more granular classification of the data. We then performed a spatial linear regression between the networks found in EEG and in fMRI. The very good match between the EEG networks combination and the fMRI networks shows that both modalities share the same information structure.

Spatial linear regression between the EEG networks and the fMRI motor network. Results for the visual and default mode networks.

Mo-187 - Disrupted spectral and directional cortical connectivity explain impairment in an object motion discrimination task during egomotion in a patient with a left occipital lobe infarct

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To investigate the neural dynamics underlying object motion detection during egomotion, we used psychophysics and MEG with a task of object motion discrimination by a moving observer. We studied six healthy subjects (HS) and patient PF with an infarct involving the left occipital-temporal cortex. In one of the two experimental conditions only visual information was available (VS task) while in the other an auditory cue moving in depth and co-localized with the target was also present (VAS task). This cue significantly helped improving performance in HS when its direction was congruent with the object motion. However, PF was severely impaired on both conditions of this task. Anatomically constrained source estimates showed same active cortical areas in both HS and the patient. Dynamic Granger Causality (DGC) computed for the stimulus presentation period in the VS task, shows that MT sends motion information to MPFC, phase-locking values (PLV) showed communication concentrated to the alpha band, which may support attentional functions, and it may also have a role in the suppression of task-irrelevant neuronal processing. In the VAS task, MT and auditory cortex (aud) send information in parallel to STP. PLV between STP and aud indicates strong alpha and beta-band coherence and communication. This may be related to attention (alpha band) and decision formation while subjects are performing the task. In PF, who is impaired on both tasks, the spatio-temporal networks underlying these tasks are disrupted, in spite of the fact that the lesion does not involve any of the cortical areas critical for task performance. Also MPFC-STP beta-band coherence may be supporting the poor performance, beta-band oscillations are not present in PF. Notably, in PF, MPFC does not connect back to aud and STP in DGC, which seen also in PLV as a loss of alpha-band connectivity with MPFC.

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We applied this approach to extract redundancy features from a robust frequency domain functional connectivity measure, the imag-
inary part of coherence (Nolte et al., Clin Neurophysiol 2004), in resting state MEG data. A statistical comparison with a benchmark
dataset of random networks, having the same number of nodes and links of the MEG nets, revealed a significant (p<0.05) difference
for all the indexes.
In particular, the redundancy in the MEG networks, for each frequency band, appears higher than random graphs, thus revealing a
natural tendency of the brain to present multiple parallel interactions between different specialized areas, as also recently reported
with EEG networks (De Vico Fallani et al., Int J Bifurc Chaos, In press). Notably, the matrix redundancy showed a high value
(p<0.05) between the channels over the parieto-occipital areas in the alpha range of MEG oscillations (7.5-13 Hz), as expected in the
resting state condition.

Mo-189 - Brain network connectivity during morpholexical processing: an MEG/EEG study

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The goal of this research is to characterize the neural circuitry that responds to linguistic complexity as indexed by a potential
inflectional morpheme (play-ed). Within the neural language system, linguistic complexity engages primarily left lateralised pro-
cesses, whereas general processing complexity - as indexed by lexical competition - engages a more bilateral network (Bozic et al.
2010). To track the dynamics of this network we investigate cortical oscillatory synchrony in a combined magneto- and electro-
encephalography (EEMEG) auditory study. Participants listened to lists of words that varied on these two core processing dimensions.
Linguistic processing complexity was manipulated by the presence or absence of a potential inflectional morpheme (played). General
processing complexity was engaged by the presence of onset-embedded lexical competitors (claim).
Phase-locking values (PLV, Lachaux et al. 1999) based on source estimates (MNE, Hamalainen et al. 1993) were computed to
determine trial-by-trial covariance of the posterior superior temporal gyrus (pSTG) and Heschl’s Gyrus (HG) with other regions of
interest. Results time locked to the onset of an inflectional morpheme revealed that phase synchrony increased in the gamma-band
(30-50 Hz) between L-pSTG and left pars opercularis (L-BA44). In contrast, processing an onset-embedded competitor induced
synchrony in a network linking the L-HG and left pars orbitalis (L-BA47). These findings suggest that enhanced cross-cortical in-
teractions between left temporo-frontal areas are necessary and highly specific for morpho-syntactic computations. Synchronisation
in oscillatory dynamics reflects the transient coupling of functional networks related to specific computational processes in language
comprehension.

Mo-190 - Dominant Component Analysis of MEG Functional Connectivity Networks

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Objective: Connectivity matrices obtained from various modalities (e.g. DTI, MEG and fMRI) provide unique insights into brain
network processes. Their high dimensionality combined with typically small population sizes necessitates method development for
population-based statistics. We present a dominant component analysis (DCA) method that identifies a basis of functional connec-
tivity (FC) components, characterizing the patterns associated with brain pathology. Projection of subject-wise connectivity matrices
into this basis allows for dimensionality reduction, facilitating subsequent statistical analysis on the coefficients.
Methods: FC is defined using synchronization likelihood (SL) computed between pairs of MEG sensors. A DCA technique (specifi-
cally, projective non-negative component analysis (PNCA)) is designed for learning localized and part-based sparse dominant com-
ponents of positive connectivity matrices, using positive projections which produce positive bases and coefficients, minimizing a
Frobenius norm of reconstruction matrix error using gradient descent.
Results and Conclusion: The proposed method was applied to MEG derived SL matrices computed for 26 subjects with autism
spectrum disorder (ASD) and 22 typically developing (TD) controls. The dominant components that can be used to assemble the individual connectivity matrices of ASD showed short-range and frontal connectivity (Fig. a) while long-range connections were seen in the TD components (Fig. b). The two-sample t-test between the projections of the connectivity matrices of pooled ASD and TD onto the fundamental dominant connectivity components (Fig. c), revealed significant group differences ($p<0.02$ in Fig. c(1)). The presented framework identifies the dominant components in the functional networks, defining the connectivity differences between ASD and TD based on resting state MEG. The framework is, however, general and applicable to any type of functional or structural connectivity networks.

![Connectivity components](image)

PNCA connectivity components obtained from the delta band SL connectivity and sorted based on the descending average of their corresponding projection coefficients in the ASD (a), TD (b) and pooled subjects (c).

Mo-191 - Group analysis of MEG functional connectivity and resting state signal complexity in autism

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Objective: We investigate autism spectrum disorder (ASD) using statistical group analysis (SGA) of functional connectivity (FC) and resting state complexity of MEG data in ASD and matched typically developing (TD) children. Connectivity measurements assess brain FC networks while complexity describes the repeatability of signal patterns in any specific region.

Methods: Using MEG signals from 274 sensors, we computed FC networks between sensors by using synchronization likelihood (SL) at each of six frequency sub-bands of delta (DL), theta (TH), alpha (AL), beta (BT), gamma (GM), and broadband (BB). We used multi-scale entropy (MSE) to evaluate the complexity of MEG signals at each sensor, computed at 60 scales for each of the six sub-bands. The maximum MSE in each sub-band was retained for SGA. SL and MSE values were computed for 26 children with ASD and 22 TD.

Results: The SGA of unthresholded connectivity showed that the ratio of the long-range significant connections in TD to those in ASD to be approximately 4, 25, 1, and 14 in DL, TH, AL, and BB, respectively, with no significant coherence in BT, GM. The SGA of MSE measurements showed different ($p<0.05$) in DL, TH, AL, BT, GM, and BB, respectively. Comparing connectivity and complexity measurements revealed high negative correlations between group differences of MSE and SL graph node strengths per sensor at each sub-band ($R=-0.53$, -0.40, -0.82, -0.65, -0.48, and -0.71). (See Fig.)

Conclusion: Resting-state MEG complexity and connectivity analysis, measured by MSE and SL, may reveal underlying anomalies in brain activity and connectivity in ASD. Significant deficits in long-range FC were measured in ASD. Negative correlations between the complexity and SL graph node strength suggest that the group differences apparent in complexity are due to the FC network differences between ASD and TD. Alternatively, more complex signals in ASD may lead to impaired long range coherence.
SGA of MSE (column 1) and thresholded SL (column 2) for DL (row 1) and AL (row 2) sub-bands. Red shows group mean is higher in ASD (and blue in TD). Column 3 shows the high correlation between the group differences in SL graph node strength and MSE.

Mo-192 - Creating MEG-DTI markers of pathology using partial data
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Introduction: Multi-modality classifiers are difficult to construct when data is missing from a modality due to technical factors, movement, or generally their inability to complete the imaging protocol, which is especially common in patient groups, or younger children. We design MEG-DTI classifiers using subjects with partially missing data, thereby broadening the scope of the classifier to include severe pathology and more generalizable age-ranges.

Method: We use an ensemble based approach to create the multi-modal classifiers. Several subsets of complete data are identified. Linear discriminant classifiers are created by training on the features for each of these subsets. MEG features used are the latency of auditory evoked neuromagnetic M100 component and magnetic mismatch field, a response component reflecting detection of change in the auditory stream. DTI features are fractional anisotropy and mean diffusivity from 37 ROIs created by a normalized cuts clustering of WM areas associated with language, providing 74 feature values. The output from these classifiers is fused using a weighted aggregation step which associates an optimal probabilistic score to each subject, quantifying the degree of pathology.

Results: This was applied to data from 98 ASD (autism spectrum disorder) subjects and 42 controls with 58% subjects missing some features. The fusion classifier distinguishes between ASD and TD with a mean 5-fold cross-validation accuracy of 83.3%. This performance is better than the deletion classifier trained by eliminating subjects with incomplete data (79.5%). The subset classifiers in the ensemble provide an insight into the relative contribution of MEG and DTI towards the quantification of pathology.

Conclusion: As more modalities are needed for comprehensive characterization of pathology, the likelihood of missing data increases. Our method can be generalized to any number of modalities to create classifiers from subjects with partial data.
Mo-193 - Large-scale cortical correlation structure of spontaneous oscillatory activity

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Little is known about the brain-wide correlation of electrophysiological signals. Here we show that spontaneous oscillatory neuronal activity exhibits frequency-specific spatial correlation structure in the human brain. We developed an analysis approach that discounts spurious correlation of signal power caused by the limited spatial resolution of electrophysiological measures. We applied this approach to source estimates of spontaneous neuronal activity reconstructed from magnetoencephalography (MEG). Overall, correlation of power across cortical regions was strongest in the alpha to beta frequency range (832 Hz) and correlation patterns depended on the underlying oscillation frequency. Global hubs resided in the medial temporal lobe in the theta frequency range (46 Hz), in lateral parietal areas in the alpha to beta frequency range (823 Hz), and in sensorimotor areas for higher frequencies (3245 Hz). Our data suggest that interactions in various large-scale cortical networks may be reflected in frequency specific power-envelope correlations.

Mo-194 - Source-space waveform reconstruction for coherent brain signals - Can phase information be used for brain connectivity measure?

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In order to study brain connectivity, source localization technique is generally required since sensor measurements are mixed up with signal sources. In addition, most brain sources are likely to be activating coherently, so for these coherent sources conventional localization technique may not be the proper way to obtain reconstructed waveforms in the source space. In this work, we apply linearly-constrained minimum variance spatial filter with source suppression to avoid power leakage interference between correlated sources. The phase difference between true and reconstructed waveforms is analyzed to show that the phase information of coherent sources from the reconstructed waveforms may be good applicable to the connectivity analysis. Linearly-constrained minimum variance spatial filter with source suppression, reconstructed waveforms are compared with conventional spatial filter without suppression. In Figure 1 (top), we see the phase distortion behavior by interference of a coherent source with respect to the SNRs. Interestingly, the phase distortion of the reconstructed wave gets smaller when suppression area gets smaller or SNR gets lower. It is understood that the noise plays a crucial role in yielding reduction of the phase distortion. Through careful investigation, we found that this phenomenon is related to the regularization factor of covariance matrix of measurement. Figure 1 (bottom) represents localization error with respect to SNRs. Evidently, lower SNR yields bigger localization error. We see that phase distortion and localization error are traded off. This finding tells that connectivity analysis in the source space should be attempted in a very careful manner.
manner and phase distortion should be taken into account. This work is supported by the KRCF through Basic Research Project managed by KRISS.

Figure 1. Phase distortion (deg) and source localization error (mm) by interference of a coherent source

Mo-195 - Synchronization of hippocampal and prefrontal rhythms in human decision-making

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Making optimal decisions requires integrating memory signals about previous decisions with value signals concerning rewards and punishments. As these signals are likely to be represented in different brain regions, optimal decision-making requires a neural mechanism for orchestrating distant neural populations. In many scenarios, this should involve orchestration of memory signals in the hippocampus and the value signals in the prefrontal cortex. Studies in rodents have shown that the hippocampus and medial prefrontal cortex can be synchronized by neural oscillations in the theta frequency range (4-8Hz). Because these studies involved spatial navigation working-memory, episodic memory and fixed reward magnitudes, the cognitive function of hippocampal-prefrontal theta synchrony in decision-making has remained unclear. Here, using magnetoencephalography (MEG) recordings we report selective theta synchronization between the anterior hippocampus and the medial prefrontal cortex while healthy humans engaged in a decision-making task. Our task was devoid of spatial learning and included active choice trials, with different levels of reward and punishment in which decisions were informed by memory for past trials, as well as forced decision trials. Stronger theta-synchronization in active as compared to forced choice trials was related to decision making per se and not the magnitude of reward. Also, the extent of synchronization between both structures was negatively correlated with the number of decision errors. These findings indicate that theta synchronization between the hippocampus and prefrontal cortex supports non-spatial, memory guided decision-making as a general mechanism, which is not limited to rewards.

Mo-196 - Convolution models for continuous M/EEG time-frequency data

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Unlike brief evoked responses, induced changes in power can last for many seconds. There are several issues that confound the analysis of these responses: (i) In many behavioural tasks, the responses to different events overlap and confound each other, making it difficult to characterise them separately. (ii) When the task involves subject’s responses and there is inevitable variability in the reaction time, it is difficult to interpret the average because the same peri-stimulus time in different trials may correspond to different stages of neural processing. Furthermore, if experimental conditions differ systematically in the reaction time there will be systematic differences in the corresponding time-frequency activity confounding statistical analysis of experimental effects. In the standard framework it is impossible to distinguish true differences in power from these reaction time confounds. (iii) When baseline correction is used as part of the analysis, systematic differences in the baseline between conditions may also confound the results.
(iv) Finally, in naturalistic tasks (e.g., continuous navigation in virtual reality environment) it might be difficult to define discrete epochs for averaging and baseline periods. To resolve these problems we propose a new statistical model for time-frequency data. The General Linear Model (GLM) with Fourier basis set modelling an induced response function was applied to continuous time-frequency data. The estimated GLM coefficients were multiplied with the basis functions above to reconstruct frequency-specific induced responses for each event. The resulting images were compared to images obtained from averaging and subjected to statistical analysis at the second level. We show on simulated and real MEG data that the proposed method can separate power responses to temporally overlapping events. We also show that the method can dissociate true condition effects on power from the effects of reaction time.

**Mo-197 - Extracting resting state networks from Elekta Neuromag MEG data using independent component analysis.**

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Spontaneous synchronisation of neural oscillations between spatially separate brain regions is postulated to underpin brain function. These resting-state networks (RSNs) have previously been detected using fMRI, via their correlated haemodynamic activity. Magnetoencephalography (MEG) can provide direct insight into the electrophysiological basis of RSNs at a high temporal resolution. Recently, it was shown how RSNs can be extracted (without providing spatial information a priori) by applying temporal independent component analysis (ICA) to MEG data acquired on a 275-channel whole-head CTF system. Here, we independently reproduce these findings by applying the methodology to MEG data collected using an Elekta Neuromag system. Additionally, we investigate whether signal space separation (SSS) affects the ability to detect RSNs. Twelve participants were scanned at rest. A beamformer was used to estimate the source space activity for three frequency bands and the oscillatory envelope of the source space data was estimated via the Hilbert transform. The envelopes were down-sampled using a 1s windowed average, then temporally concatenated across subjects and decomposed into 25 temporally independent components (tICs) using fastICA. The tICs were converted into correlation maps (by computing the Pearson correlation coefficient between each tIC and every voxel time course in the concatenated data). These maps were compared with spatial maps of RSNs found by using spatial ICA on fMRI data.

Figure 1 shows 11 fMRI spatial maps and corresponding correlation maps estimated from the MEG data without and with SSS. These findings show that resting-state electrodynamical networks can be imaged using MEG, reinforcing previous findings. Furthermore, we have demonstrated a robust analysis pipeline for extracting RSNs from Elekta Neuromag data. We have shown that SSS processing can be applied to Elekta data but that it does not improve the quality of the RSNs extracted.

![Figure 1: A comparison of resting-state networks extracted using ICA from fMRI, MEG data and MEG data with SSS applied.](image-url)
Mo-198 - Investigating the frequency composition of resting state networks in MEG using ICA

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Magnetoencephalography (MEG) has the potential to provide direct insight into the electrophysiological basis of resting-state networks (RSNs). Previously, RSNs were extracted from MEG data using temporal independent component analysis (ICA) on the amplitude envelope of individual frequency bands. However, using single frequency bands could affect the RSNs that are found. Here, we use temporal ICA to decompose multiple frequency bands simultaneously. In particular, this enables robust extraction of the default mode network (DMN), which can only be weakly detected in a single frequency band.

Twelve participants were scanned and the data filtered into 4 frequency bands: 4-8Hz, 8-13Hz, 13-30Hz, 30-70Hz. For each band, a beamformer was used to reconstruct neural activity across the brain. The oscillatory amplitude envelope of the source space data was estimated via the Hilbert transform and down-sampled using a 1s windowed average. Each subjects’ envelopes were temporally concatenated across all subjects, yielding a concatenated data set for each frequency band. These four sets were spatially concatenated, giving a single 2-dimensional data matrix. This matrix was decomposed into 50 temporally independent components (tICs) using fastICA. The tICs were converted into correlation maps for each frequency band by computing the correlation between each tIC and every voxel in the individual frequency band concatenated data. Figure 1 shows the correlation maps for each frequency band of 2 components that show strong presence in multiple frequency bands (alongside spatial maps of RSNs from fMRI data).

Decomposing multiple frequency bands with temporal ICA is a powerful extension of the Beamformer-ICA method. It allows for robust detection of networks that are present in multiple frequency bands, such as the DMN. It can also be used to elucidate the frequency content of RSNs, yielding a greater understanding of the electrodynamics of resting state brain function.

Mo-199 - Brain connectivity in permanent non-responsive patients: a DCM study of responses to tone duration violation

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A critical issue in clinics is the assessment of the brain functional state of permanent non-responsive patients. Recent studies have suggested that neurophysiological markers (MMN and P3) could provide a more objective diagnosis and help distinguishing between vegetative (VS) and minimally conscious states (MCS).

Advanced methods have been proposed to test alternative hypothesis on the cortical networks that generate evoked responses. Such hypothesis can be framed in terms of different Dynamic Causal Models (DCM) and compared using Bayesian inference. Several studies have applied DCM in healthy subjects, to explain the differences in evoked responses to standard and deviant tones, in terms of...
of modulations of effective connectivity (1). Interestingly, Boly and colleagues applied DCM to tone frequency violations in both healthy controls and non-responsive patients (2). In an attempt to reproduce those results, we compared DCMs in 15 healthy subjects and 26 patients in VS (n = 16) or MCS (n = 11). Using 32-sensor EEG, we ran a passive oddball paradigm with 75 ms standard tones and shorter deviants (30 ms, p = 0.14) (3). In comparing the same eleven models as in (2), our preliminary results indicate that indeed, the differences in evoked responses are best explained by a five-source model that include intrinsic, forward and backward connections in all groups. However, contrary to results in (2), we robustly identified as the best model, the one that does not include lateral connections between hemispheres. For this winning-model, we found no significant difference in the backward connection between frontal and temporal cortices, between VS and MCS. Complementary analyses are required to confirm this finding, which could be due to several differences between the two experimental designs.

(2) Boly et al. Science 2011

Mo-50 - Signal detection and evaluation for SQUID based fetal magnetocardiography

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Fetal magnetocardiography (fMCG) is a sophisticated non-invasive diagnostic technique to investigate the electrophysiological activity of the fetal heart. By using high sensitive low Tc DC SQUIDs with field sensitivity of 3-5 fT/sqrt(Hz), a multi-channel fMCG system was set up in a magnetically shielded room (MSR). Two different noise cancellation methods were employed: (I) first order axial gradiometers compensated by a vector reference magnetometer module, (II) synthetic first order gradiometers by using two planar magnetometers with a baseline along the axial direction. In order to compare the effectiveness of the two methods, an simulated experiment was carried out by simplifying the maternal and fetal heart sources into two coils with a horizontal distance of 200 mm and a diameter of 50 mm and 20 mm respectively. The maternal MCG and fMCG signals were simulated by using individual electrocardiography (ECG) signal to drive the two coils with adjustable amplitude and frequency. Four key indexes ‘signal-to-noise ratio (SNR), relative heights and correlation coefficients in time and frequency domain’ were used to evaluate the performances of the noise cancellation methods and the integrity of the extracted simulated fMCG signal. Based on the evaluation results, the fMCG system was optimized, and real fMCG signals with good quality from the 24th week of gestation onward were successfully detected.

Mo-51 - Screening IHD Patients with Volume Integral Value within an Extrema Circle in Magnetocardiography

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Magnetocardiography (MCG) is a non-invasive approach for diagnosing preclinical ischemic heart disease (IHD). Recent years, several methods for IHD screening using MCG data were proposed, in one of which reported by K. On in 2007, the sensitivity and specificity reached up to 71% (10/14) and 80% (24/30) when the cutoff point was set as JTi/QRSi < 1.0 for diagnosis of IHD. We presented a novel method to extract a parameter from MCG data, which is a volume integral value (Vi) in the extrema circle defined in our previous studies. The diameter of the extrema circle is the distance between two extrema in the MCG map. The effectiveness of this Vi parameter is examined by a screening test, in which the MCG data are measured by using a 36-channel superconducting quantum interference device (SQUID) system in a magnetically unshielded room in a hospital. The 66 measurement sites are arranged in a 20 cm x 20 cm measurement plane above the thorax of a subject. In this study, the data from 11 healthy subjects and 10 patients with IHD are used. Eight cases were statistically analyzed for all subjects, which are the combinations of using the normal or tangential component of the magnetic induction, using data in the extrema circle or in the whole measurement plane, and using the integral value or its time average. A comparison of these cases shows that the best screening approach is using the Vi parameter calculated by the normal component of magnetic induction within the extrema circle and averaged over time. This method

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Mo-53 - Statistical pattern recognition of mice MCG map for detection of abnormal cardiac excitation

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Various genetically modified mice are now available for pathophysiological and pharmaceutical studies of heart diseases. Magneto-cardiogram (MCG) is a useful tool to non-invasively and continuously monitor the electrophysiological characteristics of the heart of these mice.

We have developed a statistical pattern-recognition algorithm that automatically detects an abnormal cardiac excitation from MCG map of the mice and further applied it to the MCG maps of control (NZW/NSl) and MI(myocardial infarction)-model ((NZW/NBXSB)F1) mice. We measured 32 MCG maps from six control mice with their age ranging from 9 to 24 weeks in order to determine the discrimination criterion of normal MCG pattern. We estimated current dipoles using the least-squares method during R, S, and T periods of the MCG, calculating the angles of the current dipoles at each time point. We defined a two-dimensional feature vector by the time and the angle of the current dipole estimated. Using the cluster analysis we further classified the feature vectors of all control mice into 3 clusters. The normal ranges of the time and the angle of current dipoles during R, S, and T periods were determined so that each cluster contains 95% of the feature vectors estimated during the corresponding period. We determined that the MCG pattern is abnormal if any of the feature vectors located outside of the normal range of any cluster. Using this criterion, we classified 6 MCG data of control mice that we did not use for determining the criterion and 2 of MI-model mice that were confirmed to have an old MI in the postmortem assessment. The sensitivity, specificity, positive predictive value, and negative predictive value of the classification were 100%.

Our results showed that this technique would help researchers quantitatively detect the abnormal cardiac excitation of disease-model mice even without any specialized experience in MCG.

Mo-54 - Prediction of obstructive stenosis in patients with intermediate pretest probability of the chronic CAD: Value of MCG index

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Background: The noninvasive detection of coronary artery disease (CAD), especially in ‘difficult-to-diagnose’ cases, remains a clinical challenge. Magnetocardiography is a completely noninvasive method that permits the registration of cardiac electrical activity at multiple sites in a plane above the chest cage without the need for electrodes.

The purpose of this study is to investigate predictive value of the integrated MCG-index (CI) in the coronary artery stenosis diagnosis in chronic coronary artery disease patients with intermediate pretest probability of disease and uninformative results of routine tests. Methods: The study has been carried out in the clinic of cardiology of the Main Military Clinical Hospital of Ukraine, Kiev (Clinic 1) and in the II-nd Medical Clinic of University Witten-Herdecke, Essen, Germany (Clinic 2).

The main group (Group 1) has been composed of 94 patients without a history of myocardial infarction, with normal resting ECG and EchoCG, underwent coronary angiography due to chest pain. Depending on the results of coronary angiography, this group was divided into two subgroups: with 470% stenosis in at least one of the main coronary artery (62 patients, subgroup 1a) and without haemodynamically significant stenosis (32 patients, subgroup 1b). Control group consisted of 43 healthy volunteers.

All persons examined underwent MCG-examination by a 7-channel MCG system installed in unshielded location. Integrated MCG-index (CIMCG), consisting of 6 parameters, has been calculated. These parameters in collection allow performing multilateral estimation of current density distribution maps, reconstructed from magnetocardiographic data. CI has been varied from 6 up to 23 grades.

Results: CIMCG was significantly higher in patients with stenosis compared to the patients without stenosis and healthy volunteers 416 ± 3, 1 vs. 8.7 ± 2.0. Diagnostic accuracy of the CIMCG was as follows: sensitivity 93%, specificity 84%, PPV 85%, NPV 93%.

Mo-55 - Clinical usefulness of fetal actocardiogram using fetal magnetocardiogram in prena-
A fetal actocardiogram (ACG) using a fetal magnetocardiogram (FMCG), first introduced by Zhao (2002) and Wakai (2003) draws the QRS amplitude and instantaneous fetal heart rate (FHR) obtained from FMCG simultaneously and serially. This ACG is useful for detecting fetal trunk movements and the initiation and/or termination of fetal paroxysmal tachycardia. However, the clinical advantages of a FMCG ACG for the diagnoses of other fetal heart diseases are still unknown. In this study, we examined FMCG ACGs of various fetal heart diseases to clarify the clinical usefulness. We used 36 FMCGs recorded for 2 or 20 min using a 64 channel SQUID magnetocardiograph installed in National Cerebral and Cardiovascular Center, Suita, Osaka, Japan. Twenty-nine FMCGs for 2 min were obtained from 12, 3, and 14 normal and arrhythmic fetuses, respectively. Seven FMCGs for 20 min were recorded from one normal and 6 arrhythmic fetuses. ACGs for 2 min from the normal fetuses showed two different patterns: RR intervals changed following alterations in R amplitudes in 3 ACGs, although both R amplitudes and RR intervals showed small changes in the other 8 ACGs. Abrupt changes in R amplitudes and RR intervals were also observed in ACGs from 4 fetuses with severe structural heart diseases. The characteristics of 20-min ACGs from a normal fetus were similar to those of a 2-min ACG. Abrupt changes of RR intervals without preceding changes of R amplitudes were observed five times in 20-min ACG in a fetus with paroxysmal supraventricular tachycardia. Abrupt changes in R amplitudes and RR intervals in 2-min ACGs might relate to structural abnormality of the heart. ACG might be useful in prenatal diagnoses of fetal heart diseases.

Mo-56 - Development of a Magnetocardiography Algorithm for Localizing the Origin of Idiopathic Ventricular Outflow Tract Tachycardia

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Introduction: Idiopathic ventricular outflow tract tachycardia or premature ventricular contractions (OT-VT) can originate from both the left and right ventricle (LV, RV) in the outflow tract. Although there are several reports concerning characteristic 12-lead ECG findings of OT-VT, accuracy of the ECG criteria to predict OT-VT origin is sometimes limited due to physical characteristics of the patients, anatomical rotation of the heart, and changes in ECG electrode placement. In particular, precise differentiation of LVO-T-VT from RVOT-VT is meaningful in catheter ablation because success rate and complication rate depend on the side from which the arrhythmia originates. The aim of this study was to develop a magnetocardiographic (MCG)-imaging-based method to differentiate LVO-T-VT from RVOT-VT.

Methods and Results: This study comprised 63 patients with normal sinus rhythm as the baseline rhythm and OT-VT as a target of catheter ablation. An algorithm was developed by correlating the MCG findings with the catheter ablation site. The ablation sites were verified by 3D electroanatomical mapping and multiplane fluoroscopy. The outflow tract was classified as RVOT or LVOT. We evaluated the following 3 parameters obtained using 3-D MCG imaging: 1) distance between the earliest atrial activation site, i.e., the sinus node, and the origin of OT-VT, 2) depth of the origin of OT-VT in the anteroposterior direction, and 3) initial angle/vector of arrhythmia propagation. ROC analyses determined that depth of origin was the most powerful predictor among the 3 parameters, with sensitivity of 81% and specificity of 92% (p<0.01, AUC=0.90). Discriminant analysis also revealed that depth of origin had the highest accuracy for localizing the left- or right-side origin (84%). Moreover, combined analysis including all 3 parameters improved accuracy of the localization to 93%.

Conclusion: A novel method combining 3 MCG-imaging parameters could precisely discriminate a left-side origin from a right-side origin of OT-VT.
We developed an analytic solution of reconstructing equivalent current dipoles, according to the relationship between the normal magnetic field measured by SQUID system and its gradient field. With this method, using the extrema of measured magnetic field data enables us to solve the MCG inverse problem in a best way. The obtained source parameters can be used for imaging of cardiac electrical activity in two or three dimensions, revealing the electrophysiological characteristics of some heart diseases and screening patients with ischemic heart disease (IHD) and so on. For instance, the common characteristics of cardiac electrical activity regarding patients with left/right bunch conduct block have been shown by the time-dependent source parameter curves in T wave period based on the inverse calculation of the measured MCG data.

**Mo-58 - Magnetic field patterns due to normal, retrograde and uncoupled gastric electrical activity**

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Aim: We seek to use biophysically based simulations of gastric electrical activity (GEA) and resultant magnetic fields to determine the feasibility of noninvasively characterizing the underlying GEA.

Method: An anatomically realistic torso and stomach models were used. The GEA was represented by a propagating isopotential band. Two or three slow waves were present at the same time which mimics the recent high-resolution mapping studies (1). Three source configurations representing normal, retrograde or uncoupled state were simulated (2). The magnetic fields were calculated at 110 evenly spaced sensors located on the anterior of the body surface. The point mid-way (red squares in Fig 1) between the maximum and minimum amplitudes of magnetic field were located and tracked.

Results: For normal propagation (Fig 1(a)) the mid-point moved from the upper right quadrant to the lower left quadrant, reflecting the overall propagation direction. With retrograde propagation (Fig 1(b)) the mid-point moved from the lower left quadrant to the upper right quadrant, again reflecting the overall propagation direction. At T=7s for both the normal and retrograde case, a second maxima was observed possibly reflecting the emergence or loss of a source term. In the uncoupled case (Fig 1(c)), the magnetic field and mid-point location had a sudden change when two slow waves collided. After the waves collided the magnetic field map remained static for approximately 7s. The slow wave frequency for all cases was able to be predicted from the field patterns.

Conclusion: The magnetic field maps were able to differentiate normal, retrograde and uncoupled gastric electrical activity. The frequency and direction of slow wave propagation in the antrum was reliably resolved by tracking the mid-point of the magnetic field map.

References

![Fig1](image)
Mo-59 - 5-Year Long-term Results of MCG map-guide minimal AF surgery in the patients who has a long-standing persistent AF

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Map-guided AF surgery will be a good help to treat AF successfully. We introduced the magnetocardiography action potential activity mapping, non-contact and higher sensitive method to detect atrial F-wave for tracing abnormal conduction route than conventional EKG. Using this method, we conducted the MCG map-guide minimal AF surgery and report their 5-year long-term results.

To detect weak atrial excitation, we utilized a high sensitive low-Tc 64-channel MCG system with application software KRISSMCG64 to make a MCG map on the three-dimensional atrial surface. From the information of MCG map, from 2006 June to 2008 June, we conducted the minimal AF surgery in 8 long-standing persistent AF patients having concomitant structural heart disease, such as valvular or coronary disease. Their mean age is 63 years old, AF duration is 17 months, AF burden is 1.0, LA size is 60 mm, LVEF is 54%. Monthly-based standard 12-lead ECG was used for follow-up examination.

Among the 8 long-standing persistent AF patients who had underwent MCG map-guide minimal AF surgery, there are two early loss patients due to CRF sepsis and CVA stroke (at 21 and 15 postoperative days, respectively) and two follow-up loss patients because of pneumonia (at 25.3 and 5.7 months, respectively). The remaining 4 patients show 100% (4/4) drug-off AF-free rhythm at 69.1, 63.3, 59.5 and 57.4 months follow-up periods (mean follow-up 62.3 months, 5.2 years). Their final rhythms are NSR, SR, SR with 1st degree AV block, and junctional rhythm. There are no sick sinus syndrome, no permanent pacemaker insertion cases. Using MCG map-guide, we conducted minimal AF surgery in the patients who has long-standing persistent AF, and their 5-year long-term rhythms converted all regular AF-free rhythm successfully with drug-off status. It is a good method to treat AF with long-term feasible results.

Example of MCG map-guide minimal AF surgery and EKG rhythm pre and postoperative

Mo-60 - Optimizing a magnetic sensor vest for cardiac source imaging

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Magnetcocardiology non-invasively provides information about the electrical heart activity. New room temperature optically pumped magnetometers allow for placement of sensors around the body rather than enclosed in a cryostat. Therefore the question arises of where to optimally place the sensors.

We measured the magnetic field produced by the heart of a 72 year old cardiac patient. A boundary element model of the torso (0.2 S/m) and lungs (0.04 S/m) was created from a T1 weighted MRI. We modeled the cardiac sources with 13 dipoles arranged regularly.
around the left ventricle. The dipole orientations and amplitudes were fitted to the averaged PQRST interval of the MCG using a minimum norm approach and L curve regularization. We optimized the positions and orientations of a set of sensors with particle swarm optimization (PSO) with respect to the condition number (CN) and the Skeel CN of the leadfield matrix. Because the solution is non-unique, we sampled the solution space of optimized sensor setups by optimizing repeatedly with random initialization and clustering the sensor positions to elicit generalizable patterns.

The results indicate that sensors on the back of the torso are capturing relevant information. The optimized sensor distribution is non-uniform and denser at the front of the torso. The Skeel CN produces denser clusters, indicating more specific sensor placement, with better reflection of the heart’s anatomy and excitation patterns, e.g. through the resemblance of the Wilson lead line. The smallest distance between optimized neighboring sensors is approximately 4-5 cm.

We conclude that a customized optimal field sampling on the whole torso surface can be derived using a representative volume conductor and source model. The vest concept is practical for clinical diagnostics in cardiology and for long-term monitoring such as a 24 hour MCG and might facilitate the definition of a robust standard for magnetic field imaging.

Mo-61 - On sensitivity of magnetocardiography to atrial and ventricular activity

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Magnetocardiography (MCG) is frequently used in the study of atrial electrical activity [Jurkko et al. 2009, Nakai et al 2008]. Due to the complicated atrial geometry and low signal-to-noise ratio, it is often difficult to characterize, which region of the atria gives rise to the measured signals, sensitivity analysis can help in this. In this work, we present model-based MCG sensitivity distributions for atria and ventricles in realistic noise conditions.

A realistic-geometry volume conductor model for MCG was built with the boundary element method (Stenroos et al. 2007), using meshes from ECGSIM software (van Oosterom et al. 2004) and the sensor setup of the Neuromag MCG system. The sensor setup comprises 33 magnetometers and 66 planar gradiometers in triplet layout over the anterior thorax. A distributed double-layer source model was spanned over the atrial and ventricular surfaces. Lead-field matrices (LFM) for atria and ventricles were built, the variation in the density of the source meshes was corrected for by normalization.

Noise variance estimates for both sensor types were estimated from real MCG measurements. These were used for whitening the LFM to signal-to-noise basis, enabling the combination of different sensor types. The sensitivity was assessed in terms of L2 norm of the whitened lead-vector for each source location.

The sensitivity from the atria was significantly lower compared to that of the ventricles: The ratio of mean sensitivities was 0.60. For magnetometers only the ratio was 0.65. The normalization of sources guarantees that the amount of the total muscle mass does not contribute to the strength of the modeled signal. Therefore, the atria produce weaker signal compared to the ventricles also due to their deeper location inside the thorax and not only due to having less muscle mass. The highest sensitivity is on lateral walls, where the surface normal direction differs most from the sensor axis direction.

MCG iso-sensitivity distributions for atria (upper row) and ventricles (lower row) in anterior and posterior views on left and right, respectively. Brighter (yellow) color means more sensitivity.
Mo-62 - MCG-parameters in automatic classification of patients with arterial hypertension and postinfarction cardiosclerosis

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We investigated MCG parameters of ventricular repolarization in patients with arterial hypertension (AH) and postinfarction cardiosclerosis (PICS), evaluated their diagnostic capabilities for detecting myocardial electrical heterogeneity and compared with the method of standard electrocardiography.

The study included 104 persons aged 45 to 75 years. Apparently healthy persons did not have significant abnormalities of the cardiovascular system according to the results of clinical, laboratory and instrumental examinations. In the group with AH/PICS complete number of surveys using the ECG and MCG-method was performed for 49 patients.

In analyzing of MCG the software package is automatically counted more than 100 parameters that characterize the recorded heart magnetic field distribution and the recovered distribution of the current density vectors (after solving the inverse problem) in the myocardium. We allocated 3 most diagnostically significant MCG-parameters in patients with AH/PICS and obtained a decision rule that included the following parameters: 1) an indicator of the direction of the current density vector (DCDV), which characterizes the homogeneity of ventricular repolarization process, 2) the parameter of the average variability of the magnetic field (PAVMP) for the period of ventricular repolarization and 3) the parameter of synchrony and correlations (PSC) of the MCG in all 36 points of the measurements on the ST-T interval.

Initial classification of the results showed a difference of selected parameters in patients with AH/PICS, compared with those of the control group. Threshold values separating the ‘norm’ and ‘pathology’ of the patients studied by these MCG parameters. Integral use of all three informative parameters of MCG allowed to separate the group of patients with AH/PICS and healthy subjects with a sensitivity of 88% and a specificity of 96%, significantly higher than the same parameters obtained by conventional methods of ECG.

Mo-63 - Magnetocardiographic assessment of intraventricular conduction delay in patients with left bundle branch block using simulated and measured data

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Magnetocardiography (MCG) are usually recorded the weak magnetic field, which is generated from the electrical currents in the heart, over the anterior chest wall. The amplitude of the magnetic field rapidly decays with the distance between electrical cardiac currents and a magnetic sensor. Thus, the magnetic field of the anterior measurement mainly does not reflect the electrical sources at a distance such as the left ventricular posterior wall (LVPW), and may not provide sufficient information to evaluate the whole heart’s electrical excitation.

Our aim was to see whether MCG signals of anterior and posterior measurements give the information that can be used to evaluate the intraventricular conduction delay in subjects with complete left bundle branch block (CLBBB). We calculated the anterior and posterior MCG (aMCG and pMCG) signals in patients with CLBBB by using MCG simulation software. Furthermore, we recorded the anterior and posterior MCG signals for 5 CLBBB patients. To assess the intraventricular conduction delay, the end of QRS complex was semi-automatically determined from the simulated and measured MCG signals.

In the MCG simulation of CLBBB, the QRS lasted longer (9 ms) in posterior MCG signal than that in anterior MCG signal. Subjects with CLBBB also showed longer QRS (14 +/- 8 ms) in posterior MCG signal than that in anterior MCG signal. These results might indicate that posterior MCG signal could reflect the conduction delay in LVPW of patient with CLBBB, reliably. We concluded that anterior and posterior MCG measurements were useful for evaluating the intraventricular conduction delay of CLBBB.

This present study was partially supported by Strategic Promotion of Innovative R&D in Japan Science and Technology Agency.

Mo-64 - Is there a critical time period for neurovegetative development in the fetus?

Uwe Schneider1, Ekkehard Schleussner1, Anja Rudolph1, Susann Jaekel1, Ulrike Wallwitz2, Dirk Hoyer3

1BIOMAG 2012 - August 26-30, 2012 - Paris, France

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Regulation of the fetal heart rate pattern (fHRP) reflecting the development of the autonomic nervous system (ANS) can be assessed by fetal beat-to-beat heart rate variability (fHRV). The aim of this study is to elucidate evidence on the question of a critical developmental window between 28-32 wks GA.

42 healthy singleton fetuses were studied longitudinally on 2-3 occasions during the late 2nd and 3rd trimester of pregnancy by fetal magnetocardiography (fMCG) over periods of 30 minutes. The time series of fetal QRS complexes were drawn to reconstruct the fHRP and to perform fHRV. fHRP were pre-classified into quiet patterns (fHRP I) and active patterns (fHRP II). fHRP I was under-represented in the sample. In unselected time series (30 min) and segments of fHRP II (10 min) fHRV was performed: mHR, SDNN, RMSSD, fVLF, fLF, fHF, ratio fVLF/fHF, AIF\_NN, AIF\_fLF and AIF\_fHF (autonomic information flow). Developmental steps were intra-individually studied between 4 gestational segments (GS): (a)23/1-28/0, (b)28/1-31/0, (c)31/1-35/0, (d)≥35/0 wks GA.

Particularly considering fHRP II, short term parameters significantly increase first (GS a-b) accompanied by a drop in AIF. Overall/long-term fHRV parameters are following at GS a-c. There are no significant changes between GS b-c. Beyond that GS, there are trends for increase both in the overall and short term parameter sets irrespective of the fHRP. At GS c-d a gain in fHF is accompanied by increasing AIF\_fHF. A decrease in AIF\_NN is lost in association with another increase in SDNN during fHRP II.

Different rhythms of regulation mature at a different pace. The observed results elucidate separate phenomenons: increasing complexity of ANS regulation at (GS a-b), an emphasis on sympathetic activity near term during periods of fetal activity, development of fetal respiratoiy sinus arrhythmia and increasing cardiac self regulation reducing short-term beat-to-beat predictability that is overrun by sympathetic drive.

Mo-65 - His bundle activity by Magnetocardiography with QRS-onset as fiducial point

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We had reported the non-invasive tracking of the His Bundle (HB) activity by signal averaged magnetocardiography (SAMCG) earlier (1). We had reviewed the prior art and presented hitherto the most conspicuous and resolved signature for the activity. A key issue was the recognition of the importance of the QRS-onset as the fiducial point for signal averaging instead of the R-peak, owing to the inevitable modulations of the autonomic tone causing beat to beat changes of the QRS-onset to the R-peak duration. A stated limitation of the work (1) was the manual identification of the beat to beat QRS-onset.

In the present work, we describe a method for automatic identification of the QRS-onset in each cardiac cycle. The method involves fitting the absolute values of the differentiated MCG time traces to Gaussian shapes. The QRS-onset in each cycle is identified by a user defined threshold on the rise time of the fitted Gaussian. The alignment accuracy of the traces in this procedure has been evaluated by subjecting an oscillator generated cardiac signal. At a sampling rate of 5013 Hz, the standard deviation of the measured QRS-onset is calculated to be + 348 , much smaller than the duration of the HB activity (~ 8ms). The stability of the algorithm at various noise levels is investigated with increasing additive white Gaussian noise (AWGN) with SNR ranging from 100 dB to 30 dB and also by smoothing of traces using adjacent point averaging when the fitting becomes inferior with fall in SNR.

The method is applied to MCG measurements using a 37-channel SQUID system and the averaging revealed HB features comparable to our earlier work (1). H-V durations measured are in the range of 35-42 ms for the three healthy subjects and 56 ms for a subject with RBBB.

SAMCG traces using the automated QRS-onset detection show PR segments with widely differing slopes at several locations over the thorax of a normal subject (right) and a subject with right bundle branch block (RBBB) (left).

Mo-66 - Characterization of Blocked Atrial Bigeminy Using Fetal Magnetocardiography: Comparison with Pulsed Doppler Ultrasound

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Purpose: We and other groups have shown that fetal magnetocardiography (fMCG) is a highly effective method of diagnosing cardiac arrhythmia in the fetus. In this study we utilize fMCG and pulsed Doppler ultrasound to identify measurement parameters best suited to distinguishing blocked atrial bigeminy (BAB) and second degree atrioventricular block (2 AVB), two of the most common fetal bradycardias.

Methods: We retrospectively analyzed fMCG recordings from nine BAB patients in order to characterize their heart rate and rhythm patterns, and to compare them with those of second degree atrioventricular block. The fMCG recordings were made using a 37-channel SQUID magnetometer, housed in a high permeability magnetically shielded room.

Results: Distinguishing BAB and 2° AVB with fMCG is easy because in BAB the ectopic P-wave (P) occurs very early, resulting in a bigeminal (short-long) atrial rhythm. The normalized coupling interval of the ectopic beat (PP of blocked beat to PP of conducted beats) was 0.27 ± 0.03. Using ultrasound, however, the normalized mechanical coupling interval of the ectopic beat (AA/AA) often was near 0.5, which makes it difficult to distinguish BAB from 2° AVB. An important finding was that the BAB and 2 AVB patients could be distinguished largely on the basis of the higher rates of the BAB patients (83.4 ± 4.48 vs. 68.9 ± 2.12 bpm), although heart rate not always a reliable indicator. In addition, we observed one case of supraventricular tachycardia, a serious arrhythmia that also involves an accessory connection.

Conclusion: fMCG provides accurate differential diagnosis of BAB versus 2° AVB and other forms of fetal bradycardia. Furthermore, we have shown that PP interval measurements can be an electrophysiological characteristic used to distinguish between BAB and 2° AVB. In addition to the PP intervals we have also demonstrated that the heart rates and PP/PP ratios of the two arrhythmias can be used to distinguish between the two.

Monday, August 27th, 2012, 13:30-15:00

MEG and MCG Instrumentation

Mo-1 - Spherical coil array for calibration of sensors used in magnetoencephalogram systems

Yoshiaki Adachi¹, Masanori Higuchi¹, Daisuke Oyama¹, Gen Uehara¹
For the accurate estimation of brain activities using a magnetoencephalogram (MEG), the position and direction of the superconducting quantum interference device (SQUID) sensors must be precisely determined. However, the sensor array must be nonmagnetic and hence is usually made of plastic. The plastic sensor array is inevitably strained at cryogenic temperature. Therefore, the position and direction of the sensors are unpredictably shifted from the designed values, and the calibration after cooling becomes crucial to improve the accuracy of the MEG.

In this study, a spherical coil array was manufactured to improve the calibration of MEG systems. The coil array consisted of 16 copper wire coils wound along grooves on the surface of a plastic sphere (see figure), which was precisely crafted using a numerically controlled cutting machine. All coils and the sphere were concentric, and their diameter was 150 mm. To determine the orientation of each coil, a regular icosahedron concentric with the sphere was assumed. Six coils were oriented in the directions of the 12 vertexes of the icosahedron, and 10 coils were oriented in the directions of the centers of the 20 faces of the icosahedron.

The spherical coil array was positioned in the helmet-shaped SQUID sensor array of a 160-ch whole-head MEG system. Each coil was excited individually to generate a standard magnetic field. The standard magnetic field to be measured was accurately calculated. Accordingly, 16 sets of values of the measured and calculated magnetic fields were obtained for each sensor. The position and direction of the sensor were determined by nonlinear optimization based on the Hooke-Jeeves direct search method to minimize the difference between the measured and calculated values.

To evaluate the result of the calibration, a set of marker coils attached to an MEG phantom was localized using the calibrated 160-ch MEG system.

A spherical bobbin of the coil array

Mo-2 - SQUID biomagnetometer for magnetospinography

Yoshiaki Adachi1, Jun Kawai1, Shigenori Kawahata1, Dai Ukegawa1, Kensuke Sekihara2, Gen Uehara1

SQUID biomagnetic measurement systems optimized for the detection of the spinal cord evoked magnetic field (SCEF) have been developed. The SCEF signals were successfully recorded with a sufficient signal-to-noise ratio. The electric current distribution around the spinal cord was visualized along with an anatomical structure obtained by the in situ acquisition of X-ray images using magnetic source analysis by spatial filter techniques. The functional imaging of the spinal cord, known as magnetospinography (MSG), was achieved by measuring the SCEF, and this provided new information that would have significant implications for the accurate diagnosis of spinal cord disorders.

The latest SQUID biomagnetic measurement system was equipped with an array of vector SQUID gradiometers having a baseline length of 68 mm arranged in a 5 x 8 quasi-matrix. At any given time, a magnetic field in an area of 90 mm x 140 mm was observed as a vector map. The cryostat has a protrusion that is 540-mm long and 170-mm wide from the side surface of the cylindrical main body to store liquid helium as shown in the figure. The sensor array was positioned along the upper surface of the protrusion. This unique shape of the cryostat was designed to detect the SCEF from the back of a subject lying on a bed. The SCEF signals induced by peripheral nerve stimulation were clearly observed at the cervix and lumbar. We demonstrated that the
signal-to-noise ratio of the SCEF signals could be considerably improved owing to the improvement in the measurement system, the stimulation condition, and the signal processing for removing the stimulus artifacts.

Mo-3 - Auditory Cortex Signal Detected by Potassium Alkali Vapour Magnetometer

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Applying the current dipole model we present the source localization estimation of the auditory evoked magnetic field measured by a noncryogenic potassium vapour atomic magnetometer (1). The magnetometer was operating in spin-exchange relaxation-free (SERF) regime at low magnetic flux densities and high alkali-metal vapour density (2). Audio stimulation of short 1 kHz pulse trains has been applied by pneumatic earphone. After rejecting the subject's heart beat signals, signals originating from eye movements and disturbances due to mechanical vibrations, the N100m could be seen in several channels of the 256 channel atomic magnetometer. Using these channels with the best signal to noise ratio the approximate dipole source localization of the auditory evoked field was determined. The position of the estimated auditory evoked field source is located at the place as expected (3).


Mo-4 - GMR-based sensors arrays for biomagnetic source imaging applications

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New sensors have been recently proposed to detect biomagnetic signals as alternative to SQUIDs. In particular, by exploiting the new possibilities offered by spin electronics, a new mixed sensor has been developed (1). At low frequencies the sensitivity of these mixed sensors is about 1 pT by the 1/f noise. Thanks to their good performances, it has been recently demonstrated that mixed sensors are able to record magnetocardiographic (MCG) signals (2).

Here, we present the realization of a mixed sensors array, and its performances in detecting low magnetic signals from model and real sources. The recording of several channels is fundamental since it permits to drastically reduce the data acquisition time. Moreover, the sensors can be used in gradiometer mode, which could permit to employ the sensors outside a magnetic shielded environment. The array is realized by taken into account the results of numerical simulations, aimed to minimize the cross-talk between sensors.
Its performances are first measured using test signals, permitting us to verify the negligibility of cross-talk and to study the cross-correlation of noise sources (and notably the disturbing 50 Hz noise coming from the electricity supply). Thanks to this latter result, we could use the sensors in gradiometer configurations, which permitted to effectively reduce the 50 Hz noise down to a factor 20. On the basis of these findings, the MCG signal from a healthy volunteer was successfully detected by using two sensors simultaneously (see Figure). The rapidity of the measurement, together with its relative feasibility (in terms of complexity and costs), make mixed sensors promising candidates to extend the clinical use of MCG. Moreover, if their sensitivity will be further improved, mixed sensors arrays could be employed to detect MEG signals.


Mo-5 - Calibration of a multichannel MEG sensor based on Signal Space Separation method

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To make best use of multichannel MEG systems, an accurate sensor calibration is extremely important. This includes the knowledge of both channels sensitivities and sensor geometry, which can deviate from original system plans. In this work, we propose a new solution to the calibration of multichannel MEG sensors based on the Signal Space Separation (SSS) method (1). The SSS is a method for rejecting external interference and instrumental artifacts from MEG measurements. It has been shown (2) that an inaccurate knowledge of sensor calibration limits the performances of the SSS method, introducing a mismatch between the measured neuromagnetic field and its SSS reconstruction. Provided a suitable magnetic source, we show that a cost function, which strongly depends on sensor geometry, can be derived from the principal angle between the measured vector signal and the SSS basis. Hence, the calibration of the MEG sensor is carried out by minimizing the cost function using a large-scale optimization technique (L-BFGS) (3). Details of the magnetic source and calibration procedure are presented here. Finally, an application to the calibration of the 165-channel whole-head MEG system installed at University of Chieti is discussed.

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(3) D.C. Liu and J. Nocedal, Mathematical Programming, 45 (1989), 503-528

Mo-6 - Device ground truth using a single dipole phantom

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We describe the construction of a single magnetic dipole phantom with a hardware-independent microcontroller operated on a DC voltage input. Thus the phantom and microcontroller can be taken to different MEG labs regardless of manufacturer and power line voltages. The phantom dipole was driven by a sinusoidal signal from a constant current source using the microcontroller. Data from the phantom was collected at different MEG sites from different manufacturers in North America and in Europe. Two sets of data were collected at each site. Data was preprocessed using device specific software to remove environmental noise such as 3rd gradient correction for CTF data and signal space separation for Elekta data. All preprocessed data were converted to CTF format for further analysis. A modified dipole-fitting program was created with a point magnetic dipole forward model. The phantom dipole moment, and positions were fitted for the data from each site. From the MEG machines we have measured so far, the dipole moments were fairly consistent, varying by about 4% from each other. This phantom offers a potential ground truth for comparing MEG devices providing a controlled and reproducible magnetic field to compare MEG machines directly for projects that span different sites.

Mo-7 - Localization of Neuromagnetic Evoked Responses by using a Single Channel High-Tc-Squid

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After the first recordings of magnetic brain signals in 1968 by David Cohen Magnetoencephalography (MEG) became a common method. Today almost all systems are comprised with low Tc (LTC) squid sensors to detect extremely small magnetic fields generated by the human brain. LTC squid systems require liquid Helium. Although the technique is well established, construction and handling requires special materials and precautions. Furthermore liquid Helium is quite expensive and resources are limited.

With this study we test the feasibility of MEG signal acquisition and source localization utilizing a single High Tc (HTc) squid with 16 mm magnetometer input coil. Liquid Nitrogen kept the HTc squid at about 77 K. Results of at least one subject will be compared to data from the same subject(s) using a commercial 248 channel wholehead MEG system (Magnes WHS 3600, 4-D Neuroimaging). All experiments took place in a magnetically shielded room. Binaural stimulation was applied using 300 beeps (1000 Hz). To avoid magnetic interference the beeps were created by speakers outside of the shielded room and the sound was transmitted via flexible tubes to the ears of the subject. The same stimulation hard- and software was used for both, the HTc Squid and the wholehead acquisitions. Therefore within one subject the data can directly be compared. For the single channel HTc system the acquisition of the auditory evoked fields was repeated several times at different positions. Positions with maximum response obtained from wholehead recordings were used as starting positions for the HTc recordings. Measurements at 18 different positions around the maximum position were recorded. To establish a sensor coordinate system positions of the HTc sensor relative to the head frame were determined using the Fastrack® system manufactured by Polhemus.
Mo-8 - Feasibility of measuring cerebral hemodynamics with SQUID susceptometry

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Human brain function involves complex neuronal activity and spatiotemporal variations in metabolism, blood flow and blood oxygen level. In this project, we investigate the feasibility of simultaneous multimodal imaging of neural dynamics and hemodynamics with a modified magnetoencephalograph (MEG). Solenoid coils were added to a MEG instrument to apply a 20 microTesla DC magnetic field and noise levels in the magnetically shielded room (MSR) were then re-evaluated. We first measured the magnetic susceptibility response of deionized water that was pumped into an inverted flask under the array of superconducting quantum interference (SQUID) gradiometers. The magnetic field variations from the water compared favorably to theoretical magnetic susceptibility contrast. We conducted simulations to determine the susceptibility response to hemodynamics from the brain and from the scalp. Contrast to noise for cerebral hemodynamics was estimated from the water flask experiment and head model simulations. For this pilot study of 10 human subjects and 10 epochs per subject, we determined that a whole brain hemodynamic activation would be needed to obtain a measurable signal with a DC applied magnetic field and our MSR shielding level. Subjects performed the Valsalva maneuver to induce a global hemodynamic response in a blocked paradigm with pillows used to restrain the head. Subjects alternated eyes open and closed to cause changes in the alpha rhythm. Respiratory movements were recorded and used to exclude epochs with motion artifacts (37.5 percent of epochs excluded). Concurrent measurements from the prefrontal region were made using near-infrared spectroscopy (NIRS). The NIRS deoxyhemoglobin signal was found to correlate significantly with the SQUID readouts ($R^2 = 0.85$, $p < 0.05$). We conclude that it is feasible to measure intrinsic hemodynamics using a modified MEG instrument while simultaneously measuring MEG signals. Future work will focus on improving contrast to noise.

Mo-9 - Magnetoencephalography with high-Tc DC SQUID magnetometers

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Whole-head magnetoencephalography (MEG) systems are based on low-Tc (LTc) superconducting quantum interference devices (SQUIDs), which rely on liquid helium. In contrast, high-Tc (HTc) DC SQUIDs are cooled by cheap and easy-to-handle liquid nitrogen. Besides the unlimited availability and the low cost of liquid nitrogen, the major advantage of HTc SQUIDs is that they can be placed closer to magnetic sources when compared to LTc SQUIDs. The problem, however, is to reduce the intrinsic noise of HTc SQUIDs down to 10 fT/rt(Hz) at 77 K, as required for MEG. Here, we introduce home-built multilayer HTc SQUID magnetometers that have a magnetic field resolution of 4 fT/rt(Hz) at 77 K. We demonstrate results from MEG measurements obtained using our HTc...
SQUIDs and a commercial LTc system for neuromagnetic brain responses recorded from one volunteer subjected to auditory stimuli. The low intrinsic noise of the HTc SQUIDs and the closer distance to the cortex result in a signal-to-noise ratio that is comparable to commercial LTc MEG systems. Our results confirm the feasibility of using HTc SQUIDs for neuromagnetic measurements and open the way for upgrading MEG systems using HTc SQUIDs. This technology promises to make MEG systems independent of helium and more user-friendly. It would also reduce running costs, which in turn hamper the widespread utilization of MEG systems in clinical practice and research.

Results of measurements of an auditory evoked field obtained using a HTc SQUID sensor (red and green curves) and LTc SQUID sensors (blue curves).

Mo-10 - Determination of Cardiac Output by analyzing records of bioelectric heart activity

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In intensive care units most medical and paramedical staff are familiar with the measurement of cardiac output by thermodilution method. This technique however, has some limitations, as in patients with tricuspid regurgitation, very common in critically ill patients, in addition to being influenced by factors such as fluid injection rate, temperature, rhythm disturbances. Registering the analysis of the reproducibility of the signal record bioelectric heart activity, Figure 1, using a recently patented medical device, which has the distinction of recording the curves of arterial and venous pressure as those obtained using the standard technique gold in these assessments, cardiac catheterization. Is obtained by the measurement of cardiac output on 4 persons, this technique has the advantage of avoiding direct damage to the vessels by measuring variations in the intensity of a magnetic field generated by a magnetic marker at a fixed distance from a transducer that converts mechanical motions analog signals - digital expense applying the formula \( x = \text{VS} \times \text{FC} \) (VS: systolic volume ejection, FC: heart rate), where VS is under normal conditions (D=70 ml/beat) and FC is the average value of signal) obtained by measuring variations in the intensity of a magnetic field generated by the magnetic marker.
Mo-11 - A barrier free magnetic shield and its application to MCG measurements by a flux-gate array

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We have developed a barrier free magnetic shield that would be suited for the use in the hospital. The structure of the shield is cylindrical with both ends open and designed to be placed horizontally, in this case, however, magnetic shells of the shield are separated so that one can move them and access the inside easily. The size of the magnetic shield is 2.4 m in horizontal length, 1.4 m in height and also in width. Magnetic shells were fabricated by placing many layers of amorphous tapes of 5 cm in width to cover outer surfaces of the half-cut cylinders together with carbon and/or glass fiber woven clothes and resins, resulting in a fiber reinforced plastic and magnetic layer composite. The total weight of a shell pair was 540 kg. The two shells are stood to have a cylindrical space inside of them with a spacing of 30 - 40 cm at facing edges running along the cylinder axis which allows for insertion of, for example, a long dewar of SQUIDs through the top spacing and allows for standing legs of a bed on the floor. Active compensation is added for perpendicularly to the two shells and also the vertical direction to which sensor’s sensitivity axes are parallel. We will present our barrier free magnetic shield and demonstrate this time that MCG can be detected by fluxgate magnetometers in the magnetic shield. Our early result of MCG measurements by fluxgates is shown in Fig. 1. The fluxgate magnetometers used are fundamental-mode orthogonal fluxgates originally proposed by Sasada (1) and currently have white noise density $3 \sim 4 \mu T/\sqrt{Hz}$ at 10 Hz. Averaging over 30 beats was taken by using the most visible MCG signal from one of fluxgate channels as a trigger. The frequency band observed was 2 - 20 Hz. We are further developing a fluxgate array (6 by 6 with 3 cm spacing) and tuning the parameters of active compensation. We will show improved results of MCG at the conference.

Mo-12 - Magnetomodulation Superconducting Sensor of Weak Magnetic Field

Levan Ichkitidze

High-temperature superconducting ceramic materials (HTSC) as a rule are granular superconductors, represent ‘Josephson medium’ with a high nonlinear magnetic susceptibility in a weak magnetic fields $B < 1$ mT. This property is used in magnetomodulation sensors (MMS), using as a magnetosensitive elements moderate cylindrical sample (with a diameter 1-6 mm and a length 5-15 mm) made of ceramic HTSC material. MMS principles of operation are analogous those of a flux-gate magnetometer.

Pilot MMS characteristics greatly improve on using ceramic HTSC material Bi-2223 system as a magnetosensitive element (1). Furthermore, Josephson current density between granules in Bi-2223 materials by temperature $\sim 77K$ much higher as in material Y-123. Therefore, quadratic component response in it must be presented until far greater external magnetic field values ($B_* \sim 1 mT$) then those in Y-123 materials ($B_* \sim 0.3 mT$).

Thus, lower assessed value of threshold magnetosensitivity $B < 10 – 12T$ and higher limiting value of measuring field $B_* \sim 1 mT$ in HTSC ceramic Bi-2223 in comparison with those in ceramic Y-123 permit to create on basis of they the MMS with the parameters values $B \sim 10 – 12T$ and dynamic range of measurement $\sim 140dB$ which are closely related to corresponding HTSC SQUID parameters.

Proposed MMS parameters make their attractive for using their in biomedicine applications, in particular for liver, lungs, other internal and tissues and other biomedicine objects in noninvasive diagnostics. Also they can be demanded in various areas of a science and technics, including in not destroyed control of materials and over a magnetic location.

Prof. Selischev S.V. is acknowledged for supporting this work.


Mo-13 - Hybrid Magnetic Field Sensor with Superconductive Magnetic Flux Transformer for Detection of Carbon Nanotubes

Levan Ichkitidze

Carbon nanotubes (CNT) are detected by the magnetic field sensor (MFS) if magnetic nanoparticles are encapsulated into CNTs. For this purpose, very sensitive sensors, or example, SQUID sensors and MFS based on the effect of giant magnetic resistance (GMR) are used. Particularly, the hybride MFS, which consists of the film superconductive magnetic flux transformer (SMFT) and magnetosensitive elements (MSE) based on the GMR effect, is comparable with the high-temperature superconductive (HTS) SQUID sensors in regards to its resolution by magnetic field.

The possibility of increasing the gain factor $F$ of the SMFT and thereby improving the main MFS parameters is investigated. A typical hybrid MFS that consists of the dielectric substrate, the MSE based on the GMR effect, and insulating film arranged between the active strip of the SMFT and the MSE is considered (1).
It is found that in the case of optimal division of the active SMFT strip (7 \( \mu m \) wide) into parallel branches with nanodimensional widths (90-350 nm), \( F \) increases relative to the case of the active MFST strip prior to its division by a factor 25 to 80. For the low-temperature superconducting films, i.e., the films with small London penetration depth 4 of the magnetic field (e.g., for Nb, \( \sim 50nm \)), the higher values of \( F \) relative to HTS films are attained (e.g., for Y-123, \( \sim 200nm \)). An increase in \( F \) promotes attaining the resolution level \( 1 \) pT at temperature 77 K, which is more effective that the resolution (\( B \sim 10pT \)) of HTS SQUID. Thus, the suggested hybrid high-resolution magnetic field sensor will allow us to noninvasively monitor the concentration, distribution, and migration of CNTs in biological objects as well as to monitor various magnetic objects (particularly, mesoscopic magnetic particles, nanoelectronic elements, and superparamagnetic nanoparticles) in other systems.


Mo-14 - Superconducting Film Magnetic Field Concentrator for the Sensor of Magnetic Field

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As shown in (1), the magnetic flux transformers efficiency increases with optimal fragmentation of its active stripe to multiple parallel branches and slits. They have micron or submicron sizes. Similarly, magneto sensitive elements (MSE) resolution and biomedical magnetic systems efficiency can be also improved.

The object of this study is a magnetic field multiplication (concentration) factor \( F \). Magnetic field sensor geometry consists of a superconducting film magnetic field concentrator (MFC) with a tapered active stripe and a film MSE based on GMR effect. The MSE is overlapped with the MFC active strip and is separated with an insulator film.

For different fragmentations, the \( F \) was found to change insignificantly - it is reduced less than by 10% of its maximum value. At the same time, when the slits were significantly approximated to the edges or the middle of the active strip, the value \( F \) is reduced by a few times, and with the growth slits width and London penetration depth - the value \( F \) is reduced monotonically.

Analysis of the results leads to the conclusion that the fragmentation of the active strip on a small number of nanoscale canals (3) and slits (2), i.e. topological nanostructuring of the active strip, increases the multiplication factor and make it possible to achieve a larger magnetic field concentration on the MSE in 4. The calculations take into account: the width of slits 20-500 nm, the thickness of MSE \( \sim 50nm \), the London penetration depth \( \sim 50nm \). Therefore, characteristics of magneto sensitive element are improved accordingly.

The results will be in demand in different magnetic systems, registering weak magnetic fields (~10 pT): in the noninvasive biomedical diagnostics, destructive testing of solids, the electrical circuits in a field short circuit.


Mo-15 - Magnetic cytological detection system using high-Tc SQUID operated by module type flux-locked loop circuit

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A single-channel magnetic detection system using HTS-SQUID was developed to detect a magnetic field obtained from a cardiac activity and a magnetic particle in animal organ. The system was equipped with a HTS-SQUID gradiometer, a liquid nitrogen cryostat and a magnetically shielded box, and a module type flux locked loop (FLL) circuit with low amplifier noise (0.66 nV/ Hz/\( 1/2 \)). The HTS-SQUID gradiometer had a baseline of 5.5 mm and an effective area of 0.125 mm\(^2\) to improve the spatial resolution, and then it was mounted on the top of a sapphire rod inside the cryostat for cooling to liquid nitrogen temperature. The FLL circuit consists of a FLL unit and a PC interface. The FLL unit was set inside the magnetically shielded box. The cryostat had a 7L liquid nitrogen capacity to cool down the HTS SQUID for over 2 days. The two-layer structured magnetic shielded box has been constructed of permalloy with high shielding factor (50 dB), and it had a small window in the front door to set easily the bio sample under the HTS SQUID without opening the whole door. The window made it possible to access the sample without exposure to magnetic interference noise. The system noise in the permalloy shielded box was 80±0 Hz/\( 1/2 \) at white noise level. The 1/f noise of HTS SQUID was removed by AC bias operation (1) of the FLL circuit. Although the reduction of the system noise depending on the HTS SQUID is needed to detect the bio sample, the single-channel magnetic detection system is a promising tool for a magnetic cytological evaluation.

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Mo-16 - Optical Pumped Magnetometer Operated by Mixed D1 and D2 Laser Beams

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High sensitivity optical pumped magnetometers (OPMs) which can detect very weak biomagnetic signals have been studied intensely in recent years. Our aim of this study is find optimal optical transition to improve performance of OPMs. To find the transition, we investigated magnetic resonance in cesium vapor using either optical transition (D1 line, D2 line, or mixed D1 and D2 lines).

We used a cesium cell filled a buffer gas (neon and argon at partial pressures of 4.5 and 0.8 kPa). Two external-cavity-diode-lasers whose frequencies were actively locked to the D1 (894 nm) and D2 (852 nm) lines were prepared. The cell was set up in a coil configuration composed of a solenoid coil and an rf coil in a magnetically shielded box. Each beam was coaxially mixed by a half mirror, and the mixed beams were incident on the cell. The mixed beams passing through the cell were separated into D1 and D2 beams by a diffraction grating, and either D1 or D2 beam was detected. Static magnetic field (B0) was applied to the cell by using the solenoid coil, and an angle between B0 and the beam direction was adjusted to 45. In addition, rf magnetic field (Brf) was also applied to each cell at orthogonal direction to B0. We detected magnetic resonance spectrum by sweeping the Brf frequency, and measured value of \( \text{SNR}/\sqrt{\text{df}} \) to find the optimal optical transition. Where, df and SNR were the line width and signal-to-noise ratio in the magnetic resonance spectrum, respectively.

As a result, the \( \text{SNR}/\text{df} \) value obtained by using mixed beams was respectively 10 and 160 times larger than that obtained by using D1 and D2 beam.

In conclusion, the sensitivity of OPM using mixed D1 and D2 lines is much higher (10 or 160 times) than that using D1 or D2 line.

Mo-17 - Summing magnetometer outputs in an elektaval view for novel purposes

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We have been summing the output traces of the magnetometers in a whole-head MEG helmet (Elekta VectorView). We are using real-time custom Graphical User Interface (GUI) written in Matlab, which reads real time data from MEG systems. We assign different weights and polarities to each magnetometer, depending upon the purpose of the experiment. Because the data is handled in real time, a number of novel measurements become possible, as the parameters can be changed quickly and results seen instantly.

First, we may be able to detect the Johnson and/or magnetic domain noise of the inner permalloy layer of the shielded room, apparently not clearly seen before, this would show the sensitivity limit of MEG magnetometers in shielded rooms. We expect an instrumental noise, for an approximate uniform field distribution at the helmet, of about 0.2-0.4 fT/square-root Hz. Second, with rearrangement of weights we may be able to search for sources in the brain occurring as magnetic dipoles (current dipoles in a circle), at a higher sensitivity than normal. There is a hint that these might be present with interictal epileptic spikes, where MEG signals are occasionally seen without obvious EEG counterparts. If such magnetic dipoles are seen, this could clarify a new way to get unique information from this type of clinical MEG.

Third, looking at deep brain structures such as the hippocampus and basal ganglia. These are important in multiple brain functions and their related disorders. Here we would 'tune' for deep brain structure by appropriately adjusting weights of the magnetometers, resulting in higher sensitivities than usual MEG scanning methods. If successful, this may open new possibilities of using the MEG in clinically looking at neurological disorders such as Parkinson, Huntington and Alzheimer diseases.

So far, preliminary traces of the general method look promising. Actual results of these various novel experiments are presently being gathered and will be presented.

Mo-18 - First Order Gradient Compensation Technique in an Unshielded Multi-channel Magnetocardiograph System

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For an unshielded magnetocardiography (MCG) system, environmental noise suppression is a great challenge. The status of working site is of great importance for the stability and performance of MCG system. In Shanghai downtown area, where there are many cars and trams underground, the magnetic field fluctuation in daytime is more than 2 micro Tesla (04:00-24:00) and in quiet nighttime also will be 800 nT (00:00-04:00).

By using the conventional software gradiometer, which combines a second order wire-wound axial gradiometer with a three-axis reference magnetometer module, the noise level could be reduced from 2 micro Tesla to about 5 pT. But in practice, a gradiometer still has some response to the uniform magnetic field and the gradients with lower orders, especially along z axis (the direction along the gradiometer baseline). To solve this problem, a novel software gradiometer configuration is presented by introducing three magne-
tometers along z-direction in reference module to produce three first order gradient components: \( \Delta(Bz)/\Delta(x) \), \( \Delta(Bz)/\Delta(y) \), \( \Delta(Bz)/\Delta(z) \). By using the adaptive spatial filter algorithm, the noise level could be further reduced from 2 micro Tesla to 2 pT, about 2.5 times lower than that with the traditional method. This novel scheme with gradient compensation module was successfully applied in our unshielded MCG system. The integrity of MCG signal is also evaluated and analyzed in time and frequency domain.

**Mo-19 - Multi-channel Magnetocardiograph System with a Novel Low Tc DC SQUID Gradiometer Module**

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A novel niobium (Nb) SQUID gradiometer module with an Nb wire-wound antenna is designed and fabricated. In this design, the antenna is connected to a dual-loop SQUID chip onto which a voltage feedback circuit is integrated to suppress preamplifier noise contribution. Here, the dual-loop SQUID is employed to suppress the external magnetic disturbances and provide sufficient space for all coils coupling to the SQUID individually. In a magnetically shielded room (MSR), the sensitivity of the SQUID gradiometer module is measured to be about 1 fT/cm/rtHz in the white noise range.

A multi-channel magnetocardiograph (MCG) system with simplified readout electronics is set up by using such SQUID gradiometer modules. Different axial antennas are designed for human heart signal measurements in unshielded laboratory environment (ULE) or in MSR. An adaptive compensation is achieved by combining this SQUID gradiometer module with some additional planar reference SQUIDs, which effectively suppresses the noise in ULE. Here, the optimal compensation factors are in situ calculated with a software developed by us. The MCG signals measured in ULE and MSR are evaluated and compared. In addition, the performance of the MCG system based on the novel SQUID gradiometer module is compared with that based on the traditional flux modulation SQUID module.

**Mo-20 - Development of wide dynamic range SQUID magnetometer using analog FLL with flux-quanta counting**

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In present biomagnetic measurement, a magnetically shielded room (MSR) is required on environment magnetic noise which generates from cars and trains. However, the MSR is very expensive and heavy. In recent years, it has been demonstrated by several groups that digital SQUID electronics with digitally controlled flux-locked loop (FLL) system achieves biomagnetic measurements outside the MSR. There is the Flux-Quanta Counting (FQC) method in one of these methods, and microcontroller and DSP are used for the control part.

We had developed analog FLL (A-FLL) system using the FQC method by all analog circuit in order to realize even more wide dynamic range. This A-FLL was operated of the FQC using high-speed analog switch and comparator. However the switching behavior of this A-FLL became unstable by the noise which was included for the signal. Therefore, there was a problem which could not operate the high-speed switch.

In this study, the stabilization of the switching behavior was realized with the aim of wide dynamic range of A-FLL. The comparator used the high-speed device and gave the hysteresis property. As this result, high-speed operation and stability behavior became possible than the conventional system. Figure shows an active area of the A-FLL system. It means the system can measure magnetic signal just in this area. The dynamic range of developed SQUID system became 165dB at 1Hz, 151dB at 10Hz. The magnetocardiogram measured using developed system will be shown in the presentation.

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Mo-21 - Optimum combination of axial gradiometers and magnetically shielded rooms for high-sensitivity economic magnetocardiography measurements

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Typical applications of magnetocardiography (MCG) technology are detection of coronary artery disease or ischemia, and detection of arrhythmic current activity. For the accurate diagnosis of non-repetitive events using un-averaged data, such as, stress-MCG or arrhythmia, high-sensitivity superconducting quantum interference device (SQUID) system is needed. Traditionally, a SQUID magnetometer system operating inside heavy magnetically shielded room could provide best signal-to-noise ratio (SNR). For economic approach, we need to find optimum combination of magnetic field sensor and shielded room, so that most of the real-time events can be measured with acceptable SNR economically. We fabricated several magnetic sensors, magnetometer, axial gradiometers of first-order and second-order with different baseline lengths, and operated them in several shielding conditions, heavily shielded, moderately shielded, and lightly shielded room. And we compared the SNRs of each magnetic sensor depending on the shield each combination, and found that a long-baseline first-order axial gradiometer combined with moderately or lightly shielded room provided good SNR in real hospital environments.

Mo-22 - Measurement of Biomagnetic Signals with a Multi-channel Chip-Scale Atomic Magnetometer System

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We report on measurement of biomagnetic signals with an array of four fiber-coupled chip-scale atomic magnetometer (CSAM) sensors. The sensors are based on absorption of laser light in a heated, micro-machined atomic vapor cell of volume (1.5 mm)³ enclosed in a thermally isolating vacuum package of volume 1 cm³. Each sensor had sensitivity of 20 fT rms/√Hz with a bandwidth of 200 Hz and a dynamic range of ±10 nT. Compensation fields generated by coils on the sensor packages were used to reduce the ambient field to within this range.

The sensors were directly placed on the skin of healthy human subjects, similar to contactless ECG or EEG electrodes, for measurements of magnetocardiograms (MCG) and magnetoencephalograms (MEG), such that the component of the magnetic field perpendicular to the body was detected. The measurements were conducted in the magnetically shielded room BMSR-2 in Berlin, which has a static residual magnetic field of < 2 nT. The MCG was measured with the sensors attached simultaneously to the chest and back of the subjects during resting phases and while the subject was paddling in an ergometer. The QRS and T waves are clearly visible in the unprocessed data. Similar measurements were conducted in standard conventional shielded room Ak3b with a static residual field of < 50 nT, thus demonstrating the viability of operating these unique biomagnetic measurement systems in most of the conventional magnetically-shielded environments available worldwide. In addition, evoked MEG signals were measured.
Auditory-evoked M100m signals and somatosensory-evoked N20m signals were recorded simultaneously with the 4 CSAMs and a superconducting quantum interference device (SQUID) array. All the important features were clearly visible in the averaged data of both sensors. These proof-of-principle experiments are important milestones in eventually developing a low-cost, uncooled alternative to SQUIDs for measurement of biomagnetic signals in a clinical setting.

Mo-24 - Performance of a triple-sensor MEG system with additional tangentially oriented sensors

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This study was performed to evaluate the interference suppression capability (‘software shielding factor’) when 18 tangentially oriented triple-sensor units (one magnetometer overlaying two perpendicular planar gradiometers) were added to a standard 306-channel MEG system (Figure 1a).

A series of recordings was performed in a magnetically shielded room with a small coil at varying distances from the sensor array. In addition, data from four healthy volunteers were recorded to compare the auditory and somatosensory evoked fields (AEF, SEF) obtained with the 360-channel and 306-channel sensor helmets.

All recordings were processed with the signal space separation (SSS) method to suppress external interference. The SSS expansions utilized 80 and 15 multipoles for the regions inside and outside of the helmet, respectively. Software shielding factor was determined as the ratio of the norms of the magnetometer-channel signal vectors before and after SSS processing. Suppression of the interference due to the coil is presented in Figure 1b. The shielding factor was 150 for the 306-channel and 290 for the 360-channel case when the coil was 2 m away from the sensor array.

Mean correlation between 360- and 306-channel averaged AEF and SEF signals was 0.97. Higher sensor noise and larger remaining interference in the 306-channel data reduced the correlation. Frequency spectra of two channels after SSS processing are shown in Figure 1c. The 360- and 306-channel average spectra are very similar below 30 Hz, but SSS with 360 channels results in significantly lower noise at all frequencies than the standard with 306 channels.

According to the results, adding the 18 tangentially oriented sensor units: (1) Improves significantly the SSS shielding factor. (2) Does not affect the brain signals but decreases the inherent sensor noise levels after SSS processing. (3) Increases the numerical stability of SSS and removes the need to omit multipole terms with marginal contributions.

Figure 1. a) Positions of the additional tangentially oriented sensor units. b) Software shielding factors as a function of distance from the interference source. c) Averaged FFT spectra of an evoked response recording.

Mo-25 - Rapid generation and evaluation of sensor arrangements for novel helmet shapes

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Quick evaluation of different MEG helmet shapes is desirable in development projects. However, each novel helmet geometry requires a corresponding sensor arrangement, which are cumbersome to create manually. We implemented an automatic algorithm for approximate positioning of Elekta Neuromag triple sensors, based on simulated annealing and sensors confined on a dense mesh representing the sensor surface. It can operate on arbitrary-shaped confinement surfaces. As is typical of simulated annealing, convergence to reasonable solutions happens in a small number of iterations (computable on the order of minutes), while more computation time can be used to refine the solutions.

With the algorithm, fast evaluation of different sensor helmets becomes feasible. As an application, we evaluated a reduced-size array created by scaling the existing Elekta Neuromag array. All dimensions were reduced by 15%. The array was then populated with 72 triple-sensors (total of 216 channels). Despite the reduced number of sensors, the resulting smaller array has good performance in the signal space separation algorithm, with SSS shielding factor comparable to the existing 306-channel system. The sensitivity of the array to sources in a small spherical volume (r=6 cm) is increased by a factor of 2.7, due to the decreased sensor-source distance.

Figure 1: a) Dense confinement surface created by scaling and interpolation of existing array. b) Random initial sensor positions on the confinement surface. c) Positions after annealing has converged. d) Corresponding triple-sensors with orientations

Mo-26 - Development and Evaluation of Fifty-Coil Phantom for MEG Systems

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Magnetoencephalography is one of the most promising applications of biomagnetics. In order to expand and establish MEG applications, an evaluation standard for MEG systems is necessary. We have proposed and fabricated a dry phantom that is composed of two isosceles-triangle coils based on Ilmoniemi’s model. In this paper, we developed a more practical MEG phantom composed of fifty isosceles-triangle coils (left). It is constructed to imitate a human head. The conductive sphere in the ‘wet’ model can be assumed to be the assembled coil-sets, and then every equivalent current dipole (ECD) is positioned the midpoint of each isosceles-triangle coil. The coil-sets were placed inside a domed cover, which has several types of markers to indicate the position of the MEG phantom in the MEG helmet.

Moreover, the uncertainty level of the phantom itself and the intrinsic difference between the ideal models and the practical coils have not always been stated in the literature. In this study, we evaluated the intrinsic difference and uncertainty of the phantom by measuring shapes and positions of the fifty isosceles-triangle coils using an X-ray computed tomography (X-ray CT) device and a coordinate measuring machine (right). The intrinsic difference for ECD position and intensity of every coil were measured, and the mean values were 0.19 mm and +7.62 %, respectively. The uncertainty of the measurement was estimated at 0.04 mm and 0.85 %. We demonstrated the experimental evaluation of our MEG system using the new phantom. The intrinsic difference should be included in the expected position and moments for each coil, when estimated ECDs analyzed from measured magnetic field data are evaluated. The mean difference of ECD position and moment were 1.3 mm and -5.6 %, respectively. We concluded that these result have come from the MEG system or operation in experiment, because these values were more than the uncertainty level of the
Mo-27 - Publication criteria for evoked magnetic fields of the human brain: a proposal

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Magnetoencephalography (MEG) is a record of the magnetic fields produced by the electrical activities of the brain using MEG systems. There are three types of sensors for MEG systems: magnetometer and two types of gradiometer. Among them, two types of gradiometer, axial and planar, have been used worldwide. However, the waveforms of individual MEG sensors inherently differ between the two types of gradiometer, for the planar gradiometer, the response with the maximal amplitude is recorded from the sensor located just above the equivalent current source, for the axial gradiometer, the maximal positive and negative responses are obtained from a pair of sensors apart from each other that sandwiches the equivalent current source. A unit of amplitude of the MEG waveform also differs between the two types of gradiometer. These pose a serious problem in comparing and evaluating the data from the two gradiometers, perhaps precluding extention of clinical application of MEG testing. We consider that the MEG study should be published in a way that allows other workers using different types of gradiometer to evaluate and replicate the results of MEG studies. There have been, however, no publication criteria for reports of studies on stimulus-evoked or event-related magnetic fields in human subjects. Here, we propose publication criteria for evoked or event-related magnetic fields of the human brain: original waveforms of selected channels covering a region of interest, a root mean squared (RMS) waveform, and a contour map at an appropriate time. These three set will allow comparison of evoked or event-related MEG signals recorded with different MEG sensors. We hope that the publication criteria we proposed will facilitate the multicenter study on evoked or event-related MEG and establishing the normal database of evoked or event-related MEG signals and thereby, expand clinical application of MEG.
Somatosensory evoked magnetic fields with an axial gradiometer (A) (Yokogawa, MEGVision) or a planar gradiometer (B) (Neuromag, Vector View). Superimposed MEG waveforms, root mean squared (RMS) waveforms and contour maps are similar.

Mo-28 - Atomic magnetometry: present and future applications

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Over the last decade there has been a huge development of atomic magnetometry that has given rise to an increasing interest in using it as an alternative to SQUID-base devices for measuring weak magnetic fields. The not requirement of cryogenic cooling and a shielded room, the advancements in miniaturization and potential portability, and its excellent sensitivity, make atomic magnetometers one of the most promising devices in the measurement of extremely weak magnetic fields.

Our aim is to provide an introduction to these technologies and review the nowadays important applications of these atomic magnetometers as well as point out the possible future applications in biophysics and other fields.

Mo-29 - Atomic magnetometer pumped with intensity-modulated light

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We present an all-optical chip-scale atomic magnetometer. It uses pump-light intensity modulation (IM) like the original Bell-Bloom (BB) magnetometer, combining pumping, phase synchronization of the spins, and measurement in one laser beam. In contrast to the BB setup, where only the secular change of the transmission was evaluated, we detect the resulting modulation of the transmitted light signal phase-sensitive. Various pump-light modulation patterns were tested, revealing rectangular modulation with 100% modulation depth and 50% duty cycle as the best choice for high magnetic field resolution.

In array setups, one single laser source can be used for multiple channels. As an example, we show the noise-reduction by the subtraction of the signal of a reference magnetometer cell from the measurement channel. In this way, the shot-noise limit of the magnetic field resolution (220 fT/√Hz in our 50mm³ Cesium cells) is approached for measurements even in the micro-tesla field range. In the IM configuration, various errors which may occur in the common Mx method (for example phase errors due to misalignment between pump light and phase synchronization direction, crosstalk between various channels in magnetometer arrays) are excluded per se.

Due to all these features, the intensity-modulated magnetometer will be attractive for the setup of biomagnetic sensor assemblies.
Mo-31 - Experiences with a third party Helium Recycling system

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Swinburne University of Technology recently made the decision to install a commercially available helium recovery and reliquefaction system designed for use with MEG systems. The recycling system is designed to be used without a purification stage (avoiding the need for liquid NO2), making use of metal storage containers in place of the customary gas bag to avoid permeation of impurities through the wall of the bag. We will describe our experiences with installation and commissioning of the system and its space requirements, as well as discuss day-to-day issues and changes to refill procedures required to optimise efficiency and minimise impurity ingress into the system, which is by necessity non-closed loop. The absence of a purification stage implies the necessity to ‘recharge’ the reliquefaction plant on an occasional basis, and we will report the frequency of this form of maintenance, the efficiency of the system (weekly losses), and running costs, in particular electricity required to run the reliquefaction unit.

Mo-134 - Neural Correlates of Emotional Expressions in Individuals with High and Low Autistic Tendencies

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Faces are considered to be processed holistically rather than on the basis of features. The face inversion effect disrupts holistic processing through altering the familiar configuration of facial features making the face more difficult to identify if presented inverted. Individuals with autism have difficulties in both face recognition and processing of emotional expressions. They usually show absent or reduced face-inversion effect. Early event-related potential (ERP) components are suggested to reflect basic structural encoding of faces, whereas later components are thought to reflect categorization and attention to motivationally relevant information, including emotion, gender, or identity. However, some recent findings reported ERP effects of facial expressions in both early and later components. The current study investigates the relationship between neural response to facial expressions (neutral, fearful, happy and sad) and autistic-like traits in the general population as measured by the Autism Spectrum Quotient (AQ). It looks at interaction between neural encoding of structural face information and facial emotions by presenting emotional faces upright and upside-down and by looking at early and later ERP components. We particularly investigate the face-specific N170 component, which is considered to represent the structural encoding of faces and is found to be larger and slower for inverted than upright faces. We hypothesised that differences in high and low AQ will be the most significant during inverted faces, suggesting more general effects of facial features rather than emotion-specific effects during processing of facial emotions.

Mo-135 - Complexity analysis of resting-state MEG activity in Traumatic Brain Injury patients

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Introduction

Due to the difficulty in determining the localization of focal brain lesions in a large percentage of TBIs, the underlying anatomical basis for TBI has been largely unclear. Recent neuroimaging studies show neural functional changes and white matter disruptions in TBI. These suggest that regardless of an absence of apparent focal lesion, the neural network connectivity might be disrupted in TBIs. A promising measure that can characterize such connectivity objectively is complexity. Lempel-Ziv complexity (LZC) is a model-independent estimator of system complexity by estimating the number of different patterns in a sequence. It is thought that brain illnesses impair the normal patterns of brain connectivity. Presumably, due to the potential damage of connections between regions, TBIs would show a reduced level of complexity.

Methods

MEG data were obtained from 32 diagnosed TBI patients (15 military and 17 civilians at mild/ moderate level of severity) and 15 healthy controls during resting conditions. LZC values were obtained for each channel and each subject and averaged in different
sensor groups.

Results
Normals vs. civilian TBIs vs. showed a significantly higher LZC scores in frontal and posterior regions centering on the midline. Normals vs. military TBIs showed a significantly higher LZC scores in multiple regions in a more diffuse manner: bilateral frontal, temporal and posterior parietal area.

Discussion and conclusions
Our results indicate reduced complexity in multiple brain area in TBIs. This is likely due to impairment of connection either anatomically or functionally. Location-wise, the civilians showed reduced complexity in frontal and posterior regions, which might be explained by the cause of injury mostly being car collisions with the force coming from the anterior frontal part. Military TBIs showed more spread-out reduced complexity, which is likely due to injuries caused mostly by blasts resulting in damages in a more diffuse manner.

Mo-136 - Efficient estimation of cross-frequency coupling from Parkinson’s disease recordings

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Phase-amplitude cross-frequency coupling (PAC) has been spotted as an intriguing phenomenon widely observed in human and animal EEG, MEG and local field potential (LFP) recordings. It is considered to reflect an essential relation between large scale low frequency oscillations and the activity of microcellular level neuronal assemblies associated with high frequency oscillations. This study presents a formal analytical definition of PAC. An estimator called ‘normalized direct PAC’ (ndPAC) is derived based on this definition. We also introduce a parametric statistical formula supplemented to this estimator enabling a fast and reliable PAC assessment. The confidence limit of ndPAC depends solely on data length and confidence level making it superbly efficient when compared with many other traditional PAC estimators relying on permutation based statistical tests.

The proposed estimator is applied on LFP and MEG data acquired from a Parkinson’s disease patient for various medical (levodopa OFF and ON) and movement (rest and move) conditions. The performance results are compared with those of a traditional method called statistically normalized modulation index. Moreover, we demonstrate numerical simulations replicating the commonly observed PAC patterns between beta band and very high frequency oscillations in Parkinson’s disease recordings. The synthetic data are produced by Hanning tapered smooth high-frequency activity added to a specific phase of a beta cycle.

Real and simulated data results indicate that ndPAC reveals the cross-frequency couplings in brain signals accurately. The computational efficiency owing to a plain statistical thresholding allows ndPAC to be a promising methodology to capture PAC relations embedded in large neurophysiological data sets. This is especially crucial while searching for connectivity between different numerous combinations of brain regions.

Normalized direct PAC (ndPAC) and statistically normalized modulation index (MIS) estimates for dopamine OFF and ON conditions. Please note that the execution of ndPAC takes much less time (~ 100 times less) than that of MIS.
Mo-137 - Decreased reactivity of somatosensory and motor cortex oscillations (10 Hz and 20 Hz) in cerebral palsy

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Cerebral palsy (CP) is characterized by difficulty in the control of movement and posture as a result of a damage to the brain during early development. People with spastic CP have hypertonia of the muscles in the affected limb(s) hindering its usage. In addition to motor problems, tactile discrimination deficits are prevalent in people with CP.

In order to elucidate both the motor and somatosensory aspects of cortical functioning in CP we studied, with magnetoencephalography, the reactivity of the ~10–Hz and ~20–Hz rhythms, suggested to be generated mainly in the primary somatosensory and motor cortices, respectively. We recorded rhythmic brain oscillations during median nerve stimulation in 13 adolescents with hemiplegic CP caused by early unilateral brain damage of various etiologies and in 13 age- and sex- matched controls. The stimulus-induced suppression and subsequent rebound of the oscillations were quantified with temporal-spectral evolution method.

The reactivity of the oscillations to contralateral hand stimulation was lower in the affected than in the unaffected hemisphere in the CP group (Wilcoxon Signed Ranks Test, 20-Hz suppression Z = 2.9, P = 0.002, 20-Hz rebound Z = 2.62, P = 0.006, 10-Hz suppression Z = 3.11, P < 0.001, 10-Hz rebound Z = 2.41, P = 0.013) with no difference between the hemispheres in the control group. Furthermore, the strength of the 20-Hz rhythm rebound in the affected hemisphere was significantly weaker in the CP group than in the controls (Mann-Whitney U = 39, P = 0.02).

The reactivity of oscillations in both motor and somatosensory cortices in the affected hemisphere (contralateral to the side of hemiplegia) of adolescents with CP was decreased in line with observed motor and sensory deficits.

Mo-138 - Imbalanced synchronized oscillatory activity of the primary motor cortex in early stages of Parkinson’s disease

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Pathophysiological changes in basal-ganglia-thalamo-cortical circuits are well established in idiopathic Parkinson’s disease (PD). However, it remains open whether such alterations already occur at early stages representing a characteristic neurophysiological marker of PD. Therefore, the present study aims at elucidating changes of synchronized oscillatory activity in early PD patients. In the present study whole-head magnetoencephalography (MEG) was performed in a resting condition and during steady state contraction of the more severely affected forearm in 10 de novo patients without any anti-parkinsonian medication, in 10 early stage patients with medication and in 10 age-matched control subjects.

While cortico-muscular coherence (CMC) did not differ between groups, motor cortical power at beta frequency (13 - 30 Hz) was shown to be increased in patients as compared to controls during rest as well as during isometric contraction. In healthy controls power of the contralateral hemisphere was significantly suppressed during isometric contraction. In contrast to this, in de novo patients both hemispheres were activated equally strong while in medicated patients the pattern was found to be reversed. Contralateral beta power was significantly correlated with motor impairment during isometric contraction but not during rest. The present results suggest the reduced ability of the primary motor cortex to disengage from increased beta band oscillations during the execution of movements as an early marker of PD.

Mo-139 - Neuromagnetic assessment of cross-modal sensory gating in Asperger syndrome

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It is well established that individuals with Asperger syndrome (AS) often show extreme sensory processing patterns. Our study seeks to determine the relationship between behavioral measures of sensory processing and neuromagnetic brain responses in children and adolescents with Asperger syndrome vs. healthy individuals. Sensory profiles were assessed using the Children Sensory Profile or Adolescent/Adult Sensory Profile questionnaires in a small sample of 15 participants (8-16 years) classified in 2 groups: high functioning AS with sensory sensitivity (n=6), and typically developing participants (n=9) with normal sensory profile.

MEG recordings were performed using uni-modal (auditory) and cross-modal (visual-auditory) gating paradigms. Stimuli were
delivered in pairs, with the second (test) stimulus in each pair being always a broadband noise (4-msec duration, 88 dB) auditory stimulus, and the first (conditioning) stimulus being either an identical auditory stimulus, a visual checkerboard pattern (16 ms duration), or a simultaneous auditory-visual stimulus, respectively. The delay between stimuli in each pair was set to 500 msec. The dipole strengths at the peak latency of the averaged P1m component of the auditory test responses were divided by the corresponding dipole strength of the unconditioned auditory responses, and were analyzed for each condition using mixed-design 2x2 ANOVAs with between-subjects factor of Group and within-subjects factor of Hemisphere. A significant main effect of Group (F=12.4, p=0.003) and a Group x Hemisphere interaction (F=8.5, p=0.01) emerged for responses to the test stimuli in the cross-modal gating condition, with higher P1m amplitude on the left hemisphere in the AS group. No group differences were detected in the other experimental conditions. The results indicate that the neuromagnetic responses are a sensitive measure of atypical cross-modal interactions, which are part of the unusual processing of sensory inputs in AS.

Mo-140 - Corticomuscular coherence following stroke

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Functional brain imaging studies have demonstrated substantial reorganisation in the brain following stroke. In particular, activation in ipsilateral/contralesional motor cortex is often seen, but its functional relevance is still unclear. In this study, we determined the location of the peak corticomuscular coherence (CMC) in the beta band between cortex and muscles involved in a hand grip task. Our aim was i) to investigate the distribution of cortical peaks in both healthy controls and stroke patients and ii) to determine whether the location of the coherence peak in patients was associated with level of motor impairment. Twenty stroke patients and twenty healthy age-matched controls were recorded performing a simple hand grip task with visual feedback. MEG was recorded as well as EMG from the forearm muscles involved in the grip. DICS was used in order to find the peak cortical source of task-related beta CMC. In healthy controls, this peak was located in contralateral primary motor cortex (M1). However, in the stroke patients, the peak location of coherence was much more variable. The Euclidean distance (in mni space) of each patient’s peak coherence from the control group average correlated with impairment, i.e. in patients with greater impairment, the coherence peak was further from the control average. A measure of how much the stroke lesion overlapped with the corticospinal tract of the contralateral M1 positively correlated with the distance of each patient from the control average, suggesting that the greater the anatomical damage to the descending corticospinal tract, the further away the coherence peak is from the control average. A number of the patients were found to have coherence peaks in the ipsilateral sensorimotor cortex, supporting a functionally relevant role for this region during grip.

Mo-141 - Neuromagnetic auditory response and its relation to cortical thickness in ultra-high-risk for psychosis

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Higher cognitive dysfunction, lower perceptual disturbance and its relation to the structures that implicate such processes have been considered as key features in patients with schizophrenia. However, little is known about the relationship between perceptual processing and structural deficits in ultra-high-risk for psychosis. We investigated the dipole moment of M100 auditory evoked response using a magnetoencephalography in 18 patients with schizophrenia, 16 ultra-high-risk for psychosis and 16 healthy controls, and their relation to cortical thinning on Heschlí’s gyrus and planum temporale. The auditory evoked M100 dipole moment was decreased in the ultra-high-risk subjects and in the patients with schizophrenia. Ultra-high-risk subjects showed impaired right M100 dipole magnitude, similar to patients with schizophrenia. Robust correlations between the cortical thickness of left Heschlí’s gyrus and the left M100 dipole moment were found in patients with schizophrenia. Moreover, correlations were also evident between right Heschlí’s gyrus and right M100 in subjects at ultra-high-risk for psychosis. The primary feature of auditory perception in ultra-high-risk subjects and schizophrenia patients is an encoding deficit that manifests as a reduced M100 dipole moment. The relationship between abnormal M100, thinning of cortical generators and their symptomatology were shown to exist prior to the onset of overt psychosis and progressively worsen over time. Therefore, they may be a potential indicator of the development of schizophrenia.
Mo-142 - Exploring Connectivity in Schizophrenia using Joint ICA to Combine MEG and DTI

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Schizophrenia is now recognized as a disorder characterized by focal and network cortical deficits which directly impact cognitive functioning. Combining diffusion tensor imaging (DTI) to assess white matter integrity with MEG provides a unique approach to link structural deficits with functional outcome. In this study we employed an auditory/visual multisensory integration paradigm to probe posterior cortical connectivity in schizophrenia. MEG data were collected using the 306 channel Elekta Neuromag system and DTI data were collected using a Siemens 3T TIM Trio MRI system. We report here on 29 schizophrenia patients (SP) and 29 age-matched healthy controls (HC). The MEG data were preprocessed and registered (Maxfilter) to an average head position allowing for waveform comparisons across participants. The planar gradiometer MEG waveform data were combined into local field power waveforms for 12 regions (left and right - frontal, central, anterior and posterior temporal, parietal and occipital). The DTI data were preprocessed and analyzed with FSL to produce fractional anisotropy (FA) maps. The MEG/DTI data were analyzed using joint independent component analysis (jICA). This software identifies co-variation across modalities [temporal variation in MEG and spatial variation in DTI FA maps]. We identified components with significantly different (p < 0.05) co-variation in MEG/FA across diagnostic group (SP vs. HC). One component indicated larger amplitude FA values in posterior superior corona radiate associated with greater MEG amplitude (120-170 ms) in HC. A second component showed greater FA in the right anterior corona radiate associated with larger amplitude late MEG activity (300-400 ms) in SP relative to HC. Significant correlations between the ICA loading factors and reaction times suggest behavioral implications for the structure/function relationship identified using multi-modal analysis in schizophrenia and demonstrate the importance of joint analyses.

Mo-143 - A Neural Basis of Sleep Spindles -As an Indicator of Recovery Following Stroke and Brain Injury

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Sleep spindles are the rhythm generated within the thalamus, during the human sleep stage II, the recurrent inhibitory circuit in the reticular thalamus causes hyperpolarization of thalamocortical neurons and induces a sequence of spindles over most of the cortex that can be detected on the EEG. Simultaneous EEG and MEG recordings can provide valuable information of cortical activation of sleep spindles. The cortical activation of spindles centered in four areas, pre-central and post-central areas of both hemispheres. Fast spindles were associated with more frequent activation of post-central areas with stronger activation strengths, whereas slow spindles were associated with more frequent activation of precentral areas with stronger activation strengths. Using this method, analyses of spindles of 10 patients following hemispheric stroke with putaminal or thalamic hemorrhage were performed. It revealed valuable findings concerning the functional asymmetry between hemispheres from the relationships between the amplitude and patterns of cortical activation associated with spindles. Also analyses of spindles of 8 patients following diffuse axonal injury were performed with in relation to clinical recovery. In the sub-acute stage, significant decreases were detected in the frequency, amplitude, and cortical activation source strengths of spindles, but these recovered during the chronic stage. In the chronic stage, the Wechsler adult intelligence factor scale and subset patterning of patients revealed significant improvement in cognitive function, memory and attention, and they had all favorable 1-year outcomes. Slow wave sleep and REM sleep, as well as stage 2 NREM sleep, may all be involved in memory consolidation. Spindles may be related to and reflect recovery following diffuse axonal injury and comprise a very important predictor of the outcome and recovery of consciousness and cognitive functions, especially memory of these patients.

Mo-144 - Attention modulated oscillatory activity in Parkinson’s Disease is normalized by dopamine

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Next to the impairment of motor skills, patients with Parkinson’s Disease (PD) suffer from disturbed executive functions such as attention-allocation. Most symptoms of PD seem to arise from disturbances within the dopamine-network. We investigated how the oscillatory network underlying visuospatial attention is modulated by dopamine using MEG (Elekta neuromag, Vectorview, Helsinki, Finland). We focused on alpha band activity (7-13 Hz) since this is modulated by spatial attention, i.e. increases ipsilateral to the attended hemifield (e.g. van Dijk et al. 2010). Eleven patients with Parkinson’s Disease (akinetik type, Hoehn & Yahr scale < 3) were recorded following withdrawal from (OFF) and on dopaminergic medication (ON) on the same day. Motor skills we tested using the Unified Parkinson’s Disease Rating Scale (UPDRS) which was scored in OFF and ON. The visuospatial attention task consisted of a 1s baseline period followed by an attention cue: an arrow (100 ms) that indicated which hemifield to covertly attend to (right or left). Following a 1s delay, inward moving circular sine-wave gratings were presented in both hemifields. At a random moment in
time, one grating changed color. Patients were instructed to detect the color-change only in the attended hemifield. UPDRS scores showed an improvement of motor skills in ON compared to OFF (p = 0.0002). Subsequent to attention cue presentation, we observed lateralization of alpha power ipsilateral to the attended hemifield, but only in ON. This power was increased in sensors overlying the occipital (p = 0.002) as well as the sensorimotor (p = 0.038) area. In OFF no lateralization of alpha power was observed during the delay period. These results suggest that next to motor-skills, allocation of attention by alpha lateralization is normalized by administration of levodopa.

Mo-145 - Auditory evoked field of a speech stimulus in 3- to 7-year-old normally developing and autistic children

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OBJECTIVE: We examined the auditory evoked field (AEF) of 3- to 7-year old typically developing and autistic children in response to a Japanese speech stimulus. Results were compared with scores on an assessment test of cognitive functioning, with particular focus on indices of language development. METHODS: AEF was obtained from a group of 35 typically developing children (6 females and 29 males, 66 ± 11 months old) and 35 autistic children (6 females and 29 males, 66 ± 11 months). Participants listened to a repetitive series of the Japanese mora /ne/ as spoken by a female speaker. AEF was obtained through magnetoencephalography (MEG), with a system optimized for monitoring cortical functioning of young children (Yokogawa Electric Co., Japan). Testing of the children’s cognitive functioning was done with the Japanese adaptation of the Kaufman Assessment Battery for Children (K-ABC). RESULTS: Dipole source estimation for 30 sensors over the left and right hemisphere was performed. Fischer’s tests showed a significant relation (p<0.05) between the dipole latency over both hemispheres of the typically developing children during a temporal window of 40 - 150 ms and their score on a language development index in the K-ABC test (the ‘riddle’ score). No significant relationship was found between the auditory response evoked by the speech stimulus and the language development index in autistic children. CONCLUSIONS: The present study shows that cortical measures of developing language abilities in typically developing and autistic children, aged 3- to 7-years old, can be assessed with MEG. The correlation between the dipole characteristics and psychological test results suggests that both measurement types can work in tandem as a diagnostic tool of autism and cortical development related with language development of young children.

Mo-152 - Fuzzy Entropy analysis of the electroencephalogram background activity in Alzheimer’s disease

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The analysis of non-linear dynamics has provided new ways to obtain ‘hidden information’ from biomedical signals. Non-linear analysis of the electroencephalogram (EEG) might provide useful information for diagnosis. Entropy analysis of the EEG has become increasingly popular since the introduction of Approximate Entropy (ApEn) and Sample Entropy (SampEn). They characterise regularity by comparing a sequence with a delayed version of itself and provide reliable entropy estimates for short and noisy signals. Two input parameters, a run length m and a tolerance window r, must be specified to compute them.

In this pilot study we have analysed the EEG background activity in 11 patients with Alzheimer’s disease (AD) and 11 age-matched control subjects with a newly introduced entropy measure: Fuzzy Entropy (FuzzyEn). FuzzyEn overcomes some limitations of SampEn and ApEn by importing the concept of fuzzy sets to estimate regularity, which is defined on the basis of exponential functions whose shape depends on parameters m, r (as in ApEn and SampEn) and n. More than five minutes of EEG data were recorded using the international 10-20 system for each subject and FuzzyEn was computed for artefact-free 5 s epochs with different input parameters. FuzzyEn was lower in AD patients than in controls. The best results were obtained with input parameters m=2, r=0.25 and n=1, with significant differences at electrodes P3, P4, O1, O2 and T6 (p < 0.01, Student’s t-test). The ability to discriminate AD patients from controls at these electrodes was evaluated using Receiver Operating Characteristic curves. We obtained accuracies (proportion of subjects correctly classified) ranging from 77.27% (at O1) to 86.36% (at O2). The significant decrease in irregularity found in the EEG of AD patients at P3, P4, O1, O2 and T6 shows a temporal window of 40 - 150 ms and their score on a language development index in the K-ABC test (the ‘riddle’ score). No significant relationship was found between the auditory response evoked by the speech stimulus and the language development index in autistic children. CONCLUSIONS: The present study shows that cortical measures of developing language abilities in typically developing and autistic children, aged 3- to 7-years old, can be assessed with MEG. The correlation between the dipole characteristics and psychological test results suggests that both measurement types can work in tandem as a diagnostic tool of autism and cortical development related with language development of young children.

Mo-153 - Potential Utility of Resting-State Magnetoencephalography as a Biomarker of CNS Abnormality in HIV Disease

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There is a lack of a neuroimaging biomarker for HIV Associated Neurocognitive Disorder. The purpose of this study was to analyze neuromagnetic (MEG) data from patients with HIV disease and risk-group controls to determine the MEG frequency profile during resting state, and its stability over 24 weeks. We also accessed neuronal functional connectivity measures to identify HIV-associated changes in brain function.

18 individuals (10 HIV+, 8 HIV-) completed neurobehavioral evaluations and 10 minutes of resting-state MEG acquisition, which were repeated 24 weeks later (1 HIV- control lost to follow-up). Relative MEG power in delta (0-4Hz), theta (4-7Hz), alpha (8-12Hz), beta (12-30Hz) and low gamma (30-50Hz) bands was computed for 8 predefined sensor groups. Baseline eyes closed data were analyzed using mutual information (MI) between all MEG sensor pairs.

The median stability of resting-state relative power was 0.80 with eyes closed, and 0.72 with eyes open. The relative gamma power in the right occipital (t(15)=1.99, p<.06, r=-.46) and right frontal (t(15)=2.15, p<.05, r=-.48) regions was associated with serostatus. The effect of age on delta power was greater in the seropositive subjects (r² = .51) than the seronegative subjects (r²=.11). Individuals with high theta-to-gamma ratios tended to have lower cognitive test performance, regardless of serostatus. After permutation testing (at p<.005) only one network of MEG sensors was significantly related to HIV serostatus. This network was located above the right anterior region and connected to the left posterior region. A mean MI value distinguished between the serostatus groups with only one error (sensitivity=1.00, specificity=.88 (X²=15.4, df =1, p<.01, Relative Risk=.11).

The stability of the wide-band MEG frequency profiles over 24 weeks supports further exploration of MEG as a biomarker, that - through a measure of functional connectivity - may be able to distinguish between HIV-infected and uninfected individual.

Mo-154 - Gamma Band Power During Verbal Memory Encoding Differentiates Between Better and Worse Recognition Memory Performance

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There is a need for a reliable biomarker for HIV Associated Neurocognitive Disorder (HAND) that is not limited to clinical signs and neuropsychological testing. Identification of such a biomarker could distinguish between HAND and other factors affecting memory. In the hopes of discovering a variable sensitive to cognitive dysfunction we examined neuromagnetic responses during a memory task.

MEG data was acquired for 17 individuals (10 HIV+, 7 HIV-) while they completed a verbal recognition memory task. The experiment consisted of 4 words presented for encoding, and recognition memory was tested immediately with 8 words (4 targets, 4 foils). A new set of 4 words were then presented to be encoded for the next trial, and new foils are used at test. Success requires the subjects to actively forget the words previously presented in order to reduce proactive interference. We examined the MEG response to each of the words presented during the encoding phase as a function of recognition memory performance. The group of 17 subjects was divided at the median d’ value (i.e., memory strength) to create ‘good’ vs. ‘bad’ performers (although all subjects performed the task relatively well). Within the first 150 msec after stimulus presentation, the subjects who would subsequently have better memory strength (i.e., d’) had an increase of power in the gamma band (30-50 Hz), expressed as a percentage of the pre-stimulus baseline. The finding was relatively specific, in that there was no difference in the relative power as a function of HIV serostatus.

These results show that we are able to detect differences in the MEG signatures associated with memory task performance. The next step in this ongoing analysis is to perform source localization, compare the MEG responses during hits and correct rejections, and eventually discern features of the data that can identify individuals with HAND.
Mo-155 - Functional connectivity in Alzheimer’s disease and Mild Cognitive Impairment: an EEG study in the framework of DECIDE project

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Alzheimer’s disease (AD) is the most common cause of dementia in geriatric patients. To date, diagnosis of AD is based on NINCDS-ADRDA, DSM-IV, and recent guidelines on the use of neuroimaging and cerebrospinal fluid markers (1). In this framework, resting state electroencephalographic (EEG) markers are under evaluation since they are cheap, widely available, and can provide measurements of brain functional connectivity, namely the functional coupling of EEG rhythms between electrode pairs. Among these measurements, Directed Transfer Function (DTF) is a multivariate estimator robust in respect to noise and volume conduction (2). Previous evidence has shown that when compared to normal elderly (Nold) subjects, mild cognitive impairment (MCI) and Alzheimer’s disease (AD) patients were characterized by changes of parietal-to-frontal DTF markers, especially at alpha frequencies (around 10 Hz) (3). Herein we report a topological analysis of DTF computed from resting state EEG data recorded in Nold, MCI, and AD subjects. The MVAR model was fitted simultaneously to signals from 19 electrodes (10-20 electrode montage system) and DTFs as a function of the frequencies from delta (< 4 Hz) to gamma (≥ 30 Hz) bands. The obtained propagation DTF patterns revealed clear differences among the groups not only for parietal-to-frontal directions and alpha frequencies but also for other regions and frequencies, thus enlightening the complex picture of the abnormal functional coupling of resting state EEG rhythms along the progress of disease, at least at group level. Future analysis will test the clinical value of these results for application in the DECIDE e-infrastructure.

Ref:

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Mo-156 - Visuo-spatial attention and simple action decision in ageing and dementia.

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Deficits in visuo-spatial orienting in age-related dementia, such as Alzheimer’s disease, and their use as possible markers for early diagnosis have recently elicited increasing interest [1,2]. Despite conflicting evidence in the behavioural literature, such deficits appear likely considering the involvement of parietal areas and cholinergic/noradrenaline systems in attention processes, both affected in Alzheimer’s disease. Our study focuses on two standard behavioural tests of visuo-spatial attention, namely voluntary covert orienting of attention and automatic alerting by neutral cues. We measure behavioural performance in these tasks in the MEG on patients with Alzheimer’s disease or vascular cognitive impairment, as well as young and elderly healthy controls. In the alerting experiment, participants had to quickly press the left or right button in response to a left or right visual target. On half the trials, a non-predictive central cue appeared 200 ms before the target. We observed reduced alerting effect with age (reduced manual RT benefit of central cues), which correlated individually with reduced alpha synchronisation in occipital cortex in response to cue onset during the cue to target interval. In the voluntary attention orienting task, participants responded only to left targets or only to right targets in two successive blocks. We observed reduced differences between the two blocks in both healthy elderly people and in patients. We also measured the contrast eyes open vs eyes closed and observed reduced desynchronisation in occipital alpha with age. This project is funded by the BRACE charity.


Mo-157 - Atypical memory traces in adolescent schizophrenia: A magnetoencephalographic study of the auditory mismatch negativity response

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Abnormal mismatch negativity (MMN) responses are a robust feature in chronic schizophrenia. Recent evidence suggests that such MMN abnormalities relate to altered connectivity in fronto-temporal networks (Dima et al. 2012), however, still relatively little is known about the precise mechanisms underlying auditory sensory memory in schizophrenia.

12 adolescent patients fulfilling DSM-IV criteria for schizophrenia and 12 matched healthy controls participated in this study. An auditory roving oddball paradigm was used to measure the effect of memory traces on MMN (Baldeweg et al. 2004). All tones within a train were of one frequency and were followed by a train of a different frequency (length between 5=short and 11=long tones). MEG data were recorded using the scanner at Oxford University. MaxFilter\textsuperscript{\textregistered}TM and ancillary techniques were used to ensure artifact free epochs. Event related fields (ERF) were analyzed using signal space techniques (Braeutigam et al. 2004) and Dynamical Causal Modeling (DCM, Friston et al. 2003).

Compared to controls, MMN amplitudes between 140 - 250ms were smaller and less adaptive in patients, where train length had a long lasting modulatory effect on the neural response to tones well into the following sequence. Only in patients, the neural responses at early latency (40 - 100 ms) were stronger for deviant tones following short compared to long trains. DCM identified a common model for deviants after short trains in both groups and long trains in patients. The model for deviants after long trains in controls was of reduced complexity.

These results suggest ERF measures of auditory system adaptability can be obtained in adolescent patients with schizophrenia. The memory trace effect observed here might indicate abnormal network architectures in general and atypical recruitment of primary auditory processes in particular. Possibly, neither networks nor processes are abnormal per se, only their invocation within a given context is.
Mo-158 - An MEG study of high-frequency brain oscillations in autism and first-degree relatives during picture naming

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Fusiform gyrus (FG) hypofunction is reported in individuals with Autism Spectrum Disorders (ASD), and it is still unknown whether this is an inheritable abnormality. Because of the importance of face processing to successful social functioning, the FG has been studied as being a part of the visual system specialized in facial recognition. However, other functions have been attributed to the FG, such as its role in language processing. High-frequencies brain activities, such as gamma oscillations, are abnormal in the visual and auditory cortices of ASD patients and in adult first-degree relatives, suggesting an autism endophenotype. Participants were 12 persons with ASD, 16 parents of an autism child and 35 controls. Whole-head MEG recordings were acquired during a picture naming task, in which subjects were asked to subvocalize names of objects presented on a screen. Virtual sensors were created in the FG and oscillatory activity between 5 and 120 Hz was analyzed across a 1 second window using wavelet-based time-frequency methods. Measures of evoked power and phase-locking factor (PLF) were derived for each subject. Mass univariate, non-parametric statistical analyses were performed across the entire time-frequency space and corrected for multiple comparisons using cluster size metrics, \( p < .05 \). Whereas there was no significant difference among groups within the low-gamma oscillations, PLF showed significant reduction at high-gamma frequencies between 160 and 600 msec after stimulus presentation in both the parent and autism groups, relative to control subjects. This supports the known impaired activation of the FG in autism but also suggests that the high gamma-band range may be important for higher cognitive functions that are mediated by FG activation. The finding in parents suggests that the previously described gamma-band ASD endophenotype may be relevant to higher order visual object processing and possibly to aspects of language function.

Mo-159 - Contributions of the Calcarine Cortex to Mechanism of Obsessions in OCD

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Obsessive-compulsive disorder (OCD) is a common, severely disabling and heritable disease. The core symptoms of OCD are obsessions, manifested by recurrent, persistent anticipation of unwanted, disturbing events, yet the neural basis of intrinsic anticipatory processing in OCD is unknown. We studied nonmedicated young adults and adolescents with pediatric-onset OCD (n=10) and case matched healthy controls in a visual-spatial working memory task. We used magnetoencephalography (MEG) to examine the medial and lateral cortex responses during anticipation of to-be-inhibited distractors and to-be-facilitated target stimuli. In OCD anticipatory activation to distractors was abnormally reduced within the posterior cingulate area and lateral parietal cortex, as compared to prominent activation in controls. Conversely, OCD subjects displayed significantly increased activation to retrieval stimuli within the dorsal and rostral anterior cingulate and supplementary motor cortex. This previously unreported discordant pattern of medial anticipatory activation in OCD was accompanied by high performance accuracy. Importantly, the retrieval stage of processing evoked significantly increased and task specific activation in the primary visual cortex of calcarine sulcus. Our follow-up MEG studies in perception of symmetry in OCD subjects elucidated the possible role of primary visual cortices in the mechanism of obsessions in OCD. Additionally, we argue that while increased anterior cortex activation in OCD is commonly viewed as a marker of faulty inhibition, the current pattern of data suggests consideration of the operation of an anterior compensatory mechanism amending the posterior medial self-regulatory networks disrupted in OCD. The significance of the latter and the above finding on calcarine cortex engagement in cognitive processing is crucial for future studies on developmental etiology of OCD.

Mo-160 - Temporal Dynamics for Cortical Processing of Working Memory in Subjects with OCD

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One of the most debilitating phenomena in obsessive-compulsive disorder (OCD), apart from obsessions and compulsions, is the slowness of processing. Prolonged time of behavioral and cortical responses have been found in neuropsychological and neuroimaging studies. These events do not concur with the model of OCD as a disorder of disinhibition with increased concentrations of glutamate. Thus, the brain mechanisms underlying slowness of responses in OCD remain a puzzle. We test two hypotheses: (i) If the reason for slowness is a global deficit, such as reduced density of white matter, the time of processing will be increased across all phases of a task, (ii) If the reason for slowness is a poor top-down selective inhibitory control, the time of processing will worsen with consecutive phases of a cognitive task. We examined the temporal characteristics of regional cortical activation in 12 young...
unmedicated OCD subjects and matched controls using MEG recordings during performance on a visual-spatial Delayed-Matching-to-Sample Task with distractor. Source estimates were constructed for every 10 ms in each task phase: Encoding, Distractor and Retrieval. Time of peak activation was determined for the most dominant signals. During Encoding (250 ms post-Sample) over 70% of OCD subjects displayed not longer but shorter cortical responses than controls ($\sim 30 $ms). The first delayed responses in OCD were observed during Distractor phase ($\sim 20 - 40 $ms). Increasingly more right anterior larger delays occurred in Retrieval ($\sim 20 - 60 $ms) and were displayed concurrently with high performance accuracy and a significant increase in regional activation. The results provide some support to the second hypothesis. Thus, the commonly reported slowness in subjects with OCD is not an overarching property of the brain, but it is modulated increasingly in a task-phase-specific manner. Such a view is consistent with a gradually forming cognitive compensatory mechanism in the course of the disease.

Mo-161 - Effects of Medication upon Low-Frequency Frontal Activity in Schizophrenia Patients

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Schizophrenia is characterized by neural and cognitive deficits ranging from subtle to debilitating. Here we examined oscillatory brain activity of 29 schizophrenia patients (SP, 37.9 ± 11.6 yrs, 23 male) and 29 healthy control participants (HC, 37.7 ± 15.3 yrs, 19 male) using magnetoencephalography (MEG) while participants responded to auditory and visual stimuli. We first projected noise from the raw data, performed motion correction, and re-registered each participant’s dataset to a mean head position using MaxFilter. Trials were excluded in which the signal exceeded 7 pT, or participants responded incorrectly in the behavioral task. Mean MEG baseline power (-100, 0 ms) was obtained from the Morlet wavelet time frequency analysis (Fieldtrip). We used separate one-way ANOVAs to examine the group differences in mean baseline power within theta (4-8 Hz), alpha (9-13 Hz), beta (14-25 Hz), low-gamma (25-34 Hz), and high-gamma (35-45 Hz) frequency bands in frontal (FR), left temporal (LT), right temporal (RT), left parietal, right parietal, left occipital (LO), and right occipital (RO) sensor regions. We excluded 4 subjects (2 HC and 2 SP) from analyses due to power measures greater than 3 SDs from the mean. Results indicate increased power globally for SP relative to HC, with significant differences in LT sensors in all frequency bands except low-gamma (all $p < 0.05$). Significant differences were also present for RT, RO, LO, and FR theta power (all $p < 0.05$). Interestingly, FR theta power was significantly correlated with medication (Olanzapine equivalents) dose in SP ($r = .546$, $p = 0.004$). These results are consistent with greater cortical noise reported previously in SP relative to HC, yet may be in part related to medication use. Further work is needed to understand these effects and their relevance to outcome measures in SP.

Mo-162 - Alterations of cross-frequency coupling in MEG resting state recordings in Mild Cognitive Impairment patients.

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There is a growing interest in cross-frequency coupling (CFC) in neuroscience. It seems to play an important role in neural communication and learning. There are several algorithms to assess such coupling. Here we focus on Phase-Amplitude Coupling, which has been proven relevant in the literature. Specifically, we study the relation between the phase of the low frequency signal and the amplitude of the high frequency signal. High frequency activity is commonly associated with local processing and low frequency with a more distributed one. Cross-frequency would then be a way to connect both scales. Additionally, it has been shown in ECoG (subdural electrocorticogram) and MEG (magnetoencephalography) experiments that CFC intensity is dependent on the task performed, and correlates with performance. Here we want to study CFC in MEG recordings of healthy elderly (40 subjects) and patients with Mild Cognitive Impairment (MCI) (30 patients with amnestic MCI, 30 with multidomain MCI). MCI has been considered an intermediate state between healthy aging and dementia and it has been associated with power spectral variations: increase in the power of delta and theta bands (low frequency) and decrease in alpha, beta and gamma bands (high frequency). These spectral variations would affect the coupling between different frequencies. We analyze the CFC with 3 different methods: Modulation Index, envelope to signal correlation and difference between the amplitudes of the high frequency signal corresponding to peaks and troughs in the low frequency signal. Moreover a comparison between groups yields differences in the coupling strength and distribution.
Mo-163 - Reversed brain lateralization during metaphor processing in individuals with schizophrenia: A MEG study

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Previous studies have suggested that schizophrenic patients (SZ) have a reversed pattern of lateralization for language: reduced left hemisphere (LH) function and enhanced right hemisphere (RH) function. The present study examined this claim, focusing on metaphor processing. In neurotypicals, the processing of conventional metaphors (CM) is based on the retrieval of stored linguistic knowledge (LH specialization), whereas novel metaphor (NM) processing may require the unique ability of the RH to connect distant semantic concepts and coarse semantic processing. Thus, we hypothesized that a reversed pattern of lateralization would yield SZ an advantage in NM comprehension. We tested this hypothesis using a semantic judgment task with two-word expressions. Twenty subjects (10 SZ, 10 neurotypicals) were presented with a centrally located prime word for 150ms, followed by a fixation sign for 600ms and then a target word for 180ms. The stimuli consisted of four types of expressions: literal, CM, NM and unrelated word pairs. Participants had to decide whether the expressions were meaningful. MEG was recorded using a whole-head, 248-channel, magnetometer array. Results show that while SZ were characterized by RH dominance in early stages of language processing, neurotypicals showed an early LH dominance which developed into bi-lateral activity. These differences were found to interact with the type of expression, so that in SZ there was more activity in RH areas during NM processing whereas in neurotypicals there was greater bi-lateral activity in the rest of the conditions. Results suggest that semantic processing in SZ occurs mainly in the RH. This is consistent with the view that SZ rely mainly on coarse semantic processing during language comprehension.

Mo-164 - Normalization of high gamma band activity following cognitive training in patients with schizophrenia

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Speech perception, memory and production are impaired in schizophrenia, and recent research shows that these deficits are amenable to intensive computerized cognitive training. We used 275-channel MEG to study cortical activity during both a syllable identification and a syllable reproduction task in 40 patients with schizophrenia. Subsequently, 22 patients underwent 50 hours of targeted cognitive training (TCT) that focused on auditory/verbal processes, while the remaining 18 spent an equal amount of time playing commercial computer games (CG), as a control. Time-frequency analysis and source localization using the NUTMEG spatially adaptive filter provided high spatial and temporal resolution of auditory and memory-encoding processing streams in multiple frequency bands (4-12Hz, 12-30Hz, 30-50Hz, and 63-117Hz). We compared changes in neural activity before and after TCT to changes before and after CG in patients with schizophrenia and to 14 matched healthy subjects. Controlling for performance, schizophrenia subjects at baseline showed lower power in the high gamma band in many areas, compared to healthy subjects. Cognitive training led to enhancement of high gamma activity in the TCT patient group, as compared to the CG group. This increase involved areas important for audiomotor processing, especially within the tempo-parietal junction and inferior frontal gyrus, and the resulting patterns of brain activity resembled what was seen in healthy subjects. In inferior parietal lobule, training-induced enhancement of high gamma correlated with task performance. These data suggest that intensive computerized training can normalize disrupted patterns of neural activity involved in auditory and verbal processing in schizophrenia.

Mo-165 - Intracortical inhibition of primary and secondary somatosensory cortex in paroxysmal kinesigenic dyskinesia? An MEG study

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Paroxysmal kinesigenic dyskinesia (PKD) is a rare neurological condition which is characterized by sudden brief episodes of dystonic movements triggered by sudden voluntary movements. The condition responds well to antiepileptic drugs but the pathophysiological basis of the disease is still unclear. The purpose of this study is to assess possible abnormalities of somatosensory system in PKD patients. Whole-head magnetoencephalography was used to record somatosensory evoke fields (SEFs) elicited by paired-pulse median nerve stimulation in 18 controls and 9 PKD patients. Eight of the patients were studied both in drug-off/on states. The intracortical inhibition was measured as paired-pulse inhibition (PPI) ratio, which is evaluated by calculating the ratio between the response amplitudes to second and first stimuli. The larger PPI ratio indicates reduced inhibition, and the smaller PPI ratio represents stronger inhibition. The P35m ratio was larger in drug-off PKD compared to controls, and there was no significant difference
between drug-on PKD and controls. SII response PPI ratio showed a trend to be larger in drug-off PKD compared to controls, and there was no statistical difference between drug-on PKD and controls. Comparison of PPI ratio between drug-off/on states showed that PPI ratio for SII was larger in drug-off state compared to drug-on condition. Patients with PKD were impaired in somatosensory inhibition, and treatment of carbamazepine, phenytoin and oxcarbazepine could remediate this hyperexcitability phenomenon. The present data suggests dysfunction of intracortical inhibition in somatosensory system in patients with PKD.

Mo-166 - Quantitative analysis on the MEG using automated ROI constitution for assessing cerebral ischemia

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Objective
We reported the imaging of the cerebral neural activity in ischemic areas using magnetoencephalography (MEG) with standardized low-resolution brain electromagnetic tomography modified for a quantifiable method (sLORETA-qm). Quantitative evaluation of the ischemic areas is inevitable for clinical indication. We formulate the method for quantitative evaluation using automated region of interest (ROI), decided by regions of the cerebral arteries.

Methods
We evaluate the 11 patients with internal carotid artery or middle cerebral artery stenosis. Using a 160-channel whole-head-type MEG (MEG vision, Yokogawa), spontaneous cerebral magnetic fields were obtained. For quantitative images, voxel-based time-averaged intensities of slow waves (2-6Hz) were obtained by the proposed technique based on sLORETA-qm. Single-photon emission computed tomography (SPECT) and positron emission tomography with 15O gas inhalation (15O-PET) were performed to evaluate the cerebral blood flow (CBF). These MEG, SPECT and PET images were converted to normalized images using Statistical Parametric Mapping (SPM) to set the ROI automatically and determine quantity using NEUROSTAT. In the same coordinate system, we compared the magnetic fields using MEG images and CBF images using SPECT and 15O-PET.

Result
Quantity of the automated ROI based on sLORETA-qm about the spontaneous magnetic fields was well determined. Slow wave intensity was well visualized in the region of the affected side which was perfused by middle cerebral artery, but did not always correspond to the deteriorated area of CBF. The tendency of the inverse correlation between the CBF and the magnetic field was recognized.

Conclusion
MEG analysis of sLORETA-qm using automated ROI setting is useful for evaluating the quantity of the regions decided by cerebral arteries without arbitrariness. Normalized images may have the potential of prospecting the cerebral neural activity after the ischemic changes.

Mo-167 - Prefrontal deficits in the M50 network correlate with neuropsychological function in dementia of the Alzheimer’s type

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The amplitude variability of P50/M50 components of electromagnetic responses is commonly used to explore the neural ability to modulate its sensitivity to incoming sensory stimuli in both pathological and healthy aging. The focus of this MEG study was on the dynamic cortical network underlying the M50 complex evoked by a passive auditory oddball paradigm. We used MEG measurements acquired from a 275 channel CTF whole-head system and a multi-dipole, Calibrated Start Spatio Temporal (CSST) localization technique to identify the topology and dynamics of the M50 cortical networks in an effort to discriminate between patients diagnosed with mild cognitive impairment (MCI) or probable AD (n=10) compared to the age-matched controls (n=10, mean=74 age). Binaurally presented stimuli consisted of 400 standard (1,000 Hz) and 100 deviant (1,150 Hz) tones. After neuropsychological testing, evoked magnetic fields were recorded at the Mind Research Network, New Mexico. Multivariate statistical analysis techniques, including PCA and MCDA, were performed for the discernment of categories in the data. Spatio-temporal analyses identified three brain regions active in the 30-100 ms time window: superior temporal gyrus (STG) activity in 20/20 subjects (18/20 bilateral) and prefrontal
Mo-169 - Manetoencephalographic analysis using sLORETA-qm for spontaneous cortical activity in patients with brain tumors

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Abnormal focal slow wave activity on magnetoencephalography (MEG) is often seen in patients with various brain pathologies. We had reported a technique of standard low-resolution brain electromagnetic tomography modified for a quantifiable method (sLORETA-qm) to analyze spontaneous neuromagnetic fields in patients with cerebral ischemia. In this study, we used this technique to image activity in patients with brain tumors and analyzed the tomographic distribution of slow wave activity. (Method) Using a 160-channel whole-head-type magnetoencephalographic system, spontaneous neuromagnetic fields were obtained in 16 patients with brain tumors. The distribution of slow wave activity in 4 frequency bands (0.3-2 Hz, 2-4 Hz, 4-6 Hz, 6-8 Hz) were evaluated by the technique based on sLORETA-qm. Statistically-determined voxels of slow wave activity in 4 frequency bands were displayed tomographically and overlaid on individual magnetic images. (Result) The distributions of abnormal slow wave in the cortex adjacent to a tumor were obtained in 14 patients except 2 patients with meningingomas without peritumoral edema. Volumetric analysis by counting statistically-determined voxels revealed that the distributions of tumor-related focal delta band (0.3-2, 2-4 Hz) in 8 patients with neurological symptom were larger than 8 patients without neurological symptom. But patients with focal delta activity by subcortical edema exhibited recovery of function in early postoperative period. (Conclusion) The distribution of delta activity may reveal functional alterations of cerebral neural condition in patients with brain tumors. Cortical state with delta activity related only subcortical edema may be potentially reversible.

Mo-170 - Alterations in spontaneous brain oscillations during stroke recovery

The patients with hemifacial spasm often suffer from non-motor symptoms such as vision, speaking, acoustic change, and tinnitus. These non-motor symptoms are known to be associated with changes in cortical activity. Only a few studies have focused on these subtle changes in the hemifacial spasm (HFS) patients. Magnetoencephalography (MEG) is a useful method that can record brain activity, noninvasively. We measured neuromagnetic auditory response using Korean MEG system to investigate changes in cortical activity associated with non-motor hearing symptoms in HFS patients.

We used Korean MEG system (152-channel helmet type axial gradiometer, KRISS, Daegun, Korea) to evaluate the reactivity of the auditory cortex in 13 hemifacial spasm patients. This MEG system has a double relaxation oscillation (DROS) SQUID based on the relaxation oscillation of a hysteretic SQUID and a reference junction. We analyzed neuromagnetic data with a spasm and healthy side, respectively. The latency and amplitude of the most prominent deflection, N100m, was compared between the two analyzing parts. All patients showed a normal hearing activity in the pure tone audiogram (< 20dB HL). After stimulation on the spasm side, the amplitude of the N100m peak in the contralateral hemisphere was lower in the spasm side stimulation than in the healthy side stimulation. And the latency of the N100m peak in the spasm side stimulation was also delayed than that of the healthy side (5-20ms). There was a significant difference between spasm side stimulation versus non-spasm side stimulation in the difference between the latencies of the N100m peaks.

Our results indicate that MEG can detect differences in cortical activity between hemifacial spasm patients. This suggests that MEG can identify the subtle changes in cortical activity associated with non-motor symptoms in the patient with HFS. This work was supported in part by the KRISS-WCL project (12011085-34)
Mo-171 - Advances in pre-surgical functional brain mapping for tumor patients using MEG

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A brain tumor patient’s post-operative quality of life is dependent on the surgeon’s ability to avoid functional cortical regions during resections. The correlation of brain anatomy with its function is a critical aspect of modern neurosurgery, especially as traditionally relied upon anatomical landmarks are displaced by the presence of mass lesions. This correlation can be facilitated by modern functional imaging techniques, such as magnetoencephalography (MEG). Equivalent current dipole modeling has conventionally been the recommended analysis for clinical MEG applications. However, this method may be inappropriate for identifying extended and distributed activity such as in language processing. Therefore, we have investigated three alternative methods to enhance the practice of pre-surgical mapping. First, we employed the recently developed volume-based distributed analysis utilizing MNE. The traditional implementation of the analysis in the MNE software is computed on a reconstruction of the cortical surface, however, the presence of tumors disrupts this reconstruction process, making a volume based implementation a more practical choice. The outcome of this analysis can be downloaded in the Operating Room to neuro-navigational software that visualizes and tracks surgical instrument positioning relative to the analysis images. A second approach in development is a steady state analysis exploiting the spectral characteristics of the data to create maps of network activity during an active task state. Finally, we are in collaboration with colleagues who complete high definition fiber tracking (HDFT) scans of tumor patients, and are in the early stages of combining these two data sets to generate a more complete structural and functional map of the activated networks in individuals. Efforts such as these advance the application of MEG for clinical purpose and may play a critical role in the preservation of quality of life for neurosurgical patients.

Mo-172 - Neural synchronization analysis of the MEG auditory steady-state response (ASSR) to evaluate high-risk subjects for schizophrenia

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Individuals with high-risk for schizophrenia are those who do not satisfy diagnostic criteria for schizophrenia but have increased risk for conversion to the schizophrenic disorder. Therefore, the identification of biomarkers sensitive to the prodromal signs could facilitate the evaluation of interventions that might delay, alleviate, or prevent the emergence of psychosis. Recently, several neuroimaging studies tried to investigate the pathognomonic features specific to high-risk for psychosis. In addition, brain electromagnetic studies...
using EEG or MEG elicited abnormal neural circuits for the schizophrenic patients and high-risk individuals for schizophrenia. Especially, abnormal patterns of auditory information processing have been revealed from the EEG/MEG studies using auditory oddball paradigm and ASSR. From the brain-computer interface (BCI) perspective, the synchrony analysis of ASSR showed the possibility of its efficient use for the measure of BCI system. Similarly, we investigated the neural synchronization measures based on the Hilbert-Huang spectra of MEG ASSR to evaluate the manifestations for high-risk schizophrenic subjects other than schizophrenia and normal controls in the present study. Finally, we conclude that synchrony analysis of MEG ASSR may provide a promising modality for the assessment of psychiatric manifestation.

Mo-173 - Alterations in beta power during a working memory task in depressed subjects

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Patients with major depressive disorder (MDD) and bipolar disorder (BD) exhibit working memory impairment. The neuroanatomical correlates of these deficits have been investigated extensively using fMRI, however, the electrophysiological underpinnings of the abnormalities in brain activity are poorly understood.

MEG was acquired for 28 healthy control (HC), 17 BD, and 25 MDD subjects during performance of a modified N-back task using a 275 sensor CTF system. MRI scans were acquired for coregistration and source localization. Non-brain material was removed from MRI scans using the AFNI tool 3dSkullStrip, and a surface of the brain was created and used in a Nolte realistic head model. Synthetic aperture magnetometry (SAM) was used to generate Mann-Whitney U maps of power differences between the 2- vs. 1-back, 2- vs. 0-back and 1- vs. 0-back conditions, t-tests were performed at the group level. The combined patient group was compared to HC, and results were corrected for false discovery rate (FDR). BD and MDD groups were compared to subgroups of matched healthy controls individually, and results were FDR corrected over a mask created from the p=0.05 FDR corrected mask of the combined group result.

There were no significant differences between patients and controls in the 1vs0 or 2vs0 conditions. The combined patient group exhibited greater power (less beta desynchronization) between the 2- and 1-back conditions as compared to controls in areas of middle and superior temporal gyri, posterior cingulate (PCC), precuneus, thalamus, caudate, superior and middle frontal gyri, and insula. Differences in superior and middle frontal gyri were more prominent in MDD, while the PCC result was present only in the BD group.

The frontal/posterior divergence indicates that patient groups differ in underlying pathophysiology. The presence of differences in the 2vs1 condition may indicate that the 1-back is relatively more effortful in patients compared to controls.

Differences between depressed and healthy subjects in beta band power in the 2-back vs. 1-back condition of a modified N-back task
Mo-32 - Acute Alcohol Intake Affects Emotional Responses in Human Brain

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Acute alcohol intake affects the human emotional state possibly through neurotransmission modulation. Social drinkers enjoy both inhibition and excitement following inebriation. However, the effect of alcohol on human brain responses to different kinds of emotional stimuli remains unclear. To determine this modulation and the brain structures involved, magnetoencephalography (MEG) signals were recorded from 15 males who passively viewed emotion-eliciting pictures both after having consumed an alcoholic beverage (0.48 g/kg) or placebo. The order of the sessions was counterbalanced among participants. The affective pictures were selected from the International Affective Picture System (IAPS) according to their arousal and pleasure ratings. Four stimuli sets that manipulated the level of arousal within pleasant and unpleasant pictures were used. The pictures were presented in a random order. To increase the signal-to-noise ratio the procedure was repeated four times resulting to 160 trials for each kind of affective stimuli. MEG signals were band-passed filtered between 2-40 Hz and their Global Field Power (GFP) was calculated. A general GFP decrease on middle (200 ms) and late (400 ms) components was observed following alcohol vs. placebo if the types of the affective pictures were merged. Alcohol interacted with pleasure on middle components (200 ms) causing significantly (p < .05) lower GFP only for pleasant pictures. There was also an interaction of alcohol by arousal, GFP was significantly (p < .05) lower following alcohol for high arousing pictures. Results obtained so far, suggest that acute alcohol intake has a stronger impact on the pleasant and high arousing images, while does not influence correspondingly the brain responses to unpleasant and low arousing ones. To accurately investigate the localization of this phenomenon extensive neuroimaging analysis is underway in order to map the MEG activity on individual brain anatomies and study the involved dynamics.

Mo-33 - Dynamics of evidence accumulation in subliminal and conscious conditions: an EEG/MEG study

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Recent models of visual awareness propose that sensory evidence is accumulated over time and either crosses the threshold for conscious access (conscious trial) or, on the contrary, remains below threshold (subliminal trial). In the present experiment we took advantage of the high temporal and spatial resolution of simultaneous magneto- (MEG) and encephalographic (EEG) brain recording to investigate this issue and track the neural dynamics of conscious versus non-conscious evidence accumulation in a parametric masking task.

We used a design similar to Del Cul et al.’s (Plos Biology, 2007, Brain, 2009) in which participants performed a number comparison task on a masked digit, while perceptual evidence was systematically manipulated by varying the target-mask Stimulus Onset Asynchrony (SOA). Assessing target-visibility on a trial-by-trial basis, this design allow us to study how different processing stages, from visual integration to response programming are modulated both by objective available evidence (SOA) and consciousness. For specific time-windows, we monitored the variations of event-related potentials (ERPs) and fields (ERFs) and their underlying cortical sources as a function of target-mask SOA and response accuracy, separately for trials reported as conscious or subliminal. Our results replicate and extend those obtained by Del Cul et al., showing that early processing stages in occipito-temporal regions remain stable in conscious and subliminal conditions but are nevertheless sensitive to evidence accumulation (SOA). Crucially only late stages associated with fronto-parietal and motor activations show a non-linear dissociation for conscious accessed stimuli. Moreover, only in conscious condition, motor preparation shows a clear breach for erroneous responses, reflecting the conflict between the correct response, computed consciously and the response actually made.

Mo-34 - EMG-coherent EEG maps suggest communication between SMA and muscles during a manual precision task.

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The present experiment was performed in order to study the implication of corticospinal projections from primary and secondary
cortical motor areas in precise hand muscle force control. We analyzed the EMG-coherent EEG maps during a precise visuomotor tracking task controlled with a precision grip, the latter known to maximally mobilize corticospinal projections. Corticomuscular coherence (CMC) is a non-invasive method to analyse communication between cortical areas and motoneurons.

Nine subjects were instructed to keep a cursor on a force curve (Fig. 1A) by applying a force with their right thumb-index precision grip on a device containing a force sensor. The force curve was moving from the right to the left side of a computer screen and was continuously visible in a ten-second window. The cursor’s horizontal position was fixed in the middle of the screen while its vertical position was varying according to the force applied on the device, the cursor moving upwards with increasing force. Activity of two hand muscles was recorded at the same time as 64 channel EEG (ANT, Enschede, The Netherlands). We analysed CMC during stable force production periods (see Fig. 1A). The spectral analysis (multitaper method) and statistics (cluster-based permutation tests) were done using FieldTrip, an open-source Matlab toolbox for neurophysiological data analysis (Maris et al., 2007, Oostenveld et al., 2011).

Besides the well-known CMC over the contralateral primary sensorimotor area (Fig. 1B, D), the EMG-coherent EEG maps show significant CMC over the SMA region (Fig. 1C, D). Therefore, our study revealed the functional role of corticospinal projections from SMA in a manual task requiring high-precision motor control.

Mo-35 - Cortical oscillations accompanying inhibitory control: Is response withholding different from response switching?

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In a recent MEG study, we found that the ability to switch motor responses to infrequent targets in a rapidly presented stream of digits (switch task) was associated with increased right frontal theta activity prior to movement and early motor preparation reflected by decreases in beta oscillations in motor cortex (Cheyne et al., submitted). We interpreted frontal theta activity to reflect inhibition of the prepotent response and beta suppression to indicate anticipatory preparation, both of which influenced successful switching. Here we describe the same analyses in 6 subjects who also performed a no-go version of the task (withhold task) to determine if preparation or inhibition differed for a task requiring complete inhibition of motor output. For the withhold task, subjects similarly demonstrated early beta suppression in MI, but the amount of suppression was significantly larger and more strongly time-locked to the cue, rather than movement onset, and slightly delayed and reduced on correct withhold trials. Beta suppression was reduced only on error trials in the switch task, suggesting differences in the degree and timing of response preparation between tasks. Right frontal theta activity was observed for both correct switch and correct withhold trials with differences in peak location and latency, including delayed theta activity in left frontal regions for the withhold task. In both tasks, errors elicited theta activity in the right anterior cingulate that was larger in the withhold task. These preliminary results suggest that tasks requiring either switching to an alternate response, or simply withholding a response, activate similar areas associated with inhibitory control (e.g., right frontal cortex) and error processing, but with different patterns of activity possibly related to response selection requirements in the switch task, and differences in response preparation that may reflect the requirement to suppress all motor output in the withhold task.
Mo-36 - Binding visual social cues: a study coupling EEG and fMRI

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Communicative intentions are transmitted by many perceptual cues, including gaze direction, body posture and facial expressions. Yet, these social signals can take on new significance once merged. In particular, processing of these social signals will vary according to their self-relevance. However, little is known about how visual social cues are integrated over time in the brain. To experimentally address this question, we manipulated three visual cues that affect the appraisal of the self-relevance of social signals: gaze direction, emotion and posture. In order to induce a parametric variation of self-involvement at the neural level, our experimental design capitalizes on the ability to change the number of social cues displayed by the actors toward the self, i.e. one (gaze direction only), two (gaze direction and emotion or gaze direction and posture) or three visual cues (gaze direction, emotion and posture). We then combined functional magnetic resonance imaging with electroencephalography (recording of event related potentials) to identify the spatiotemporal characteristics of social cues binding mechanisms. We were able to show that, 200 ms after stimulus onset, the premotor cortex integrated gaze, posture and emotion displayed by a congener. At earlier stages, emotional content was processed independently in the amygdala (170 ms), whereas directional cues (gaze direction with pointing posture) were combined at around 190 ms in the parietal and supplementary motor cortices. These results demonstrate that the early binding of visual social signals displayed by an agent engaged the dorsal pathway and the premotor cortex, possibly to facilitate the preparation of an adaptive response to another person’s immediate intention.

Mo-37 - Effect of force-load on cortical activity preceding voluntary finger movement

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Neural activity preceding force-loaded voluntary finger movement (the Bereitschaftsfeld) was recorded using 143-channel whole-scalp magnetoencephalography (MEG) in order to determine how the level of force produced during voluntary finger movement is represented in activity over different premovement time intervals localized to different cortical areas. Eighteen healthy subjects performed voluntary right index-finger extension movements against an inertial load of either 0, 100, or 200 g. Results showed that the earliest component of premovement activity, beginning between 1.5 and 1.0 s prior to movement and localized to the central midline around the region of supplementary/cingulate motor areas, was not modulated by the level of force required for movement. However, later premovement activity, occurring between 500 and 200 ms prior to movement onset, was significantly greater for the highest force movements compared with both intermediate (p<0.05) and no weight-load conditions (p<0.01). This component was localized to primary sensorimotor cortical areas, with greater source strength on the left side contralateral to movement. Results indicate that, although early premovement activity of the supplementary/cingulate motor areas does not appear to encode movement force, later premovement activity of the primary motor cortex is significantly greater for movements made with more force, not only during movement execution but also up to 500 ms prior in readiness for intended movements of greater force.

Mo-38 - The affective impact of person density perception in public transport: an MEG study

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Co-presence is the mere fact of being in a face-to-face situation with another person (from one to many). Numerous studies in the field of ethology, and social psychology have shown a negative impact of high density of persons (1). A key structure of the emotional brain, the amygdala seems to be involved in both personal space regulation and social emotional perception (2). Nevertheless, there has been no attempt at providing an objective measure of the affective impact of person density on brain responses. We propose here to use magnetoencephalography (MEG) to investigate the time course of these responses in relation with the perception of person density. We have built a database of 237 real-life stimuli consisting in photographs from the public transport. The person density depicted by these stimuli was evaluated by 115 subjects in a pre-test. This allowed selecting a set of 90 stimuli that were of low, medium and high density (30 stimuli per category). A phase-scrambled version of these stimuli was created. These stimuli will be used in an MEG experiment. Subjects will have to perform a valence evaluation task where they will judge the stimuli as positive, negative or neutral. Normal and scrambled versions of the stimuli will be presented in different blocks. Using an automated method of amygdala segmentation (3), we will localize amygdala sources of magnetic activities in every subject and assess the involvement of these sources in the perception of person density. Following the MEG session, the anxiety level and the sensitivity to interpersonal distance of every subject will be measured, and an affective evaluation of the pictures will be obtained, in order to examine the
correlations between these variables and amygdala responses.

Mo-39 - TMS of SMA evokes similar motor potentials on intrinsic hand muscles as TMS of M1 during a precise visuomotor tracking task.

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A recent human EEG/EMG study performed in our team has suggested communication between supplementary motor area (SMA) and hand muscles during a precision grip task (Chen et al., 2012, in preparation ), which strongly suggests that corticospinal projections from SMA are functional during a manual precision task. In the present study, we further explored these projections by single pulse transcranial magnetic stimulation (TMS). We used neuro-navigated TMS (Nexstim NBS) for precisely targeting two stimulation zones (Fig. 1A), located in the hand areas of respectively left primary motor cortex (M1L) and SMAL according to the somatotopy by Picard and Strick (2002). With help of the NBS, we equalized the electric field at the target level for the two anatomical sites.

Eight subjects were instructed to keep a cursor on a force curve by applying a force with their right thumb-index precision grip on a device containing a force sensor. The force curve was moving from the right to the left side on a computer screen. The cursor’s horizontal position was fixed in the middle of the screen while its vertical position varied according to the force applied on the device, the cursor moving upwards with increasing force. TMS occurred during steady-state force production. Electromyography (EMG) of two intrinsic hand muscles was recorded. We analyzed the amplitude and latency of the motor evoked potentials (MEPs) and the duration of the silent periods (SPs) induced by TMS.

The results clearly show that TMS of SMAL evokes MEPs with similar latency and amplitude followed by SPs with similar durations as those obtained by M1L stimulation (Fig. 1B). This strongly suggests that the corticospinal projections from SMA are indeed functional during precise manual tasks. Moreover, although it has been shown in monkeys that the spinal projections from SMA are weaker than those from M1 (e.g., Boudrias and al, 2006, Macpherson and al, 1982), this seems not to be the case in humans.

Figure 1. A. Estimation of the magnetic field induced by TMS of the two anatomical sites of interest, M1 and SMA. B. EMG responses to TMS of M1 respectively SMA. The TMS artifact can be seen at 0 ms.
Mo-40 - Evidence for a motor gamma-band network governing response interference

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The gamma-band response is thought to represent a key neural signature of information processing in the human brain. These brain signals have been associated with a variety of sensory modalities (vision, sensation, audition) and also following basic motor responses, yet the functional significance of the motor gamma-band response remains unclear. We used the Multi-Source Interference Task (MSIT) to assess the sensitivity of these cortical motor-gamma band rhythms to stimuli producing response interference. We recorded MEG from adult participants (N=21) during MSIT task performance and compared motor gamma-band activity on Control and Interference trials.

Reaction time on MSIT Interference trials was significantly longer (~ 0.2s) for all subjects. Response interference produced a significant increase in motor gamma-band activity including ~ 0.5s sustained increase in gamma-band activity from bi-lateral anterior (BA6) motor areas directly preceding the response (much stronger contralaterally). In addition, an unanticipated activation of increased right Inferior Frontal Gyrus (R-IFG) was observed at gamma-band frequencies ~ 0.2s prior to the button press response. Post-hoc analysis of R-IFG gamma-band activity was observed to correlate with reaction time.

Our study is the first to record MEG during MSIT task performance. We observed novel activity of the motor-gamma band on interference trials which was sustained for ~ 0.5s prior to the response and in novel locations including bi-lateral (BA6), and R-IFG. Our results support the idea that R-IFG is specialized structure for response control. Together, these data provide evidence for a motor gamma-band network for selection and control of motor responses in the context of interfering stimuli.

Mo-41 - Statistical regularity encoding in the human brain

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We constantly look for patterns in the environment that allow us to learn key regularities about the world, enabling us to make predictions about what is likely to happen next. The study of regularity extraction has primarily focused on repetitive sequence-based rules. Here we ask whether we can implicitly and efficiently encode sequence-independent statistical regularities (and detect irregularities). We recorded magneto-encephalographic (MEG) activity evoked by a stimulus embedded in a stream of events sampled from two normal distributions of pure tone sounds, characterised by equal means and different variances (low and high). We found that responses to auditory events depended on the statistical context, or distribution variance, in which they occurred. Importantly, this effect was not due to local adaptation. The parietal cortex was more active for rare events that occurred in the context of a low, as compared to high, variance distribution. Thus we show that the human brain efficiently encodes statistical regularity, and is sensitive to variations in sufficient statistics such as mean and variance in environmental stimuli. Such sensitivity may provide a computational basis for our ability to make perceptual inferences in noisy environments and for making decisions in an uncertain world.

A) Experimental design B) Scalp sensitivity to contextual variance (p<0.05 FWE) C) Source sensitivity to surprise, MSP solution for 100-200 ms. D) ERFs (first DCA) to trials that exclude at least n (n = 1,2,4,15) tones preceding rare events.
The color-word interference Stroop task has been used in functional neuroimaging studies to understand the underlying neural processes of response inhibition and cognitive control. While these techniques have been used to identify the cortical structures that serve these functions in pre-frontal cortex (PFC), little is known about either the timing of activity between these regions or the oscillatory dynamics of activity within these areas. To examine these processes, we used time-frequency optimized reconstructions of magnetoencephalographic imaging (MEG-I) data during a modified stroop task. Data (100 trials) were collected using a 275-channel whole head biomagnetometer (MISL). During recording, participants were required to provide a manual response (button press) while covertly reading the color of a word, which could be congruent or incongruent with the word definition. Both stimulus and response-locked reconstructions were generated across the theta (2-8Hz) alpha/beta (9-20Hz), high beta (20-30Hz) gamma (30-55Hz) and high gamma (65-90Hz, 90-140Hz) frequency bands. At stimulus onset, greater alpha/beta power during the incongruent trials was observed over medial PFC, with increased gamma power over extrastriate visual cortex ~ 300ms post-stimulus. In the response-locked analyses, increased oscillatory power during incongruent trials in the high-gamma range (90-140Hz) was observed over medial PFC and over left dorsolateral PFC in the theta range ~ 75ms post-response. When oscillatory power was correlated with reaction time (RT) in the response-locked analyses, a positive correlation was seen during post-response time periods between RT and theta power over anterior PFC and high-gamma power over medial PFC. These findings suggest both response inhibition and error monitoring processes in higher-order association cortex, defining interactions within a pre-frontal cortical network during cognitive control.

Mo-43 - Oxytocin attenuates feelings of hostility depending on emotional context and individuals’ characteristics.

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In humans, oxytocin (OT) enhances prosocial behaviour. However, it is still unclear how the prosocial effects of OT are modulated by emotional features and/or individuals’ characteristics. In a placebo-controlled design, we tested 20 healthy male volunteers to investigate these behavioural and neurophysiological modulations using magnetoencephalography. As an index of the individuals’ characteristics, we used the empathy quotient (EQ), the autism spectrum quotient (AQ), and the systemising quotient (SQ). Only during the perception of another person’s angry face was a higher SQ a significant predictor of OT-induced prosocial change, both in the behavioural and neurophysiological indicators. In addition, a lower EQ was only a significant predictor of OT-induced prosocial changes in the neurophysiological indicators during the perception of angry faces. Both on the behavioural and the neurophysiological level, the effects of OT were specific for anger and correlated with a higher SQ.

Mo-44 - Event-related changes in gamma-band brain activities during eye gaze perception between directly facing subjects

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Recent neuroimaging studies on the perception of facial expression have elucidated that the changes in eye gaze directed to the observer evoke specific neural responses in the middle frontal, the inferior temporal, superior parietal and the posterior superior-temporal regions. However, it is still unclear how the changes in the eye gaze direction between the directly facing subjects changes the spontaneous brain activities in the both subjects. Here we used neuromagnetic recording (magnetoencephalography: MEG) to measure brain responses while the observer perceives changes in eye gaze, namely (a) the eye-contact and (b) the avverting conditions, of the directly facing person. The MEG signals were analyzed in the time-frequency domain to evaluate event-related changes in the spontaneous brain activities induced by the onset of eye movements. Significant increase in the gamma-band power was observed in the eye-contact condition compared to the avverting condition in the bilateral superior-temporal and frontal areas. Frequency-domain Granger-Geweke causality was used to test if there were causal connectivity between the areas where significant changes in gamma-band power were observed. The current results indicate that the connectivity between (a) the bilateral frontal areas, and (b) the right frontal and parietal areas might be crucial for the perception of eye gaze of the directly facing person.
Results of the time-frequency analysis of even-related changes in spontaneous brain activities during eye gaze perception task

Mo-45 - Neural correlates of the reproduction of temporal intervals as revealed by MEG and EEG.

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When participants are asked to reproduce an earlier presented duration, EEG recordings typically show a slow potential that develops over the central regions of the brain. This contingent negative variation (CNV) has been linked to processes such as anticipation, motor preparation and interval timing (e.g., Walter et al. 1964, Elbert et al., 1991, Macar et al., 1999). However, a still open question is whether this electrophysiological component has a magnetic counterpart (CMV). N’Diaye et al. (2004) have shown that a CMV can be found at parietal regions in a temporal discrimination study with durations below 1 second, and Elbert et al. (1994) have shown that during the estimation of a 4 seconds duration multiple sources might contribute to a buildup of a CMV. To assess the robustness of the CMV, we have conducted a temporal reproduction study with multiple durations while co-recording EEG and MEG. In the study we report on, 17 participants who were presented intervals of 2, 3 or 4 seconds which had to be immediately reproduced, similar in setup to the seminal work of Elbert et al. 1991. The EEG data shows a clear CNV in the central and fronto-central areas which develops during the whole interval. The amplitude of a slow potential measured at the centro-parietal and left primary motor regions was significantly bigger for the 2 seconds condition than for the 3 and 4 seconds conditions. However, we did not identify a sustained magnetic variation that resembles the CNV. Instead, initial analyses hint at the development of a magnetic field at centro-parietal locations that is initiated by the onset of the interval but dissolves after 1 second, again with a greater amplitude for the 2 second interval. Its centro-parietal location and timing suggest that this might be a magnetic counterpart of iCNV, potentially related to early anticipatory process (Fischer et al. 2010).

Mo-46 - Age-related differences in neural activation during emotional processing

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Emotional face processing is critical to successful social interaction. Although an innate predisposition for orienting towards faces is present at birth, perceiving and interpreting emotional faces involves more complex functions that develop over childhood. Maturation of emotional face processing has been suggested to reflect protracted development in the neural areas recruited during this
process. The current study explored the temporal and spatial properties of neural activation during implicit emotional face processing in adolescents and adults with MEG. Seventeen adults (9M, 23.0±1.9 years) and 14 adolescents (11M, 14.2±1.1 years) were tested. Rapid presentations were shown of an emotional (happy or angry) or neutral face, concurrently with a scrambled pattern (target), on either side of a central fixation cross. Participants indicated the location of the target by pressing a corresponding button, while fixating on the cross. Structural MRIs were obtained in all subjects to facilitate accurate source localization. We conducted event-related beamforming analyses on the MEG data contrasting happy-neutral and angry-neutral comparisons in an early time window (80-120 ms). In response to happy faces, we found left middle frontal activation in adults, and left anterior cingulate, bilateral middle frontal, and right inferior frontal activation in adolescents. In response to angry faces, adults showed left middle frontal, right inferior frontal, and left cingulate activation while adolescents showed early left medial frontal, bilateral middle frontal, and right inferior frontal activation. Overall, adolescents and adults showed similar frontal but divergent limbic activations for processing of emotional faces. The time courses of these activations are undergoing further analyses. These data demonstrate, however, that even in adolescence the neural mechanisms underlying the development of rapid, implicit emotional processing are continuing to mature.

Mo-47 - Behavior of motor-cortical 20 Hz oscillatory activity in movement inhibition and execution

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Purpose
The behavior of 20 Hz rhythm of central area contralateral to the movement is known as motor-related. To clarify cerebral processing of motor control, activity of 20 Hz was analyzed in response to transient motor inhibition and execution.

Method
Ten healthy volunteers were recruited.

Omission auditory stimuli: Auditory tone bursts were presented in fixed interval of 0.7 s stimulus onset asynchrony. In the auditory sequence, 20% of the stimuli were omitted randomly.

Paradigm: 1. Omission-NoGo. In a train of auditory stimuli, subjects were requested to move their right thumb in response to the tones. Subjects should not move their thumb in response to the timing when tones would be omitted (omission).
2. Omission-Go. Contrary to Omission-NoGo, subjects had to make response to omissions exclusively. No response was requested to tones.
3. Rest. Subjects were requested just to listen to the same stimulus sequence.

Recording: Whole-head MEG (Neuromag Vectorview) was used to sample data at 600 Hz. Frequency power centered at 20 Hz was calculated in each channel from 1.6 s before and 1.4 s after the omission onset. The power was normalized with respect to that from -1.6 to -1.4 s.

Results
In the left central area (contralateral to the movement) in all subjects, clear event-related synchronization (ERS) of 20 Hz was found in Omission-NoGo, and event-related desynchronization (ERD) appeared in Omission-Go. In Rest, there was no significant change in any sensor. In both Omission-NoGo and -Go, 20 Hz change exceeded the significant level peaking at 0.2 s after the omission onset as compared to preceded responses to tones.

Discussion
Motor-related oscillation usually involves preparation and execution process. In the present study, motor preparation was completed before omission. Process just after the omission must indicate alteration of motor program without movement.

Conclusion
The 20 Hz change in this short period directly relates to update of motor program.
Mo-48 - Modulation of auditory-cortex lower alpha-band rhythm by anticipated emotional sounds

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A spontaneous 'tau' rhythm within the lower alpha-band (8-10 Hz) has been recorded with MEG from the auditory cortex and found to be suppressed by auditory stimuli. We were interested to find out whether the tau rhythm can be modulated just by the anticipation of emotional sounds.

We recorded whole-scalp MEG (Vector View, Elekta-Neuromag) from 15 right-handed subjects who were anticipating for 2 s and then hearing for 6 s emotional sounds, selected among 8 pleasant & low arousal (P), 8 unpleasant & high arousal (U), and 8 neutral (N) sounds (IADS-2 library, Florida University). The frequency (0.5, 1, or 2 kHz, order randomized across subjects) of a 100-ms sound, presented 2 s before each emotional sound, cued the valence (P, U, or N) of the emotional sound. About 40 sounds of each category were presented.

Because the sources of the tau rhythm are located close to the N100m sources in the supratemporal cortex, 10 sensors around the most prominent N100m response were selected for statistical analysis.

During the 2-s anticipation period, the tau rhythm (8-10-Hz level averaged over the 10 channels of maximum N100m amplitude) was suppressed more for U sounds than for N and P sounds (U < N with p < 0.001 and U < P with p = 0.018 at 1.5-2 s), without interaction between hemispheres and sound categories. The sounds themselves suppressed the tau rhythm in both hemispheres. These results suggest that the tau rhythm can be modulated by anticipation of emotional sounds and that the suppression depends on the anticipated emotional content.
Mo-103 - Amygdala timing reveals the underlying neural mechanisms for 5-HTTLPR Polymorphism variation: a MEG/SAM study

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INTRODUCTION Carriers of the low expression (LE: short alleles/S&Lg) of the 5-HTTLPR polymorphism show hyperreactivity in the amygdala to emotional stimuli compared to carriers of the high expression (HE: long allele/La). However, it is unknown whether this reflects increased responsiveness of the amygdala generally or interactions between the amygdala and the input systems. It is argued that the amygdala receives input via a quick subcortical and a slower cortical pathway. If the elevated amygdala response in LE reflects a general amygdala response property, then such difference should be seen both earlier in the subcortical route and later in the cortical route. However, if the difference is a secondary reflection involving interactions between the amygdala and cortical areas, then such difference should only be evident later in the cortical route.

METHODS 40 subjects (14LE/25HE) viewed faces with fear, anger or neutral expressions. A dynamic SAM analysis in the gamma band was done. Group contrasts were made for fear vs. neutral and anger vs. neutral across groups.

RESULTS Although both LE and HE started showing amygdala activity as early as 50ms, the between-group contrast on fearful faces showed an increased activity in the amygdala for LE only at a later time (200-320ms). LE also showed an elevated response in cortical regions including superior temporal sulcus (STS, 130-240ms) and PFC (100-190ms). The between-group contrast on anger faces also showed an increased activity in the amygdala at a later time (160-320ms). SA also showed an elevated response in cortical regions STS (200-240ms), anterior cingulate (ACC, 250-350ms) and parietal cortex (270-370ms).

CONCLUSIONS An elevated amygdala response to emotional expressions in LE appears only at later components of the time-course. This suggests that the effect is not due to the general responding properties of the amygdala, but due to interactions between the amygdala and cortical systems like STS, PFC, ACC.

Mo-104 - Brain regions sensitive to the facial color processing: an fMRI study

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Facial color provides important clues to recognize someone’s emotion and health condition. Therefore facial color is important
information for our social communication. Our previous EEG study shows that face sensitive ERP component (N170) is modulated by facial color, which suggests that face color is important for face detection (Inami et al. 2011). Moreover, facial color sensitivity of N170 was found at the left occipito-temporal site (Nakajima et al. submitted). Although the EEG study indicates that N170 at the left occipito-temporal site is related to facial color processing, it is unclear which brain region is involved in facial color processing because EEG measurement has low spatial resolution. Thus the present study aimed to identify the brain regions related to facial color processing by using functional magnetic resonance imaging (fMRI) with higher spatial resolution. We measured the brain activity from 25 participants during the presentation of natural- and bluish-colored face and their scrambled images. The participants were asked to silently count the number of dummy target monkey images to concentrate on the experiment. Face-selective regions of interest (ROIs) were identified separately for each subject and hemisphere. The bilateral fusiform face (FFA) area and occipital face area (OFA) were identified as brain areas activated more to natural-colored faces than to natural-colored scrambled images. For the ROI analysis, percent signal change data were extracted and averaged by condition within each subject’s predefined ROIs. The left FFA was sensitive to facial color, whereas the right FFA was not. Further, the right and left OFA was also insensitive to facial color. In combination with our previous EEG result, the present study showed that the left FFA is related to facial color processing.

Mo-105 - Motor planning network of processing categorical action sequences

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Shima (2007) discovered neurons from the primate dorso-lateral prefrontal cortex which fired specifically prior to the execution of a certain action sequence category. In the current study, we aimed to find the neurophysiological representation of sequence category within the areas involved in motor planning in healthy humans. A 306 channel magnetoencephalography (MEG) device was used and data analyzed from 22 subjects, while they performed a 4-sequence action, composed of one or two simple movements. There were 11 sequences and 3 categories, ‘Paired’, ‘Alternative’, and ‘Repetitive’. MEG data for the correct trials were preprocessed and the time-frequency representation was calculated via wavelet transform for each category for 204 gradiometers. The channel and frequency band with the most prominent beta-band (15 ~ 30 Hz) event-related desynchronization (ERD) was identified for each subject, and the corresponding beta-power time-course was compared across the category-wise amplitudes of beta-ERDs. We found beta-ERD in all categories for all subjects, mostly in the contralateral frontal/parietal lobe channels starting shortly after visual cue onset. Also, in 20 out of 22 subjects, a subsequent power increase, a ‘rebound’ relative to the maximum ERD, was found. The amount of beta-power decrease and subsequent increase was quantified as a peak-to-peak amplitude difference, and was compared across categories. Differences in amplitudes among categories were detected in 20 subjects for both beta-ERD and rebound. For 18 out of 20 subjects the ‘Repetitive’ category showed the largest ERD and rebound compared to ‘Paired’ and ‘Alternative’. However, the beta-ERD/beta-rebound amplitude for ‘Paired’ and ‘Alternative’ sequences did not reach a statistical significance. Based on the current results, we have found that the beta-power in the contralateral frontal/parietal areas during planning for upcoming movement is differentiated by the category of action sequences to perform.
A. Beta-power time-course for 22 subjects. The vertical axis is power (decibel), and the horizontal axis is time (second). Green lines are 'Paired', red is 'Alternative' and blue is 'Repetitive'. The dotted and solid vertical lines depict zero (visual cue).

**Mo-106 - Simultaneous EEG-MEG study of feedback responses during Brain-Computer Interaction**

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In cognitive tasks, error and correct trials give rise to distinct neurophysiological responses. In EEG, incorrect compared to correct feedbacks evoke a feedback-related negativity (FRN) and both evoke a P3. However, the mental processes they reflect and their underlying neural mechanisms remain largely unraveled. Besides, the MEG equivalents of those signals have not yet been clearly identified.

In brain-computer interfaces (BCI), it has been shown that these responses are maintained, although no motor action is being produced. This is fortunate since they can be used for automatic error detection (1). However, this detection is challenging since it applies on noisy single-trial responses. A fine cortical characterization of those responses might help optimizing their detection.

We used simultaneous EEG (56 channels) and MEG (275 sensors) recordings in a BCI-task. Each participant (N=11) performed 340 trials of an EEG-based P300-speller (1). At the end of each trial, the feedback appeared on screen, displaying either the correct or incorrect letter. We compared activity evoked by good and bad feedbacks, in both EEG and MEG. We then fused EEG and MEG responses and performed group inversion at the latency of the FRN using SPM8 `[2,3]`.

In EEG, we obtained the expected feedback-evoked responses, namely the FRN and P3. Interestingly, although the hypothesized radial mediofrontal sources of the FRN are thought to be hardly visible in MEG, we did observe a large difference between the two conditions in MEG too, at the latency of the FRN (Fig. 1).

Simultaneous localization of EEG and MEG differences in evoked-responses yielded a source network made of the left fusiform gyrus and bilateral superior temporal gyri. Although very preliminary, the latter result is in line with previous EEG findings (4).

(1) Perrin et al., Graz BCI workshop, 2011
(2) Litvak et al., Comp. Intel. Neuro. 2011
(3) Henson et al., Front. Hum. Neuro. 2011
(4) De Pascalis et al., Clin. Neurophysiol. 2010
Mo-107 - I have just seen a face: Neuromagnetic oscillatory activity in somatosensory cortex indexes recognition of facial affect expression

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It has been shown that disrupted activity in the somato-sensory face area (SFA) impairs accurate perception of emotional face expression and that passive viewing of static face images reduces oscillatory activity in the alpha frequency band (8-12Hz) over central electrodes. This suggests that re-activation of those somato-sensory brain regions that are involved in facial expression mediate recognition of affect in other people’s faces. The neural dynamics of this re-activation, in particular, the contribution of ongoing brain oscillations have not been specified. Using high-resolution MEG and single-trial oscillatory analyses, the present study sought to clarify the neural dynamics and the corresponding brain networks associated with this re-activation. Thirty volunteers watched 120 5-sec videos of human faces, which changed their expression from neutral to either fearful or happy emotional expression, or changed facial features while expression remained neutral (control condition). Changes from neutral to emotional expression were associated with 10-15 Hz power increase in bilateral SFA prior to and a relative power decrease following the time point when emotional expression recognition exceeded 80% accuracy (determined in a separate session). Graph theoretical analysis revealed that this power in- and decrease pattern was associated with relative de- and increased coupling of the SFA with all other brain regions.

Results suggest that facial affect recognition involves re-activation of those somatosensory areas that are involved in expression of the observed emotion. Ongoing alpha oscillatory activity is a candidate to mediate this processing.

Mo-108 - Cross-frequency coupling of neuromagnetic oscillatory activity: A window on neural mechanisms of emotion regulation?

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Hemodynamic and electromagnetic imaging methods can clarify brain activity and its dynamics relevant to emotion regulation. Research suggests a spatio-temporal sequence of activity in subcortical (amygdala) and prefrontal and cingulate brain regions during down-regulation of responses to emotional stimuli. Interregional coupling of frequency-specific oscillations is believed to index coordinated activity within and across neural networks. Complementing conventional averaged event-related activity, such oscillatory phenomena should provide insight into neural mechanisms that contribute to processing of emotional stimuli. Neuromagnetic activity was measured from 24 volunteers during instructed down-regulation of unpleasant pictures and during passive viewing of neutral and unpleasant pictures. Alpha (10-15 Hz) and gamma (60-80 Hz) activity was analyzed using dynamic imaging of frequency-specific coherent sources (Gross et al., 2001) and phase-amplitude coupling (Voytek et al., 2010). Picture onset prompted event-related
Mo-109 - Self-monitoring of internal clock shifts: automatic vs. conscious access to time

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The proper selection and programming of actions in time are a requirement of daily functioning. The accuracy of such judgments is cognitively monitored, specifically leading to internal error signals when the outcome does not match the prediction. The Error Related Negativity (ERN), an EEG component that captures this internal error, occurs a few milliseconds after errors. Additionally, the Feedback Related Negativity (FRN) is considered an equivalent of the ERN but only when the error is signaled by an external feedback (FB). Both ERN and FRN have been studied when errors pertain to the selection of a motor program. However, much less is known about the extent to which cognitive monitoring is involved when the required response is a judgment of when to act (e.g. time estimation) as opposed to how to act (e.g. which key to press). Here, we asked whether duration estimations and the internal clock are subject to similar error detection monitoring. To test this, we tested participants with combined MEG-EEG while they performed a duration estimation task (1.45 sec). Crucially, and unbeknownst of the participant, the internal clock was actually calibrated by external FB. The experiment consisted of three main conditions, each tested with two runs: the first run provided participants with an accuracy FB on their temporal estimations (too short, correct, or too long) whereas the second run did not provide any FB. In the first condition, the FB was valid i.e. based on the actual difference between the estimated and the objective duration. In the other two conditions, the FB was invalid and calibrated to a shorter (1.2 sec) or a longer (1.7 sec) objective duration. Preliminary data show that the FRN reflect the information provided by the FB and is particularly sensitive in blocks with invalid FB. This suggests that internal monitoring of the internal clock does occur and keeps track of the discrepancies between the external and internal temporal estimations.

Mo-110 - The role of cerebellum in the temporal regulation of emotional processing

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The cerebellum contributes significantly to cognitive processing and emotional control in addition to its role as critical modulator of movement. Burgeoning neurophysiological evidence implies that non-motor cognitive processing in cerebellum is sub served by posterior hemispheric lobules, whereas affective processes by posterior midline cerebellar structures. Nevertheless, the precise nature of cerebellar contribution in emotional processing is still unclear. MEG recordings were performed on 12 healthy individuals exposed to affective stimuli from the International Affective Picture System collection. Four stimuli sets that manipulated the level of arousal within pleasant and unpleasant pictures were used. Global Field Power (GFP) was estimated at sensor level of these sets’ averaged data in the gamma band. Source power was estimated using a beamformer. Virtual sensors (VS) at regions of interest presented significant differences between high and low arousal and/or valence. GFP results demonstrated significant gamma modulation indicating that the same affective information (arousal and/or valence) is processed over several distinct time instances (fig. A). Arousal was localized on cerebellum’s right midline and hemispheric posterior lobe (fig. B) as well as on the left lingual gyrus. Arousal’s interaction by valence involved the cerebellum’s left hemispheric posterior lobe (fig. C). VS results complemented the GFP ones implying that significant early differences between high and low arousal occur as early as 100 ms and that this may be processed in cerebellum’s right posterior lobe. Arousal’s interaction by valence occurred at longer latency responses (≥300 ms) on left cerebellar hemispheric posterior lobe. These significant components at sensor and source level may place the current opinion on the suggestion that distinct cerebellar sub-lobules exhibit unique functional roles on emotional processing, while reserving timing mechanisms that aid in emotional regulation.
Mo-111 - Embodied spatial transformations: The brain rotates 3D objects like it controls ice skating spin

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The neuronal recycling hypothesis posits that existing structures evolved for other purposes during evolutionary development, thereby cognition exapted sensorimotor functions. Likewise, the ability to imagine someone else’s viewpoint has developed from physical alignment of perspectives. Using MEG, we compared the spatio-temporal unfolding of the neural mechanisms underlying a shape-matching task, where two objects (either familiar: human bodies, or unfamiliar: cube assemblies) were displayed under similar or different viewpoints. Subjects had to indicate whether these two objects were identical, or mirror. Activity in the superior parietal lobe (SPL) and in the supplementary motor area (SMA) was stronger when a spatial transformation was required. Moreover, activity in SMA increased from the ‘body’ to the ‘cube assemblies’ condition. In line with the neural recycling hypothesis, we consider that mental spatial transformations rely on the same cerebral areas than actual spatial transformations do, but at a more cognitive level. A sport metaphor can help understanding this phenomenon: SPL first triggers the spatial transformation (ice skater impulsing its spins), then SMA strengthens the structure during the rotation (ice skater maintaining its posture during the spin), and finally SPL predicts the visual consequence of spatial transformation (the ice skater stops spinning).

Mo-112 - Neural mechanisms underlying socially-induced preferences

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We live in a social world. In order to interact with others we must decode social signals conveyed by conspecifics. Eye gaze direction is a particular and powerful cue that indicates the focus of attention and the potential targets of actions of others. It has previously been shown that objects looked at by others are preferred to objects that did not fall under others’ attention. However, the neural correlates underlying such socially-induced liking effect are unknown. We have tested the liking effect induced by others’ gaze using a modified version of a Posner-like attention cueing paradigm. A first phase consisted of successive blocks of attentional orienting induced by eye gaze, where a central face gaze directed to the right or left side of the screen served as the cue and target stimuli appeared either at the gazed (cued) or at a non gazed (uncued) location. The subjects had to categorize the target stimuli. In a second phase the cued and uncued objects were seen again and evaluated affectively along a 9-point rating scale. This paradigm has been effective to show a liking effect for cued stimuli such as letters and symbols. In a next step, we will use the same paradigm to study the neural correlates of the liking effect with magnetoencephalography (MEG). In order to uncover the brain activity underlying this effect we will: i) compare the brain responses to cued and uncued target stimuli (attentional effect of gaze), ii) examine the brain activity that correlates with the affective evaluation of these stimuli (liking effect). We expect to find activations in brain areas associated with affective valuation like the orbitofrontal (OFC) and ventromedial prefrontal (vmPFC) cortices. We will test whether these activations correlate with the attentional modulation of target stimulus processing induced by gaze cues. The excellent
The gastrectomy is a surgical procedure that constitutes the partial or total stomach recession, which causes modifications in some gastrointestinal tract properties. The Alternate Current Biosusceptometry (ACB) is a biomagnetic method that uses induction coils on the acquisition of magnetic flux variation obtained in response to the magnetic material ingested or fixed in the tract. This paper proposes the partial gastrectomy influence and consequences analysis in gastric emptying time and orocecal transit time by the ACB.

This work was divided in three steps, before surgery, right after surgery and two months later. Each stage consisted of monitoring the magnetic intensity values on both stomach and cecum projections on the abdominal surface by ACB in a group of six male Wistar rats. All raw signals were analyzed in MatLab® by visual inspection and the statistical moment was calculated. Using this approach, it is appropriate to quantify the following parameters: Mean Gastric Emptying Time (MGET), Mean Cecum Arrival Time (MCAT) and Mean Small Intestine Transit Time (MSITT). The statistical values obtained in the stages before surgery, right after and two months after the procedure was: MGET, 168 ± 20, 127 ± 6 and 110 ± 3 minutes, MCAT, 327 ± 26, 263 ± 15 ± 221 ± 8, and MSITT, 159 ± 15, 135 ± 11 ± 110 ± 8, respectively. This gastric emptying time reduction is related to the physiological consequences of the gastrectomy. Different kind of surgery should cause different effects on the gastric emptying and orocecal transit time, keeping a large whole of applications for the gastrectomy technique. By these results, this biomagnetic method showed efficiency evaluating alterations provoked by surgical procedures. The association of these obtained parameters to other properties as gastric contraction activity frequency and intensity should provide a better understanding of these procedure consequences.

Tu-137 - Proliferation of the cell culture line HEK 293T under different concentrations of ferromagnetic fluid

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Introduction: The cultures of cell lines are widely used in various areas of the biomedical research. The embryonic kidney cells HEK belong to a cellular line generated in the 70’s, they are usually used in cell biology research and their growth parameters and behavior are well known (1). There are many reagents for handling, testing and maintenance of cell cultures, nevertheless, such products can affect significantly the cell viability and proliferation and, in many cases, those effects have not been studied in depth. Objective: To observe the changes in viability, proliferation and cell death of the HEK 293T line (2) under different concentrations of a ferromagnetic fluid. Materials and methods: A variant of the HEK 293T cell line is used in this research, which contains in addition the SV40 Large T-antigen that allows its replication. Cells were cultured in an incubator with complete medium culture DMEM (Gibco-Invitrogen), low glucose and glutamine, supplemented with Fetal Bovine Serum (FBS, Gibco-Invitrogen). The proliferation and viability of the cell culture were studied at different concentrations of ferromagnetic fluid, from 0 (control) to 200 , observing changes in proliferation or encumbrances. Results and discussion: The results show a resistance of the cell culture line HEK 293T to the toxicity at concentrations up to 50 of ferromagnetic fluid. There was an increment of 13 % (see Fig) Fin the cell proliferation at a concentration of 30 of ferromagnetic fluid. (1) F. L. Graham, J. Smiley W. C. Russell, R. Nairn (1977). Characteristics of a Human Cell Line Transformed by DNA from Human Adenovirus Type 5. Journal of General Virology (1977), 36, 59-72. (2) G L. Pardo Andreu, Y Nuñez Figueredo, V G. Tudella, O Cuesta Rubio , F P. Rodrigues, C R. Pestana, S A. Uyemura, A M. Leopoldino, L C. Alberici, Carlos Curti (2011). El Agente Anticancerígeno Nemorosona, es un Nuevo y Potente Desacoplador Pro
Behavior of the cell line HEK293T under a ferrofluid

Tu-138 - Colon Pharmacomagnetography by AC Biosusceptometry

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Colon is an important target of drug delivery and is commonly used in therapy. Nevertheless, experimental determination of tablet disintegration uses a standard in vitro apparatus and it does not precisely fit the in vivo disintegration properties. AC Biosusceptometry (ACB) has become an alternative method for pharmaceutical research as a tool for in vivo studies. The aim of this study was to employ the ACB to investigate the behavior of magnetic enteric coated tablets as well as the in vivo determination of their drug release in combination with pharmacokinetic outcome. The study was carried out in eight healthy volunteers (age: 20-40, 3 male, 5 female). Tablets were obtained by direct compression of 1 g ferrite (magnetic marker), 100 mg of diclofenac sodium (model drug), excipients and coated with a pH-responsive polymer. Enteric coated tablets were tested under requirements of pharmacopeia. Drug levels were measured in the plasma, and the transit of the enteric coated tablets was followed by ACB, monitoring of the abdominal surface to determine gastric residence time (GRT), colonic arrival time (CAT) and disintegration time (DT). Each monitoring was recorded at 15 min intervals up to 8 h. Images were obtained from magnetic monitoring and then segmented to calculate the pixels area. Blood samples were collected simultaneously at pre-defined time intervals and analyzed in HPLC. GRT were 90.00 ± 34.02 min and CAT 215.63 ± 41.61 min. DT for enteric coated tablets were 28.25 ± 11.35 min. The tablets had variable in vivo performance (Tmax ranging from 266.5 ± 52.42 min, AUC 436.513 ± 312.238 ng.h.ml⁻¹). The tablets were colon-specific since drug was detected in the blood only when the dosage forms had reached the region. From the results presented, we conclude that ACB associated with pharmacokinetic data, a method termed pharmacomagnetography, was reliable into provide valuable data concerning drug release processes from magnetic enteric coated tablets.

Tu-139 - Analytical solutions for the flow of blood in the presence of an external magnetic field

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The movement of a conducting fluid in an externally applied magnetic field, B₀, is governed by the laws of magnetohydrodynamics (MHD). When the body is subjected to a magnetic field, as it is the case in Magnetic Resonance Imaging (MRI), the charged particles of the blood get deflected by the Lorentz force thus inducing electrical currents and voltages across the vessel wall and in the surrounding tissues. These voltages perturb the ElectroCardioGram (ECG) that is used for cardiac gating. During MRI examinations, the largest potentials are induced in the aortic arch, since it is perpendicular to the magnetic field and presents the highest flow rate. An optimal modelisation of blood flow in that case should thus include the pulsatility of flow, the deformability and conductivity of the vessel wall, together with the induced electrostatic and electromagnetic fields.

We addressed this quite complicated problem by studying separately the influence of each factor (rigid or deformable tube, steady or
pulsatile flow, conducting wall or not). It is hoped that such analytical solutions will improve the understanding of magnetohemodynamics in the context of MRI, and that they may also be used to validate the 3D computational fluid dynamics codes developed by other groups.

**Tu-140 - Electron Spin Resonance Spectroscopy study of Paramagnetic ions in Subthalamic Nucleus of patients with Parkinson’s disease**

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Subthalamic Nucleus (STN) is a dense cluster area of neurons in the center of subthalamus and which is of great significance in Parkinson disease (PD). From a functional point of view, the subthalamic nucleus is part of the basal ganglia system. The motor signs and symptoms of PD result primarily from dysfunction of the basal ganglia system. Moreover, PD and related syndromes are associated directly with the concentrations of paramagnetic ions and its bonding molecules in the basal ganglia system, such as ferritin and neuromelanin. Even more, nowadays it is discussed the possible protective role of neuromelanin by the sequester redox active iron ions, reducing the formation of free hydroxyl radicals and therefore inactivating the iron ions that induce oxidative stress. In this work we study the concentration ratios between paramagnetic ions and neuromelanin in subthalamic nucleus of patients with PD using Electron Spin Resonance (ESR) spectroscopy. Necropsy samples of subthalamic nucleus from six human brains were studied: three non-affected by any neurodegenerative disease and three with PD. ESR experiments were carried out on a JEOL FA-200 X-Band spectrometer at different temperatures between -170°C and room temperature. The relative concentrations of each species were estimated from peak to peak amplitudes and from the double integral values of the fitted spectra. All samples showed an ESR spectra composed of three different signals. One signal was attributed to high-spin ferric ions ($g \sim 4.3$) in rhomboedric symmetry, Cu(II) ions (close to $g=2.0$) and neuromelanin ($g \sim 2.01$). Our preliminary results indicated a small increment of copper and a significant increment of iron concentration related to neuromelanin in PD samples, which agrees with previous histochemical and biochemical reports. These results and the reduction of neuromelanin concentration in PD samples suggest the possible role of neuromelanin as paramagnetic ions storage.

**Tu-141 - Metabolism of Magnetic Nanoparticles in Rats**

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As we know, bio-functional magnetic nanoparticles (MNPs) have been well synthesized and widely used in biomedical applications recently. For some in-vivo applications, such as drug delivery, hyperthermia, and images etc., the metabolism of MNPs is the most important issue before carrying on vivipерception. In this work, the metabolism of MNPs in rats with two types of form: (1) without bioprobes coated, and (2) with bioprobes coated were studied by a homemade novel scanning SQUID biosusceptometry (SSB), and also general biological methods such as blood tests, tissue stains, etc.. The feasibility of SSB for tracking free MNPs was demonstrated. The complete metabolism model of the uncoated MNPs was established. Next, for the metabolism studies with anti-Alphafetaprotein (anti-AFP) as a bioprobe targeted to the liver cancer tissues, SSB was paralleled with MRI. The good agreement was found among the metabolism results of SSB, MRI and the biological assays of tissue stains. In order to establish an inspection method of the tumor cells, the dynamic magnetic labeling results for the normal rats and the liver-tumor rats will be demonstrated in the meantime. Finally, by means of the level tests of Glutamate Oxaloacetate Transaminase (GOT) and Glutamic Pyruvic Transaminase (GPT), the toxicity results of the anti-AFP will be revealed.

**Tu-142 - Magnetic Nanoparticle Uptake in Tumor Cells quantified by Temperature Dependent Magnetorelaxometry**

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Magnetorelaxometry (MRX) is proven to be a powerful tool for the quantitative detection of magnetic nanoparticles (MNP) utilized
in magnetic drug targeting and magnetic hyperthermia. So far we applied MRX measurements at room temperature for quantification of MNP in blood and tissue samples. Since the MRX relaxation time depends on the MNP size, particles with less than about 17 nm in diameter at room temperature decay too fast and are not detectable within the recording time window of present MRX devices. To circumvent this limitation we performed temperature dependent MRX measurements.

HeLa and Jurkat tumor cells were incubated with small iron oxide MNP, CD021110 (carboxy dextran coated preclinical MNP, Charité Berlin, $d \sim 4 \text{nm}$) at varying concentrations. After 30 h, samples of about $10^6$ cells were harvested. A conventional SQUID magnetometer was utilized for temperature dependent MRX between 5 K and 300 K. By normalization of the reference relaxation amplitudes to the amplitudes of the cell samples a straightforward quantification was carried out. For cross validation the cell samples and references were analyzed by M(H) measurements using the same device and by non-linear ac-susceptometry using an MPS spectrometer. Temperature dependent amplitudes were compared with reference data from individual MNP fractions with different diameters.

The cell samples showed an iron uptake in the range scaling with the concentration of MNP during the incubation as confirmed by M(H) and MPS measurements. From the temperature dependent MRX measurements of the references a detection limit of about 100 ng iron was estimated. Furthermore, size specific uptake of MNP is expressed by a shift in the temperature dependence of the relaxation amplitudes.

Performing MRX measurements at lower temperatures allows the in-vitro quantification of MNP of smaller sizes with extremely short relaxation times at room temperature. A size specific cellular uptake of MNP can be quantified.

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Tu-143 - Imaging of a magnetic nanoparticle distribution using a single sensor and multiple magnetizing coils

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Quantitative spatially resolved imaging of magnetic nanoparticles (MNP) is essential for the control of new MNP-based therapies against cancer. In magnetorelaxometry (MRX) a distribution of nanoparticles is quantified by measuring its relaxation after changing an external magnetic field. Previous theoretical work suggests an improvement of the spatial resolution by sequentially application of inhomogeneous excitation fields. Here we experimentally tested this hypothesis using a single-sensor setup.

The MRX setup consisted of 30 magnetizing coils ($d=6\text{mm}$) radially placed on the surface of a cylinder (5 rings with $l=7.5\text{ mm}$, 6 coils with $\alpha = 60\text{ per ring}$, each ring shifted 30) as shown in figure 1A.

The volume directly outside the cylinder surface was divided into 9 subvolumes (voxels). In each of the 9 voxels an MNP-sample (300mg iron oxide powder) was sequentially magnetized by the 30 magnetization coils and the relaxation response was measured by a single SQUID system. The voxel magnetization was reconstructed by inverting the forward problem of 30 equations relating magnetizing field and relaxation amplitude using a Truncated Singular Value Decomposition. The reconstruction of more complex
source distributions was evaluated on superpositions of the results of the single voxel measurements. The measurement of MRX signals using 30 excitation coils was feasible. A quantitatively accurate reconstruction of the amount of nanoparticles was achieved for all single voxels and also for complex distributions. The mean difference between the reconstructed MNP amount and the actual value was about 10 percent. Meaningful reconstructions were also obtained after virtual enlarging the spatial resolution up to 9 by 9 voxels. We demonstrated the possibility of MNP imaging with MRX using inhomogeneous magnetizing fields and only one sensor. Further works will focus on larger source volumes and multi-sensor systems.

**Figure 1:** A) Schematic of the measurement setup and each measured sample position for building a complex source distribution B) Reconstructed iron mass (negative values excluded) of the distribution in A using 3x3 and 9x9 voxels in the reconstruction grid.

**Tu-144 - Increased survival of human lymphocytes by combined effect of magnetic stimulation and mitogenic**

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Introduction. Electromagnetic fields are a combination of electric and magnetic fields. They occur both naturally and due to human activity. In the present study, we observed the effects produced by an oscillating magnetic field on human lymphocytes in a frequency range from 100 to 2500 Hz. Materials and Methods. Mononuclear cells of peripheral blood from subjects clinically healthy were isolated by differential centrifugation in a gradient density Ficoll-hypaque. The magnetic stimulation was performed in several stages by means of a computational algorithm, a signal generator, which are set the shape parameters of the generated signal, these parameters are selected by a switch at time intervals of 360 seconds for each frequency to complete one cycle of two hours. In the computer is generated the sine waveform and sent to the amplifier to finally remit to a coil Rodin in which magnetic field is generated. To increase the effect of magnetic stimulation in cells were added a ferromagnetic fluid. The cell cultures were performed under standard conditions of temperature, humidity and CO2. Cells were labeled with CFSE, exposed to the magnetic field and incubated for various periods of time in the presence and absence of Concanavalin A (mitogen). Survival was evaluated with the parameters of size vs granularity (Forward and Side scatterer) and retention of CFSE by flow cytometry. Results and Discussion. There was an increase around 12% (see figure) in viability and survival of cells exposed to the magnetic field and stimulated with Concanavalin A (Con A) as compared to cells not stimulated with Con A and subjected to the magnetic field as well as cells stimulated with Con A but not subject to magnetic field.
Tu-145 - Inspection Method of Magnetic Nanoparticle for Biomedical Analysis

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OBJECTIVE: We have developed a detection method of magnetic nanoparticle using AC susceptibility measurement technology. Using this method, we studied the inspection of magnetic nanoparticle for biomedical assays, such as the cell detection and immunoassay.

BACKGROUND: Previously we developed the HTS SQUID system for small amount of magnetic nanoparticle which bound to protein-coated polystyrene microspheres. We have also developed the inspection method because of the study for the property of magnetic nanoparticle in more detail. Therefore, we can study the frequency magnetic properties of varied sized nanoparticles using the difference of Brownian motion of particles.

METHODS: In this experiment, the magnetic nanoparticle made of Fe₃O₄ for cell separation was used. Since several nanoparticles formed complex each other in dextran polymer, the size of complex was enlarged to be 110nm. Then we measured the magnetic frequency properties of varied sized magnetic nanoparticle complex. Furthermore, we also detected the signal intensity of free-magnetic nanoparticle unbound to protein-coated polystyrene microspheres (≥1E+7 beads/mL) and mammalian cells.

RESULTS: We detected the peak frequency of the magnetic nanoparticle complex at 100-130Hz of imaginary part. In addition, the low magnetic intensity which was caused by consumption of magnetic particles bound to polystyrene microspheres was measured (decrease ratio ≥80%). Therefore, it was revealed that the most magnetic nanoparticle was bound to protein-coated polystyrene microspheres.

CONCLUSION: We could have detected the frequency properties of varied sized magnetic nanoparticles using AC susceptibility measurement technology. Thus, our method will be useful for inspection of magnetic nanoparticle and biomedical assays. The present study was partially supported by Strategic Promotion of Innovative R&D in Japan Science and Technology Agency.

Tu-152 - Analysis of spatial resolution of the ac biosusceptometry gradiometers by implementation of modulated transfer function

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The Alternate Current Biosusceptometry (ACB) is a biomagnetic technique able to evaluate different parameters related to the gastrointestinal tract through the external monitoring of ferromagnetic materials used as markers or tracers.

The magnetic sensor consists of two coils pairs (induction and detection) to excite and monitor, respectively the magnetic materials ingested and/or fixed to the gastrointestinal tract.

The high magnetic susceptibility of these materials generates an imbalance between the induction/detection coil pair. This response obtained produces an electrical signal proportional to the variation of the magnetic flux also proportional to the magnetic material concentration and position, which gives the characteristics of a linear system to the ACB. The signal produced enables the formation of images, relating to the pixel tone from the magnetic field variation. Making use of computational techniques was possible to form
phantom images, revealing the need for signal processing and image analysis of this system. Currently one of the most established methods for analyze the spatial resolution of linear systems is the Modulation Transfer Function (MTF). The MTF is the Fourier transform of the Point Spread Function (PSF), the latter being the function that allows the visualization of a system response to a stimulus. As the ACB system is relatively new, until now there are no studies regarding its resolution. Since this technique produces a signal linearly proportional to the amount of magnetic material present in the sample, it is possible to assess the system spatial resolution by MTF. In this study, was compared resolution for ACB sensors with different diameters (3cm, 4cm, 5cm, 6cm, 7cm and 8cm).

The results obtained from this study correlation shows high (0.94) between MTF and half the bandwidth at half height. This method can be used to and assist the choice of specific sensors to be used in the practical routine of the BAC application.

Tu-153 - AC Biosusceptometry to study gastrointestinal motility in pregnant rats

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Several hormonal and physiological changes that occur during pregnancy seem to affect the gastrointestinal (GI) motility, however very little is known about relationship between electrical and mechanical activities of the stomach and their implications. The aim was to compare female sex hormones with GI motility profile, using AC Biosusceptometry (ACB) in pregnant rats. Seven female Wistar rats (weighting 250-350 g) were used and all procedures were approved by the local Animal Ethics Committee. Laparotomy was performed in anesthetized rats and a magnetic marker (3.5 mm diameter and 3.0 mm height) was implanted in distal stomach. After 10 days of recovery, mating occurred until pregnancy confirmation. Fed animals were anesthetized (pentobarbital, 30 mg/kg) and kept supine for the 30 min signal recording with an ACB sensor placed on the abdominal surface in day-1, -7, -14 and -20 of pregnancy. Statistical analysis was performed by Student’s unpaired t-test Newman Keuls and a P value of 0.05 was considered statistically significant. The frequency of stomach contraction was 74 ± 3mHz, 67 ± 7mHz, 59 ± 6mHz (p<0.05 vs day-1), 71 ± 5mHz in day-1, -7, -14 and -20, respectively. The values of 44 ± 15pg/mL, 31 ± 9pg/mL, 25 ± 6pg/mL, 22 ± 9pg/mL in day-1, -7, -14 and -20, respectively, obtained for 17ß-estradiol were not statistically significant. Progesterone values were 13 ± 6pg/mL, 54 ± 15pg/mL, 127 ± 42pg/mL (p<0.05 vs day-1), 22 ± 13pg/mL in day-1, -7, -14 and -20, respectively. The linear correlation (Pearson’s test) between decreased gastric frequency and increased of progesterone levels was 80 % (p<0.0000001). To date, relationships between hormone and motility changes have not been described in detail because, in part, of methodological constraints. Our biomagnetic technique offers new insights about bradygastria provoked by progesterone during pregnancy with accuracy and without interfere with normal physiology.

Tu-154 - ACB Tomography of regular phantom

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Alternate Current Biosusceptometry (ACB) is a gradiometer based instrumentation that has been successfully implemented on biological sciences research during the last two decades, where the major concerns were signal and planar images to evaluate motility, transit, and meal distribution on the gastrointestinal tract. Once ACB had good performance on planar image acquisition, we aimed to evaluate the reconstruction of ACB tomographic images. Initially we built four different bar phantoms (3mm diameter and 1.9g ferrite each bar) that were moved by a computerized driving system during the data collection, a process very similar to the first generation x ray tomography. To detect the phantom response to the excitation magnetic field a multi-channel ACB system with 13 first-order gradiometers was placed close to the phantoms and its position was set up to guarantee simultaneous readings of at least two sensors. From the multi-channel acquisition, we run a filtered backprojection reconstruction algorithm with Hamming filter and cubic interpolation on MatLab. The ACB tomography had very promising results when operating with multiple sensor acquisition. On the final axial slices it was possible within a field of view of 50mm locate all objects of interest, measure its shape, position and concentration, regardless some distortions and artifacts induced by misalignments and driving systems vibration during the acquisition. We conclude that ACB tomography is viable and with the implementation of more adequate reconstruction algorithms it could become a very interesting instrumentation for small animal and pharmaceutical research.

Tu-155 - Biosusceptometry to evaluate in vitro swelling processes and drug release on hydrophilic matrix tablets
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Hydrophilic matrices are modified release solid dosage forms obtained from hydrophilic polymers, such as cellulose derivatives. Drug release from these systems is dependent upon pharmaceutical and physicochemical factors highlighting diffusion as the dominant mechanism. The aim was to employ the AC Biosusceptometry (ACB) technique associated with standard methods to evaluate in vitro swelling as well as the drug release profile of magnetic hydrophilic matrices. Formulations (F1 and F2) were obtained by direct compression (30 kN) in a single punch machine using hypromellose (10% and 30%, respectively), ferrite, sodium diclofenac and excipients. Magnetic monitoring was realized to obtain magnetic images and to calculate the imaging area at pre-determined time intervals. Variations in the weight gain, swelling and volume were also obtained. Dissolution tests were carried out in phosphate buffer pH 6.8 at 37°C in vitro. Variations in the weight gain, swelling and volume were also obtained. Drug release at the same time intervals was 80% and 40% for F1 and F2, respectively. Polymer concentration influenced significantly all the parameters analyzed. Hydration of polymer promotes the formation of a gel layer that controls the drug release rate. Increases in the polymer concentration results in lower hydration rate and, consequently, decreases the drug diffusion through the gel layer. ACB associated with standard method has allowed to analyze biopharmaceutical processes in polymeric matrices.

Tu-156 - AC Biosusceptometry to evaluate gastrointestinal transit in renal transplant recipients

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Gastrointestinal (GI) complications after renal transplantation are often associated with immunosuppressant therapy, however, motility disorders have been scantily studied. The aim of this study was to employ the Alternating Current Biosusceptometry (ACB) to investigate the influence of immunosuppressants on GI transit after renal transplantation. The protocol has been approved by local Ethics Committee. Eighteen renal allograft recipients and 12 healthy volunteers, were enrolled in the study. All the patients were receiving three immunosuppressive therapy: 12 were taking prednisone (PRED), azathioprine (AZA) and tacrolimus (FK) and 6 were taking PRED, AZA and Cyclosporin A (CsA). After an overnight fast, subjects consumed a standard 500 Kcal breakfast and 4 g ferrite. ACB sensor was used to monitor gastric and colonic region at 10 min intervals for at least 8 h. Magnetic images were obtained to quantify GI transit parameters. From the gastric emptying (GE) and colonic arrival (CA) time-intensity curves, mean GE time (MGET), mean CA time (CAT) and mean small bowel transit time (MSBTT) were calculated. The results were expressed as mean ± standard deviation. Differences were evaluated by ANOVA. P value <0.05 was considered statistically significant. MGET obtained for FK, CsA and control was 44 ± 33 min, 147 ± 88 min and 166 ± 52 min, respectively. MGET was significantly faster (P<0.001) in FK group than CsA and healthy controls. MSBTT for FK, CsA and controls was 183 ± 93 min, 137 ± 65 min and 196 ± 66 min, respectively (P=0.52). MCAT was 220 ± 101 min, 283 ± 59 min and 363 ± 55 min for FK, CsA and controls, respectively (P=0.002). Since patients were taking concomitant drugs, we conclude that the differences may be due to the use of FK which is a macrolide and stimulates the gastric motility. There are still gaps in our knowledge regarding the influence of immunosuppressants on GI tract. ACB sensors are versatile tools for monitoring GI transit under such conditions. CNPq/FAPESP
Tu-157 - Employment of a noninvasive magnetic method in the evaluation of gastrointestinal transit in rats

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The gastrointestinal transit (GIT) in rats is usually quantified by measuring the propulsion within the gut of charcoal or dye which requires death and large number of animals. The aim was monitoring in real time GIT of liquid and solid meals using AC Biosusceptometry (ACB). Magnetic intensity values were obtained by an ACB sensor placed on gastric and cecal abdominal projection. Subsequent measurements were made in awake animals at these two points at regular 10-min intervals for at least 7 hours. Liquid meal (Ferrofluid 1.0 ml 4 50 mg/mL) was diluted in 1.5 ml of water and administered by gavage while solid meal using powder magnetic material (0.5 g) incorporated into the laboratory chow (1.5 g) was ingested by animals. The statistical moment was obtained through the temporal average pondered by magnetic intensity curves, normalized by area under curve through following parameters: Mean Gastric Emptying Time (MGET) defined as the amount of magnetic meal that emptied of the stomach at time t, Mean Caecum Arrival Time (MCA T) defined as the increase of amount of magnetic meal that arrived in caecum at time t, Mean Small Intestinal Transit Time (MSITT) quantified as the difference between MCA T and MGET. Student’s t-test was used and a P value of 0.05 was considered statistically significant. The results showed that gastric emptying time was markedly different between both meals in the same animal. MGET values were statistically significant (p < 0.04) between liquid (99.58 ± 13.50 min) and solid meals (140.52 ± 35.51 min). MCA T values were also statistically significant (p < 0.04) between liquid (202.86 ± 16.31 min) and solid (243.74 ± 62.12 min) meals. There is no significant difference between MSITT for both liquid (103.28 ± 18.73 min) and solid (103.22 ± 37.26 min) meals. Our magnetic technique allows repeated in vivo experiments while preserving the physiological conditions. Also this protocol can be applied in drugs and medicinal plant tests without unnecessary animal death.

Tu-158 - Absorption and distribution patterns of magnetic nanoparticles through the gastrointestinal tract using ACB technique

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The alternative current biosusceptometry (ACB) system is a biomagnetic technique quite used for studies regarding the gastrointestinal (GI) tract. The association of an ACB system to magnetic nanostructured particles provides new approaches able to evaluate a whole other class of biological properties. By this new method became possible to analyze the absorption of a magnetic tracer from the stomach and gut through liver and its arrival on kidneys. These magnetic tracers can still be monitored and related to the capability of each organ to absorb, retain and release a specific material, so the main objective of this study is to associate the GI transit of marked solutions and its absorption, with the arrival of these particles in the liver and kidneys to insure the relation between the particle ingestion, its absorption, arrival and clearance at those organs. This technique principle is based on a magnetic flux transformer where this variation is related to the magnetic tracer concentration in the analyzed region. A marked solution was injected...
by gavage in a group of 6 male Wistar rats. After monitoring the variation of the tracer concentration in 5 pre-determined regions of each animal, related to stomach, cecum, liver, right and left kidneys, was plotted a magnetic tracer concentration through time for each region (figure 1). Then, by monitoring the magnetic tracer arrival and clearance of each organ, was possible to observe the relation between gastrointestinal transit, absorption and distribution patterns, and also the organs function. From the obtained data, it can be anticipated that will be possible to constitute a normality parameter for each function and its relations, analyze the normal behavior of each organ and process, and also the influence of drugs on the relation between two or more physiological process.

Tu-159 - Non-destructive quantitative imaging of magnetic nanoparticle distributions in arteries by multipole expansion

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The accurate determination of magnetic nanoparticle (MNP) distributions in biological tissue is an important question for understanding the basic physical and physiological mechanisms of MNP based novel medical applications like drug targeting and hyperthermia. Magnetic measurement techniques such as magnetorelaxometry, susceptometry or remanence measurements so far allow the direct quantification and localization of point-like MNP accumulations in tissue or the quantitative reconstruction of MNP distributions from measurements of a dissected organ. In contrast, for the non-destructive reconstruction of spatially extended nanoparticle distributions from a measured magnetic field pattern, an ill posed inverse problem has to be solved to obtain the underlying distribution. Here, we present an approach to model the linearly extended MNP distribution in an artery, based on a magnetic multipole expansion. The multipole moments of a spherical harmonic multipole expansion are evaluated for an MNP distribution along an artery magnetized either longitudinal or perpendicular to the artery. It is shown that for both magnetization directions each multipole order of the magnetic field can be characterized by only one principal multipole moment, since all other moments of a multipole order can be related to the corresponding principal multipole moment and carry the same information about the linear MNP distribution. It follows that each order is characterized by a typical magnetic field pattern.

In a first approach, we investigated the relationship between multipole moments and distribution parameters for a homogeneous MNP distribution. Furthermore, we considered the experimentally more realistic model of an inhomogeneous distribution resulting from drug targeting by a magnet tip near the artery. For both models the principal moments were used to determine characteristic features like the amount, the spatial extent, and the density profile of the linearly extended MNP distribution.

Tu-68 - Combined EEG and MEG Source Analysis of Epileptic Activity

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Epilepsy
Our contribution will focus on improved source analysis using combined EEG/MEG data of pre-surgical epilepsy patients. We measured EEG (74 channel and 6 channel EOG) and MEG (304 channel whole head) simultaneously to benefit from their complementary information. Furthermore, to allow for a combined EEG/MEG source analysis, we need to take into account the different sensitivity profiles of both modalities. We therefore propose to use a calibrated realistic finite element head model consisting of 6 tissue compartments (skin, skull compacta, skull spongiosa, CSF, anisotropic grey and white matter) for each patient. Geometry and brain conductivity anisotropy are extracted from individually measured T1-, T2- and diffusion-tensor- (DT-) weighted magnetic resonance images, while calibration (conductivity fitting) is performed by means of additionally measured somatosensory evoked potential (SEP) and field (SEF) data. We present here the first results of a case study, where more than 100 epileptic spikes were detected from a patient with left sided temporal lobe epilepsy and the averaged spike waveform was reconstructed using different inverse approaches. We will compare reconstruction results for EEG and MEG alone versus their combination and when using calibrated anisotropic six compartment versus the standard three-compartment isotropic volume conductor modelling.

Tu-69 - Towards source volume estimation of interictal spikes in focal epilepsy using magnetoencephalography

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Intercital spikes are a hallmark of cortical epileptogenicity, their spatial distribution in the cortex defines the so-called ‘irritative’ zone or spiking volume (SV). Delineating the SV precisely is a challenge during the presurgical evaluation of patients with epilepsy. Magnetoencephalography (MEG) recordings enable determination of the brain sources of epileptic spikes using source localization procedures. Most previous clinical MEG studies have relied on dipole modeling of epileptic spikes, which does not permit a volumetric estimation of the spiking cortex.

In the present study, we propose a new source modeling procedure, Volumetric Imaging of Epileptic Spikes (VIES). In VIES, the SV is identified as the 3D region where sources of the high frequency activities (≥20 Hz) associated with epileptic spikes are distributed. We localized these sources using a beamforming approach (DICS, Dynamic Imaging of Coherent Neural Sources). To determine the optimal parameters and accuracy of the method, we compared the SV obtained by VIES with the SV defined by the invasive gold standard, intracranial stereotactic EEG recordings (SEEG), in 21 patients with focal epilepsy. Using rigorous validation criteria based on the exact anatomical location of SEEG contacts, we found that the overall sensitivity of VIES for detecting spiking SEEG contacts was 76 % and its specificity for correctly identifying non-spiking SEEG contacts was 67 %, indicating a good agreement between VIES and SEEG. Moreover, we found that classical dipole clustering was not informative in 9/21 patients, while VIES enable to delineate the SV in all patients. For the 12 patients having a SV delineated both with VIES and dipole clustering, VIES method had higher sensitivity and lower specificity. This proof-of-concept study shows that VIES is a promising approach to non-invasive estimation of the SV in focal epilepsy.

Tu-70 - Motor cortex oscillations, motor pathways and motor control in rolandic epilepsy

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Aims
There is increasing evidence that rolandic epilepsy, characterised by focal motor seizures arising from rolandic cortex and interictal spiking activity over centro-temporal cortical regions, is associated with motor coordination disorders. This was investigated using psychobehavioral measures, diffusion weighted imaging (DWI) and neuromagnetic induced motor responses.

Methods
Children aged between 8 and 14 years with a diagnosis of rolandic epilepsy were assessed using the Movement-ABC (MABC-2, Henderson et al., 2007), DWI, and cued unilateral index finger movements in MEG.
For each individual, cortical locations of MEG motor responses were identified using a beamforming approach. Mean magnitude and peak frequency were extracted from time-frequency windows of interest. Mean DWI fractional anisotropy (FA) was computed for motor tracts in the dominant hemisphere between the following ROIs: supplementary motor area (SMA), M1, thalamus, cerebellum, basal ganglia.

Results
MABC-2 scores were variable but significantly below the population mean and several children scored below the 5th percentile. Greater magnitude of post-movement beta rebound activity (PMBR) and ipsilateral movement-related beta desynchrony (MRBDi) during movements of the dominant index finger predicted better scores on the MABC-2 aiming and catching sub-test. Greater PMBR and MRBDi were predicted by higher FA of thalamus to SMA tracts.

Conclusion
Smaller MRBDi and PMBR in patients with poorer motor co-ordination may reflect abnormal motor network activity. The magnitude of these induced beta band responses, believed to reflect inhibitory control (Engel & Fries, 2010, Curr. Op. Neurobio.), may be partially determined by structural characteristics of specific motor pathways, reflected in their FA. Induced cortical oscillatory responses and DWI of motor pathways may provide markers of impaired motor skills during development.

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Tu-71 - Linking resting-state MEG and fMRI brain networks in epilepsy

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Resting-state MEG and fMRI studies have independently shown that epilepsy is associated with disturbed network topology, but the overlap between them remains unknown. In healthy subjects, the default mode network of fMRI and the envelope of particularly beta band MEG signals seems similar. We investigated the association between fMRI and MEG network parameters and determined optimal features from both methods to describe epilepsy parameters. Epilepsy patients (N=49) underwent 6 minutes of resting-state MEG and BOLD fMRI. Preprocessing of MEG involved removing channels with artifacts and filtering in the beta band (13-30 Hz), while fMRI data underwent standard resting-state preprocessing. A 138 ROI parcellation was used. MEG data were analyzed in two ways, by (1) using the raw beta-filtered time-series, and (2) applying a Hilbert transform on the data and downsampling to 6Hz. The phase lag index (PLI), which takes only non-zero phase lagged correlations into account, was calculated on all three time-series. From these connectivity matrices, local clustering, path length, modularity, number of modules and eigenvector centrality were calculated. Whole-brain connectivity did not correlate between fMRI and the two MEG methods, nor did the network parameters. However, connectivity and eigenvector centrality in individual ROIs did correlate (figure 1). In terms of relation with duration of epilepsy, only beta-filtered MEG data yielded significant results, increased path length and clustering were related to longer history of seizures. Thus, regional network measures within an ROI (e.g. connectivity/centrality) yield similar results between resting-state fMRI and MEG data, although more global network topology cannot be compared easily between modalities, also when using the envelope of the MEG signal. Furthermore, duration of epilepsy is best predicted by 'regular' MEG analysis of path length and clustering, indicating that this method may be optimal for use clinically.
Tu-72 - Presurgical workup in refractory epilepsy: The search for interictal MEG correlates of the seizure onset zone

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The aim of presurgical workup for patients with drug-resistant epilepsy is to localize the seizure-onset-zone (SOZ) and aid in planning of surgery to eliminate seizures, while sparing regions of critical function. Video-EEG, PET/CT and MRI may localize the SOZ noninvasively. However, intracranial EEG remains the gold standard for identifying the SOZ. The role of stereo-EEG (SEEG) depth electrodes for delineation of the SOZ is well established. Research continues to identify and validate interictal MEG correlates of SEEG recordings that could delineate the SOZ noninvasively.

A patient undergoing presurgical workup for treatment of drug-resistant epilepsy was enrolled in a research study to develop the use of MEG for language laterality mapping. Surface EEG was not conclusive for seizure localization. Ultimately the SOZ was delineated using SEEG (Figure 1), in correlation with MRI and PET/CT findings. The SOZ was selectively resected and histologically classified as a Type IIB focal cortical dysplasia (FCD). Six months following surgery the patient is completely seizure free and off all antiseizure medication (Engel class 1).

Herein, we compare ictal and interictal epileptiform activity obtained from SEEG to interictal activity obtained from MEG ‘virtual electrodes’. Virtual electrode positions that co-localized with the surgical resection zone were determined by interictal best-fit equivalent current dipole locations (Figure 1) and regions identified by the Elekta-Neuromag Beamformer Spikiness algorithm. MEG correlates to interictal activity characteristic of FCD as measured by SEEG (i.e., 0.5 to 10 Hz) were investigated, and high-frequency (≥ 25 Hz) interictal activity within the surgical resection zone was also characterized.

Figure 1. Average PLI per ROI of (A) beta MEG signals, (B) the envelope of the beta MEG signals, (C) fMRI signals. Warm colors indicate high PLI, cool colors indicate low PLI.
Tu-73 - Comparison of beamformer kurtosis measures on epilepsy surgery candidates measured on two different MEG platforms.

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Objectives: To compare kurtosis beamformer localisations of inter-ictal epileptiform activity measured on two different MEG hardware/software platforms in candidates for pre-surgical assessment.

Methods. Five patients of paediatric age (11-16) referred for presurgical evaluation of epileptogenic cortex, were measured on two different MEG systems in the same recording session.

MEG data acquisition: Achieved using a 275-channel whole-head CTF system and a 306 channel Elekta TRIUX system, both located in magnetically shielded rooms. All patients underwent over 1 hour of recording at a sampling rate of 2kHz. A Polhemus Isotrak 3D digitizer (Kaiser Aerospace Inc.) mapped the surface shape of each patient’s head and the positioning of the electromagnetic coils with respect to that surface. The surface was then co-registered with the individual patient’s anatomical MRI acquired on 3T Siemens Magnetom Trio using a surface matching algorithm.

MEG Data analysis: Inter-ictal transient epileptiform MEG activity was defined in terms of excess kurtosis by SAM (g2) and the Elekta kurtosis beamformer with band-pass filter settings of 10-70 Hz and 6-45Hz. Intra-trial localisations were compared, but in order to compensate for trial/re-trial variations, Elekta files of spontaneous data were converted to CTF format to enable the two kurtosis measures to be applied to the same data set. Finally, the order of the standardised moment used for spike detection in the Elekta software was varied, to compare detection and localisation variance with pre-established SAM(g2) criteria of excess kurtosis.

Results. Detection rates and localisations were highly similar between systems when a bandpass of 10-70Hz and spike order 4-6 were employed. Confidence gained in over 150 pre-surgical assessments using a CTF system and SAM(g2) beamformer was transferrable to an Elekta TRIUX, kurtosis beamformer protocol.

Tu-74 - Paradoxical lateralization of spikes with HR-EEG and MEG

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INTRODUCTION

Medial posterior cortex epilepsies (PCE) may be characterized by interictal spikes whose surface projection is contralateral to the side of the epileptogenic lesion. This so-called paradoxical lateralization has been for the first time described by Tukel & Jasper
(1952) in patients with epileptogenic foci on the mesial surface of one hemisphere. Paradoxical MEG lateralization has been more recently described, in cases of para-sagittal generators. We present here such a case studied with HR-EEG, MEG and SEEG.

**PATIENT AND METHODS**

This patient had a drug-resistant medial PCE. Seizures were characterized by an initial ictal amaurosis. MRI showed a focal cortical dysplasia in the superior edge of the right calcarine fissure. HR-EEG, MEG and SEEG (stereoelectroencephalography) were recorded. Interictal spikes were selected. Realistic head model, beamformer and MUSIC algorithms were used. Source localizations were compared to SEEG recordings.

**RESULTS**

A focal irritative zone involving both medial posterior cortices, was characterized by very different amplitude maps in HR-EEG and MEG. HR-EEG as well as MEG interictal spike amplitude maps displayed a paradoxical lateralization. However, MEG amplitude map was quadripolar, suggesting two almost synchronous generators localized in homotopic areas. SEEG demonstrated that the irritative zone was strictly medial and characterized by a co-activation of both medial occipito-parietal junctions with a time precession of the right source. Despite this paradoxical lateralization, SEEG validated accuracy of source localizations provided by HR-EEG and MEG.

**CONCLUSION**

This paradoxical HR-EEG and MEG lateralization is likely due to the spatial orientation, especially obliquity of the cortical generator (here, the calcarine fissure). MEG was more precise and more complex than HR-EEG amplitude map, suggesting through its quadripolar shape two intracerebral generators (with time lag between them) further validated by SEEG.

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**Tu-75 - Beta-band oscillatory activity in magnetoencephalography correlates with focal cortical dysplasia type IIb in patients with symptomatic epilepsy**

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**Introduction:** Focal cortical dysplasias type IIb (FCD) are epileptogenic lesions, for which anatomical complete resection is associated with a good postsurgical outcome. Invasive recordings of FCD have shown intrinsic repetitive or continuous spikes, spike waves and burst-like spike series in the frequency band of 10-30 Hz within the lesion. This project aims to correlate beta-band oscillatory and interictal epileptic activity in MEG/EEG recordings with the lesion.

**Methods:** Six patients with symptomatic drug resistant epilepsy caused by neocortical FCD underwent resting eyes closed recordings using a 306 channel Elekta MEG system. In four of six patients MEG was combined with a 60 channel surface EEG cap. One patient underwent MEG and combined intracerebral EEG/MEG recordings and one patient had MEG and subsequent intracerebral EEG recordings. MEG/EEG data were visually evaluated for epileptic spikes and spikes were localized using BESA software suite. Frequency analysis in the beta-band of artefact free intervals with deselected spike epochs of at least 2 minutes duration was performed using fieldtrip.

**Results:** Beta-band activity and epileptic spikes were recorded in all patients in MEG and EEG. Averaged spikes from MEG and EEG could be localized in the border zone of the FCD. In three of six patients beta-band-activity correlated with the epileptogenic lesion regionally. In the other three patients there was pronounced beta-band-activity correlated to the lesion ipsilateral, but also contralateral activity. In one patient MEG beta-band activity could be shown to be coherent with intraleisional beta-activity. Frequency analysis of the surface EEG supported the findings of the MEG recordings.

**Significance:** Beta-band frequency analysis might be able to supplement clinical MEG/EEG analysis in patients with FCD. It may give additional electrophysiological localization information, especially in patients with rare epileptic spikes.

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**Tu-76 - Localizing extratemporal lesion-related epileptogenic zone using magnetoencephalography in patients with dual pathology**

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**Objective:** Dual pathology (DP) is defined as a pathological state where extrahippocampal lesions coexisting with hippocampal sclerosis. Numerous studies have revealed a better seizure outcome by removing both abnormalities than lesionectomy or mesial temporal resection alone. However, it is necessary to demarcate the precise extratemporal lesion-related epileptogenic zone (ETL-EZ) for optimal seizure outcome. This study demonstrated that magnetoencephalography (MEG) could demarcate the ETL-EZ for presurgical evaluation in patients with DP.

**Methods:**

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We retrospectively analyzed MEG data in 6 patients who underwent resective surgery based on intracranial video-EEG (IVEEG). MEG was performed with 204 channels of planar gradiometers (306-channel whole-head type, Elekta-Neuromag System). We classified distributions of an equivalent current dipole (ECD) into clusters and scatters (Iida K et al., 2005), and compared the ECD-based distribution of epileptic areas, IVEEG results, and seizure outcome.

Results:
Single-cluster ECDs were located over the posterior peri-sylvian region in 2 patients and the anterior temporal region in 1 patient. Two independent clusters were observed in the mid-temporal and inferior parietal regions in 1 patient. The other 2 had no epileptic spikes on MEG recording. Except for an ECD cluster over the anterior temporal region, the other ECD clusters and IVEEG showed colocalized inter-ictal spikes demarcating the ETL-EZ in 3 patients (2 single-clusters and both of 2 clusters). All patients underwent anterior temporal lobectomy (including hippocampectomy) and lesionectomy (total: 5, partial: 1) with (5) or without (1) additional cortical resection of ETL-EZ on IVEEG. Five patients had excellent seizure outcome (Engel class I), and the patient with partial lesionectomy indicated more than 90% seizure reduction (Engel class II).

Conclusion:
MEG identifies the extent of ETL-EZ in patients with DP, and facilitates planning of IVEEG implantation.

Tu-77 - EEG spectral topography and functional connectivity in temporal lobe epilepsy: a comprehensive survey

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Resting state brain dynamics captured particular interest in recent years showing great promise for a better understanding of the human brain in health and disease. In EEG and MEG, resting state spectral rhythms originating from distinct brain regions have been shown to be associated with specific brain functions. Disruptions in spectral topographies in the diseased brain have been observed in a host of diseases. Here we systematically characterize the spectral topographies as well as functional connectivity of 7 patients with left temporal lobe epilepsy (LTLE) in comparison with 10 healthy controls. All subjects were scanned in a quiet room using a 64-channel EEG system at rest with eyes closed (EC) and eyes open (EO) for a total of 3 minutes per condition. We show that LTLE results in elevated power in the delta and theta bands for both EC and EO, and reduced power in the alpha band in EC. While the overall power in the 2-20 Hz range is elevated in LTLE patients, the elevation in the lower band results largely from an overall shift of the alpha spectrum toward lower frequencies, with the alpha peak shifting by more than 1 Hz relative to controls. Furthermore, while both groups show increased synchronization with EC, consistent with the suggested role of alpha in mediating connectivity, LTLE patients show increased synchronization in both EC and EO relative to controls. Topographically, the high synchronization is largely concentrated over the frontal and parietal regions. We conclude that although TLE has been traditionally viewed as a focal impairment, changes in spectral rhythms as well as functional connectivity are observed across a wide spatial range, lending support to the hypothesis that epilepsy is a network disorder. This analysis will be further extended to patients with right TLE and bilateral TLE for a better understanding of the altered resting state dynamics accompanying TLE.
Noninvasive magnetoencephalography (MEG) has been regarded as a useful tool for the localization of epileptogenic zone. According to a recent study, patients with a single spike cluster had better postoperative outcomes compared with patients with multiple spike clusters (Stefan et al., 2011), which suggested that unifocal epileptic activity detected by MEG may be a predictor of favorable postoperative outcome compared with multifocal activities. However, in case of multifocal clusters, the issue of how to determine epileptogenic zone among multiple foci of MEG spike clusters has not been resolved. In the present study, we propose a possible way to address this issue in terms of brain connectivity, which has recently received explosive attention. There are three types of connectivity, i.e., structural, functional, and effective connectivity. Among them, an effective connectivity is a concept defined as the direct or indirect influence that one neural system exerts over another. Thus, it describes the causal relation between components of a network. Here, we used a PSI (phase-slope index) measure to estimate the direction of information flow in multivariate time series (Nolte et al., 2008). Four focal cortical dysplasia Type I patients, who had multifocal clusters, were studied. All of them classified as Engel class III corresponding to worthwhile improvement. After applying the PSI and permutation test for statistical analysis, we were able to differentiate the potential informational source location between multiple foci of spike clusters. All of locations were included or near the surgically resected area (<3cm) with good reproducibility across different epochs. We presume that there is a good possibility that informational source would be associated with epileptogenic zone. Our results imply that effective connectivity measure could provide additional information for epileptic brain networks in the situation where multiple foci of MEG spike clusters were found.

Tu-80 - Effective connectivity as a tool for the determination of epileptic networks in multifocal MEG clusters

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Noninvasive magnetoencephalography (MEG) has been regarded as a useful tool for the localization of epileptogenic zone. According to a recent study, patients with a single spike cluster had better postoperative outcomes compared with patients with multiple spike clusters (Stefan et al., 2011), which suggested that unifocal epileptic activity detected by MEG may be a predictor of favorable postoperative outcome compared with multifocal activities. However, in case of multifocal clusters, the issue of how to determine epileptogenic zone among multiple foci of MEG spike clusters has not been resolved. In the present study, we propose a possible way to address this issue in terms of brain connectivity, which has recently received explosive attention. There are three types of connectivity, i.e., structural, functional, and effective connectivity. Among them, an effective connectivity is a concept defined as the direct or indirect influence that one neural system exerts over another. Thus, it describes the causal relation between components of a network. Here, we used a PSI (phase-slope index) measure to estimate the direction of information flow in multivariate time series (Nolte et al., 2008). Four focal cortical dysplasia Type I patients, who had multifocal clusters, were studied. All of them classified as Engel class III corresponding to worthwhile improvement. After applying the PSI and permutation test for statistical analysis, we were able to differentiate the potential informational source location between multiple foci of spike clusters. All of locations were included or near the surgically resected area (<3cm) with good reproducibility across different epochs. We presume that there is a good possibility that informational source would be associated with epileptogenic zone. Our results imply that effective connectivity measure could provide additional information for epileptic brain networks in the situation where multiple foci of MEG spike clusters were found.

Tu-81 - Surgical outcome for MRI-negative epilepsy: predictive value of MEG modeling of Spiking Volume

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Surgical treatment for patients with MRI-negative epilepsy is considered as challenging in many epilepsy centers. Moreover, intracranial EEG is usually mandatory in that situation to localize precisely the seizure-onset zone. It is not known whether MEG predicts the success of the intracranial EEG recordings and of the surgical outcome. We recently described a new analysis pipeline in MEG, VIES (Volumetric Imaging of Epileptic Spikes) aimed at delineating the Spiking Volume (SV) in partial epilepsy. Here, we test the hypothesis that the extent of the SV determined by VIES is predictive of the surgical outcome for MRI-negative epileptic patients.

21 patients suffering from pharmacoresistant epilepsy, and candidates to surgical treatment were included in the study. All patients underwent both MEG modeling of the SV using VIES and intracranial EEG with stereotactically implanted intracranial electrodes (SEEG). Depending on its spatial extent, the SV is considered as focal, lateralized or non-lateralized. We measured the proportion of patients having localized epileptogenic zone during SEEG and the proportion of patients becoming seizure-free post-operatively for each SV extent. We found that 17/21 patients had spikes during MEG recording. For each of the 17 patients with MEG spikes, a spatial overlap was found between the MEG SV and intracranial seizure-onset zone. For the 8 patients with focal SV, 8/8 had localized epileptogenic zone during SEEG. 7 were operated and 6 are seizure-free. For the 7 patients with lateralized MEG SV, 3/7 had localized epileptogenic zone during SEEG and 2/3 were operated and are not seizure-free post-operatively. For 2 patients with non-lateralized MEG SV, none had localized epileptogenic zone during SEEG, 1 was operated and is not seizure-free post-operatively. Those results show that VIES is a promising tool to predict the probability of success of SEEG and surgical treatment for patients with MRI-negative epilepsy.
Tu-82 - Lobar localization information in epilepsy patients: comparison between long-term video-EEG monitoring and MEG

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Purpose: Magnetoencephalography (MEG) and magnetic source imaging (MSI) are techniques that have been increasingly used for preoperative localization of epileptic foci. To help elucidate the value of MEG, we assessed the results of whole-head MEG versus video-EEG (vEEG) in the case management of patients undergoing epilepsy surgery.

Method: We studied 19 patients with suspected focal epilepsy who underwent interictal and ictal vEEG and, subsequently, interictal and ictal MEG. Out of 19 patients studied 14 were with suspected neocortical epilepsy, 5 with mesial temporal lobe epilepsy. Nine patients underwent surgical resection of suspected epileptogenic zone and seven of them invasive electrocorticography (ECoG). The results of MSI were classified to define epileptogenic foci according to the clustering of interictal and ictal spikes recorded during a 4-hour recording session. The data were analyzed to determine to what extent the results of MSI correlated with vEEG determined irritative zones.

Results: In 4 of 19 cases MSI - determined localization regionally correlated to vEEG data (that is, showed the same lobe). In thirteen patients MSI showed 20 additional epileptogenic foci that ictal vEEG was unable to identified. These undetected sources were localized mainly in the frontal lobes (70%), and at the lobar surface level - at the medial and the basal aspects of cerebral lobes (70%). In six cases, MSI was used to guide invasive electrodes to locations that otherwise would not have been targeted and provided unique localization data, not evident from other imaging modalities, that strongly influenced the surgical management of the patient. In seven patients, for whom data from invasive ECoG were available, the MSI was highly correlated with the zone of seizure origin identified by EcoG.

Conclusion: Magnetic source imaging can provide critical localization information that is not available when other noninvasive methods, such as vEEG and MRI, are used.

Tu-83 - Sedation effects on language mapping in a clinical population

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There are now several robust language mapping paradigms in use in MEG centers. To date, however, these protocols have been used for patients and participants who are able to cooperate with the task demands. In a pediatric clinical setting, however, some patients require sedation to complete their scans. This provides an opportunity to examine the effects of sedation on language processing to determine if we can lateralize language function even when patients are sedated.

Participants: There were 128 patients seen in the MEG Center at Le Bonheur Children’s Medical Center who underwent language mapping between January 2009 and May 2011. A total 41 Sedated patients were included (mean age = 7 years, 6 months) and 70 Awake patients (mean age = 16 years, 0 months).

Methods: MEG data was digitized at 678 Hz for 1000 ms post stimulus, with a 100 ms pre-stimulus baseline, using a 248-channel whole head system (Magnes 3600, 4D Neuroimaging). Data was digitally filtered off-line with a bandpass of .1 to 20 Hz. All patients listened to a series of 180 words, following a procedure adapted from the one developed by Papanicolaou and his colleagues. Propofol was used for all sedated patients.

Results: There was a significant difference in age between the Sedated and Awake patients (t=6.89, p<.001). In addition, there was a significant difference in the magnitude of the MEG signal, both in the early (0 4 250 ms) and in the later (300 4 800 ms) windows. The success rate for determining language lateralization was 93% for Awake patients and 83% for Sedated. There was no significant difference between the groups for success rate or pattern of lateralization.

Discussion: The results show that, although the signal is significantly attenuated by propofol, some language processing remains and language function can be mapped in sedated children. This suggests a high degree of automatic processing in a simple language listening task.
Tu-84 - Spatial MEG Laterality Maps for Language

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Functional neuroimaging has been used with increasing prevalence in recent years as a non-invasive method of language laterality assessment. Historically, laterality of language and memory has been assessed using the intracarotid sodium amobarbital test (i.e., the Wada test). This is an invasive investigation and provides spatially limited measures of laterality. Despite advances in neuroimaging, recent laterality assessments suffer similar limitations, such as a one-dimensional laterality index (LI). This oversimplification has neglected the potential value of functional neuroimaging.

We demonstrated a language laterality assessment that uses magnetoencephalography (MEG) to produce 'complex laterality vectors'. These values were used to create 'laterality maps' that indicate both the strength of activity and degree of laterality for a function. To demonstrate, language was assessed in healthy controls and in patients with epilepsy. It was shown that laterality maps provide information about the spatial characteristics of language activation, and that this information would be unavailable using the traditional LI. Importantly, it was possible to differentiate between weak LI scores that resulted from weak vs. strong bilateral activation, as well as strong LI scores that resulted from weak vs. strong unilateral activation. The ability to clarify these ambiguous situations, and to display complex patterns of activation, make laterality maps an ideal representation of language dominance.

Tu-85 - Ictal gradient magnetic-field topography for intractable epilepsy

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Purpose: Conventional equivalent current dipole analysis in magnetoencephalography (MEG) can show the ictal onset of intractable epilepsy, but cannot show elapsing changes in neuronal activity or the gradient of seizure. The purpose of this study was to identify the gradient of seizure as well as ictal onset by ictal MEG using gradient magnetic-field topography (GMFT).

Methods: Before resective surgery, 4 patients (1 female, 3 males) with intractable epilepsy (mean age, 18 years, range, 6-28 years) underwent ictal-MEG and were analyzed using the GMFT method.

Results: GMFT of ictal MEG showed onset from the left frontal pole before propagation to the other side in Case 1, from the left temporal lobe before propagation to the ipsilateral occipital and frontal lobes in Case 2, from the right temporal lobe before propagation to the ipsilateral frontal and occipital lobes in Case 3 and from the left frontal lobe before propagation to the ipsilateral temporal lobe in Case 4. In all 4 patients, seizures were eliminated after focus resection and ictal onsets of GMFT were concordant with...
Tu-86 - Functional analysis of epileptic spike at focal cortical dysplasia with spatial filtering analysis

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Introduction
Focal Cortical Dysplasia (FCD) is a major cause of intractable epilepsy of infants and children which usually results in catastrophic prognosis and severe developmental delay. Our aim is to detect FCD directly by analyzing the shape of MEG spikes, using spatial filtering analysis: dynamic statistical parametric mapping (dSPM) which enables to show epileptiform activity with spatiotemporal source distribution with millisecond temporal resolution (Dale,2000).

Objects and Methods
We studied 11 patients (mean±SD, 17.6 ± 10.5 years old) with symptomatic localization-related epilepsy using a 204-channel, whole-head gradiometer system (Vectorview, Elektra Neuromag Inc., Stockholm, Sweden). We divided FCD group and Non-FCD group according to the pathologic diagnosis and existence of FCD in Magnetic resonance imaging (MRI). We selected 10 epileptic spikes from each patient and analyzed by dSPM. We projected the results to normal standard brain model to minimize the differences in shapes between the patients’ brain. Thus, we investigated characteristic features of epileptic spikes by analyzing strength and temporal activity of epileptiform.

Results
The form of epileptic spike in FCD group is single and sharp in peak, emerging and vanishing within a same location of the brain without expanding its area. In contrast, that of Non-FCD group is multiple and diverse, expanding the area to the circumference and vanishing toward different lobe. A case categorized as Non-FCD group with no lesion in MRI initially revealed to have the same epileptiform activity as FCD group which indicates the existence of FCD. This patient underwent cortical resection and became seizure free.

Discussion
Functional analysis of MEG with dSPM can disclose the characteristic features of epileptic spikes with high spatial and temporal resolution. This method will help diagnose the existence of FCD as well as the case with invisible lesion in MRI and detect surgically treatable epilepsy.
Tu-87 - A MEG connectivity study on frontal epilepsies and idiopathic generalized epilepsies

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Thirty epileptic patients were studied using magnetoencephalography (MEG): fifteen patients with Frontal Epilepsies (FE) and fifteen patients with Idiopathic Generalized Epilepsies (IGE). For the characterization of epileptic syndromes the seizure classification and other criteria, e.g. case history, age of first manifestation, neurological findings, EEG and MRI were used.

MEG recordings were completed with the 306-channel Elekta Neuromag® system (102 magnetometers and 204 planar gradiometers in a helmet-shaped array covering the entire scalp). Eye movements were monitored and artefacts were controlled with four head position indicator coils (HPI) placed on the scalp that measure head movement during the session. MEG data was acquired at a sampling rate of 1 kHz, with on-line band-pass filter of 0.10-330 Hz. Acquisition occurred in a single 20 min session of resting state: 10 min with eyes open followed by 10 min with eyes closed. To correct the head position and the associated movement-related artifacts, a spatio-temporal signal space separation method (tSSS) with movement compensation was realized using the MaxFilter® software.

Spike-wave series were seen in all patients. For every patient, a connectivity analysis was performed. Functional connectivity was studied through phase synchronization indexes: Phase Locking Value (PLV) and Phase Lag Index (PLI). Effective connectivity was studied through the classical Granger causality (GC) approach, and though the information theory approach, transfer entropy (TE). Statistical significant results were found in both groups, during the intervals preceding seizures (pre-ictal periods) and during the intervals far away from any seizure activity (inter-ictal periods).

Tu-88 - Lateralized interictal MEG dipoles of generalized spike and waves in children with intractable epilepsy

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Objective: Scalp EEGs often show paroxysmal generalized spike-and-waves (GSWs) during non-REM sleep in children with intractable partial epilepsy. MEG can localize the spike dipole at the earliest spike peak of the GSWs. We assessed the lateralization of interictal MEG dipoles of the GSWs in children with intractable epilepsy.

Methods: We retrospectively identified 28 patients who had interictal GSWs during non-REM sleep on prolonged scalp video-EEG recording among 103 patients who underwent intracranial video EEG (IVEEG) and MEG. Lateralization of MEG was determined when the number of MEG dipoles in one hemisphere occurred more than twice compared to the contralateral hemisphere.

Results: During non-REM sleep, 21 out of 28 patients had continuous/frequent GSWs, 6 intermittent and one rare. During wakefulness, 8 patients had continuous/frequent GSWs, 7 intermittent and 4 rare. The other 8 patients showed focal discharges, and one had no interictal discharge. 26 patients showed lateralized MEG dipoles. Cortical resections were performed over one lobe in one patient, 2 lobes in 10, 3 lobes in 11 patients, and 4 lobes in 3 based on the IVEEG results. The remaining 3 patients did not undergo resective surgery due to overlapping ictal onset and functional zones on IVEEG.

Conclusion: MEG can help lateralize GSWs in children with intractable epilepsy. Even when patients show the continuous/frequent GSWs during non-REM sleep, they can be considered for epilepsy surgery if MEG shows lateralized MEG dipoles. The resection areas, however, tend to be multi-lobar, thus the relation between the epileptogenic and functional zone needs to be critically analyzed.

Tu-89 - Functional connectivity analysis of generalized epileptic discharges using MEG

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Aim: To describe the spatial and temporal profiles of connectivity networks preceding generalized spike-and-wave discharges (gSWDs) in childhood absence epilepsy (CAE)

Methods: MEG recordings were performed for 30 patients (6-15 years of age) with absence seizures, ranging from patients with typical CAE, who can be treated quite successfully with anti-epileptics, to more complex atypical forms and children who had absences and complex partial clinical features. Nonlinear associations of MEG seizure activity and local connectivity measures obtained within the framework of graph theory (1) were determined for all patients. Furthermore, the identification of a preictal period enabled us, together with the beamformer analysis to identify the driving source of the SWDs.

Results: Studying in detail the changes in time and space of the cluster values revealed, like in the study of Westmijse et al. (2), a rhythmic pattern of lateral parietal and frontal focal regions during the spikes alternated by a generalized pattern during the waves,
indicating a common network of the activity underlying the gSWDs for all the patients studied. However, the changes in local and global connectivity measures indicated a transition from the normal to the ictal phase in the period preceding the gSWDs (preictal period), thus enabling us together with beamformer analysis to identify the cortical node activity preceding the gSWDs. The results indicate that the location of the driving source activity of the SWDs differs for the distinct patient groups, with either a parietal (3), frontal or frontotemporal location.

Conclusion: The occurrence of early preictal source activity demonstrates that SWDs are not suddenly arising but gradually build up in a dynamic network. Studying the changing connectivity networks underlying the MEG SWDs in time and space appeared to be helpful in identifying the driving cortical node of these discharges for the distinct types of CAE.

**Tu-90 - Consistent MEG results in tuberous sclerosis complex achieve the best seizure outcome by epilepsy surgery**

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**Purpose:**

Tuberous sclerosis complex (TSC) often causes intractable epilepsy. Epilepsy surgery is an option to control seizures in subset of TSC patients with multiple tubers. MEG has been applied for presurgical evaluations before the epilepsy surgery. This study analyzed characteristicst of MEG spike sources (MEGSSs), surgical resection and seizure outcome in patients with TSC.

**Methods:**

We retrospectively analyzed data from 12 patients who underwent MRI, scalp video EEG, MEG, intracranial video EEG and epilepsy surgery. We used single moving dipole analysis to localize MEGSS at the beginning of epileptiform discharges. We compared the surgical outcome with resected ratio of number of MEGSSs and consistency of MEGSS distribution.

**Results:**

We analyzed total 20 MEG studies. We divided two groups, (A) 7 seizure free patients, (B) 5 residual seizure patients. In group A, 2 patients had twice MEG studies. In group B, 4 patients had twice MEG and one patient had three times MEG studies. Group A showed 28-107 MEGSSs (mean, 65) and group B showed 6-108 (54). The distributions of MEGSSs were inconsistent in each MEG studies in all 7 patients (group A, 2, group B, 5) who had repeat MEG. Less than half of MEGSSs were resected in any MEG study was confirmed in 2 patients of group A, comparing 4 patients in group B.

**Conclusion:**

MEG can show inconsistent results of serial MEG studies in patients with intractable epilepsy secondary to multiple TSC. The concordant MEG result with other investigations represents the epileptogenic zone to be resected for seizure control.

**Tu-91 - Magnetoencephalographic measures of abnormal sensory oscillations: A window on photosensitive epilepsy**

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**Aims**

Photosensitivity is a common trait in a number of epilepsy syndromes. Measuring visual responses with magnetoencephalography (MEG) provides a unique opportunity for the non-invasive study of abnormal cortical oscillations in these patients. Of particular interest are gamma oscillations (30-100 Hz), which are thought to reflect GABAergic inhibitory processes. Evidence points to photosensitivity being driven by an abnormal state of cortical 'hyperexcitability' due to abnormalities in neuronal inhibition, and this may be reflected in differences in the gamma-band response in photosensitive patients relative to non-photosensitive controls. The aim of the present study was to use MEG to identify and characterise such differences.

**Methods**

Data were collected from patients with photosensitivity and from two age-matched control groups. Participants’ visual responses were recorded using a 275-channel CTF MEG system while viewing static square-wave gratings. Induced activity was localised to the visual cortex using Synthetic Aperture Magnetometry, and the relationship between visually-induced oscillations and stimulus parameters (contrast and size) were compared between the different participant groups.

**Results**

Contrary to our expectations, we did not find clear evidence for a difference between groups in the main gamma-band response (40-70Hz). Instead our results suggest differences at a lower frequency around 28Hz and in the alpha frequency (8-12Hz) range.

**Conclusions**

Our evidence suggests that there are indeed characteristic differences in visually-induced oscillations between individuals with photosensitive epilepsy and control participants, which may have potential use as a diagnostic marker. In future, the linking of photosen-
sitivity to differences in neuronal oscillations at specific frequencies may also help to identify the neurophysiological abnormalities that lead to seizures in photosensitive epilepsy.

Tu-92 - The value of MEG as a presurgical evaluation tool: Adult nonlesional neocortical epilepsy

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Introduction
There have been few electrophysiological studies including MEG on the diagnostic value in the nonlesional epilepsy population. Here, we compared various modalities including SPECT, PET, video-EEG, and MEG with intracranial EEG (iEEG) to identify the value of individual modalities in surgical decision of the nonlesional adult neocortical epilepsy patients.

Methods
We retrospectively analyzed 23 adult patients (30.7 ± 9.0 years) with no abnormal MRI findings, who underwent surgical resection for intractable epilepsy. Localization of individual presurgical test was determined by visual analysis. For the MEG, interictal spike was visually inspected and localized using the single equivalent current dipole method. Each localization result was then compared with ictal onset zone (IOZ) defined by iEEG to calculate concordance rate. Then, we elucidated the value of preoperative MEG results in predicting surgical outcome.

Results
Postoperative seizure outcome was Engel class I in 5 patients, class II in 3, class III in 10, and class IV in 5 patients. MEG showed best concordance rate with IOZ in either hemisphere or lobe level. The highest to the lowest hemispheric concordance rates are as follows: compared to iEEG IOZ, MEG (83%) ≥ ictal EEG (78%) ≥ interictal EEG=PET (70%) ≥ SPECT (57%). The lobe concordance rates are as follows: ictal EEG=interictal EEG=MEG (65%) ≥ PET (61%) ≥ SPECT (52%). Statistical analysis showed MEG has higher hemispheric concordance with the IOZ than SPECT (p<0.05). The differences of concordance rate regarding to the surgical outcome did not reach significance. We analyzed the effects of MEG clustered area resection on surgical outcome, and patients who had resection of MEG cluster showed a better surgical outcome (p<0.05).

Conclusion
Our results show that MEG has the highest concordance with iEEG IOZ. Furthermore, MEG cluster resection has a prognostic significance in predicting surgical outcome.

Tu-93 - Increased Fluctuations in Phase Synchronization Activity in Seizure Areas On Different Days Measured with 256 Channel Scalp EEG

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Our objective was to examine if short duration, interictal, spike-free 256 channel high density (dEEG) scalp EEG data can be used to noninvasively localize the epileptogenic areas. We studied one patient with refractory epilepsy who underwent intracranial EEG to establish the localization of seizures. Prior to invasive EEG studies, the subject underwent dEEG recordings. Three minutes of spike-free, epileptiform-free interictal dEEG data from first day, second day and from the eleventh day were selected for analysis. The analysis was performed in theta (3-7 Hz), alpha (7-12 Hz), beta (12-30 Hz) and low gamma (30-50 Hz) bands. The phase synchronization index (SI) was computed after taking Hilbert transform of the EEG data. The SI for each electrode was averaged over the nearby six electrodes. A detrended fluctuation analysis was used to find the stochastic behavior of the SI. Contour plots with 10 sec intervals were constructed using a montage of the layout of 256 electrode positions. Contour plots displayed over the scalp show that the stochastic behavior of the SI becomes stronger with time in the proven epileptogenic area while in other areas it becomes fragmented and scattered. It was also found that low gamma band was the best to localize epileptogenic area. A stable pattern of stochastic behavior in or near to the epileptogenic area was observed after 80 seconds. This was observed on all three selected days and it is shown in the figure. On the first day, the stronger behavior of SI is near to the upper left side of the rectangle that marks epileptogenic area as mapped with intracranial grid recordings. On the second day, it matches very well. On the eleventh day, the match is poor with some higher SI activity near to the left and upper edge of the rectangle. These are preliminary results and show some potential in localizing epileptic sites from dEEG. However, further studies with more subjects are needed.
Tu-94 - MEG epileptic gamma and ripple activity in a patient with focal cortical dysplasia

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Background
Fast oscillatory activity has been recognized as substrate of epileptic networks. High frequency oscillations (HFO) above 80Hz show high specificity for epileptic areas. In MEG, HFO analysis has been used for epileptic focus localization (Xiang et al., 2009), as well as gamma activity superimposed on spikes (Guggisberg et al., 2008). Such patterns may be especially valuable in patients without spikes. In this study, we present a case with focal epilepsy due to focal cortical dysplasia (FCD), in which we observed localizing MEG gamma activity independent of spikes, as well as spike-related ripple activity.

Methods
MEG focus localization was performed in a patient with focal epilepsy due to left central FCD. Ten minutes of MEG data were recorded (Magnes 3600WH, 4D Neurormaging, San Diego, USA, sample rate 2kHz, 0.1-800Hz). Data was filtered for visual inspection: 50Hz notch, 1-70Hz for spikes and 30-70Hz for gamma activity. Detected events were inspected for ripple HFO using spectrograms (80-250Hz). sLoreta source localization was performed on filtered data (Curry 7, Compumedics, Singen, Germany).

Results
A total of 15 spikes and 8 gamma bursts were identified, localizing to the FCD. Two of the bursts were superimposed on spikes, the remainder had no spike correlate. The two spike-related gamma bursts were also accompanied by short HFO in the ripple range, localizing into the FCD.

Conclusions
Gamma bursts and HFO may occur independent of spikes and can be utilized for MEG focus localization in workup for epilepsy surgery.

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Tu-95 - Clinical Application of MEG Source Localization Algorithms in Presurgical Epilepsy Evaluation: Comparison to ECoG and Clinical Outcome

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Clinical Application of MEG Source Localization Algorithms in Presurgical Epilepsy Evaluation: Comparison to ECoG and Clinical Outcome

MEG source localization algorithms perform well in simulation studies with low noise, little is known regarding relative strengths and limitations of algorithms for real clinical data. We compared algorithms with a common presurgical evaluation clinical dataset. We recorded MEG interictal discharges for 351 patients (ages 1 mo-26 years) with medically intractable epilepsy. Of this group 340 had epileptiform discharges and we analyzed all these recordings with equivalent current dipole models (ECD) and a beamformer, synthetic aperture magnetoencephalography (SAM). We additionally analyzed recordings in 169 patients with dipole scan (DS), (multiple signal classification -MUSIC) and distributed dipole models (DD) (minimum norm estimate - MNE, standardized low resolution brain electromagnetic tomography - sLORETA). We compared each to presurgical scalp interictal/ictal EEG findings. We compared MEG to ECoG localization for 112 patients. Use of several methodologies limited errors from each, when multiple algorithms indicated a similar region, the localization more often agreed with ictal onset by ECoG. MEG source localization algorithms highlight different aspects of the irritative zone associated with interictal discharges based on different a priori assumptions and different approaches to the inverse problem. Use of several different MEG source localization methodologies may improve localization non-invasively of
the irritative zone prior to placement of intracranial electrodes and prior to epilepsy surgery.

Tu-96 - Detecting increased high frequency oscillations and slow wave activity in the epileptogenic area using MEG

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Treatment with antiepileptic drugs (AED) is successful in the majority of patients with epilepsy, but in some cases AED therapy is inefficient. Surgery can be an alternative for those with focal epilepsy, however precise focus localization is required prior to that. Conventionally, source localization is based on interictal spikes and rarely ictal rhythms. In addition, high frequency oscillations (HFO) and slow wave brain activity exhibit association with epileptogenic tissue.

In this study, we examined 5 patients with intractable focal epilepsy and 3 healthy controls. In all patients, epilepsy etiology was focal cortical dysplasia (FCD). We recorded whole-head MEG with high sampling rate (≥2000 Hz) and analyzed the brain activity in 4 frequency bands: slow wave (2-6 Hz), high gamma (50-100 Hz), ripple (100-250 Hz), and fast ripple (250-500 Hz). For each patient, we determined a region of interest (ROI) around the FCD and a control ROI in the homologous brain area of the other hemisphere.

Activation in all frequency bands was higher for patients than for controls (figure). In the ripple and fast ripple bands we found higher activation in the ROI around the FCD than in the contra-lateral ROI in 4/5 patients. The difference was more distinctive in the fast ripple band. For the slow wave and high gamma bands no difference was found.

The results show that activity in low and high frequency ranges is increased in patients with epilepsy compared with healthy controls. These findings are an important step towards new approaches in localizing epileptic foci for presurgical evaluation. They show that activity in certain frequency bands is higher in the epileptogenic area and that it can be recorded non-invasively by MEG, independent of spikes and seizures.

Tu-97 - Magnetoencephalography as a prognostic tool for epilepsy surgery in patients with hippocampal sclerosis

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Integration of normalized power over different frequency ranges for patients and controls
Objective: Magnetoencephalography (MEG) estimates the distribution of epileptic activity more accurately than electroencephalography (EEG), because the magnetic field is free from volume conduction. MEG is also good for detecting tangentially oriented current to the scalp. In this study, we used MEG to estimate the distribution of epileptic activity in patients with hippocampal sclerosis before standard anterior temporal lobectomy and compare them with the outcome after operation.

Methods: Eleven patients were enrolled for the study. For each patient, we analyzed 3-5 recordings lasting 3-5 minutes each. The sessions were analyzed by independent component analysis (ICA), using second-order blind identification. The distribution of the strongest component was estimated by minimum norm estimation (MNE), and overlaid on the individual brain MRI for each subject.

The surface of each hemisphere was separated into nine regions: medial temporal, medial occipital, medial parietal, mediadorsal frontal, medioventro frontal, lateroventro frontal, laterodorsal frontal, lateral parioto-occipital, and lateral temporal. Interhemispheric differences in current intensity in the nine regions were analyzed using paired t-tests.

Results: Six patients (male, 3, right resection, 2, age, 23 ± 8.6 years, disease duration, 15.7 ± 5.0 years) became seizure-free after the operation (Engel class 1a). Five patients (male, 2, right resection 2, age, 38.8 ± 12.8 years, disease duration, 31.0 ± 15.0 years) were free of disabling seizures (Engel class 1b). Patients with outcome 1a were younger and had shorter disease duration, and epileptic activity on the resected side was increased in five regions: medial temporal, medial occipital, medioventro frontal, and lateral temporal. Patients with outcome 1b showed no such laterality.

Conclusion: Our results suggest that MEG is useful as a prognostic tool for standard anterior temporal lobectomy in patients with hippocampal sclerosis.

Tu-98 - Magnetoencephalography is Useful for Postsurgical Evaluation in Patients with Catastrophic Epilepsy

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Objective: Early presurgical evaluation and radical surgical procedure are indispensable for patients with catastrophic epilepsy (CE). For better postsurgical outcome, postsurgical evaluation is also important, especially for patients who need additional multiple surgical treatments. We used magnetoencephalography (MEG) for postsurgical evaluation in patients with CE.

Method: The subjects were 3 children (M=1, F=2) with hemimegalecephaly (case1), congenital middle cerebral artery (MCA) thrombosis (case2) and multi-lobar focal cortical dysplasia (FCD) (case3) who underwent radical surgery in early childhood. All subjective patients have been seizure free after the last surgery. MEG scanning was obtained before and after operation in order to evaluate the effect of surgical procedure.

Results: Case1 and case 2 underwent functional hemispherectomy. Presurgical MEG showed diffuse spikes and slow waves in affected hemisphere in case1 and both hemisphere in case 2 respectively.Postsurgical MEG showed isolated aberrant multifocal spikes in divided hemisphere in both cases. Case3 underwent triple cortical resection in the guidance of MEG findings and finally MEG spike sources were isolated in resected lobes.

Conclusion: MEG directly showed the aberrant epileptic currents from cerebral cortex and also critical evidence of success of radical surgery in patients with CE non-invasively. Sequential multiple MEG analyses after surgery are also valuable for postsurgical evaluation in the patients with CE.

Tu-99 - The dynamics of gradient magnetic-field topography (GMFT) proved by simultaneous electrocorticography 4 magnetoencephalography.

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Purpose: Gradient magnetic-field topography (GMFT) is one of MEG analysis without resolution of inverse problem. We previously reported the usefulness of GMFT on epilepsy (Hashizume, 2007, Shirozu, 2010). The purpose of this study is to validate the spatiotemporal accuracy and reliability of GMFT by simultaneous recording of electrocorticography (ECoG) and magnetoencephalography (MEG).

Methods: We reviewed the simultaneous ECoG-MEG recording data of the three patients underwent epilepsy surgery based on chronic intracranial EEG (iEEG) monitoring. Ictal onset zones of each patient were lateral frontal lobe, insula to parietal operculum and basal temporal lobe. ECoG was analyzed by voltage topography (VT) using selected 32 or 60 electrodes of concerned area. Total number of intracranial electrodes ranged 112 to 192 channels. We compared the spatial and temporal change in VT and GMFT on simultaneously detected interictal epileptic discharges of ECoG and MEG.

Results: Despite slight difference of spatial distribution or temporal phase, the results of GMFT were concordant with those of VT. The accuracy of spatial distribution was in gyrus as a unit. These results corresponded with the ictal onset zones of iEEG.

Conclusion: Although the number of intracranial electrodes was restricted, we proved that GMFT accurately showed reliable epileptogenic activity of the brain and spatiotemporal distribution was affected by the difference of the source and/or sensitivity of EEG and MEG.
An illustrative case of focal cortical dysplasia on the left insula to parietal operculum (A, yellow arrow). 32 channels of intracranial electrodes were selected in concerned area (B, green circles). We analyzed simultaneous spike on MEG and ECoG (C).

**Tu-200 - Identification of Neuromagnetic High-frequency Oscillations in Pediatric Epilepsy using Autofocus Beamforming**

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Introduction: High-frequency oscillations (HFOs) in epilepsy have been well investigated with invasive intracranial recordings. However, noninvasive identification of HFOs has rarely been studied. According to our pilot data, one main challenge in the detection of HFOs using magnetoencephalography (MEG) is that HFOs are very weak and commonly obscured by lower frequency signals. The aim of the present study is to develop a new MEG method for the detection of HFOs in epilepsy.

Methods: Building on our previous results, this new method was developed to classify and extract spatially constrained neuromagnetic HFOs. Since weak HFOs typically appeared in a small group of sensors, a focal beamformer based on the spectral power of a small group of sensors (auto-focus beamforming) was used to scan the magnetic sources. Sixty patients with clinically diagnosed epilepsy were studied using our new method and conventional beamformers. MEG data were digitized at 4,000 Hz and de-identified. Blinded analyses were performed. Three-dimensional magnetic resonance imaging (MRI) was obtained for each patient to produce magnetic source imaging (MSI).

Results: Our preliminary data have demonstrated that neuromagnetic HFOs in epilepsy could be reliably detected in 53 of the 60 patients (88%). In the 60 patients, 46 patients (77%, 46/60) had visually identifiable spikes. There were 16 of these 60 patients had HFOs without spikes (23%, 16/60).

Conclusion: These results have provided evidence that patients with epilepsy have associated HFOs which can be detected with advanced MEG methods. The concordance and independence of HFOs and spikes suggests that HFOs are potential new biomarkers for clinical management of epilepsy in the future.

**Tu-129 - N400m does not differ significantly between phonological, semantic or morphosyntactic processing.**
Studies using fMRI have found that distinct cortical areas are activated by the phonological, morpho-syntactic and semantic aspects of words. This study addressed whether these differences could be observed with MEG, by comparing responses evoked across three matched tasks requiring phonological processing (determining if the presented word rhymes with a target), semantic processing (determining if the presented word refers to something that would fit in a breadbox), or morphosyntactic processing (determining if the presented word would end in '-ed' if placed in the past tense). In all paradigms, the word was presented visually for 300ms and half of the words repeated multiple times. In all tasks, repetition resulted in modulation between 300 and 500ms (frontal, temporal and parietal areas). The location, timing, and task correlates of the N400m suggest that it may reflect the activation of task-relevant information. Nine healthy males participated in 306 channels MEG recordings (Electa-Neuromag). At the group level, we compared response patterns for the 3 tasks for the repetition effect (repeated ANOVA for time window between 300 and 500 ms) and did not observe reliable task-dependent differences of N400m. In conclusion, the topography of the N400m, and presumably its underlying cortical generators, does not differ significantly across tasks accessing phonemic, semantic or morphosyntactic information. This remarkable finding may indicate that the N400 process automatically activates all types of information associated with a word, with post-access processes drawing upon this information to guide the response to the task at hand. In this view, the dissociation between MEG and fMRI results would result from fMRI revealing post-access activity following the N400. Alternatively, the N400 process may only reflect modulation but not activation. In this case, the fMRI results would reflect neuronal activation that is not seen with MEG.

Tu-130 - Categorical processing by hierarchical oscillations: a MEG study of speech perception

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Phonological processing during speech perception extracts phonetic information from a highly variable acoustic signal. A powerful theory assumed that this phenomenon, categorical speech perception, corresponds to the perception of oppositions between phoneme categories. According to this theory, it should exist a synergy between a phonological and a psychoacoustic determination of the boundary between two phonemic categories. We used two continuum of acoustically varying sounds for testing the identification of distinct phoneme categories (/ba/-/da/ and /da/-/ta/). The continuum /ba/-/da/ varied on second formant values which is a frequency variation and the continuum /da/-/ta/ varied on Voice Onset Time values, corresponding to a temporal variation. Using MEG recording, we found that listening to speech stimuli varying in small and acoustically equal steps caused a fundamental and qualitative change in both the frequency and spatial distribution of cortical activity. The present study showed that cortical population response patterns were organized by their sensitivities to critical acoustic features: ERF amplitudes were correlated to frequency and temporal variability across stimuli. Source-reconstruction method enhances that phonetic categorization was present in A1/A2, but also in BA22 and was accompanied by theta and gamma oscillations. Using time-frequency analyses, we confirmed that theta activity is correlated with the amount of voicing, a temporally slow varying acoustic feature. We also showed a dominance of gamma activity in left auditory cortices during syllable processing. These findings provide evidence for acoustic-to-phonetic level encoding of speech sounds in human language perception cortex.


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Theories of semantics propose that word meaning is mentally represented in 'semantic spaces' in which different words are represented as nodes, and semantic similarity relationships are expressed by the distance between them. What is the neural basis of semantic spaces? How are the neural codes supporting meaning of different words related to one another? We recorded high-density (64 channels) EEG on 20 subjects using a parametric semantic priming paradigm whereby target words are preceded by prime words which semantic relation to the target varies along a continuum of semantic similarity (e.g., CAT-DOG, DOLPHIN-DOG, HAMMER-DOG). We selected a set of word pairs which relative semantic distances were evenly distributed along a 4-levels range (three within and one across semantic domain), on the basis of previously acquired similarity judgments. Words belong to two semantic domains: animals and tools. Targets were presented visually, while primes could be written or spoken words. For both visual and auditory prime words, ERPs to target words were modulated between 300 ms and 500 ms by the semantic relation with the prime word, reflecting the 4 semantic distances. Importantly, however, this word semantic distance effect was category-specific in both time and space: while for words of animals it
emerged as a fronto-central negativity at about 350 ms, resembling the classic N400 effect, for tools it appeared significantly later (between 400 and 450 ms) and was confined to posterior electrodes. Source reconstruction confirmed two anatomically distinct substrates for these modality-independent category-specific semantic effects: the lateral anterior temporal cortex for animals, and the medial posterior temporal cortex as well as the anterior parietal cortex for tools. Results demonstrate that distinct categories of concepts are coded in different brain regions, and that, within each category, the neural code is graded, directly reflecting the metric of the semantic spaces.

Tu-132 - Identical spatio-temporal patterns of rapid motor-cortex activation for action-related nouns and verbs: MEG study

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Background and Objectives. Perception of action verbs is known to selectively activate the respective representations in the motor cortex at the early stage of word recognition. We investigated, for the first time, whether the action nouns follow the same spatial-temporal activation patterns as that known for action verbs. Furthermore, we aimed to specify, using distributed source modelling of MEG data, whether the action words activate primary and/or secondary areas of motor cortex as well as the time-course of this activation.

Methods. We selected three pairs of Russian words related to actions performed by hand, foot and mouth, and each pair included a verb and a noun having the same word stem. The stimuli were presented within the mismatch field (MMF/MMN) paradigm in three blocks corresponding to the word pairs, which were used as rare unexpected deviant stimuli, while the frequent standards were pseudo-words chosen for each word pair in such a way that their onsets were phonologically identical to the test words, and the acoustic disambiguation point between the 2 deviant words and the standard pseudo-word always occurred at 260 ms after the word onset. The MMF source activation time courses in the motor cortex were analysed.

Results and Conclusions. We demonstrate for the first time that both lexical categories of Russian action words activate the motor cortex somatotopically but source distribution is shifted somewhat anterior to primary motor cortex (Fig.1). Moreover, cognate verbs and nouns have very similar spatial-temporal pattern of motor cortex activation that reaches its peak just ∼100 ms after the word disambiguation point and ∼30 ms ahead of the MMF response in the auditory cortex.

Tu-133 - Distinct brain networks underlying word segmentation revealed by Independent Component Analysis

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Word segmentation (i.e. detecting word boundaries from a continuous speech) is one of the most difficult problems that learners
should face when learning both first and second language. Although previous neuroimaging studies have shed light on the neural processes supporting it, functional connectivity studies during this process are lacking. In the present work, we used a multivariate method, Independent component analysis (ICA), to examine the brain functional networks active while participants were required to learn artificial language streams made by concatenated syllables. These speech streams contained both statistical regularities and prosodic cues that could be exploited for segmentation. ICA method allows the separation of the underlying brain activity into a set of spatially independent networks each of them synchronized in their time course. It has been proposed that ICA can extract the networks that represent the functional integration of an active brain. Results showed three different active networks while subjects were segmenting speech: i) an audio-motor network that showed activation mainly in bilateral superior temporal gyri, precentral gyri and supplementary motor area, ii) a sensory-motor network extending mainly through both pre and post central gyri and the supplementary motor area, iii) a network showing a more left lateralized activation covering the classical language related areas in left frontal, temporal and parietal lobes. In addition, the default network appeared negatively correlated with the task. These results provide further evidence and support the functional integration hypothesis considering that complex cognitive processes as language learning are subserved by different identifiable separated brain networks.

Tu-146 - Effects of navigated rTMS on object and action naming

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Transcranial magnetic stimulation (TMS) is widely used in brain research and in clinical studies. Repetitive TMS (rTMS) has previously shown potential in disturbing ongoing speech tasks. Lately, navigated TMS has shown results comparable to direct cortical stimulation in mapping the motor cortex. In this study, we used navigated rTMS to map the language processing in the human brain by disturbing speech performance in connection with different language tasks. Five healthy right-handed subjects were asked to name actions and objects while rTMS was targeted over different sites of their left hemisphere. First, a baseline naming was carried out to monitor subjects’ performance without rTMS. Thereafter, rTMS was delivered at 5 Hz, 300 ms after presenting action and object pictures on a computer screen once every 2.5 s. The mapping sessions were video-recorded for off-line analysis. rTMS produced no-response errors, delayed responses, and phonological and semantic paraphasias. In four out of five subjects, rTMS disturbed more object than action naming. In particular, no-response errors were observed more frequently in object than action naming tasks in all subjects. The results show that object naming is more vulnerable to rTMS distraction than action naming, and suggest that object and action naming are processed in a slightly different manner in the human brain. However, further studies are needed to strengthen these conclusions.

Tu-147 - Right-hemisphere language lateralization without a corpus callosum

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Speech production is a dynamic process that typically relies on left hemispheric dominance. Individuals with agenesis of the corpus callosum (AgCC) offer a unique opportunity to examine the role of the corpus callosum development on language processing dynamics including hemispheric lateralization. Here, we use time-frequency MEG imaging to quantify changes in neural oscillations during language tasks in patients with partial (pAgCC) and complete (cAgCC) agenesis of the corpus callosum and matched healthy controls (HC). Subjects participated in an auditory verb (AV) generation task and Boston picture naming (BPN) test during MEG recording. MEG data were collected using a 275-channel whole-head biomagnetometer (MISL). For VG, a single auditory noun is presented and subjects were instructed to generate a verb. For BPN, an image of an object is projected onto a screen and subjects are instructed to name the pictured object. Data were analyzed in the time-frequency domain using an adaptive spatial filtering technique (nutmeg.berkeley.edu). Changes in beta oscillatory power (12-30Hz) were used to compute a language laterality index (LI, a ratio of power change between the left and right hemispheres). While we found the expected leftward language lateralization healthy controls (mean LI=-0.6) only 20% (mean LI=-0.06) of cAgCC individuals showed left hemisphere language dominance. The pAgCC group demonstrated an intermediate left lateralization at 47% (mean LI=0.08). In the group comparison, an increase in beta power suppression was identified in the AgCC group over the right medial frontal gyrus and the right pre-central gyrus ∼ 450ms prior to the vocal response. In the left hemisphere, significantly reduced beta suppression in the AgCC group was identified over the angular and the superior occipital gyrus. This report demonstrates a direct relationship between abnormal callosal development and impairments in cortical recruitment during language production.

Tu-148 - What you say is what you are: Theta power differences during perception of speech from substance abuse treatment sessions

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Motivational interviewing (MI) is a directive, client-centered therapeutic method employed in the treatment of substance abuse, with strong empirical evidence of effectiveness. The mechanism of action in MI with the most consistent empirical support is ‘change talk’ (CT), which is generally defined as within-session speech in support of a behavior change. ‘Sustain talk’ (ST) incorporates speech in support of the status quo. MI is grounded in self-perception theory and posits that during treatment, clients essentially talk themselves into change via these CT and ST utterances. In the present study MEG was used to measure brain activity while alcohol users heard repetitions of their CT and ST recorded from their MI sessions. Previous results indicated significantly more activity for CT than for ST in right-hemisphere regions including inferior frontal gyrus, insula, and superior temporal cortex. Using these sources we computed induced power and phase locking in a 1000-ms epoch following the auditory offset of each phrase. Significant differences were observed in insula in the theta (4-8 Hz) range within the first 300 ms following offset. Insula has been implicated across a broad range of cognitive processes, as well as in emotion and mood. In particular, increased theta band activity in the insula has been associated with emotional stimuli, with higher activity for emotional stimuli than for neutral. The timing of the theta band activity in the present study may suggest sensitivity of the insula to subtle differences in emotional content between CT and ST during MI sessions. Given the strong relationships seen in multiple studies between CT counts and substance abuse outcomes (Aharonovich et al. 2008, Moyers et al., 2007, 2009, Vader et al. 2010), these results suggest that the emotional content of client speech within treatment sessions may underlie subsequent behavior change in substance abuse treatment.

Tu-149 - Mapping of neural generators of electrophysiological responses to semantic and syntactic anomalies using MEG

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Introduction
Language processing depends on the interactions between frontal and temporal brain regions. The interactions between these regions are mediated by two main pathways with complementary functions: a ventral temporal-frontal route essential for semantic processing, and a dorsal parietal-frontal pathway subserving syntax and phonology. In the present study, we mapped the neural networks that generate electrophysiological responses to semantic (N400) and syntactic anomalies (P600) using Magnetoencephalography (MEG), while participants performed a sentence comprehension task in the auditory and visual modalities.

Methods
Experimental items consisted of 400 sentences selected from a set of normed materials. To elicit N400 responses, semantic anomalies were created by substituting the final word of the sentence with an unexpected completion of the same part of speech (e.g., She will go to the bakery for a loaf of books). The P600 was elicited by introducing a grammatical error in the verb tense agreement earlier in the sentence (e.g., She will going to the bakery for a loaf of bread). Participants performed a sentence acceptability judgement task.

Results
Oscillatory changes in MEG event related synchronization/desynchronization (ERS/ERD) in alpha and beta frequency bands were localized using beamforming and synthetic aperture magnetometry (SAM). The results indicated that ERD in the 8 to 30 Hz frequency range was observed in the temporal-frontal regions for semantic anomalies, and in the parietal frontal regions for syntactic anomalies (see Figure 1).

Discussion & Conclusions
The results indicate that the neural generators of the N400 and P600 responses can be mapped using MEG beamforming of 8-30 Hz ERD. As predicted, semantic and syntactic responses were localized to the ventral and dorsal language networks. These results will form basis for the study of compensatory reorganization of these language networks after stroke to support recovery.
Tu-150 - A Mirroring System for Language: Using MEG to Explore Developmental Changes in Sensory-Motor Connections for Speech

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Shared perception-action networks for speech are essential for imitation and learning of the sound patterns contained in ambient language. An interesting cognitive science question can thus be posed regarding brain activation in response to speech: Does the brain respond to the auditory presentation of speech in auditory areas alone, or in motor speech areas as well, and if so, what role does experience play in the patterns of brain activation in these brain areas? The answer addresses theoretical issues related to the nature and existence of shared or mirroring systems for perception and action, as well as the role of experience in the development of these systems. In MEG experiments using the oddball paradigm, we tested 6- and 12-month-old infants, as well as adults, to address this question. Listeners were presented with syllables containing native speech sounds, and syllables containing non-native speech sounds. Our results show activation in both motor and auditory speech areas in response to both kinds of speech signals. These results address the theoretical implications of shared patterns of brain activation in auditory and motor speech areas, how these patterns change with age, and implications for theories of neuro- and cognitive science.

Tu-151 - Connectomic signatures of language network in the spontaneous MEG

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It is well established that the resting networks such as memory or default network represent fairly robust correlation with pathological or performance states. Unlike the aforementioned resting networks, resting language network has yet been less established. Much benefit is expected when language faculty is assessed without explicit tasks, especially in the patients less cooperative. We are particularly interested in elucidating the language network in the resting brain and investigating information flow in this network. To this end, directed connectivity was investigated among so-called language connectomes during a rest while the oscillation was recorded using a whole-head MEG system (Vector-View, Elekta, Neuromag, Oy, Helsinki, Finland) from 2 anteriorly callosotomised patients, which were then compared with those from 13 healthy controls. Artifact-free signals were submitted to time-frequency analyses for computing partial directed coherence (Baccala and Sameshima, 2001). The time-series data was shuffled through permutations using a surrogate approach. The connectivity surviving the significance level of .99 between the pairs confirms that overall intra-hemispheric pathways for speech was evident in task-independent resting and highlights that this pattern was preserved in the patients. The same or enhanced language performance after the operation can, expectedly, be related with the overall increased connectivity in the language network after the operation, markedly in the left. The interhemispheric connectivity between the frontal areas was drastically reduced without any damage on language. This paradox may imply that interhemispheric connection could be redundant, or that a compensatory function transfer might have occurred, or that there might be other interhemispheric communi-
Directed connectivity pattern in the language network in the healthy (A) and the anteriorly callosotomised participants (B).

Inter-hemispheric connectivity in the frontal and the temporal regions (C)

**Tu-184 - Audio-visual speech integration is predicted by coupling of low frequency coherence and high gamma-power**

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At any moment, several functionally specialized, but spatially distributed areas are involved in processing sensory stimuli or cognitive functions. Dynamic and flexible interaction between these areas is essential for effective brain functions. Several studies have suggested that neuronal oscillatory synchronization provides a candidate mechanism for effective and flexible interaction between neuronal groups. Here, we studied the role of oscillatory neuronal synchronisation in audio-visual speech perception.

11 subjects viewed congruent audio-visual stimuli of a speaker articulating vowels /a/ or /o/. In addition, we presented modified, incongruent versions of the stimuli in which /a/ was provided by audio signal and /o/ by the visual signal (or vice versa). Subjects’ task was to report whether stimuli were (in)congruent while we recorded neuromagnetic activity with a 306-channel MEG.

We found an early (-50 to 400 ms) significant increase of low frequency (4-12 Hz) power for incongruent stimuli around left primary auditory cortex (A1). In addition, beta (20-30 Hz)-power was enhanced for congruent stimuli in left BA 40 (supramarginal gyrus) at 425-750 ms and high gamma (120-140 Hz) was enhanced in left BA 44 (Broca’s area) between 675-875 ms after auditory onset.

In addition, we found a linear increase of coherence between A1 and BA 44 for congruent stimuli between on- and offset of auditory stimuli. In contrast, coherence decreased linearly for incongruent stimuli. Interestingly, we found that this difference in coherence was positively correlated with the above mentioned increase of gamma-power in BA 44.

In summary, our results demonstrate that oscillatory power in several frequency bands predicts successful integration of audio-visual speech on a large spatio-temporal scale. The findings reveal that parts of this network are coupled by coherence in the theta/alpha band and that low frequency coherence and high frequency power modulations are correlated.

**Tu-185 - Oscillatory brain activity during reading of word and consonants measured with MEG.**

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Introduction: Printed word reading has been shown to correlate with oscillatory MEEG activity at different frequency bands across the brain, indexing differential patterns of connectivity at the cortical level. Among others, Goto et al. (2011) reported theta band ERS (event-related synchronization) in the bilateral occipital, anterior temporal and medial prefrontal cortices, also, alpha, beta and low gamma ERD (event-related desynchronization) were reported in the left posterior inferior frontal gyrus, the left anterior superior
Methods: We compared oscillatory brain activity generated when reading Spanish Words and Consonant strings up to 400 ms post stimulus onset across different frequency bands. Twenty Spanish speakers performed a visual low-level Go-NoGo task. NoGo trials were Words (CASA, home) and Consonant strings (FGCJ), while Go trials were the same strings with a letter substituted by a dot (C-SA or FG-J). MEG data were collected continuously using a Elekta Neuromag 306 channel system. A time frequency analysis focusing on the axial activity recorded from magnetometers was performed both at a sensor and at a brain level. The neural source activity at different frequency bands were reconstructed using linear constrained minimum-variance beamforming.

Results: In the 0-200 ms interval we found similar ERS oscillatory activity in occipital regions in both beta and alpha bands for Consonant strings compared to Word reading. In the 200-400 ms interval we observed higher ERD oscillatory activity in the beta band in the VWFA for Words compared with Consonant strings.

Discussion: Our study investigated the dynamics of oscillatory activity related to visual word recognition. VWFA was found to be more relevant for word than consonant processing at all frequency bands. Involvement of occipital areas was found independent regardless the string of letters formed a word or not.

A) Average beta band oscillatory activity across subjects at the sensor level from 0-200 and 200-400 ms. B) Beamforming inverse solution in beta band for one participant.

Tu-186 - Spatio-temporal dynamics of semantic priming effects on words and word stems: anatomically-constrained MEG

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Lexical-semantic processing has been studied extensively with both temporally-sensitive and hemodynamic neuroimaging methods. Nevertheless, the neural underpinnings and temporal dynamics of the process that underlies 'building meaning' from partially available information is still poorly understood. The aim of the present study was to examine the spatio-temporal activity pattern during processing of complete or partial words as a function of contextual facilitation. Participants were presented with word stems or real words that were primed or not and were asked to indicate whether they rhymed with the last word in each triad (e.g. open - cl - expose, tile - story - score).

High-density magnetoencephalography (MEG) signal was recorded with a whole head device (Elekta Neuromag) and analyzed with an anatomically-constrained MEG (aMEG) approach. Noise-normalized distributed minimum norm inverse estimates of activity to target words and word stems were constrained to each person’s cortical surface reconstructed from anatomical MRI scans. Inverse solutions from all of the subjects were averaged by aligning cortical folding patterns.

Starting in the visual cortex, the estimated activity spread in the anterior direction and was left-dominant for words and right-dominant for word stems after ~ 200ms. A typical effect of priming was observed only in the left fronto-temporal areas as the N400 was larger to incongruously primed stimuli in both categories. Conversely, the N400 to congruously primed word stems was greater in the right temporal cortex at a later latency. These findings suggest that the two hemispheres are differentially sensitive to words and word-like stimuli. Even though lexical-semantic processing is primarily subserved by the left temporo-prefrontal cortical areas, the
right hemisphere contributes to semantic processing of incomplete words.
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**Tu-187 - Event-related theta power during lexical-semantic retrieval and decision conflict is modulated by alcohol intoxication: anatomically-constrained MEG**

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Language processing is commonly characterized by an event-related increase in theta power (4-7 Hz) in scalp EEG. Oscillatory brain dynamics underlying alcohol’s effects on language are poorly understood despite impairments on verbal tasks. To investigate how moderate alcohol intoxication modulates event-related theta activity during visual word processing, healthy social drinkers (N=22, 11 females) participated in both alcohol (0.6 g/kg ethanol for men, 0.55 g/kg for women) and placebo conditions in a counterbalanced design. They performed a double-duty lexical decision task as they detected real words among nonwords. An additional requirement to respond to all real words that also referred to animals induced response conflict. High density whole head MEG signals and midline scalp EEG data were decomposed for each trial with Morlet wavelets. Each person’s reconstructed cortical surface was used to constrain noise-normalized distributed minimum norm inverse solutions for theta frequencies. The overall spatiotemporal pattern is consistent with the left-lateralized fronto-temporal activation observed in language studies applying time domain analysis. Event-related theta power was sensitive to the two functions manipulated by the task. First, theta estimated to the left-lateralized fronto-temporal areas reflected lexical-semantic retrieval, indicating that this measure is well suited for investigating the neural basis of language functions. While alcohol attenuated theta power overall, it was particularly deleterious to semantic retrieval since it reduced theta to real words but not pseudowords. Second, a highly overlapping prefrontal network comprising lateral prefrontal and anterior cingulate cortex was sensitive to decision conflict and was also affected by intoxication, in agreement with previous studies indicating that executive functions are especially vulnerable to alcohol intoxication.

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**Tu-188 - Modeling Prediction within the Semantic Language Network: A Dynamic Causal Modeling Study**

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Language processing is usually performed rather effortlessly by humans. Interestingly, it has been demonstrated that the understanding of a word is significantly eased if it matches the expectation from the preceding context. This let us assume that the language network generates predictions for the upcoming input stream, but how are predictions implemented neurally? To further investigate the information flow in the semantic network, we set up a paradigm with German short sentences using two groups of verbs. Verbs were either strongly predicting which noun followed (e.g. he drives the car) or not (e.g. he gets the car). Participants listened to the sentences while MEG recordings were conducted. Evoked responses were further analyzed using dynamic causal modeling (DCM). Bottom-up and top-down processing are modeled via forward and backward connections respectively in DCM. We systematically compared models which either used backward or both connections to model our experimental manipulation, semantic predictability. For the processing of the verbs, we assumed the bottom-up processing of the two conditions is comparable, but the verbs which generate the predictive context are strongly enhancing top-down processes. Consequently, when modeling the difference between the two groups of verbs, backward connection models should be best suited. For the processing of the nouns, we expect a different scenario for bottom-up processing. Since the highly predictable nouns elicit much weaker field changes and at about 250ms the signal power drops down to zero, we interpret this observation as a shortening of the bottom-up processing. Furthermore, the non-predicted nouns are needed to complete the meaning, therefore they elicit strong top-down processes. Comparison of both noun groups should therefore lead to a preference of the forward-and-backward models. Interestingly, DCM model comparison demonstrated that the family with modulated extrinsic backward connections is clearly superior for modeling of the verb and family with modulated forward-and-backward connections for the noun. Compared to non-predictive verbs, we showed that predictive verbs induce stronger top-down information flow during verb comprehension and less overall information flow during the following noun comprehension. We take this as evidence that language processing strongly takes advantage of the comparison between self-generated predictions and the incoming information stream.

**Tu-189 - The role of brain oscillations in mediating linguistic relations**

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Children with reading impairment have subtle deficits in speech perception which may be related to their phonological processing abilities. However, little is known about how this interacts with semantic influences. The aim of this study was to examine brain oscillatory activity related to auditory word perception in reading disability under varying degrees of phonological contrast in sentence context using magnetoencephalography (MEG). Good and poor readers were tested on the effects of semantic context on auditory recognition of sentence-terminral incongruent words phonologically manipulated to be similar or dissimilar to corresponding congruent target words. Neural synchrony between task-relevant brain areas, and oscillation frequencies was examined using phase-locking values (PLV) and phase-amplitude coupling measures. Gamma band (30 4 40 Hz) PLV between auditory cortex and superior temporal sulcus in the right hemisphere appeared to be differentially modulated by the degree of phonological contrast in the two groups. Specifically, the PLV was larger in the phonologically similar (PS) than in the phonologically dissimilar (PD) condition between 400 4 600 ms related to semantic processing, in the good readers. This pattern, however, was reversed in the poor readers, whose lower synchrony in the PS condition may reveal the group’s reliance on context under perceptually challenging conditions. Cross-frequency coupling (CFC) between theta band phase and gamma band amplitude was left lateralized for the PS condition, but only in good readers and in an earlier time range (150 4 400 ms) potentially related to phonological processing, no hemispheric difference was found in poor readers. The left lateralized CFC in good readers may implicate a role for theta-gamma coupling in speech perception. The results, overall, suggest the involvement of brain oscillations in mediating between different levels of linguistic conflict.

Tu-190 - The different role of consonants and vowels in visual word recognition: MEG correlates of relative position priming

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Previous neurocognitive studies have shown that the nature of letters-consonant vs. vowel is crucial for printed word recognition. We recorded MEG evoked activity while participants read words in a masked priming experiment. Half of the words included a vowel (V) as initial, third, and fifth letters (e.g., acero [steel]), while the other half included consonants (C) (e.g., farol [lantern]). Targets were preceded 1) by the initial, third, and fifth letters (Relative position, e.g., aeo-acero and frl-farol), 2) by consonants or vowels that did not appear in the target word (Unrelated, e.g., iui-acero and tsb-farol), or 3) by the same words (Identity: acero-acero, farol-farol).

13 Spanish speakers took part in the experiment. Evoked MEG activity was recorded using a 306-channel Elekta system. Two participants were excluded due to high number of artifacts. ECD dipolar activity was fitted to a large activity peaking at 237.9 ms on average. ECDs were located in the left posterior regions: eight participants showed the effect in the occipital-temporal regions (7 in the ventral portion and 1 participant in the lateral portion), while in three participants the dipole was located in the medial part of the occipital lobe. Larger amplitudes were observed for the Unrelated conditions (C: 21.3 nA, V: 21.1 nA) compared to the Identity (C: 16.9 nA, V: 17.9 nA). The Relative condition activity in the case of Vowels (21.4 nA) was similar to the Unrelated and different from the Identity condition. In the case of Consonants (17.8 nA) the Relative condition activity was different from the Unrelated but similar to the Identity condition (see Figure).

In line with previous masked priming MEG experiments we found evidence of increased left occipital-temporal brain activity right after 200 ms elicited by the reading of a printed word. Here we bring evidence that this initial (pre-lexical) processing stage is mainly sensitive to the information brought by consonants compared to vowels.
Dipolar activity elicited by the three critical conditions for the Consonants and Vowels manipulation.

**Tu-191 - MEG responses (ASSR) to tremolo like presentation of major and minor chords.**

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In the western music, chords play a very important role in expressing emotions. Generally, major chords are associated with happy and bright feelings and minor chords with sad and dark feelings. Neural basis for this association has attracted many researchers and fMRI has been successfully yielded evidence for differences in sites of activation for the two chord categories. On the other hand, it has been difficult to see clear difference between responses to the two categories although mismatch responses are easily observed in oddball paradigms employing the two categories as standard and deviant stimuli. We used amplitude modulated major and minor triads to see possible difference in responses. The modulation frequency was set at 10 Hz which was much lower than the optimal modulation frequency around 40 Hz but somewhat near the tremolo playing frequently employed in music playing also the center frequency of the alpha band. 11 male students (non-musicians) participated in the study. Bursts of AM major and minor triads lasting 2 s were produced with Matlab using pure tones. During MEG recording, the participants watched a silent movie to ignore the sound. When all the 11 subjects were taken for analysis, there was no significant difference between the two categories, but when one subject who showed responses several times larger than the rest was excluded, the 10 Hz component to the minor chords was significantly larger than to the major chords. When all the 11 subjects were taken for analysis, there was no significant difference between the two categories, but when one subject who showed responses several times larger than the rest was excluded, the 10 Hz component to the minor chords was significantly larger than to the major chords.
Amplitude of the 10 Hz component of the dipole intensity of the equivalent current dipole estimated for responses to major and minor chords.

Tu-192 - Enhancing language comprehension with noninvasive brain stimulation

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Languages often contain lexical ambiguities. Though many words have the same pronunciation and spelling but different meanings (e.g., bank), we can select an appropriate meaning from many alternatives by using the lexical and contextual information. This resolution of lexically ambiguity is an important part of language comprehension. We previously investigated the spatio-temporal characteristics of neural activities related to the resolution of lexically ambiguity by using MEG (Ihara et al., 2007). The results suggested that multiple meanings are accessed initially with no influence from preceding contextual information, and then the ambiguity is resolved by controlled semantic retrieval and contextual selection in the left inferior frontal cortex. Thus, if the excitability of the left inferior frontal cortex can be increased, the behavioral performance of lexical ambiguity processing should improve. In the present study, we conducted an experiment using transcranial direct current stimulation (tDCS). We investigated the effect of tDCS over the left inferior frontal cortex (0.043 mA/cm²) on reaction time and accuracy rate obtained when the subjects performed a semantic judgment task. The stimuli were Japanese word pairs in which the targets were either ambiguous or unambiguous words, and these were either semantically related or unrelated to the primes. The anodal electrode was positioned over the left inferior frontal cortex, based on the MEG results, and the reference electrode was centered over Cz of the International 10-20 system for EEG electrode placement. We compared the behavioral indexes of anodal sessions (15-min anodal tDCS) and sham sessions (30-sec tDCS). Supporting the hypothesis, the reaction time was shorter in the anodal tDCS session than in the sham session for ambiguous words. The result showed that the left inferior frontal cortex is an essential region for lexical ambiguity processing.

Tu-193 - Cortical oscillations during lexical processing: MEG studies in adults and children

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Synthetic aperture magnetometry (SAM) was used to characterize the time-course of auditory cortical oscillations observed in the magnetoencephalography of the brain’s response to spoken words. SAM is a linear beamforming approach to magnetic source imaging that offers a view of event related spectral perturbations without the need for time-averaging of evoked responses. In previous work we demonstrated the timing of event-related desynchrony (ERD) and synchrony (ERS) in adult auditory cortex during a lexical decision task. Analysis of spectral power in the ERD/ERS response to high and low frequency spoken words revealed an elevated left hemispheric ERD in the alpha range (8.5 - 12.5 Hz) following words in the interval 445 - 700ms post-stimulus. Furthermore,
auditory processing was characterized by a differential burst of ERS in the gamma band (42-50 Hz) that distinguished high frequency words from low frequency and non-word stimuli in the interval 345-475ms. Here we report preliminary findings from analysis of cortical oscillations during auditory lexical decision in two pediatric populations. To examine auditory processing abnormalities frequently observed in autism spectrum disorders (ASD), we compare ERD/ERS time-course in a cohort of typically developing (n=5) and autistic (n=4) children. The data indicates that typically developing (TD) children show lexical ERD activation patterns in the theta-alpha ranges (5-15 Hz) that is comparable to adults. However, children with ASD display markedly less ERD. In the interval 400-550 ms post-stimulus, TD children display significantly enhanced ERD to words (−14.8 ± 5, M), as compared to non-word (−10.2 ± 5), t = -3 (2-tailed), p<.05. Whereas in the same time window, children with ASD show remarkably less ERD to word (−3.6 ± 5) and non-word stimuli (−2.6 ± 3), t = 0.4. These preliminary findings suggest an induced neural activity correlate to impaired auditory lexical processes in ASD.

**Tu-194 - Role of nested oscillations on speech tracking: an EcoG exploratory study**

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Cortical oscillations constitute a means to temporally organize induced neural activity. There is recent evidence that the brain preferentially tracks modulations in the delta, theta and gamma frequency ranges of speech stimuli. Phase reset of theta and gamma bands, both independently or through oscillatory nesting is a possible mechanism for parsing speech at relevant syllabic (~150 ms) and phonemic timescales (~30 ms), preparing it for higher-order computations. Here, we seek to probe if there is any concomitant processing at these bands by assessing the relation between phase and power at different frequency bins and different rates of speech. An epileptic patient underwent an intracranial (EcoG) recording while hearing sentences with a natural speech rate and with 2, 2.5 or 3 times time compression. For all sentences/conditions, phase-coupling estimates were obtained from pairings of the frequency-dependent modes obtained trough empirical mode decomposition in time-varying windows of 1 second. A sum of all the significant events of coupling for each pairing was done for the left temporal channels across all sentences.

Results did not show neither any clear condition related finding nor a time-specific conclusion but, a consistent cluster of phase-amplitude coupling around the phase frequency of modes 8, 9 and 10 and the amplitude frequency of modes 6 and 7. These modes correspond roughly to theta (8), delta (9,10) and higher beta/low gamma (6,7) ranges, resembling syllabic and phonemic scales and giving further support to the hypothesis of hierarchical processing through oscillatory nesting. Importantly, the fact that the nesting estimates did not yield a distinct pattern for the accelerated speech should be taken with caution. One can draw two alternative conclusions: the change of rate does not effect the nested oscillations or changes occur at a more narrow time and frequency scale. A MEG protocol with longer sentences is expected to provide further evidence.

**Tu-195 - Effect of external pacing on speech motor control: MEG/fMRI studies**

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External pacing such as metronome sound is known as having fluency-inducing effect on speech-related disorders like stuttering. The neural mechanisms of this effect have not been investigated sufficiently until now. Firstly, we measured event related desynchronization (ERD) with magnetoencephalography (MEG), when the subject performed either vocalization, or observation of video of vocalization. Transforming the measured signal to time-frequency representation, the ERD (ERD or ERS) with magnetoencephalography (MEG) was observed. The ERD when looking at video of vocalization also caused ERD at the timing of vocalization, which might be caused because the subjects simulated vocalization when watching video. These results may suggest that speech with the external pacing modulates neural activity of regions for speech motor control profoundly than that without the external pacing. Secondly, under MRI environment, we investigated the fluency enhancing effect of external auditory pacing on stuttering speakers. Stuttering speakers and nonstuttering controls were scanned while performing metronome-paced speech, choral speech, and normal speech. Compared to nonstuttering controls, stuttering speakers showed a significantly greater increase in activation in the superior temporal gyrus under both metronome-paced and choral speech conditions relative to a normal speech condition. The basal ganglia of the caudate, globus pallidus, and putamen showed clearly different patterns of signal change from rest, the signal change of stuttering speakers was significantly lower than that of nonstuttering controls under the normal speech condition but was raised to the level of the controls, with no intergroup difference, in metronome-paced speech. These results suggest that the external auditory pacing modulates the activity of the cortex and the subcortex of sensori and motor regions, and accordingly raises the speech fluency of stuttering speakers.
Tu-196 - Coherence analysis for language function using the spatial filter technique of magnetoencephalography

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The aim of this study is to propose a coherence of event related desynchronization and synchronization (ERD/ERS) using special filter technique in magnetoencephalography. We reported an intensive beta activity occurred in the dominant inferior frontal language area in during the silent reading and word generation task. But it is difficult to detect temporal language area in our MEG studies. Therefore, we used the coherence technique for the purpose of detecting the neuronal network of language function.

The word generation task was performed to 10 right-handed volunteers using 160 channels whole head MEG. We presented one Japanese character each six minutes and repeated this trial about 80 times. An examinee repeatedly recollected one word continued from the character. After presenting a trigger character, we analyzed 400ms length data (from 200ms to 600ms after the presentation of at trigger character) using special filter technique. We set the seed point on the left inferior frontal gyrus in MRI, and explored the coherence for there bands, alpha (8-13 Hz), beta (13-25 Hz), and gamma (25-50 Hz), in ERD analysis. The results showed various pattern of the coherence, and it was not stable and common in all cases. Alpha and beta ERD activities were detected in ipsilateral front-temporal, ipsilateral front-parietal, and contralateral relation, and beta intensity tended to be higher than alpha intensity. Some cases showed ERS beta coherence, and the other did not show the coherence at all. The neural network was found to be very complicated, and there was much discrepancy in each individual condition. This coherent analysis is useful for confirming the speech dominant side, and learning the human cognitive function.

Tu-197 - Correlation Study of the Cortical Magnetic Response to Word

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Subjects hear a real Russian word in a stream of pseudo-words 120 times during 25 minutes. MEG is recorded with Elekta Neuromag system in Moscow. We observe averaged signals over considerable part of the head. The highest amplitude waveforms in the right and left hemispheres are shown in the Figure. They are quite different. We noticed that the amplitude build-up of the averaged signal is quite uneven and looked into the data in more detail. For each channel we calculate correlation between the time course of the field gradient during each presentation of the word with the time course of the signal, averaged over 120 runs. Time span is 800 ms after word onset. The correlation coefficients for each run are evenly scattered between the highest value and nearly zero, as shown in the Figure. This feature is common for all subjects and words. It does not depend on the time window for which the correlation is calculated, provided it is longer then 300 ms. Waveforms are quite robust and do not differ much for nouns and verbs which sound nearly alike. The waveform can be considered as local cortical signature of a particular word. This signature is individual for each subject.
Left panel. Signals recorded over the right and left sides of the head during and after the word is uttered. Black and gray lines indicate gradients of the magnetic field on the same chip in two orthogonal directions. The time is indicated in milliseconds. The word is pronounced during 450 msec  

Right panel. Correlation of the signals recorded during each utterance of the word with the average signals presented in the left panel. The 120 events are ordered independently for the left and right channels with maximum amplitude. Insert. Points correspond to each word utterance and the coordinates are the correlations in the right and left channels. The sources of the signals in different hemispheres behave independently.

Tu-198 - Spatiotemporal dynamics of speech comprehension as revealed by MVPA

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Extensive evidence has revealed a bilateral fronto-temporal network supporting speech comprehension (Marslen-Wilson & Tyler, 2007) and a left-lateralised sub-system specialised for processing of grammatical complexity (e.g. walk-ed, Bozic et al., 2010). Using combined MEG-EEG, we addressed how neural activity in this network is modulated by properties of the speech input. We manipulated the presence of an inflectional affix (‘s and past-tense ‘ed) to investigate what regions are sensitive to morphological complexity. Stimuli consisted of phrases presented in 3 contexts (I walk, He walks, He walked) and acoustically-matched stimuli (musical rain), which share the auditory properties of speech but are not interpretable. Analyses were performed using representational similarity analysis (Kriegeskorte et al., 2008), which examines the information carried by patterns of neural activity in order to determine the stimulus distinctions that are emphasised in a given region at a given time. The first dissociation was between pronouns (I vs. He) and between words and musical rain at 80 ms in bilateral fronto-temporal regions. Left inferior frontal cortex (BA 44) was the only region to show sensitivity to differences between affixed and non-affixed words, from -50 ms to 100 ms after affix-onset. These results suggest speech-specificity emerges by 80 ms and is modulated by acoustic properties of the input (differences between I and He). Processing within left BA44 was sensitive to the presence of an affix, consistent with neuroimaging results showing this region plays a key role in morphological processing.

Tu-199 - Role of magnetoencephalography/ magnetic source imaging (MEG/MSI) in tailored left anterior temporal lobectomy

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Traditionally the resection margin of tailored left temporal lobectomy (LTL) is defined by electrocortical stimulation (ECS) for language mapping. In recent years, MEG/MSI has become an increasingly important alternative in the pre-surgical evaluation of epilepsy patients. We reviewed 18 patients who underwent tailored LTL following MSI language mapping. The 13 female and 5 male patients were between 5 and 53 years old (average 26 yrs) at surgery. Fifteen of the patients also underwent ECS language
mapping (one patient could not tolerate a grid and in other 2 patients no language sites could be defined). MSI language mapping was acquired with a word recognition task (1). The language data were analyzed using the single dipole model. ECS was conducted using the standard protocol for our institution, including naming, repetition, reading, automatic speech. The distance between the anterior margin of MSI language dipoles and the temporal tip was between 3.3 and 5.4 cm (mean 4.3 cm). In the 15 patients, ECS defined language sites were 3 to 6 cm posterior to the temporal tip. The resection margin was between 2.0 and 4.8 cm (mean 3.6 cm) from the temporal tip (measured at the middle temporal gyrus level on post-operative MRI). The localization of MSI and ECS language mapping is partially overlapping in the 15 patients with ECS(2). The resection was guided by both electrocortical stimulation and MSI language mapping in 15 patients while three were guided solely by MSI language mapping. There were no unexpected language deficits after resection at 6 plus months follow-up. In conclusion, MSI can provide reliable receptive language mapping in LTL patients and may be a possible alternative to electrocortical stimulation in guiding dominant temporal lobectomy.

We thank Mr. Brian Owens for his technical support.


Fig. A patient with left temporal lobectomy with subdural EEG implantation and MSI language mapping. Green dots on the left image represent the language region by ECS. The red region represents receptive language area defined by MSI

**Tu-160 - Unraveling the mechanism of perceptual bias of ambiguous stimuli in auditory cortex**

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The perception of an auditory stimulus can be modified by its surrounding context in multiple ways. Context effects can best be studied using ambiguous stimuli where the stimulus is held fixed while the context is varied. A compelling example of such a stimulus is a sequence of two Shepard tones spectrally shifted by half an octave, which can be perceived as ascending or descending in pitch. Chambers et al. found that preceding this pair by a 'biasing' sequence of appropriately shifted tones leads to stable shifts in perception, specifically, sequences above (below) the first tone in the pair induced ascending (descending) percepts.

To investigate the neural representation of this phenomenon, we recorded MEG responses in human subjects listening to these sequences. In order to measure the effect of the biasing sequence, we inserted 'diagnostic' tone sequences between the bias and test so as to measure the effects of the bias tones on cortical responses.

We find that responses co-located in frequency bands activated by the biasing sequence are reduced relative to other regions. This finding agrees with neurophysiological data we have obtained in the ferret auditory cortex (B. Englitz et al. and thus support the hypothesis that suppression and ‘contrast enhancement’ mechanisms underlie the biasing effect.

We further investigated whether temporal coherence contributes to the strength of the bias. To do so, we compared the effectiveness of synchronous versus desynchronized biasing tones in inducing the directional percept of the Shepard pair. While both stimuli individually lead to a biased percept, the synchronous tones had a stronger biasing effect.

In summary, both temporal and spectral properties of the bias seem to determine the efficacy with which it influences the directional percept of the Shepard pair. Since both of these parameters play a role in stream formation, these phenomena may be linked on the level of neuronal mechanisms.
Tu-161 - Predictability of auditory stimulus timing modulates neuromagnetic N1m responses

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To investigate the effect of temporal predictability on the N1m amplitude, auditory evoked magnetic fields (AEFs) were analyzed using a modified paired-stimulus paradigm. The auditory stimulus sequence consisted of repetitive presentation of the identical tones with controlled intervals. Each interval was ordered to configure a paired-paired-tone paradigm, in which the two successive sets of paired tones with the same S1-S2 intervals were paired. The former priming pair (pS1-pS2) and the latter testing pair (tS1-tS2) had the same S1-S2 SOA of either 0.25, 0.5, 1 or 2 s. These paired-tone pairs were presented pseudorandomly at the inter-pair intervals from 2.5 to 3.5 s. The experiment consisted of 3 sessions. In the first session, the subjects were instructed to try to ignore the auditory stimulus by attending to a silent movie. In the second session, every S2 was not triggered automatically and the subjects were instructed to trigger the otherwise-missing S2s by pressing a button and to reproduce SOAs of the previous priming pairs as precisely as possible. In the last session, the subjects were instructed to listen to the same auditory sequence as the first session, predicting the occurrence timing of the S2. The AEFs to each tone were recorded by a 306 channel neuromagnetometer and selectively averaged over 30 times in every session. In the first session, the N1m amplitude of the responses to S2 was significantly reduced than that to S1 in SOA from 0.25 to 1 s in both hemispheres. In the second session, the reduction ratio of tS2/S1 was significantly reduced than that of pS2/pS1 in SOA of 0.25, 0.5, and 2 s only in the right hemisphere. The individual behavioral accuracy of timing reproduction was significantly correlated with the N1m reduction ratio (tS2/S1) in the right hemisphere.

Some neurological disorders are known to affect mental chronometry. The task devised in this study could be a new probe to investigate human timing function.

Tu-162 - Brain dynamics of mild cognitive impairment during face encoding

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Brain oscillations are closely correlated with human information processing and fundamental aspects of cognition. Previous literature shows that due to the relation between brain oscillations and memory processes, spectral dynamics during such tasks are good candidates to study and characterize memory related pathologies. Mild cognitive impairment (MCI), defined as a clinical condition characterized by memory impairment and/or deterioration of additional cognitive domains, is considered a preliminary stage in the dementia process. In consequence, the study of its brain patterns could help to achieve an early diagnosis of Alzheimer Disease. Spectral analyses of spontaneous electroencephalogram (EEG) or magnetoencephalogram (MEG) activity at rest demonstrate that the slowing of oscillatory activity is a prominent functional abnormality in AD. However, neuronal electromagnetic activity during a memory task could provide more reliable information to study cognitive consequences of pathological aging. In order to study memory related brain dynamics of pathological aging, a total of 80 individuals underwent a MEG recording during a face delay match to sample task. The MCI group included 40 participants recruited from the Hospital Clinico San Carlos and from the Memory Decline Prevention Center of Madrid. The healthy aging group included 40 participants recruited from a Day Care Center of Madrid. A time-frequency analysis of the data showed between-group differences in the four frequency bands analyzed (theta, alpha, beta and gamma), indicating malfunctioning in the information transmission in the brain of MCI patients as well as compensatory mechanisms.

Tu-163 - Encoding and retrieval of second language vocabulary

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The subsequent memory paradigm has been used in lexical memory research to examine how the electrophysiological features of encoding are related to subsequent recall, but the characteristics of this process are not yet clear for learners of a second language.
We examined the paired-associate learning of Spanish-Basque translation pairs in a subsequent memory paradigm using magnetoencephalography. Native Spanish-speaking participants (Exp. 1, n=22, Exp. 2, n=5) heard lists of Spanish-Basque noun pairs (Exp. 1) or adjective pairs (Exp. 2) presented in an encoding phase, followed by retrieval practice in an explicit cued-recall phase. The words in the pairs were direct translations, and the entire encoding-retrieval procedure was repeated four times per list for eight lists. The behavioral results for the nouns (Exp. 1) showed that recall for the words in the pairs improved with retrieval practice, as expected, and that recall from the Spanish cue was lower than recall from the Basque cue. An equivalent current dipole model of the mid-latency (400-700 ms) evoked activity to the Spanish probe words in the recall phase showed a larger amplitude response to later-forgotten, compared to later-remembered probes (see figure), suggesting a subsequent ’forgetting’ effect. This effect was present in both the left and right superior temporal sources. The response difference to the words in the encoding phase showed a difference similar to that of the retrieval phase. In contrast to the Spanish probe words, the difference between later-remembered and later-forgotten trials with the Basque cue was greatly reduced, and statistically non-robust. The preliminary results for the adjectives show a more variable response than the first experiment with nouns. The results suggest that the electrophysiological characteristics of L2 subsequent memory are distinct from classical subsequent memory effects, which has been observed mainly in response to native language stimuli.

Tu-164 - Effects of somatic stimulation on working memory function using a dual task paradigm as measured by magnetoencephalography (MEG)

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The effects of somatic stimuli on cognitive function are of increasing interest from theoretical and clinical perspectives. For example, there is a growing literature on the effects of important and salient somatic cues such as pain given pain’s important adaptive function as a signal of potential threat and/or injury (Dick et al., 2008). The importance of somatic cues such as pain is highlighted by the marked impact on human performance, and, thereby, on human performance by disruptive somatic signals. In order to investigate the disruptive effects of somatic cues on cognitive function, the present study was designed with a salient but non-noxious stimulus. We recorded MEG data during a classic Sternberg working memory (WM) task as our primary cognitive task. We used increasing letter set sizes of 2, 5, and 8 letters randomly presented to participants over six blocks. During three of these six WM blocks, a distracter oddball task was included, wherein median nerve stimulation (MNS) was delivered and participants were required to respond to a double stimulus delivered randomly during 20% of trails. Behaviourally, (1) decreased accuracy and longer response latency were associated with longer set sizes and (2) the distractor task significantly disrupted WM function, as shown by increased reaction time. We examined the MEG data for behaviourally relevant changes in cortical oscillatory activity during the memory retention interval between conditions (i.e. set size & distraction).
Frequency-specific changes in MEG beamformer-based source activity occurred between conditions. This research suggests that a salient somatic stimulus interferes with WM function as manifested by functional impairment and changes in brain activity. Our current and next studies involve the use of painful stimuli to examine the disruptive effect of a more biologically relevant stimulus such as acute pain. We will also use this paradigm in a group of individuals who experience chronic pain.

Tu-165 - Gamma-band activity in human prefrontal cortex codes for the number of items maintained during working memory

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The maintenance of information in working memory (WM) is associated with elevated neuronal activity in several areas of the neocortex. Previous work indicates that neural oscillations reflect core properties of cortical networks during WM maintenance, but the functional involvement of distinct frequencies as well as the brain regions underlying WM maintenance remain largely unclear. To address this question, we recorded magnetoencephalography (MEG) during a WM-task in 25 human participants. Using multi-taper spectral analysis and beamforming we found elevated spectral power during the delay period in the gamma band (60-80 Hz) in right parietal and prefrontal cortex (PFC). Spectral changes were also detected at alpha frequencies but did not correlate with WM-load. Finally, we decoded MEG source activity and found that only gamma-band activity in PFC predicted the number of behaviorally relevant items maintained in WM. These results establish a close relation between gamma-band oscillations and WM maintenance in human PFC.

Tu-166 - Is the posterior superior temporal sulcus a critical locus for crossmodal integration?

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Crossmodal integration of auditory and visual stimuli is an important component of perception, with the posterior superior temporal sulcus (pSTS) hypothesized to support this. To test this prediction, we had subjects (N=13) learn 12 abstract, non-linguistic pairs of auditory and visual stimuli over 4 weeks. These paired associates were of four types: auditory-visual (AV), auditory-auditory (AA), visual-auditory (VA), and visual-visual (VV). At week four, subjects were scanned using magnetoencephalography (MEG) while performing a correct/incorrect judgment on pairs of items. During scanning, subjects were first presented with a learned auditory or visual stimulus (S1), followed by a delay period, then the simultaneous presentation of an auditory and visual stimulus (S2). MEG data were recorded at a 600 Hz sampling rate, using a 275-channel whole-head MEG system. Using a new implementation of synthetic aperture magnetometry (SAMspm), a minimum variance beamformer that computes real statistics across trials, we directly contrasted crossmodal (AV and VA) with unimodal (AA and VV) pairs from S2 onset for 2 seconds. Comparisons were made in theta (4-8 Hz), alpha (9-15 Hz), beta (16-30 Hz), and gamma (31-50 Hz) frequencies. We found pSTS showed a significant group-level difference in the beta frequency, with greater desynchronization for crossmodal compared with unimodal trials. We then used a sliding window technique to assess the timing of differences in pSTS in the beta frequency. This analysis showed that the pSTS difference began at ~ 250 – 750ms after S2 onset. Finally, we directly contrasted all paired associate types from S2 onset to 2 s. This analysis showed that the difference in pSTS was a consequence of an auditory stimulus present within a pair. Our findings thus suggest that pSTS is not simply integrating crossmodal stimuli, but rather pSTS appears to be involved in the storage and/or retrieval of dynamic, auditory stimuli.

Tu-167 - A comparison of brain networks identified using fMRI and MEG during an N-back working memory task

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Introduction: In the past decade, BOLD fMRI has revealed a number of networks involved in sensory and cognitive processing (1). However, BOLD is an indirect measure of brain activity and it is desirable to gain complementary electrophysiological information. Here we use an N-back working memory paradigm to induce changes in network activity. We apply independent component analysis (ICA) to fMRI and MEG data to independently define haemodynamic and electrophysiological networks.

Methods: The task comprised 4 phases: 0, 1, 2, 3-back and rest. During N-back phase’s letters were presented every 2s and subjects...
responded when the letter matched that presented N letters previously. Each phase lasted 33s. 10 trials were collected in fMRI and 12 in MEG. BOLD data were acquired using a 7T scanner, MEG data were acquired using a 275 channel system.

BOLD data were motion corrected, spatially smoothed (4mm), co-registered to standard space and group-level spatial ICA was performed using MELODIC. MEG data were frequency filtered ($\delta, \beta, \alpha, \gamma$ bands) and projected into source space using a beamformer. The Hilbert envelope of voxel timecourses was derived and temporally smoothed (2s). Data were concatenated across subjects and analysed using temporal ICA within frequency bands, a second level ICA was then used to collapse components across bands.

Results: Plausible physiological networks were identified using both modalities, 6 MEG networks and their closest matching fMRI networks are shown in figure 1. In some cases a single fMRI network is split into multiple MEG components, in other cases a single MEG network is split across multiple MR components.

Discussion: This work shows that task positive networks can be identified using ICA in fMRI and MEG that agree spatially across modalities. Results confirm a neural oscillatory basis to haemodynamic networks and MEG offers a means to study network dynamics with high temporal precision.

References: 1 Smith et al, 2001 PNAS 106

![Figure 1: MEG and fMRI networks.](image)

**Tu-168 - Decrease of processing speed due to switching between tasks**

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When an individual needs to switch between cognitive tasks, a so-called task switching cost is observed as a decrease in task performance speed and/or accuracy. In a typical task switching experiment, the action required to a similar visual stimulus, e.g., a letter and a number appearing on the screen, is systematically alternating between pressing buttons twice to determine whether the letter is a consonant or a vowel, and thereafter twice to determine whether the number is odd or even. In our modified version, the alternation between the tasks is not systematic, but comes to the subject as a surprise since the same task is randomly repeated 0 to 7 times before the task is switched. Such a modification is attempting to mimic more naturalistic conditions.

We recorded MEG with the Vectorview MEG device from 9 subjects in the modified task switching experiment. As a response to the visual stimulus presented on the screen we could observe, in addition to typical visual responses, responses related to the attentive actions to perform the task. These responses were observed to appear similar to the P300 responses in their latency and amplitude. In the task-related responses, a decrease in the latency and an increase in the amplitude was observed after the switching of the task compared to the same stimuli when the task was not switched.

These results show the brain processes related to the attentive demands caused by the switching of the task. In addition, these results highlight the causes of the behavioural consequences of task switching.

**Tu-169 - Theta Oscillatory Synchrony and Cross-Frequency Coupling Coordinate Spatial Memory Retrieval**

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Numerous rodent electrophysiology studies indicate that hippocampal theta oscillations play a key role in spatial memory. Interestingly, synchrony with theta in the medial prefrontal cortex (mPFC) has also been observed during spatial memory retrieval. Furthermore, recent models have examined the role of cross-frequency interactions between hippocampal theta phase and high frequency cortical gamma amplitude in mnemonic function. Based on this work, we investigated inter-regional theta synchrony and theta-gamma cross-frequency coupling when participants were coordinating the retrieval of spatial memories prior to making their
response. We used MEG recordings from healthy volunteers performing a virtual reality spatial navigation task in which they learned object locations. We specifically focused on cued retrieval of an object’s location prior to navigation. Using the LCMV beamformer source reconstruction technique, we examined power changes between this cue period and baseline, identifying peaks in mPFC in the theta band (4-8Hz, $P<0.05$ FWE) and in visual and posterior cingulate cortex (PCC) in the gamma band (65-85Hz, $P<0.05$ FWE).

We then analysed theta phase-lag index (PLI) in source space, using the mPFC as the seed. We found increased theta synchrony between mPFC and right anterior Medial Temporal Lobe (aMTL) during the cue period compared to baseline. When testing coupling between mPFC/right aMTL theta phase and the envelope of gamma power in source space, we found significant effects in PCC and dorsolateral prefrontal cortex. This evidence indicates that theta phase in key regions associated with spatial and episodic memory exhibits long range coupling effects during the coordination of retrieval of learned spatial representations.

Tu-170 - High-frequency neural oscillations in visual working memory: insights from MEG and PET-flumazenil data

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High-frequency oscillations in the so called gamma-band have been demonstrated to form a fundamental neural mechanism involved in both primary sensory and high-level cognitive processes. Recent studies have also shown that at least in the visual cortex, the frequency of gamma-oscillations depends on the concentration of GABA (1), the main inhibitory neurotransmitter in the human brain. Furthermore, in the motor cortex, injection of diazepam, a GABA-A-modulatory agent, has been shown to affect the level of rhythmic activity in the beta-band (2).

In this study, we investigated the relationships between oscillatory activity (determined with magnetoencephalography, MEG) and GABA-A-receptor density (determined from positron emission tomography, PET, flumazenil data). MEG and PET data were collected in 10 subjects, the flumazenil uptake recordings were conducted during resting condition, and MEG data were collected during a visual working memory task (0-, 1-, 2-, and 3-back tasks for visually presented letters). Functional magnetic resonance imaging (fMRI) data of the same experiment has also been collected from the same 10 subjects.

The predominant effect of the working memory task on oscillatory activity was an increase of neural activity in the 60-90 Hz range, relative to the baseline time-window and also as a function of the memory load, in particular, effects of the memory load were detected in the occipital, parietal, and medial prefrontal cortex. Preliminary results also suggest that in the occipital cortex the peak frequency of the gamma-band activity during the working memory tasks is negatively correlated with the PET-flumazenil estimates, akin to the findings from GABA-concentration studies in the primary visual cortex, the data also indicate that the amplitude of the gamma-band activity at the peak frequency is positively correlated with the GABA-A-receptor density.

(1) Muthukumaraswamy et al, PNAS 106, 2009
(2) Hall et al, Neuroimage 56, 2011

Brain areas showing a monotonic increase (yellow) or decrease (blue) of 60-90 Hz neural activity at 300-500 ms post-stimulus as a function of memory load (Friedman test, 1-, 2- and 3-back tasks, $p<0.05$ uncorrected).
Tu-171 - Neural dynamics associated with semantic and episodic memory deficit in Alzheimer’s disease: evidence from MEG

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Episodic memory deficits without comparable semantic impairments are commonly observed in the early stage of Alzheimer’s disease (AD). Furthermore, episodic memory performance in AD depends on preserved semantic memory abilities, supporting a hierarchical model of human memory. Here we used magnetoencephalography (MEG) to investigate the brain substrates of episodic memory for faces of different semantic status (famous / unknown) in a group of mild AD patients and matched normal controls. Eleven AD patients and eleven healthy control subjects participated in a memory task comprising two phases: i) during encoding, 56 faces (28 famous and 28 unknown) were presented in a famous / unknown semantic decision task, ii) during recognition, the 56 old (studied) faces and 56 paired new faces were presented in an old / new episodic decision task.

Overall patients showed reduced magnetic activity compared to normal controls. During the semantic task controls exhibited differentiated event-related fields (ERFs) in response to famous faces and unknown faces over temporal sensors, in contrast AD patients showed an early atypical activity over fronto-temporal sensors from about 350 ms (p < .05). During the episodic task, the controls showed a differentiated old/new effect for famous and unknown faces: the old/new effect culminated over temporal sensors for the famous faces and was restricted to left parieto-occipital sensors for the unknown faces. In contrast, in AD patients, the old/new effect showed a frontal distribution for the famous faces, which could reflect familiarity-based judgments, and an occipital focus for the unknown faces. Moreover preliminary results of source localization for the control group revealed a stronger hippocampus activation for the episodic compared to the semantic task. Altogether, these findings suggest a functional reorganization of neural dynamics associated with memory impairment in AD.

Tu-172 - Network analysis based on graph filtration during working memory maintenance

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Recently, a novel network approach using graph filtration was introduced (Lee et al., 2011). In this method, connected structure was defined by single linkage distance (SLD). Here, we aimed to investigate the differences in connected structure between the delay and the baseline periods during working memory task.

The data were obtained during visuospatial delayed-match-to-sample task using a whole-head Neuromag 306 channels. In our previous study, time-frequency was performed for alpha, beta and gamma frequency bands and 17 sources were defined using beam-forming technique when compared the delay and the baseline periods (Park et al., 2012). For network analysis, the single trial power values were extracted from the 17 regions of interest (ROIs) in the delay and baseline conditions. Then, the correlation between frequency bands power in each source was calculated at individual level. After computing distance matrix by 1-correlation, SLD was calculated on all pairs of ROIs based on cost-minimizing path. For group level statistics of SLD between the conditions, the distance was transformed to z value and paired t-test was performed. The significant differences were identified at p < 0.05 by 5000 permutation tests.

The left superior frontal gyrus (SFG) in the alpha band showed significant correlation with other sources in the same band (alpha) and beta band during the delay period whereas right lingual gyrus (LG) in the gamma band showed significant correlation with the posterior sources in the alpha band during the baseline period.

We examined the network structure with power values of frequency bands in source space during the working memory maintenance using a novel network approach which is called graph filtration. As in the previous report using resting PET data from clinical populations (Lee et al., 2011), we suggest that this new method could be useful for revealing functional network characteristics during cognitive processing using MEG data as well.
Oscillatory brain activity has been implicated in cognitive processing. While previous research has shown the importance of alpha (8-13 Hz) and gamma (30-100 Hz) oscillations for working memory capacity (Sauseng et al. 2009 Curr. Biol.) the specific roles of these rhythms remain to be further elucidated. One possible hypothesis is that information is gated by top-down controlled alpha activity, whereas bottom-up processing is reflected in the gamma band. We measured oscillatory magnetic activity with MEG during a visuo-spatial working memory task. Participants had to allocate their attention covertly to the left or the right visual hemifield according to a cue (1.5 s) before an array with colored dots (load individually adjusted to achieve an accuracy of 75%) appeared briefly (100 ms). Subjects had to retain the attended array (1.5 s) until probed by a second array (2 s). In our preliminary analysis, we observed a sustained hemispheric alpha lateralization during the spatial cueing and delay interval. The alpha activity decreased in the hemisphere contralateral to the cue, while it increased relatively in the ipsilateral hemisphere. In addition we observed a clear stimulus driven gamma band activity in response to the memory and probe arrays. These data suggests that the alpha oscillations reflect top-down cognitive control: alpha increases and decreases reflect respectively inhibition and release from inhibition. Gamma oscillations on the other hand reflect bottom-up processing of the stimulus sample encoding and probe comparison. To identify the involvement of GABAergic interneurons responsible for producing these effects we are currently investigating how the alpha and gamma activity in this task is modulated by the benzodiazepine lorazepam.
Figure A) Modulation Index of alpha power (8-13Hz) defined as Attention left visual hemifield - Attention right visual hemifield condition divided by the sum of both. Left column, Time-frequency plot of left sensors of Alpha Modulation Index (AMI).

Tu-174 - Object naming in a foreign language: a pre/post MEG study of language learning

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Neuroimaging studies of word learning have focused on single-session paradigms and found MEG changes in frontal and temporal language areas as well as in rolandic areas (Veroude et al., 2010). We used MEG to examine receptive and expressive language changes in cortical representation for newly learnt vocabulary before and after a multi-day training protocol. 14 adult native English speakers (mean=27.9yrs,7F), who were naïve to Romanian, participated. Prior to training, subjects completed 2 conditions as baseline in the MEG: 1) subjects were shown pictures and asked to name objects in English, and 2) subjects completed a forced-choice picture matching task to auditory words presented in English or Romanian. Subjects then completed an interactive computer training program over 2-weeks where they were taught to name 50 objects in Romanian. Subjects returned for a second MEG session and completed the same tasks. The only exception was that the naming task was completed in both English and Romanian. Behavioural data showed significant improvements in Romanian on measures of accuracy, reaction time and fluency. MEG data were processed using a beamformer algorithm. Contrasts between pre- and post-training in Romanian revealed significant changes in rolandic areas controlling the oromotor structures, suggesting improved fluency. Contrasts between post-training English and Romanian on the word recognition task identified greater activity in left inferior frontal gyrus (BA47) for English. Contrasts between post-training English and Romanian word production identified greater activity in Wernicke’s area (BA 40) for English. These results suggest that new word learning builds on the neural network for native language representation on the brain, with activation in classic language areas increasing with greater language proficiency. This study presents a unique picture of the neurological bases of word comprehension and production for newly learnt words in a foreign language.

Tu-175 - Memory load and auditory signal degradation elicit enhanced alpha power: an MEG study

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Over the last decades, alpha oscillations (~ 8 – 13Hz) are not considered an ‘idling’ state any longer but are assumed to serve a role in cognitive processes, such as functional inhibition. In line with these predictions, alpha power is enhanced during tasks with higher memory load. We hypothesized that alpha enhancement is a more general mechanism also observable for other challenges such as perceptual uncertainty, e.g. when processing degraded speech. In an auditory Sternberg paradigm, we therefore parametrically varied memory load (set size of 2, 4, or 6 auditorily presented digits) and signal degradation (noise-vocoding in 16, 8, or 4 bands). Subjects had to memorize the digits for about two seconds. We analyzed magnetoencephalographic gradiometer data from sixteen subjects by conducting a time-frequency analysis, wavelet convolution, time-frequency-channel cluster statistics, followed by beamformer source localisation.

During the retention interval, a significant alpha enhancement at centro-parietal sensors was found, in two main effects of set size
(more memory load) and of degradation (worse signal quality). Alpha enhancement during retention was positively correlated with the reaction time observed in response to the ensuing probe digit. Source projection of the overall alpha power during retention indicated a right-hemispheric parietal origin. More specifically, however, parametric group statistics on the source reconstructions showed that the anterior cingulate cortex activity increased monotonically with set size, while the posterior cingulate cortex activity increased monotonically with degradation.

In sum, our results suggest a separation of load-specific from more unspecific alpha-band effects in response to the challenges in adverse listening. This bears relevance to the aging and hearing-impaired brain and provides a general metric for effortful listening.

**Tu-176 - Atypical network oscillation dynamics in very preterm children during visual short-term memory processing**


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Children born very preterm (≤32 weeks) display selective cognitive difficulties in domains such as visual spatial processing and executive functions, even in the absence of major neurological or intellectual impairment. The alterations in functional brain activity underlying such problems remain unclear. We have previously reported altered spontaneous oscillatory brain activity, as well as oscillatory synchronization among brain regions in very preterm children.

We used MEG imaging to investigate oscillatory changes in functional brain networks during visual short-term memory processing in school-age children born very preterm. MEG was recorded using a 151-channel whole-head CTF system from 27 very preterm children (7.7 years, 19 females) and 27 full-term controls (7.7, 17 females) during the performance of a visual short-term memory (STM) task. Children with neurological or major sensory/motor/cognitive impairment or current medications were excluded from analysis. Dual state beamformer was employed to identify changes in brain activity in theta, alpha, beta and gamma frequency ranges. Time-frequency analysis of the signals originating in locations with the strongest activations or showing most significant differences between the groups was performed (Fig. 1).

STM processing involves oscillatory changes within a distributed cortical network. Very preterm children exhibit altered recruitment within several regions. Specifically, visual areas indicate an increase in alpha-desynchronization, together with an increase in early theta activity and in gamma band frequencies. Frontal cortex including L-R-medial frontal regions also express atypical oscillatory responses.

Very preterm children without major brain injuries exhibit altered recruitment of oscillatory network dynamics during visual STM processing, further suggesting a reorganization and compensation of cortical networks underlying cognition.

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Tu-177 - Functional connectivity between bilateral premotor cortices during phonological working-memory task

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Using MEG we studied functional connectivity within the premotor cortices during phonological working-memory task. Six subjects participated in the experiment and their neuronal activity was measured by a 306-channel MEG system (Vectorview, Elekta Neuromag). We used a modified version of the visual Sternberg paradigm as a working memory task. We analyzed alpha band activity in the maintenance period, in which subjects had to memorize sequentially-presented 8 alphabets. We estimated functional connectivity by following three steps. First, we used the minimum variance beamformer to determine the distribution of the equivalent current sources. Second, we applied a hierarchical grouping method with Mojena’s stopping rule to the estimated sources in order to statistically decide the number of regions of the interest (ROI). We defined the center of the ROI to be the mesh point with the largest moment amplitude. Third, we determined the connectivity between sources at the centers of ROIs by means of Granger causality.

The average number of estimated ROIs was 6.72 for each trial. Most of the ROIs were localized in the bilateral prefrontal area, mostly in the premotor area (Brodmann area 6 (BA 6)) as well as in the dorsolateral prefrontal area (BA 9) and the frontal eye field (BA 8). The center of ROIs were localized in the BA 6 of the right and left hemisphere in 74% and 67% of all trials, respectively. Among the 35% of trials in which we observed the simultaneous activation in the BA 6 of both hemispheres, 77% of the trials showed connection between them. Although previous research has shown that phonological working-memory is maintained within the left premotor cortex, Broca’s area, and temporoparietal cortex, our results suggested that the neural network, processing the phonological working memory, occasionally requires coordinated activity between the bilateral premotor cortices.

Tu-178 - Serial memory scanning regardless of the memory set presentation type during the Sternberg task : a preliminary study using fMRI and MEG integrated analysis.

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Previous EEG/MEG studies with the Sternberg memory scanning task have revealed the serial memory scanning process independent of what to be memorized. Present study posed a question if how to be memorized affected the memory process. We explored the first time the cortical activities during the two types of Sternberg task differ in memory set presentation types (simultaneous and successive), using fMRI-MEG integrated analysis. fMRI data were collected with an 1.5T MRI system (TOSHIBA Vantage) on the basis of event-related paradigm during the Sternberg task. Magnetoencephalographic responses were recorded using 306 ch Elekta Neuromag system (Electa oy) from eight healthy adults while performing the two types of Sternberg memory task. In the successive presentation, 3/5 digits were presented one by one (Memory 3/5). On the other hand, 3/5 digits were presented all at once in the simultaneous presentation. Two control conditions (Control 3/5), in which all the digits presented were same (i.e. 6/6/6) were set. Memory maintenance phase was 300 ms before the memory set to 1000 ms after it. Memory retrieval phase was 300 ms before the test item to 1000 ms. Event related Fields (ERFs) were obtained from the Root Sum Square (RSS) of each pair of gradiometers. Epochs were averaged for each phase and conditions. The fMRI result indicated two cortical areas, frontal area and posterior cingulated during the memory retrieval (p < 0.0001 uncorrected). MEG sensor space analysis revealed a significant activity peaking at the parietal area approximately 300 ms after the test item for both memory set presentation types. Although as a preliminary result, the linearly constrained minimum variance beamforming (LCMV) utilizing the fMRI result revealed dynamic transition of memory process from the encoding phase that is sensitive to the factor of stimulus input to the retrieval which was restored to the intrinsic sequential process that the Sternberg task essentially required.

Tu-179 - Time-on-task effect on workload level discriminability through electroencephalography

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Passive brain-computer interfaces (BCIs) allow one to monitor cognitive state, such as levels of workload or alertness, using as input an operator’s brain waves recorded through electroencephalography (EEG). Previous studies showed that the power of theta and delta bands at frontal sites increases with load, while the power of the alpha band at parietal sites decreases (Schober et al., 1995). When time-on-task increases, the power of low frequency (LF) bands increases as well, while the power of high frequency bands decreases (Klimesch, 1999). However, to this day, no study has evaluated the interaction of those factors at the electrophysiological level. Yet, this interaction might prevent from clearly distinguishing load levels and thus reduce classification accuracy. This study was designed to assess and characterize load and alertness levels, as well as their interaction, by using EEG power spectral density (PSD) measures. Load was manipulated using a modified Sternberg paradigm (Sternberg, 1966) in which 20 participants encoded 2
or 6 digits and responded to a probe. Alertness varied with time-on-task. Participants’ reaction times (RTs) and PSD of 7 frequency bands (delta, theta, alpha, low alpha, high alpha, beta and gamma) were evaluated using variance analyses. Preliminary results are in keeping with the literature for each factor’s effect. As regards their interaction, in the alert condition, PSD of the delta, alpha, and beta frequency bands at parietal and frontal sites significantly decreased with load, which made the load levels easy to distinguish. While in the low alertness condition, no significant change was observed between load levels, but for a decrement with load in the alpha band at parietal sites. Those results suggest that a low alertness reduces the discriminability of load levels through EEG. Passive BCIs that would take this interaction into account could adjust their parameters accordingly and increase their classification performances.

**Tu-180 - Context overlap between study and test reverses theta oscillatory subsequent memory effects**

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Successful remembering depends on the overlap of the contextual features between study and test. If a retrieval cue matches contextual features of the originally encoded episode, memory performance is higher than if the contextual features do not match. This encoding specificity principle has been proposed more than 40 years ago but no study has yet investigated the brain oscillatory underpinnings of this effect. Here we directly tested the encoding specificity principle by manipulating the overlap of contextual features during encoding and retrieval. Participants encoded words superimposed on short movies while MEG was recorded. During recognition testing, words were either presented in the same or in a different context. Following previous studies, suggesting that theta oscillations mediate item-context binding, we hypothesized that high theta power and high theta phase coherence during encoding would be beneficial for retrieval if encoding and retrieval contexts matched. The opposite pattern was expected if the contexts did not match, as strong item-context binding should impede retrieval of items which are presented in a different context. Confirming the encoding specificity principle, memory performance was enhanced if the contexts of encoding and retrieval matched. Furthermore, high theta power during encoding was either beneficial or detrimental for memory retrieval, depending on whether the encoding and retrieval contexts matched. Estimating the sources of these effects a large scale network was identified, including medial temporal lobe regions. Moreover, theta-phase to gamma-amplitude cross-frequency coupling in the prefrontal cortex was also modulated by the context match. These results confirm, for the first time, the existence of the encoding specificity principle using brain oscillations.

**Tu-181 - Modality-specific reactivation of visual and auditory processes during episodic memory retrieval.**

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**Purpose**

To reveal the effect of reactivation on episodic memory retrieval, this study examined temporal dynamics of modality-specific reactivation in the visual and auditory cortices during the presentation of recognition items in the recognition judgment task using magnetoencephalography (MEG).

**Method**

Nine right-handed healthy young adults (4 males and 5 females, 27 years old) participated in the experiment. The experiment consisted of word encoding phase and recognition phases, where 3 encoding conditions were considered: (a) encoding words were presented with related pictures (visual condition), (b) encoding words were presented with related sounds (auditory condition), and (c) only encoding words were presented (word condition). Recognition test was conducted in the MEG scanner 15 minutes after the completion of encoding phase. After the recognition test, source recognition of encoding words was conducted, in which participants were required to choose whether each recognition word was not presented or presented with which information in the encoding phase.

**Results**

The recognition test revealed that test performance in the auditory condition was higher than that in the word condition. The source recognition test showed superior performance in both the visual and the auditory conditions compared to the word condition. The equivalent current dipoles (ECDs) analysis of MEG data indicated that ECDs amplitudes in the right fusiform gyrus in the visual condition and those in the superior temporal auditory cortices in the auditory condition 450-550ms after the onset of the recognition stimuli.

**Conclusion**

This study confirmed the modality-specific reactivation of visual and auditory information presented with encoding words using MEG. Thus, Reactivation of visual and auditory information during recognition binds language with modality-specific information, suggesting that reactivation enhanced source memory judgement.
Tu-182 - Desynchronization of alpha-band rhythm corresponding to primary and recency effects in a sequential short-term memory task

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We used a sequential short-term memory task to clarify the relationship between alpha-band modulation and retrieving memory. MEG signals were recorded with a 76-ch helmet system from 10 healthy volunteers. As a memory task, seven arrow images were sequentially presented with durations and intervals of 100 and 500 ms, respectively. Afterwards, a retrieving number (1-7) was presented (e.g., '2'). Each participant memorized the order of the presented arrow directions (left, right, top or bottom) and answered the direction that was presented in the order indicated by the retrieving number (i.e., second order) by pressing a button. Envelopes of the spontaneous rhythm with the 8-13 Hz band of each channel were averaged according to answering condition (correct/incorrect) or the retrieving number (1-7). The envelopes were further averaged over 4 channels in appropriate areas: frontal region, motor area, and parietal region.

The accuracy rate of answers was 73% on average. The accuracy rate and response time demonstrated clear primary and recency effects, that is, higher accuracy rate and shorter response time were obtained at the beginning (1) and ending (7) parts of the sequence of arrow images. The amplitude of the alpha-band rhythm rose and fell in accordance with arrow presentation and interval. After presenting the retrieving number, the amplitudes dramatically decreased and were minimized at about 500 ms after the onset. The reductions of amplitude were significantly greater for correct answers than incorrect answers in the motor area and parietal region. Furthermore, primary and recency effects appeared in the amplitude as well in the right frontal region. The cross correlation coefficients of the amplitudes were 0.9 to response time and -0.82 to accuracy rate.

The results suggested that amplitude of the alpha-band rhythm, especially in the right frontal region, can be modulated by retrieving short-term memory.

Figure. (Upper) primary and recency effects shown in relationship between accuracy rate and retrieving number. (Lower) Corresponding amplitude modulation of alpha rhythm over right frontal region. Cross correlation coefficient is -0.82. Mean, n=10.
Tu-183 - Acoustic textures improve motion discrimination: indexing metamodal plasticity with MEG

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The functional specificity of sensory cortices has recently been questioned and proposed to be metamodal, namely able to operate irrespective of the sensory modality of input. For instance hMT+/V5, a well known area specialized in the computations of visual motion can be recruited for the analysis of auditory and tactile motion in blind individuals. In non sensory-impaired individuals, it has been reported that auditory events improve the discrimination of visual motion, however, no neurophysiological correlates have yet been put forward to explain such cross-sensory enhanced learning. Here, we asked whether auditory information functionally affects visual plasticity in non sensory-impaired participants. Participants were trained to discriminate a coherent population of visual dots among an incoherent one. Stimuli consisted of two equiluminant colored populations (red and green) displayed as Random Dot Kinematograms (RDK). The MEG experiment consisted in a pre- and post-test with four blocks of individually adjusted trainings in-between. Two groups of participants took part in the study: one trained visually (V), the other audiovisually (AV). During the AV training, subjects heard acoustic textures correlated to the RDK, they were unattended and orthogonal to the task. AV trained participants significantly outperformed the V trained group. The RMS of visual evoked-related fields in both groups was positively correlated with the degree of RDK coherence. However, topographical results suggest the implication of a more complex network underlying the learning in AV than in V, likely at the origin of superior learning in AV. To specifically address this observation, source analysis was conducted with MNE. The degree of coherence of target in RDK was clearly discernable in hMT+/V5 but differential so in both groups, preliminary data also suggest that differences between the V and AV groups affect other areas including the Superior Temporal Sulcus (STS) and V4.

Tu-1 - Assessment of Hippocampal Source Localization with DBA Model Using Noise Normalized Minimum Norm Estimates: a MEG study

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In this study, we quantify our ability to reconstruct subcortical activity using realistic Monte Carlo simulations applied to the imaging model of deep brain sources called Deep Brain Activity (DBA) (1). Particularly, we quantify the distortion of point source reconstruction in the hippocampus, i.e. the point-spread functions (PSF) and the Dipole Localization Error (DLE), using the wMNE, dSPM ad sLORETA inverse operators. Forward solution and inverse operators were computed thanks to Brainstorm software (2) on a 151-channels CTF system. DLE was defined as the Euclidian distance of a solution’s gravity center to the true location. The top left corner of the figure (black box) shows DLE’s spatial distribution map (in mm) on the left hippocampal surface for wMNE inverse operators. This map has a small localization error on most of the surface. Errors are mainly in the range of 0.5 cm to 2 cm. The map shows higher errors at the hippocampus edges. Three sources were tested for the PSF in the left hippocampus, one in the head, one in the body and one in the tail (see the three white boxes using the centered colormap). Anterior’s and body’s sources are well localized by wMNE with a small DLE. However, DLE is stronger in the tail and the spatial dispersion is stronger in the body and the tail sources. Indeed, for both sources the distribution has a large dispersion toward the medial and lateral temporal lobe near the actual sources. The distribution also extends in basal ganglia near the actual sources, for example in the case of the tail’s source the distribution extends in the pulvinar. We have also performed this assessment for the 306-channels Elekta system. Results are similar with less spatial dispersion especially in other deep sources.

(1) Attal et al. 2009, Modeling and Detecting Deep Brain Activity with MEG and EEG, IRBM ISSN
(2) Tadel et al. 2011, Brainstorm: A User-Friendly Application for MEG/EEG Analysis, Computational Intelligence and Neuroscience
Black box: DLEůι spatial distribution map (in mm) on the left hippocampal surface for wMNE inverse operators. White boxes:

Three sources were tested for the PSF in the left hippocampus, one in the head, one in the body and one in the tail

Tu-2 - Localization of ictal events recorded in MEG with beamforming techniques

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Background:
Recording and analysis of interictal activity with MEG has been proven to be efficient in the presurgical investigation of epileptic patient. Because of constraints such as immobility MEG is not the technic of choice for the recording of ictal activity. However ictal events can incidentally be recorded during MEG investigations. In these cases source localization could provide important information on the epileptogenic zone. However, the standard ‘equivalent current dipole’ (ECD) may not be the most practical technique for localizing the origin of this activity.

Aims:
We propose to evaluate BeamForming techniques in the temporal domain (LCMV) as well as frequency domain (DICS) for the localization of ictal events recorded with MEG.

Material and methods:
MEG ictal recordings were obtained for 6 patients with pharmacoresistant partial epilepsy, using a whole head, 248-channel biomagnetometer system (4D Neuroimaging). Three of them were in presurgical evaluation for surgery. For 3 other patients, MEG seizures were recorded after a first epilepsy surgery. Different localization strategies have been applied. The results of the localizations have been compared with intracerebral SEEG recordings. LCMV has been applied with various baselines and time window of analysis. Frequency localization has been performed after time/frequency analysis of the signal.

Results and conclusion:
Beamforming techniques have been able to localize the ictal activity where the ECD technique failed. In all patients but one localizations were in agreement with the information obtained from SEEG recordings.
Typically, Magnetoencephalography (MEG) is used to convert non-invasive measurement of magnetic fields outside the head to current flow estimates in the human brain. This is an ill-posed inverse problem and prior information including an underlying model of source activity, is required to solve it. One way to quantify the model suitability is to evaluate the marginal likelihood (or evidence) for this model by integrating over all possible parameter values (current distributions), this rewards data fit but penalises large parameter ranges (or complexity). This model evidence can be used to compare competing models but provides no quantification of how far the best solution is from reality. In this work we use the MSP (1) algorithm in which the model is a sparse set of regions of active cortex. We try to explain the same MEG data using a range of models in which the cortical surface (and hence the lead field structure) is expressed using progressively higher spatial resolution harmonic basis functions. This provides an anatomical calibration or ground truth for the model evidence. For example, in the case where the assumptions behind the inversion are nonsensical (or there is only sensor noise, see below), one expects no significant difference between the evidence for a surface shaped like a brain and one shaped like a rugby ball. However, if MEG data can be explained by cortical current flow then more anatomically accurate models should have higher marginal likelihood (as approximated by the negative free energy). Figure shows evidence for reconstructions of current distributions consisting of 2 (green triangles), 4 (blue squares) and zero (red circles) simulated sources on the true cortical surface. The saturation points of these curves give a measure of the spatial resolution of the reconstruction.

Change in log model evidence as a function of the number of spherical harmonics used to represent the cortical surface.

Tu-4 - Special Finite Elements for Dipole Modelling

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The paper focuses on the solution of the EEG forward problem, using the finite element method. The goal is to compare different dipole models for a current source in the human head, with a focus on Whitney type basis functions. For the current sources in the head a widely used model is the mathematical or current dipole. Its strong singularity poses a problem for numerical methods. Therefore we investigate a less singular dipole model based on Whitney forms. In the first part of the thesis we give an overview of the EEG forward problem and the theory behind Whitney elements. Then we investigate methods for representing a mathematical dipole in Whitney formulation, in order to validate the Whitney approach. The following comparison of the available models on tetrahedral and hexahedral meshes shows, that the Whitney model achieves the highest accuracy if the local mesh geometry can represent the dipole moment well. Otherwise interpolation techniques have to be used, which worsen the accuracy, making the Whitney approach inferior to the other methods in the general case. The attached figure shows the RDM error for different dipole models at various eccentricities without dipole moment interpolation.
Tu-5 - The need of accurate modeling in simultaneous ECoG and E/MEG studies

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Electrocorticography (ECoG) is a technique that allows to study the electrical brain activity invasively. This is done by introducing a silastic grid on the brain cortex that allows to record EEG signals without being affected by the skull. It is generally considered in presurgical evaluations due to its capability for locating the epileptogenic zone and testing the brain functions involved.

The implantation of the grid allows researchers to study the brain function and the influence of the skull in noninvasive methods. The latter aims to test the sensitivity of extracranial recording modalities for epileptic spikes in different cerebral regions, characterizing the cortical area, synchrony, and amplitude required to generate the events that are recordable noninvasively by MEG and scalp EEG. This is usually done by comparing the amplitude of simultaneous recordings, implicitly assuming that the variations in the model due to the grid implantation do not affect the noninvasive recordings. This assumption may lead to erroneous results, since the non-conducting nature of the grid and the holes in the skull may change the electric potential and current density distributions.

We analyze the influence of the grid and the holes in the skull in simultaneous ECoG and E/MEG recordings considering a realistic model taken from a patient with focal-cortical dysplasia of the frontal lobe. By means of the finite element method and considering anatomically constrained sources we solve the E/MEG forward problem and compare the results with simplified models where the grid and/or holes are not taken into account. This allows to assess their influence and evaluate the need for their inclusion in the model.

Results show that the magnitude of the EEG signals in some situations changes drastically, while the MEG signal is less affected. However, accurate models including the grid and holes must be adopted if the inverse problem is to be solved with simultaneous MEG and ECoG recordings.

Tu-6 - Multimodal EEG/MEG fusion within the Maximum Entropy on the Mean (MEM) framework

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Many studies have suggested that for an epileptic discharge to be detectable on the scalp by ElectroEncephalography (EEG) or MagnetoEncephalography (MEG), spontaneous epileptic discharges should involve a spatially extended area of the cortex (several cm\textsuperscript{2}). Source localization using Maximum Entropy on the Mean (MEM) has demonstrated good sensitivity to recover the spatial extent of the sources $s = 3 \text{ to } 30\text{cm}^2$, when using EEG only (Grova et al. NeuroImage 2006) or MEG only (Lina et al. IEEE TBME in press). Symmetrical fusion of EEG and MEG data exploits their complementarities to increase spatial accuracy of the
The aim of the present work is to evaluate the performance of a MEM-based MEG/EEG symmetrical fusion. Within the MEM framework, the proposed fusion strategy relies on a model of cortical parcelling (Lapalme et al. NeuroImage 2006) that combines the probable contribution of each cortical source to either EEG or MEG data. Using realistic simulations of spatially extended sources, we compared the performance of MEM when localizing EEG only, MEG only and multimodal MEG+EEG (MEEG) for both deep and superficial sources (Fig1.c). The visual assessment (Fig1. d) of the source localization shows a good fusion of the EEG and MEG source in the MEEG source localization. The result shows a significant improvement in the spatial accuracy with MEEG source localization.

![Figure 1](image)

**Tu-7 - Domain Decomposition to handle versatile conductivity models**

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Source localization from external data such EEG or MEG, requires a good understanding of the electromagnetic behavior of the patient head. Several models can be used, representing more or less complex geometrical shapes, and conductivity profiles. Different numerical methods allow to cope with different types of models: the Finite Element Method (FEM) can handle very general conductivity models, whereas the Boundary Element Method (BEM) is limited to piecewise constant conductivity. On the other hand, it is easier with BEM than with FEM to accurately represent sources in isotropic media. Thanks to domain decomposition, we propose to independently use BEM or FEM in different sub-domains. In the EEG forward problem considered, the BEM is limited to the domain containing sources (the brain) while the other tissues are handled with the FEM. This leads to an accurate description of the sources while allowing for inhomogeneous and anisotropic conductivity. The coupled method is first validated against analytical solutions in multi-sphere models. Results of the forward problem are presented for a four-layer realistic head-model incorporating a burr-hole in the skull. Convergence of the iterative coupling algorithm is analyzed numerically, and the results are compared to the BEM alone, and the FEM alone. For the BEM we use the symmetric BEM of OpenMEEG, and for the FEM we use a tetraedric FEM, with or without the dipole subtraction method.

The domain decomposition framework provides a way of taking the best advantage of both methods, thus significantly improving the accuracy in the resolution of the forward EEG problem, as well as time and memory consumption. As a byproduct of this research, domain decomposition can also be used for BEM or FEM by themselves, in order to break down a
Tu-8 - Improvements in MEG source reconstruction for reliable intersubject comparison

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One central topic in MEG data analysis is the reconstruction of brain signals based on the magnetic fields measured outside the head. Unless the signal sources are described with just a few parameters like in the single equivalent dipole case modelling the source currents usually poses an under-determined problem lacking an unique solution. Therefore additional constraints are required to achieve e.g. reliable localizations of field sources inside the brain. Furthermore, the absolute signal strength of the underlying generators is of interest. This is particularly important when analysing group studies involving several subjects. Here the measured neuromagnetic field changes may vary not only due to the individual processing but also depend on the distance of the MEG sensors to the sources. In general this impedes direct comparison across subjects. With this study we introduce a new measure to determine the directionality of a focal source. A variable, analogous to the thrust-variable(1), describes the directionality of the generating current distribution. For testing we implemented the new measure into magnetic field tomography (MFT), where simulated MEG data were localized and compared to results obtained by minimum norm estimates (MNE) and standard MFT. In case of highly directional sources we find that the directionality variable in conjunction with the l1-norm of the current distribution nicely represents the signal strength of simulated sources.

(1) S.Brandt, H.D. Dahmen, ZPhysC 1(1979)61

Tu-9 - Accuracy of neural-source strengths estimated from a small number of MEG trial data

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To analyze neural sources of event-related MEGs, we usually estimate locations and strengths of sources from the data that are averaged across about a hundred trials for each of conditions to be compared. However, in order to compare neural activations for many conditions, or to obtain detailed dependence of neural activations on stimulus parameters, it is desirable to estimate activations from fewer trial data than a hundred ones. A previous fMRI experiment on lexico-semantic processing showed that strengths of activations varied as semantic relatedness between two presented stimuli, but locations of activations were similar in the anterior temporal area. In the present study, we conducted a simulation study on accuracy of estimating the moment strengths of neural sources from a part of MEG trial data while source locations were determined from all of MEG trial data. In the simulation, we made artificial MEG trial data using single dipoles that were placed in seven language-related areas, and added noises to them. Using the MEG trial data, we carried out source estimations as follows. At first, we applied a minimum-norm method to the 100-averaged data that were obtained by averaging 100 trial data. Second, we selected major dipoles from the solutions by neglecting those with smaller strengths within 2 cm. Third, moments of the major dipoles were fitted to each of 100 trial data with the 100-averaged data that were obtained by averaging 100 trial data. Finally, we evaluated the variations of dipole moments in each area. A previous fMRI experiment on lexico-semantic processing showed that strengths of activations varied as semantic relatedness between two presented stimuli, but locations of activations were similar in the anterior temporal area. As a result, standard deviation of moment strengths of dipoles in the anterior temporal area was evaluated to be about 30% for 10-averaged data, when the signal-to-noise ratio was one. This suggests that the conditional difference of about 30% is significantly detected from 10-averaged data of 10 subjects at the significance level of three times standard deviation.

Tu-10 - Accuracy of spatio-temporal reconstruction using entropic technique from MEG data

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Source localization of abnormal epileptic discharges can be done non-invasively using MagnetoEncephaloGraphy (MEG) during presurgical investigation of patient with epilepsy. The Maximum of Entropy on the Mean (MEM) (Grova et al., Neuroimage, 2006)
and its equivalent within the time-frequency domain using discrete wavelet representation (wMEM) (Lina et al., IEEE TBME, in press) were proved to recover accurately the spatial extent of the generators of transient and rhythmic epileptic discharges. However, epileptic discharges often propagate along the cortex and accurate characterization of their spatio-temporal evolution is clinically relevant (Lantz et al, Journal of Clinical Neurophysiology, 2003).

The aim of the present study is to assess the ability of MEM techniques to recover accurately the time courses of the sources. Realistic simulation involving two spatially extended sources activated with a delay were considered. Real MEG background was added to simulated data. The performance of MEM and wMEM were compared to standard Minimum Norm Estimate. The ability of each method to recover accurately spatio-temporal propagation patterns was evaluated (fig. A) using: 1) the Area Under the ROC Curve (AUC) quantifies the spatial accuracy at the main peak of each source, 2) the root mean square error (RMS) of averaged time course reconstructed within each source, 3) the energy of the reconstructed sources in a close neighborhood (geodesic distance up to 14mm) around each simulated source to quantify overestimation of the spatial extent.

Based on 100 simulations involving two sources, MEM and wMEM showed the best localization accuracy (AUC) and reconstructed the time course of the simulated signals with the lowest RMS error (fig. B), whereas wMEM tended to overestimate the spatial extent of the sources.

In addition to recover accurately the spatial extent of the generators, MEM approaches demonstrated good reconstruction of the dynamics of MEG data.

Results of a simulation of an epileptic discharge, showing the propagation between 2 extended sources within a 10ms delay.

Tu-11 - Localization of vortex shaped current sources in a physical torso phantom

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The first experimental study of the influence of increasing vortex currents on electric and magnetic signals in a human torso phantom (1) proved the well known fact that vortex currents can be detected only by the magnetic measurements. The active vortex currents in (1) were modeled by a set of twelve single current dipoles positioned 15 mm apart and arranged in a circle with a circumference of 180 mm. Magnetic and electric data were recorded simultaneously while the dipoles were switched on stepwise one after the other. They found out that source reconstruction with unconstrained focal source models performed well for a single dipole only, while minimum norm source reconstruction yielded reasonable results only for a few of the dipole configurations.

In this study, we applied a source model with a constant current along the circular arc (2) to explain the measured data from (1). The current was approximated by uniformly distributed current dipoles positioned tangentially along the arc. Goodness of fit was estimated by the relative error (RE) and correlation coefficient (CC). Localization error (LE) was estimated by the difference between center of gravity (COG) of dipoles in the original source and COG of dipoles in the arc model. Reconstruction results show that the arc model gives excellent results (RE<0.02, CC>0.9997) for all sources with 2 or more dipoles switched on. However, the LEs show that the arc model can be effective only when more than a half of the circle is switched on (LE<10 mm and reconstructed radius
Recently, we presented a novel method of estimating the conductivity of cardiac tissue using Magnetocardiography (MCG) data. Although non-invasively estimating the conductivity of human tissue is a relatively difficult issue, which may be dependent on the health of the subject. At present, the cardiac conductivity is mainly obtained by measurement in vitro or in vivo. Non-invasively estimating the conductivity of human tissue is a relatively difficult issue.

The cardiac conductivity has been investigated with the aim of modeling bioelectrical activity and extracting useful information which may be dependent on the health of the subject. At present, the cardiac conductivity is mainly obtained by measurement in vitro or in vivo. Non-invasively estimating the conductivity of human tissue is a relatively difficult issue. Recently, we presented a novel method of estimating the conductivity of cardiac tissue using Magnetocardiography (MCG) data. A partial differential equation of describing the relationship of measured magnetic field and the conductivity was proposed, according to Maxwell equations and the biomagnetic inverse theory, which was used to solve the inverse problem of estimating the conductivity using MCG data. The Ritz-Galerkin method was used to transfer the partial differential equation to the ordinary differential one. Then, the Particle Swarm Optimal (PSO) algorithm is utilized to acquire the optimal solution of cardiac conductivity in different depth and different positions by the ordinary differential equation. The magnetic field data from central area is used to simplify the conductivity estimate and exclude the influence of data from boundary measurement error. Our calculation results are approaching to the cardiac conductivity, between 0.0537-0.483 S/m, which has been reported by D. U. J. Keller in 2010. Six normal subjects have been investigated and it is obvious that in the central area of the measurement plane, the conductivity of a subject is with a region of 0.02-1.2 S/m in different depth during ST segment. According to our calculation, the cardiac conductivity for most normal subjects varies time-dependently and slightly in a small region.

**Tu-12 - Estimation on the Conductivity of Cardiac Tissue in Magnetocardiography**

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The cardiac conductivity has been investigated with the aim of modeling bioelectrical activity and extracting useful information which may be dependent on the health of the subject. At present, the cardiac conductivity is mainly obtained by measurement in vitro or in vivo. Non-invasively estimating the conductivity of human tissue is a relatively difficult issue. Recently, we presented a novel method of estimating the conductivity of cardiac tissue using Magnetocardiography (MCG) data. A partial differential equation of describing the relationship of measured magnetic field and the conductivity was proposed, according to Maxwell equations and the biomagnetic inverse theory, which was used to solve the inverse problem of estimating the conductivity using MCG data. The Ritz-Galerkin method was used to transfer the partial differential equation to the ordinary differential one. Then, the Particle Swarm Optimal (PSO) algorithm is utilized to acquire the optimal solution of cardiac conductivity in different depth and different positions by the ordinary differential equation. The magnetic field data from central area is used to simplify the conductivity estimate and exclude the influence of data from boundary measurement error. Our calculation results are approaching to the cardiac conductivity, between 0.0537-0.483 S/m, which has been reported by D. U. J. Keller in 2010. Six normal subjects have been investigated and it is obvious that in the central area of the measurement plane, the conductivity of a subject is with a region of 0.02-1.2 S/m in different depth during ST segment. According to our calculation, the cardiac conductivity for most normal subjects varies time-dependently and slightly in a small region.

**Tu-13 - Extension of Basis Function Source Model: Applying Normalized-cut to the Segment of ROI for MEG Source Reconstruction**

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In this study, we use the new method of MEG source spatio-temporal reconstruction based on modeling the neural source with extended basis functions. A new model is built to describe the current source distributed on each vertex of cortex mesh, which consists of analogous basis functions (the Laplacian eigenvectors of spherical mesh) and unknown weighted coefficients. The weighted coefficients can be calculated along with leadfield. The neural source distribution on mesh is then reconstructed according to the basis functions expanded model above. However, the reconstruction results produced by the selected method still have distortions and instability comparing to the original source patterns, mainly because the larger region of cortical surface used for reconstruction leads to more plausible and less accurate results in terms of an ill-posed inverse problem. To solve this problem, it is feasible to reduce the reconstructed region to be close to the region of interest (ROI) so that the accuracy can be increased. Therefore, the normalized-cut method is applied to determine the ROI based on the geometrical information in this paper. The normalized-cut method has been widely applied for graph segmentation. The Fiedler vector of mesh Laplacian is used for the vertices clustering of ROI mesh. Then, the basis function method is applied on the ROI segmented by the normalized-cut method. The results suggest that, when the reconstruction model is segmented as close as the region that the current sources actual locate, the reconstruction is capable to obtain the more accurate result. In other words, the change of the reconstruction on the model from the global cortical surface to proper-selected localized ROI affects the accuracy and goodness of the result directly. This is a crucial feature when the basis function method is applied into the MEG source reconstruction.

**Tu-14 - Spatial Improvement of MEG Source Reconstruction by Applying Bayesian Super-resolution method**

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Bayesian super-resolution is one of the classic pattern recognition methods that are used for high-quality image recovery from a set of low-resolution images. Its principle is to improve the image by the inversion of a transformation from some unknown high-resolution image to the observed low-resolution images based on the Bayesian theory. This approach applies a regularization process for the ill-posed inverse problem. MEG shows weaknesses on spatial resolution but superior temporal resolution that generates a rapid sequence of images. The goal in this study is to use these image sequences in conjunction with the previous source reconstruction method (e.g., the basis function method), to improve the spatial resolution of MEG reconstruction. This problem can be described as obtaining a source distribution on the higher-resolution cortical surface mesh from several continuous current source frames dis-
tributed on the original cortical mesh in the temporal field, which resembles the concept of super resolution for image reconstruction. Therefore, a reasonable estimation for the spatial resolution improvement can be provided in terms of Bayesian inference. The mathematical framework of the method provides sound logic and an adequate description of the inverse problem of MEG. The numerical experiment results of parameter estimation show that the spatial resolution has effectively been improved. However, the computation complexity and inaccuracy of the reconstruction results immensely increased because the algorithm processes source distribution on 3D cortical surface mesh and contains a number of large matrix calculations.

Tu-15 - Imaging of epileptogenic zone using L2 norm spatial filter

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Purpose: Dipole mapping has been adopted in order to visualize epileptogenic zone in analyzing MEG, however, the source of interictal spikes is so wide that the dipole model is not suitable. Dipole mapping contains other disadvantages, the moment of each dipole is not expressed and epileptogenicity is underestimated when dipoles cluster tightly. We developed a new method for visualizing epileptogenic zone using L2 norm spatial filter.

Method: The formula of L2 norm spatial filter has been well-known, however, the importance of regularization of the covariance matrix has not been emphasized. By using the data of a phantom, the patient with tight dipole-clustering and the patient with wide dipole-scattering, we compare the parameter of the regularization which composes L2 norm spatial filter.

Result: The best number of eigenvalue for 204-channel system was proven to be 40.

Conclusion: Imaging of epileptogenic zone using L2 norm spatial filter is quantitative representation and is more useful than dipole mapping; however, L2 norm spatial filter leads superficial sources when the generator is located at deep structure such as hippocampus. The combination of the two methods is recommended in the presurgical evaluation of the patients with epilepsy.

Tu-16 - Influence of interior cerebrospinal fluid compartments on EEG source analysis

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It is known that incorporating cerebrospinal fluid (CSF) into realistic volume conductor models adds precision for source analysis. However, modeling interior CSF compartments like ventricles or deep sulci creates a complex source space with many deep cavities. Such a fragmented source space can cause problems for dipole fitting and other inverse methods. A solution could be to use a simplified head model, where only the superficial CSF layer between the brain surface and the inner skull boundary is included, while interior CSF compartments are ignored. The present paper aims at investigating if simplified CSF models are sufficiently accurate for forward and inverse solutions.
A simulation study using realistic volume conductor models was performed. First, a detailed and anatomically plausible reference model was created. Then, two test models were derived. Test model A ignored CSF completely, while test model B only ignored CSF in deep sulci and the ventricles. Forward computation errors were assessed by directly comparing the potentials computed in the reference and test models. Inverse errors were investigated by performing source reconstruction of single sources in the test models to reconstruct the potentials simulated in the reference model.

Large topography (relative difference measure (RDM) ≥ 0.1) and localization errors (≥4 mm) were found for superficial sources and sources close to internal CSF compartments for model A. In model B, RDM errors ≥ 0.1 were found for only few sources close to the ventricles and close to sulci of larger extent. Localization errors in model B were below 2 mm for all reference sources.

The results suggest that ignoring CSF when creating a head model leads to substantial localization errors. Ignoring only internal CSF-filled compartments, while modeling superficial CSF layers allows source localization with relatively high precision. Thus, avoiding a fragmented source space by not modeling internal CSF compartments is acceptable.

**Tu-26 - Skull Defects in MEG and EEG: Experimental Results and Modeling**

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While the influence of skull defects on the electroencephalogram (EEG) has been reported, the magnetoencephalogram (MEG) is thought to have a negligible sensitivity to skull defects. However, quantitative experimental evidence under realistic conditions is rare. Our objective is to experimentally investigate the influence of conducting skull defects on the EEG and MEG using a controlled current source under and next to the defect and to develop a finite element model and equivalent source model to explain it. We measured a 64-channel EEG simultaneously to a 16-channel MEG produced by a miniaturized artificial coaxial dipole implanted in a rabbit brain tangentially to the inner skull surface in vivo. Following a recording with intact skull, a skull defect was introduced above the dipole and filled with agar (1.0 S/m at 30°C). A CT (0.4 mm3) provided the defect geometry and the dipole position. The dipole was shifted in 0.35 mm steps from a position next to the skull defect to a position under the defect and further to the opposite side and a recording was taken at each step under otherwise identical conditions.

Our results demonstrate that both EEG and MEG were significantly and reproducibly influenced by the introduction of a conductive skull defect with a maximal relative magnitude deviation of above 300% for EEG and above 20% for MEG. Both, the EEG and to a smaller degree also the MEG topography, are altered in a fashion that is spatially corresponding to the skull defect location and geometry. These observations are reflected in our finite element models of the skull defects.

We conclude that skull defects need to be accounted for in volume conductor models used in the reconstruction of brain activity sources from EEG and also MEG, particularly in infants with open fontanels and patients with post-surgical skull conditions.

**Tu-27 - Effects of brain inhomogeneity and anisotropy on the estimation of source parameters and functional connectivity**

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We examined how tissue inhomogeneity and anisotropy affect the accuracy of MEG and EEG source estimates and functional brain connectivity measures. A FEM volume conductor model was created using T1/DT-MRIs from a 5-year old patient with a lesion in the parietal area and anisotropy in gray and white matter. We placed six equivalent current dipoles (ECDs) around the lesion (Fig. A) and computed the MEG and EEG forward solutions, which were then used to obtain the inverse solutions for each ECD with an isotropic non-lesion head model.

For ECD 2 (Fig B), the reduced isotropic model gave the dipole close to the true dipole. For ECD 3 (Fig C), the dipolar solutions based on MEG or EEG were pulled close to the lesion boundary. The orientations deviate from the actual ones and are almost perpendicular to the boundary surface. The location, orientation, and magnitude errors were 5 mm, 40°, and 800% for EEG, and 4 mm, 35°, and 300% for MEG. For ECD 5 (Fig D), the MEG fitted dipole was shifted radially, nearly 90° off the true orientation, which caused the magnitude estimate to reach an unreliable 900% error.

For the effect on functional connectivity estimates, we formulated a resolution matrix \( R' = RQ = (F'F)^{-1}F'TQ \), where the accurate forward matrix whose columns are the true dipole fields is denoted by \( T \), a less accurate forward model by \( F \), and the estimated and true dipole waveforms by \( Q' \) and \( Q \), respectively. \( R \) induces a false-positive source covariance \( RRT \) and corresponding coherence between even totally uncorrelated sources. If the model misspecification does not produce any false connectivity, the matrices in Fig. 1EF should show zero coherence. The inaccuracy of the forward model led to false linkage when the lesion was omitted. This error was stronger for EEG than for MEG.

This study provided how inhomogeneity and anisotropy can distort the MEG and EEG source estimates and functional connectivity.
Tu-28 - Hierarchical Fully-Bayesian Inference for EEG/MEG combination: Examination of Depth Localization and Source Separation using Realistic FE Head Models

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Measuring the induced electromagnetic fields at the head surface to estimate the underlying, activity-related ion currents in the brain is a challenging, severely ill-posed inverse problem. Especially the recovery of brain networks involving deep-lying sources by means of EEG/MEG recordings is still a challenging task for any inverse method. Recently, hierarchical Bayesian modeling (HBM) emerged as a unifying framework for current density reconstruction (CDR) approaches comprising most established methods as well as offering promising new methods. Our work examines the performance of fully-Bayesian inference methods for HBM for source configurations consisting of few, focal sources when used with realistic, high resolution Finite Element (FE) head models. In addition, using EEG and MEG alone is compared to a combined data analysis. The main foci of interest are the right depth localization, a well known systematic error of many CDR methods, and the separation of single sources in multiple-source scenarios. Both aspects are very important in clinical applications, e.g., in presurgical epilepsy diagnosis as well as in the analysis of evoked potential and fields, e.g., for auditory or somatosensory stimuli. Our results show that HBM provides a promising and convenient framework for these tasks. In particular, it is able to improve upon established CDR methods like minimum norm estimation (MNE) or sLORETA in many aspects. For challenging multiple-source scenarios where the established methods show crucial errors, promising results are attained. We further discuss several aspects of EEG and MEG combination like sensitivity profiles, noise characteristics and modeling.
Tu-29 - Calculating the Electric Fields in Real Human Head by Transcranial Magnetic Stimulation Using H-Coil

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Transcranial magnetic stimulation (TMS) is a noninvasive technique used to apply brief magnetic pulses to the brain that can induce electrical fields underlying cortical tissue, thereby producing a localized excitation of neurons. Standard coils used for TMS are circular or figure-of-eight shaped, which have been limited to induce stimulation in superficial cortical regions of the brain due to field reducing rapidly with distance from the coil. Only very high intensities would allow stimulation of deep brain regions and such intensities would lead to undesirable side effects. Recently, interests in stimulating deeper sub-cortical brain regions have arisen and have become an active research topic in TMS, because several studies show that activation of deeper prefrontal and limbic regions may increase the antidepressant effect.

In the last years a method to stimulate deep brain regions using TMS was obtained by a specifically designed coil: the H-coil. In this study, the H-coil was numerically designed as shown in Fig. 1. The pulse current with amplitude of 7.7 kA and operating frequency 3.6 kHz sine wave is fed into the coil. A real 3-D human head model which has 25 different tissues is employed in this study. The tissue properties are modelled using the 4-Cole-Cole method. The electric fields in head tissues were calculated by using the 3D impedance method. It was found that the induced electric fields in brain tissues are above the threshold for neural activation i.e. 150 V/m even at depth of 8 cm. While the induced electric fields in superficial cortical regions are much higher. Results in this work showed it is not obtainable by H-coil to stimulate deeper brain regions without increasing the electrical field intensity in the superficial cortical tissues.
Tu-30 - Assessment of Induced Electric Currents in Patient’s Head Exposed to Pulsed Z-Gradient Coil in Magnetic Resonance Imaging

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In magnetic resonance imaging (MRI), time-varied gradient magnetic fields may stimulate nerves and muscles by inducing electric fields and currents in patients, which may potentially cause health problem. The International Commission on Non-Ionizing Radiation Protection (ICNIRP) has set international guidelines for limiting the exposure. Based on these guidelines, the basic restrictions limit the induced current density in the central nervous system (CNS) which is set at \(2\, \text{mA/m}^2\) of exposure of the general public at a frequency of 1 kHz. The guidelines require that the basic restrictions are not exceeded at any time. However, it is impossible to measure these currents, and often they must be calculated using large scale computing.

In this study, a 3-D real human man model located inside a realistic z-gradient coil was numerically designed. The human man model with 3 mm resolution, shown in Fig.1, to simulate the patient. This model is obtained from Brooks Air Force Laboratory, USA. It is based on anatomical slices from a male cadaver and was originally obtained from the Visible Human Project. The coil was 1.055 m long and consisted of 24 rings, all with a radius of 0.35 m. Fig.1(a) shows the case for a practical body imaging. While Fig.1(b) simulates a practical brain imaging with head and neck inside the MRI bore. The pulse currents with amplitude of 180.52 A and a working frequency of 1 kHz sine wave are fed into the coils. The tissue conductivities are calculated using the 4-Cole-Cole method.

The induced current density and electric fields in man model were calculated by employing impedance method. It was found that the maximum value of the 1-cm -averaged induced current density in CNS tissues in the head increases from 81.2 mA/m² for body imaging to 247 mA/m² for brain imaging. For both cases, the maximum value of the 1-cm -averaged induced current density greatly exceeds the ICNIRP basic restriction.
Tu-31 - Comparison of Induced Electric Fields in Child and Adult Head Models by Transcranial Magnetic Stimulation

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Transcranial magnetic stimulation (TMS) is a noninvasive technique used to apply brief magnetic pulses to the brain that can induce electrical fields underlying cortical tissue, thereby producing a localized excitation of neurons. Compared to the extensive research on every aspect of TMS in adults in the past two decades, the potential application of TMS in children has not yet been fully explored. The purpose of the present study is to calculate the electric fields in realistic child head models by employing a realistic figure-of-eight TMS coil and compare the results with that of an adult model. It is hoped that this study will help in the evaluation of the safety profile involved with applying TMS to the pediatric population.

The child head models were developed by Virtual Family project. We have used the models of 6-year-old boy and 11-year-old girl with a resolution of 1\text{mm} as shown in Fig. 1(a)-(b). The adult head model as shown in Fig. 1(c) was obtained from Brooks Air Force Laboratory. We have modeled the TMS with a figure-eight-shaped coil. The inner and outer radii of the circular wings are 10\text{mm} and 50\text{mm}, respectively. The number of the wire turns in each wing is 10. Following a typical clinical procedure we use a sinusoid current with amplitude of 7.7\text{kA} and working frequency 3.6\text{kHz}. The electrical properties of head tissues are modeled using the 4-Cole-Cole method. The induced electric fields are calculated using the impedance method. It was found that field penetration into the brain is reduced quickly for child heads compared to that of the adult head. The explanation for this observation is because of the thinner skull and smaller overall dimension of the brain for a child compared to those for an adult. In the head models of children, the induced electric fields decay slowly as the age increases.
Tu-32 - EEG forward simulation through the complete electrode model for a head of a newborn

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This work concerns electroencephalography (EEG) forward (data) simulation through the complete electrode model (CEM), in which the electrode size, shape and effective contact impedance can be incorporated into computation of the electrode voltages, and both neural currents in the brain and shunting currents between the electrodes and the skin can affect the voltages values computed. The results presented compare the CEM to the point electrode model (PEM), the current standard in EEG, in which the electrodes are point-like and their impedance cannot be controlled and which can be formulated as a limit of the CEM, where the impedance of each electrode goes to infinity and the size (diameter) tends to zero. Impedance and surface area both have an effect on the simulation of the electric potential. The present focus is on these effects in 3D space with the aim of finding out if the CEM can lead to significantly different forward simulation as compared to the PEM. To achieve this aim the geometry of the human head has been modeled as realistically as possible, especially the skull and its openings. The results concern in particular a head of a newborn, an important special case, in which the electrode diameter is exceptionally large in relation to the size of the head and which can also include fontanelles and sutures, i.e. openings in the midline of the skull and areas where the bones join together, respectively. The finite element method has been used throughout the numerical experiments. The difference between CEM and PEM has been approached via numerical forward and inverse errors as well as graphically by visualizing e.g. shunting currents on the electrodes. In addition, feasibility of different impedance values for measurement purposes has been studied from the CEM point of view.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{eeg_forward_simulation}
\caption{Electrode configuration on a head of a newborn: shunting effects (left) and electrode voltages (right) in microvolts for a tangential and a radial source, respectively.}
\end{figure}

Tu-111 - Differential Contributions of Cortical Sources to Scalp EEGs and MEGs

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Our objective was to examine how electrical activity of cortical sources from left and right brain contribute to the scalp EEGs and MEGs. This may be helpful in lateralization of left and right cortical source volumes from EEG and MEG data. Our second objective was to quantify the contribution of deeper cerebral sources to EEGs and MEGs. We used a 3-D finite element method (FEM) model of an adult subject constructed from 192 segmented axial MR slices with 256x256 pixel resolution. The voxel resolution was 111 mm. Majority of the tissues were identified that included: scalp, fat, muscle, dura layer, CSF, cerebellum, gray and white matter, and hard and soft skull bone. The electrical activity of the left and right brain was represented by 60,000 dipoles each, and of the cerebellum...
by 24,000 dipoles. The dipole intensity distribution was in the range of 0.0 to 0.4 mA meter with a uniform random distribution. The electrical conductivities of various tissues were obtained from the literature. Using an adaptive FEM solver the potential and flux distribution in the whole head model were computed. The scalp potentials were extracted and referenced to a common average reference. The MEG sensor coils were assumed to be 1.0 cm above the scalp surface. The magnetic fields at the sensor locations were computed by use of Biot-Savart law. Spatial contour plots of potentials on the scalp surface and magnetic fields on the sensor surface were made. For the left brain sources, the positive peak was in front central area and the negative peak was in the left central temporal area. For the right brain sources, the positive peak was in the left front area and the negative peak was in the right mid central area. Similar results were found for magnetic field plots. This suggests that lateralization of the left and right cortical source volumes maybe possible from the scalp EEGs and MEGs. Contribution to EEGs and MEGs from deeper cerebral sources was about 15%.

Scalp potentials from (left) left brain sources, (middle) right brain sources and (right) sources in the cerebellum. Colorbars are in micro Volts.

Tu-112 - Changes in Scalp Potentials and Magnetic Fields Due to a Stroke

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Our objective was to examine how scalp potentials and fields change due to a partial stroke in the left or right side of the brain. We used a 3-D finite element method (FEM) model of an adult subject constructed from 192 segmented axial MR slices with 256x256 pixel resolution. The voxel resolution was 11.1 mm. Majority of the tissues were identified that included: scalp, fat, muscle, CSF, dura layer, cerebellum, gray and white matter, and hard and soft skull bone. The stroke volume was approximately 3 cm radius spheroid in the left or right central sulcus region with no electrical activity. The scalp potentials and fields were also simulated for a normal brain with no stroke. The electrical activity of the cortex was represented by 144,000 distributed dipolar sources with orientations normal to the local cortical surface. The dipolar intensity was in the range of 0.0 to 0.4 mA meter with a uniform random distribution. The electrical conductivities of various tissues were obtained from the literature. Using an adaptive FEM solver the potential and flux distribution in the head model were computed. The scalp potentials were extracted and referenced to a common average reference. The MEG sensor coils were assumed to be on a curved surface, 1.0 cm above the scalp. The magnetic fields at the sensor locations were computed by use of Biot-Savart law. Spatial contour plots of potentials and magnetic fields for strokes exhibited complex patterns which were different in shape and locations from a normal brain. For stroke in the left brain, the potential profile had complex spatial patterns on the left facial and scalp surface, and also a dipolar pattern on the back of the head. For stroke in the right brain, the complex spatial patterns were visible on the right side of the scalp and face. The magnetic field plots also had complex spatial patterns. These findings have possible clinical applications to differentiate between right or left stroke volume from scalp EEGs or MEGs.
Tu-113 - Multi-trial evoked EEG and Independent Component Analysis

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We study the activation cascade in the human brain after stimulating a cortical area of interest by transcranial magnetic stimulation (TMS). EEG is used to record the spreading of the activity from the target area. To identify activated neural locations and latencies, the blind source separation (BSS) is used to separate underlying neural components in EEG. The components have both a spatial EEG topography representing the location of the component and an activation time curve.

The latent neural components are assumed to be independent of each other at each EEG time instant, which is here referred to as momentary independence. Therefore, independent component analysis was chosen as a form of BSS. However, as we show, due to the non-stationarity of the evoked responses, the momentary independence does not imply independence of the components when the samples from all time instants are concatenated, as is commonly done.

We show that the preprocessing step of subtracting the mean response, taken over trials at each time instant, from all the individual responses, makes the components mean-independent. This is a weaker property than statistical independence, but sufficient for the separation by the FastICA algorithm.

To further relax the conditions by which the components are found, it is possible to form Gaussian samples for each time instant, preserving the correlation matrices of the recorded signals. The momentary uncorrelatedness is then sufficient to perform the separation with FastICA, which is beneficial in cases where the momentary independence assumption is doubtful.

The presented approach was tested with simulated data. The result shows that FastICA can effectively separate the evoked components after mean-subtraction, but not without. This novel methodology is usable with any evoked responses recorded with EEG/MEG.

Tu-114 - Improvement of beamformer source reconstructions using sensor-array subsampling

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MEG sensor records present a spatial mixture of unknown time courses of the active underlying neural sources. Inverse reconstruction techniques such as beamformers are used to unmix the sensor data into the constituent source activations. Beamformer algorithms operate on the sensor level covariance matrix in order to optimally suppress signals that do not originate from the location under consideration. For good performance, beamformers need a reliable estimate of the covariance matrix. In many practical applications the number of sampled time points is insufficient for a robust covariance estimate, resulting in a reduced quality source reconstruction and compromised statistical sensitivity.

Here, we explore the potential of sensor-array subsampling to improve the quality of beamformer source reconstructions constrained by a small amount of data. The approach relies on the fact that any neuronal source is visible on multiple MEG sensors, thus making high-density MEG-sensor arrays highly redundant for the detection of any single source. The rationale is to reconstruct the source activation multiple times, each time using a different set of MEG sensors. Each individual reconstruction provides a noisy estimate of the activity. Yet, a combination of the individual reconstructions may effectively reduce the noise, leading to a more accurate estimate compared to the single reconstruction using all channels at once.

We tested the subsampling approach using simulated data and compared its performance with that of a conventional beamformer. We found that, in the presence of limited data, subsampling may lead to a marked improvement of the accuracy with which source activations can be reconstructed (fig 1). These results suggest that this technique may be useful in real applications where the number of time points in the data is limited. The proposed technique may be particularly relevant in applications with single trial analysis, such as BCI, and connectivity analysis.
We have developed Champagne, a novel source reconstruction algorithm that is derived in an empirical Bayesian schema(1). The algorithm is designed to estimate the locations and time-courses of a sparse set of dipoles that adequately explain the observed sensor data. We have performed exhaustive performance analysis of the Champagne algorithm, and compared its performance with existing source localization algorithms. Results of such comparisons show that Champagne has superior performance over existing algorithms in terms of reconstruction accuracy and robustness to correlated sources and noisy data(2). However, since Champagne imposes sparseness on source distributions, it naturally fails to reconstruct non-sparse sources such as smoothed or diffuse sources. In this paper, a modified version of the Champagne algorithm is proposed that can handle non-sparse source distributions. We show the effectiveness of the proposed algorithm using a computer simulation whose representative results are shown in (a),(b), and (c). The original diffuse source distribution assumed in the computer simulation is shown in (a). The reconstructed results using the original Champagne algorithm are shown in (b). The algorithm fails to reconstruct one of the three sources at its correct location. The results of source reconstruction using the proposed algorithm are shown in (c). Here, the proposed algorithm can successfully reconstruct the three diffuse sources at the correct locations. The proposed algorithm is also effective in reconstructing moving sources, which the original Champagne algorithm fails to reconstruct.

References
Tu-116 - Particle filtering of static dipoles in MEG

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Most recently proposed inverse methods for EEG/MEG aim at exploiting the temporal structure of the data. In particular, Bayesian filtering has the further appeal that, in principle, it can be applied online, because the estimate at time t is only based on the data up to time t.

Here we consider Bayesian filtering of current dipoles from MEG data. We present a state space model devised to fully reflect the physiological interpretation of the dipole model: dipoles can appear and disappear, dipole orientations change slowly relative to dipole strength, and dipole locations are stationary during the dipole life time. In order to perform inference for the stationary dipole model, we have developed an algorithm based around the Resample-Move (2) and a carefully designed importance distribution approximating the optimal one (1). This marks a substantial departure from previous work (3), where, in order to use standard bootstrap particle filtering, an artificial dynamic structure was imposed, in which dipoles performed a random walk.

We apply the new algorithm to simulated data with complicated and time varying source configurations, and show that the average localization error remains below 1 cm, even when the data is produced by five simultaneous sources, by contrast, the bootstrap particle filter with the stationary model produces artefacts, resulting in an average localization error of 2 cm. In addition, the new algorithm has a higher effective sample size, indicating that the importance distribution is well designed, and a higher likelihood, indicating that the sample points concentrate more on the high-probability region of the state space.

We also consider application to an experimental data set, recorded during median nerve stimulation.

(3) Sorrentino et al. (2009) Human Brain Mapping Vol 30, p 1911-1921

Tu-117 - Comparison of BEM and FDM head modeling in SPM for EEG source reconstruction based on free energy

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The boundary element method (BEM) is commonly used in EEG source reconstruction due to its efficient computational properties. Finite difference methods (FDM) are computationally more intensive but allow more realistic head modeling. Bayesian EEG source reconstruction techniques are implemented in the statistical parametric mapping software (SPM). They admit comparison of reconstructions based on their free energy values. Only BEM head models are however available in the SPM package. This work extends head modeling in SPM to FDM models.

We constructed an FDM model based on the default BEM surfaces and brain tissue conductivity values used in SPM. This to compare FDM and BEM modeling in similar conditions. For the comparison we reconstructed scalp EEG data from 26 subjects in a visual detection checkerboard task, for bottom left stimuli, based on the default number of dipoles (5124, 8196 and 20484) and dipole locations. The accuracy of the reconstructions was validated based on the results from previous EEG/MRI checkerboard studies. For the grand averaged data there was strong evidence that the FDM outperforms the BEM, i.e. we found Bayes factors \( \geq 150 \). The
Free energy comparison for single subject reconstructions did not show strong evidence for either BEM or FDM modeling, i.e. we only found Bayes factors < 20. The results are shown in figure A. These results evidenced better performance of the FDM with higher number of dipoles. The reconstruction results for the model of 20484 dipoles are presented in figures B and C for the BEM and the FDM respectively. The evoked energy between 80-112 ms corresponding with the early P1 peak is depicted on the left. The time course of the dipole with maximum energy for the FDM head model is shown on the right. The reconstruction results based on the FDM model correspond with the results from previous studies. The results are less clear for the BEM.

Tu-118 - Analyzing trial-to-trial variability of neuronal activity using MEG/EEG source reconstruction with mixed norm priors in the time-frequency domain

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Using MEG/EEG source estimates computed from averaged evoked responses it is possible to study brain function with a high temporal and a good spatial resolution. However, the applicability of present source reconstruction methods to the study of trial-to-trial variability is limited due to the low signal-to-noise ratio of unaveraged data.

In this contribution, we present a new source localization approach for analyzing trial-to-trial variability, which considers multiple trials simultaneously to increase the information content. Our multi-trial time-frequency mixed-norm estimate (MT-TF-MxNE) is based on a composite multidimensional mixed norm prior in the time-frequency (TF) domain, which combines a sparse intra-trial prior and a smooth inter-trial prior. The intra-trial prior promotes spatial sparsity and temporal smoothness of the estimated neuronal activity in each trial by thresholding the short-time Fourier transform of the source signals. The estimated time courses are thus a linear combination of few oscillatory atoms. The inter-trial prior imposes similarity of the source activations over trials by retaining consistency of the respective sparsity structure in the TF domain, i.e. the same TF atoms are selected in each trial. However, amplitudes and phases of the selected TF atoms are allowed to vary in order to account for trial-to-trial variations such as decreasing peak amplitudes due to habituation or latency jitters.

The proposed regularization functional is non-smooth but convex. Thus, the resulting sparse regression problem is a convex optimization problem. We solved this problem using the fast iterative shrinkage-thresholding algorithm (FISTA), a first-order scheme based on proximal operators.

We tested the MT-TF-MxNE with simulated MEG/EEG data showing its ability to reconstruct location, activation and trial-to-trial variability of evoked neuronal activity.
Tu-119 - Comparison of Boundary Element and Finite Element Approaches to the EEG Forward Problem

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The accurate simulation of the electric fields evoked by neural activity is crucial for solving the inverse problem of EEG. Nowadays, boundary element (BE) methods are frequently applied to achieve this goal, usually relying on the simplification of modelling the human head by three nested compartments with isotropic conductivities (skin, skull, brain). Here, including the highly-conducting cerebrospinal fluid (CSF), whose significant influence on EEG forward simulations has been shown, is a difficult task due to the strongly folded structure of the cortex. This demands a high number of nodes to accurately model the CSF/brain interface resulting in a strongly increased computational effort.

In contrast, the CSF can be included at negligible computational costs when applying finite element (FE) forward approaches. Thus, one focus of our investigation is placed on the influence of modelling/neglecting the CSF.

First, we compare the accuracy of different FE and BE forward approaches in a three-layer sphere model and, subsequently, we investigate the accuracy of the FE approaches in a four-layer sphere model. We use the pure analytical error of neglecting the CSF as a reference for the range of the numerical errors, showing that this model error exceeds the numerical errors of the FE approaches.

Finally, we carry out similar comparisons using realistic three- and four-layered head models. Due to the lack of an analytical solution in this case, a numerical solution has to be used as a reference so that only the relative errors between different approaches can be compared.
Tu-120 - Validation and Application of Realistic Head Modelling to MEG

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While realistic head modelling is nowadays frequently applied in EEG source analysis, it is only rarely used in the evaluation of MEG measurements. One reason is the lower dependency of MEG signals on the volume conductor geometry.

A simultaneous evaluation of EEG and MEG is highly desirable for an accurate source reconstruction when considering the complementary strengths of these two modalities, e.g., their sensitivity to different source orientations. However, when aiming at a symmetric data fusion of simultaneous EEG and MEG recordings, it is necessary to simulate the magnetic field of neural sources as exact as possible. Thus, the influence of the head geometry on the magnetic field evoked by the volume (or return) currents, the so-called secondary magnetic field, should be taken into account by using realistic head models. This demands the application of numerical approaches.

Therefore, as a first step towards this goal, we investigated the accuracy of different finite element \textsuperscript{(FE)} approaches to the forward problem of MEG and the influence of realistic head modelling.

Accuracy investigations were carried out in different scenarios. As a first step, we investigated the accuracy of the numerical solutions using both artificial and realistic sensor configurations in sphere models.

Subsequently, we expanded our study to realistic head models, investigating the influence of a detailed simulation of secondary magnetic fields in realistic scenarios.

Using an analytical solution as reference, we show that all tested FE approaches achieve a high accuracy in sphere models for both realistic and artificial sensor configurations. Furthermore, our results indicate that realistic head modelling has a non-negligible contribution for realistic sensor configurations, especially when aiming at a symmetric data fusion of EEG and MEG.

Tu-121 - Sensitivity of EEG leads to volume conductor properties

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Our aim was to investigate the lead field sensitivity within realistically shaped finite element head models as a function of the model parameters.

By means of an effect-by-effect approach, the widely used (in EEG and MEG source analysis) homogenized isotropic three compartment head model (skin, skull, brain) is expanded to a more realistic six compartment head model (skin, skull compacta, skull...
spongiosa, cerebrospinal fluid (CSF), brain grey and white matter) with brain conductivity anisotropy (Olesch et al., Proc. SPIE Medical Imaging, 2010, Wolters et al., Neuroimage, 2006, Wagner, Diploma Thesis, 2011). In each successive step, an additional effect (either a further realistic tissue compartment or brain anisotropy) is incorporated into the simpler model of the previous step. For each incorporated effect the resulting changes in the lead vector field orientation and magnitude are assessed in the whole volume conductor as well as in the cortical compartment. Moreover, the direct visualization of the computed vector fields throughout selected regions of interest within the volume conductor allows an easy and intuitive result interpretation.

Results of our presentation are (1) channeling effects of the vector field in lower resistive regions, for example, in the skin, skull spongiosa and the CSF, (2) resulting vector field orientation and magnitude in the cortical compartment changes by more than 50 degrees and 250 %, respectively, (3) vectors, located in areas of higher resistive regions tend to be oriented towards the nearest less resistive tissue, (4) when modeling brain conductivity anisotropy, the vector field is oriented more parallel to the main conductivity tensor direction.

The visualization of lead vector fields offers an intuitive way to better understand volume conduction effects and our presentation demonstrates that anisotropic multi-compartment realistically shaped head models are important for an accurate source analysis.

Sensitivity distribution within realistically shaped six compartment head model with brain anisotropy. Thinned version of the calculated vector field is presented, where only the middle cone of each 4mm x 4mm block is visualized.

**Tu-122 - Comparison of direct and reciprocal forward modeling approaches in EEG source analysis**

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Our presentation will focus on a comparison between the reciprocal or adjoint approach (AA) (Vallaghe et al., Phys.Med.Biol., 2009) and the partial integration (PI) direct approach using the transfer matrix approach (Wolters et al., Inverse Problems, 2004, Vorwerk, Diploma Thesis, 2011) for realistic forward modeling in EEG source analysis. Following (Vallaghe et al., Phys.Med.Biol., 2009), the AA is deduced using the adjoint method and Riesz representation theorem is used in order to depict the connection between the AA and the EEG forward problem. Next, the PI is derived and used for a comparison with the AA (Wagner, Diploma Thesis, 2011). In order to investigate realistically shaped head models including tissue inhomogeneities and anisotropy, the finite element method (FEM) is used for numerical realization of both forward modeling approaches. The underlying theory will be discussed and the connection between lead field approach, Helmholtz’ principle of reciprocity and the AA will be demonstrated in detail.

By means of a validation of our implementation in tetrahedral as well as hexahedral anisotropic multi-compartment spherical shell
models, an estimation of the computational complexity and a derivation of closed formulas, we will show that the AA and PI are essentially identical (Wagner, Diploma Thesis, 2011).

However, the AA can be used to calculate and investigate lead field sensitivity distributions that serve as sensitivity maps for the considered pairs of electrodes (lead) in EEG source analysis. Sensitivity maps can be used to (1) assess the influence of an arbitrary dipolar source on the potential difference between a fixed lead at a glance, (2) identify the orientation of certain dipoles needed to maximize the potential difference measured between the considered lead in an intuitive way, (3) visually predict the differences in forward modeling when extending a head model from a standard homogenized three-compartment model to a more realistic one.

Tu-123 - Volume conduction effects in tDCS using a 1mm geometry-adapted hexahedral finite element head model

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Transcranial direct current stimulation is a non-invasive brain stimulation technique that can induce transient excitability changes in the stimulated cortex. Despite of the recent progress, the knowledge about the underlying mechanisms behind tDCS is still limited. In order to gain insight in the sophisticated interplay of stimulation, volume conduction and resulting cortical current density distribution, we follow an effect-by-effect approach. We start our investigations with a homogenized isotropic three compartment (skin, skull, brain) head model, where results are still rather obvious. In each consecutive step, we then extent our head model by one additional effect, which is either a tissue layer or an anisotropic instead of a homogenized isotropic tissue compartment. For each additional effect, the resulting changes in the current density distribution are deeply investigated. Our most realistic volume conductor contains six tissue compartments and brain anisotropy.

Major findings of our study include (1) channeling effects of the skin, the skull spongiosa and the cerebrospinal fluid (CSF) compartments and resulting current density vector field orientation and magnitude changes in the cortical compartment of more than 60 degrees and 300%, respectively, (2) current vectors in lower-conducting regions tend to be oriented towards the closest higher conducting region, (3) anisotropic white matter conductivity causes current flow in directions more parallel to the white matter fiber tracts, (4) highest cortical current magnitudes are not only found close to the side of stimulation.

An accurate modeling of the volume conduction effects using highly-realistic multi-compartment anisotropic head models is important for the understanding of tDCS and the guidance of its application in experiments. Finally, by means of Helmholtz’ principle of reciprocity, our results are also relevant for EEG and MEG source analysis.

Current density distribution (in A/m²) within realistically shaped six compartment head model with brain anisotropy. Thinned version of the calculated vector field is presented, where only the middle cone of each 4mm x 4mm block is visualized.
Tu-124 - Simultaneous Spectral EEG/MEG Inverse Solution Using Variational Bayes: Simulation and Analysis of Alpha Lateralization by Attention

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We implement an inverse solution for combined EEG and MEG data. The EEG forward solution is obtained from a boundary element model, and the Biot-Savart law provides the MEG solution. These models are used in a variational Bayes scheme to estimate the activity at cortical sources. Variational Bayes approximates the true posterior distribution of estimated variables with simpler distributions, often a conjugate distribution to the prior. We obtain spectral estimates of sensor noise and cortical source variance. This scheme is applied to simulated simultaneous EEG/MEG data obtained with 102 magnetometer and 128 EEG channels. Simulation studies were carried out to quantify the robustness with different numbers of samples, underlying source configurations and different levels of added noise. Relative error ranged from 8.12% to 13.3%, increasing as added noise increased.

The scheme is applied to a combined EEG/MEG attention switching experiment. The subject is directed to detect isooriented bars occurring amidst a larger number of flickering randomly oriented bars in one visual field, ignoring similar stimuli in the other field. The attended visual field is switched at random intervals. Orienting attention toward one visual field is known to lateralize EEG, particularly parietal and occipital alpha. The variational Bayes inverse is used to estimate the cortical spectrum from single- and dual-modality signal spectra. We focus on the power change that occurs when the locus of attention switches visual fields (see Figure). In left-to-right switches, the MEG-only solution shows an increase over the right hemisphere, significant \( p < .05 \) Holm-Bonferroni t-test) in a small occipital patch. The EEG and MEG/EEG show a significant decrease in potential over left occipital hemisphere and a significant increase over right occipital and parietal and left frontal areas. This similarity between EEG and combined MEG/EEG reflects the higher EEG SNR for alpha lateralization.

Single-subject left-attending to right-attending switch alpha power ratio (decibels). Channels with significant change are marked with red (increased) and blue (decreased) dots.

Tu-125 - Diffeomorphic Susceptibility Artefact Correction of Diffusion-Weighted Magnetic Resonance Images

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Diffusion-weighted magnetic resonance imaging (DW-MRI) is a key investigation technique in modern neuroscience. Since DW-MRI requires the acquisition of image volumes for several diffusion directions, fast acquisition techniques are commonly used. A
drawback of these sequences is the high sensitivity against small perturbations of the magnetic field caused, e.g., by different mag-
netic susceptibilities of soft tissue, bone and air. These inhomogeneities cause geometrical distortions and intensity modulations in
DW-MRI data and complicate the fusion with anatomical images like conventional T1- or T2-weighted MRI. In order to limit the
degradation of DW-MRI data, we present here a variational approach based on two reference scans with reversed polarity and hence
reversed distortion effects. To this end, we incorporate the physical distortion model into a variational image registration framework
and derive a tailored nonlinear regularization functional to obtain smooth and diffeomorphic transformations. By using state-of-the-
art image registration tools we obtain an accurate and fast correction algorithm.
We evaluate the applicability of our approach to highly distorted DW-MRI in a group study. For all datasets, the automatic correction
algorithm considerably reduced the image degradation. We show that after correction, fusion with T1- or T2-weighted images can be
achieved by a simple rigid registration. Furthermore we demonstrate that the novel scheme provides meaningful, i.e., diffeomorphic,
solutions independent of the actual choice of the regularization parameters.

Tu-126 - A state-space modeling approach for reconstructing the spatially focal and tempo-
 rally smooth current sources using the spatially inhomogeneous dynamical model

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State-space modeling is a promising approach for EEG/MEG current source reconstruction because the spatio-temporal behavior of
current source is explicitly modeled by the equation of dynamics (state equation). Although there have been several studies which
pursue use of state-space model for current source reconstruction, it remains underdeveloped to obtain spatially focal current sources
in the distributed source approach. Here we propose a method to obtain the current source reconstruction in high spatial resolution
while the temporal constraint is imposed by the dynamics equation. To enable focal current source reconstruction, we account for
spatially inhomogeneous dynamics by introducing the model parameters that differ for each cortical source. In particular we use
AR(1) model as the dynamics model. The model parameters and the intensity of the current sources are jointly estimated. In order
to circumvent the high dimensionality of the model (more than one thousand), we apply the full Bayesian model and the variational
Bayesian method for parameter and source estimation. The prior distributions for the model parameters effectively reduce the sen-
sitivity to modeling error, and the variational Bayesian inference reduces computational cost. Through simulation experiments and
application to real MEG data, we have confirmed that our proposed method successfully reconstructs focal current activities each of
which evolves with its estimated temporal dynamics even for the case modeling errors exist.

Results of current source reconstruction for real MEG data from the auditory experiment
Tu-127 - Statistical Theory of Beamformer-based Brain Mapping

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Reconstructing neural activities based on the measurements outside a brain is an ill-posed inverse problem since the observed magnetic field could result from an infinite number of possible neuronal sources. The challenge comes from two sides: source localization and estimation. The so-called minimum-variance beamformer mapping represents one of popular and simple solutions to the above problem. While a significant number of recent publications reported the ability of magnetoencephalography (MEG) to detect neuronal activity emanating from multiple sources in the brain, there is a lack of a general statistical theory on what can and cannot be inferred from the beamformer. In this paper, such a theory is developed. We analytically show how the spatial and temporal dimensions (i.e., lead field matrix and temporal correlation structures) of a beamformer affect its performance in brain mapping. We study the signal cancellation and interference rejection effects of a beamformer in the presence of multiple sources. A new neural activity index is also proposed for source localization based on a sparse estimator of sensor covariance matrix. Conditions are provided for convergence rate of sparse beamformer estimation. The implications of the general theory are further examined by simulations.

Tu-50 - Cortical oscillatory activity of DBS treated Parkinsonian patients

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Patients suffering from Parkinson’s disease (PD) display abnormal synchronized oscillatory activity within the basal ganglia thalamocortical circuitry. Particularly, excessive beta band oscillations are thought to be antikinetic. We studied the effects of bilateral electrical stimulation of subthalamic nucleus (STN) on cortical spontaneous activity by magnetoencephalography (MEG) in the pericentral and the occipital cortical regions in 11 PD patients. The large artifacts produced by deep brain stimulation (DBS) were suppressed by spatiotemporal signal space separation (tSSS) algorithm.

The amplitudes of oscillatory alpha and beta-band signals did not differ between the DBS on and off conditions in the pericentral region. When DBS was turned on, UPDRS (Unified Parkinson’s Disease Rating Scale) rigidity scores correlated significantly with 6-10 Hz and 12-20 Hz source strengths whilst eyes were open. When DBS was off UPDRS action tremor scores correlated significantly with pericentral 6-10 Hz and 21-30 Hz source strengths and with occipital alpha, particularly when eyes open.

Occipital alpha strength decreased when DBS was turned on and eyes were closed. The peak frequency of occipital alpha activity when eyes were closed, correlated negatively and significantly with total UPDRS motor scores and with rigidity subscores, suggesting that progression of motor symptoms in PD is associated with a decreased peak frequency of the occipital alpha.

Our results show that effects of DBS can be studied by MEG when appropriate artifact rejection methods are utilized. STN DBS modulates brain oscillations both in alpha and beta bands, particularly in pericentral cortical regions, and these oscillations apparently reflect the clinical condition during DBS.
Tu-51 - MEG Functional Connectivity Reveals a Task-Positive Sensorimotor Network

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Non-invasive mapping of neuronal networks analysis is a growing field of interest termed functional connectivity magnetoencephalography (fcMEG). However, establishing the functional relevance of the identified networks requires the task-related modulation of fcMEG measures. This study presents a novel approach for measuring ‘state-related’ (i.e. task vs. rest) changes in fcMEG. We provide evidence that this approach can effectively reveal specific ‘task-positive’ networks. Modulations in fcMEG, measured as cortico-cortical coherence (CCC) between 80 anatomically prescribed nodes, were calculated between the resting state and the performance of a visually directed motor task in a healthy cohort. Task-related increases in whole-head CCC relative to a resting state (i.e., task-positive) were identified between areas established as part of the sensorimotor network, as well as frontal eye fields and prefrontal cortices (p < 0.005). The task-positive network was activated predominantly in the beta and gamma frequency bands. This study provides evidence for the use of MEG to identify task-specific functionally connected networks in a non-invasive, patient-friendly manner.
Intra-group reliability of changes in cortico-cortical coherence between task and rest states is shown for the (a) beta and (b) gamma bands. Red and green lines indicate coherence was reliably (99.9th percentile) greater during the task and at rest.

Tu-52 - Imaging coherence in schizophrenia: a pilot MEG study

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Previous studies examining coherence and connectivity deviations in schizophrenia patients relied on standard coherence measures between recording sites. Our group has developed a coherence-imaging methodology to assess and quantify imaged brain structures that contribute to the default mode network (DMN). Magnetoencephalography (MEG) based coherence-imaging was applied to assess the coherence deviations in schizophrenia patients during the resting state. Twelve patients diagnosed with schizophrenia and twelve healthy control subjects were studied. A ten minute resting state MEG brain scan was performed with eyes open. MEG coherence analysis was carried out to determine the cortical areas that interacted strongly within each frequency bin of 2Hz from 1-50Hz. A discriminant function analysis was performed on the schizophrenia versus control data. Statistically significant increased coherences were detected in schizophrenia patients compared to controls in the left inferior frontal gyrus (BA47), left superior temporal gyrus (BA22), left superior frontal gyrus (BA8) as well as the left lateral orbitofrontal gyrus (BA47). These areas are involved in language, memory, executive and higher cognitive functioning. We conclude that resting state coherences of schizophrenia patients deviate from normal subjects in several behaviorally salient regions. Analysis of imaged coherence by MEG can provide clues to the abnormalities in the resting state.
Significant increased coherences were detected in schizophrenia patients (in red) compared to controls in the left inferior frontal gyrus (BA47).

Tu-53 - Measuring Functional Connectivity in MEG: a Multi-Variate Approach Insensitive to Source Leakage

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Introduction: Recent studies have begun to show the promise of MEG as a means to measure functional connectivity. However, a number of problems with the methodology still remain, including how to deal with the non-independence of voxels in source space (signal leakage) and how to collapse the rich time-frequency information available into a single imaging statistic. Here we describe an approach that addresses these two major problems.

Methods: Resting state MEG data were recorded in a single subject. Data were projected into source space using a beamformer and a seed voxel chosen in right motor cortex. To remove effects of signal leakage, the time series at each target voxel, y, was replaced by its residuals after regressing out the linear prediction based on the time series at the seed voxel, x. x and y were then segmented into 1s windows, Fourier transformed, the absolute value of the Fourier coefficients computed, and collapsed across frequency bands of interest to yield X and Y in which each column represents the (mean corrected) oscillatory power in a single band. A multivariate linear model, with X as the design and Y as the dependent variable, was used to quantify the relationship between X and Y at each voxel as a chi square statistic and thresholded to correct for multiple comparisons (1).

Results: Fig 1A shows cross hemisphere motor connectivity computed with leakage correction, Fig 1B shows the same thing without leakage correction, Fig 1C shows the difference. Note that significant (p<0.05, corrected) interhemispheric connectivity is observed.

Discussion: Our method enables interactions between the power envelopes of neural oscillatory processes to be identified within a multivariate statistical framework. The method is spatially unbiased, removes linear signal leakage between seed and target voxels and offers a means to capture the rich information content of MEG signals in a single statistic.

(1) Barnes et al., 2011 NeuroImage 56:1072-1081
Tu-54 - A Computational Model of Resting-state MEG

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The mechanisms underlying the spontaneous organized patterns of oscillations in the resting human brain are still unexplained. Progress has been made through the identification of spatially robust resting-state networks using fluctuations in the amplitude of alpha (8-13Hz) and beta (13-30Hz) frequency band oscillations detected with magnetoencephalography (MEG) (Brookes et al., 2011) that correspond to the results obtained with slow fluctuations (<0.1Hz) of the resting BOLD signal. Nevertheless, the origin and mechanisms underlying these cortical oscillations are still under debate.

Here, we used a computational model capable of reproducing BOLD resting-state functional connectivity (Cabral et al, 2011) to predict experimental MEG data observed in spontaneous brain activity at different frequencies. In particular, realistic alpha and beta-band oscillations can emerge spontaneously from the network dynamics of weakly coupled oscillators. Using realistic time delays, the system of coupled oscillators tends to decay temporarily to meta-stable states which oscillate at a reduced collective frequency. Interestingly, for realistic delays and using intrinsic oscillations in the gamma-band, these meta-stable oscillatory states occur in the alpha and beta frequency bands. In this dynamical regime, the fluctuation in the synchrony degree of a group of nodes modulates the spectral power density of these nodes, i.e. during periods of low synchrony, nodes oscillate at their individual frequency (i.e. gamma-band) while during higher synchrony periods oscillations slow down to reduced frequencies, temporarily increasing the power in that reduced frequency-band. In Cabral et al. (2011) BOLD fluctuations were explained by slow fluctuations in the synchrony degree. Here, we show that these fluctuations also modulate the power in the alpha and beta frequency bands, which is suggestive of general computational principles underlying spontaneous brain oscillations.

Tu-55 - Regionally specific theta, alpha, and gamma resting state abnormalities in schizophrenia

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fMRI studies indicate an overactive resting state network in patients with schizophrenia (SZ) (Fehr et al., 2003). To better understand resting state abnormalities in SZ, MEG localized resting state oscillatory activity in SZ and healthy controls (HC). Based on previous studies (see reviews in Siekmeier & Stufflebeam, 2010, Gandal et al., 2012), it was hypothesized that resting state low and high frequency abnormalities would be observed, with low frequency theta abnormalities most prominent in temporal regions and high frequency gamma abnormalities observed in multiple brain regions.

21 medicated patients with SZ (22-61 yrs) and 24 HC (21-58 yrs) participated. Six minutes of eyes-closed whole-head MEG data were collected. Frequency-domain VESTAL analyses (Huang et al., 2006) provided 3D maps of brain activity. Between-group t-tests examined 3D maps for delta, theta, alpha, beta, and gamma.

Groups did not differ in delta or beta activity. Greater theta activity in right superior temporal gyrus (STG) and in right lateral occipital cortex (LOC) was observed in SZ than HC. Greater alpha activity in SZ than HC was observed in right STG, left parahippocampal gyrus, right superior frontal gyrus, left temporal pole, and right LOC. Greater gamma activity in SZ than HC was observed in left temporal pole, left LOC, and right middle frontal gyrus. Greater alpha activity in HC than SZ was observed in right frontal areas.

Greater gamma activity in SZ than HC was observed in multiple brain regions, a finding consistent with the hypothesis of greater baseline brain 'noise' activity in SZ (Gandal et al., 2012). However, findings here and in other studies showing increased baseline activity at lower frequencies suggest that baseline 'noise' abnormalities in SZ are not specific to gamma. Brain areas showing low and high frequency abnormalities in SZ did not completely overlap. This may indicate that there are distinct neural networks abnormalities in different brain regions in SZ.

Tu-56 - Resting state network activity during mindfulness meditation

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Mindfulness meditation (MM) training promotes psychological health, yet the neuronal mechanisms associated with these benefits are largely unknown. MM is an effective prophylactic treatment for depression (1), which is associated with dysfunction of the default mode network (DMN) (e.g. 2). We investigated functional connectivity in the DMN in 13 experienced meditators. Neuronal activity was recorded using magnetoencephalography during 10 minutes rest, focussed attention meditation (FAM), and MM.

We used temporal ICA to identify networks of functionally connected but spatially distributed brain regions (3). As expected, there was temporally correlated activity in the DMN (medial prefrontal cortex including anterior cingulate cortex (ACC) and bilateral parietal regions) at rest in the alpha band (8-13Hz), see Fig. 1a. In contrast correlated activity in the DMN for the MM (Fig. 1b) and FAM (Fig. 1c) conditions was confined to the beta band (13-30Hz).

Activity in the DMN is usually reported in the alpha band (e.g. 3), but activity in the beta band has been shown to be associated with cognitive and sensory resting state networks, including the DMN (4). Studies examining DMN activity in depressed patients report increased connectivity in 'affective' regions, which may detrimentally affect connectivity in regions associated with cognitive processing such as the dorsal ACC (5). In contrast, our results show that MM (and FAM) increases functional connectivity in the DMN, which is related to higher cognitive functions such as self-reflection and attention (4). These preliminary results provide an exciting new insight into the neuronal mechanisms mediating the beneficial effects of MM for depression.

Future work will focus on a statistical comparison of DMN connectivity between these conditions (i.e. rest, FAM, and MM).

1 Segal et al.(2003)  
2 Greicius et al.(2007) Biological Psychiatry  
3 Brookes et al.(2011) PNAS  
4 Jann et al.(2010) PLoS ONE  
5 Rose et al.(2006) Neuroimage
Figure 1: Correlation maps of the default mode network during rest (alpha band), mindfulness meditation (beta band), and focused attention meditation (beta band) across 13 participants.


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Alteration of brain communication due to abnormal patterns of synchronization is nowadays one of the most suitable mechanisms for having a better understanding of brainpathologies. Very recently, it has been proved that abnormal changes in both local and long range functional interactions underlie the cognitive deficits associated with different brain disorders. Mild cognitive impairment (MCI) is a state characterized for cognitive dysfunction, such as the memory. The study of the spatial and dynamic alterations in MCI subjects’ functional networks could provide important evidences of the brain mechanisms responsible for such impairment. Moreover, there is a growing interest in the role of ApoE genotype in pathological aging. However, its relation with brain electromagnetic activity patterns needs to be looked into. Here we use magnetoencephalography (MEG) to record resting state activity of healthy elderly people and patients with MCI, with both eyes closed and eyes open. Their ApoE genotype was also determined via a genetic test. Additionally, the subjects had a neuropsychological test done to determine their MCI subtype. Our database consists in 40 healthy elderly people and 60 MCI patients (30 with amnestic type and 30 with multidomain type). In order to provide a functional connectivity pattern, we calculate the Synchronization Likelihood of the MEG time series. The analysis is done for the classical frequency bands, via a statistical test to search for differences between groups with different diagnosis and ApoE genotype. Our result shows an increased connectivity in genotype 3-4 and 4-4, when compared with 2-3 and 3-3. Thus, regardless of having multidomain or amnestic MCI, carriers of APOE allele 4 showed higher synchronization values than controls or non APOE 4 carriers. This indicates a potential link between high synchronization (as a sign of abnormal communication) and a genetic risk for the development of dementia.
Tu-58 - Effects of Oxytocin Administration on Activity in War Veterans Exposed to Combat-Related Trauma

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Exposure to severe traumatic events may lead to the development of post-traumatic stress disorder (PTSD). The hormone oxytocin (OT) has been shown to have anxiolytic effects and has been proposed as a potential therapeutic agent in severe anxiety. Our aim was to examine whether spontaneous brain activity recorded by MEG is impacted by OT administration, and whether the effect differs according to trauma exposure. Twenty-three young, physically healthy, men took part in the study. Fifteen of the participants were exposed to a severe combat-related trauma in the course of their military service (six diagnosed with PTSD) and eight were unexposed controls. All participated in two experimental sessions, 7 days apart. In a double-blind placebo-controlled crossover design, participants were administered either OT or placebo (PL) intranasally. Following administration, a 2-minute recording of resting with eyes closed was performed with a 248-magnetometer system. Data were subjected to spectral analysis using Fast Fourier Transform (FFT) at the sensor level. Mean power in four frequency bands: delta (1-4 Hz), theta (5-8 Hz) alpha (8-13 Hz) and beta (13-20 Hz), was computed for each experimental condition (OT or PL), in each quadrant (left, right, anterior, posterior) and compared between the experimental groups. Trauma-exposed and control subjects differed in alpha power in the right and left anterior regions regardless of experimental condition. Differences between the OT and PL conditions emerged in the beta band of the right and left anterior regions for both trauma-exposed and controls. Since altered beta activity has been associated with disrupted emotional functioning, if validated, the current findings may be of clinical interest. OT administration had a different effect in delta activity in exposed and unexposed individuals. After OT administration anterior delta activity increased among controls, but decreased among exposed veterans.

Tu-59 - Representation of neural plasticity and executive function in resting-state functional connectivity

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Our ability to process and use complex cognitive information depends on the ability to integrate information across multiple brain structures. We used source-space reconstructions of resting-state magnetoencephalography (MEG) data in order to identify deviations in functional connectivity in both patients with schizophrenia (SZ) and agenesis of the corpus callosum (AgCC), and correlated this data with neuropsychological measures of executive function. MEG data were collected from 18 patients with AgCC, 30 clinically stable patients with schizophrenia (SZ) and matched controls. 15 participants from the schizophrenia group were enrolled in a computer-based auditory training program. Four minutes of spontaneous recording (closed) was obtained in all participants using a 275-channel biomagnetometer (MISL). Sources of neural activity in the alpha band (≈ 8 – 12Hz) were estimated using an adaptive spatial filtering technique. Functional connectivity in the alpha band between brain voxels was computed using imaginary coherence (IC). In a group comparison between the AgCC and control groups, three regions were significantly underconnected bilaterally: dorsolateral pre-frontal (DLPFC), posterior parietal (PPC) and parieto-occipital cortex (PO). Low functional connectivity in the AgCC group was correlated with neuropsychological testing measures of processing speed and problem solving. In the SZ cohort following targeted training, increased functional connectivity was seen in left DLPFC and middle temporal cortex. Functional connectivity in DLPFC was also seen to predict the strength of recovery of global cognition scores following training. These findings contribute to an increasing body of literature that indicates that there is a strong relationship between resting-state functional connectivity and executive function impairments and illustrate that these markers can be used to monitor the progression of recovery following cognitive-based rehabilitative paradigms.

Tu-60 - Effect of menstrual cycle on beta-gamma cross-frequency coupling revealed by resting neuromagnetic activity

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Variations of cognitive ability across the menstrual cycle have been reported in the literature. However, the direct effects of sex hormone levels on resting networks in human brains have not been experimentally studied yet. There is increasing evidence that cross-frequency coupling between neuronal oscillations is related to communication between neuronal ensembles with different frequency contents and reflects brain integration. This study aimed at investigating whether cross-frequency phase-phase coupling of local resting network is modulated by sex hormone levels during different phases of the menstrual cycle. Sixteen healthy females were enrolled during menstrual period (MC) and ovulatory phase (OV). Three-minute eye-open resting magnetoencephalographic signals of each individual during each phase were recorded. For each channel, synchronization value of cross-frequency coupling between each pair of frequency bands (2, 4, 8, 12, 16, 24, 32, and 40 Hz) was estimated by calculating phase-locking value (PLV).
and the mean phase coupling z-score was obtained from significant PLV (P < 0.001 corrected with multiple comparison). Statistical comparison between MC and OV phases was performed using Wilcoxon signed rank test. The results showed in the MC phase frontal area displayed more coupling between beta/gamma oscillations whereas less coupling within the occipital area (Figure 1(a)). On the other hand, higher coupling at the frontal-parietal and cerebellum areas were found in the OV phase (Figure 1(b)), where these two regions have been reported as part of resting state networks. Significant difference of coupling between the MC and OV phases was found in the right frontal, central-parietal and left parietal areas (P < 0.01). Our findings implicate that sex hormone level modulated phase-phase coupling of beta/gamma oscillations, which reflected fluctuations of functional integration between frontal-parietal and sensorimotor networks across the menstrual cycle.

![Figure 1. Topography of beta-gamma cross-frequency coupling between MC and OV phase in healthy females. The color represents z-score statistic value which means how different the original data is from all surrogates data.](image)

**Tu-61 - The default mode network of the inebriated brain**

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Alcohol is known to induce transmission of dopamine and GABA, whose concentration is related with human brain default mode network (DMN) activation. We hypothesized that the intake of a moderate dose of alcohol will affect the brain activity of social drinkers at rest in terms of functional connectivity. Electroencephalographic recordings were performed during rest after receiving an alcoholic beverage and placebo respectively. Salivary alcohol and cortisol served to measure the inebriation and stress levels. The activity of cortical sources was estimated with the standardized Low Resolution Electromagnetic Tomography (sLORETA). The power spectrum of the sLORETA solutions and the Magnitude Square Coherence (MSC) on each pair of them were estimated for each frequency band. The networks were treated in the context of graph theory and their parameters were calculated. The power spectrum of cortical sources did not change between alcohol and placebo for any frequency band. The MSC averaged across all sources’ pairs, along with the global efficiency of the DMN, were significantly (p < 0.05) higher following alcohol intake (vs. placebo) in alpha and beta bands. The inter-connectivity of certain nodes, roughly outlining the DMN, was elevated (p < .05 corrected) in alpha band during alcohol sessions indicating a pronounced functional connectivity in the DMN (Figure A). Salivary alcohol was positively correlated with the density of the network in beta band (Figure B, C). Higher salivary cortisol was coupled with less spatially segregated function in the DMN in both alpha and beta. Our findings demonstrate that the human DMN exhibits pronounced functional connectivity following alcohol intake. As expected, measures that globally quantify the brain functional connectivity were sensitively affected by alcohol-induced alterations in the DMN function and this can be partially attributed to the alcohol-induced alterations on neurotransmission.
Tu-62 - Connectivity and task-induced deactivation in the DMN. A MEG study in Mild Cognitive Impairment (MCI)

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The default mode network (DMN) was defined by Raichle et al. (2001) to refer to the task negative network, as the function of all its brain regions is suspended during any task or goal directed brain activity. It has received growing attention since it has been found that is disrupted in neurological and psychiatric disorders such as autism, schizophrenia and Alzheimer disease.

The DMN is particularly relevant for aging and dementia since its structures are vulnerable to atrophy, deposition of the amyloid protein and show reduced glucose metabolism. Several studies made with fMRI have found that the task-induced deactivation pattern and its functional connectivity are progressively decreased along the continuum from normal aging to MCI and to clinical AD. In order to provide more information about what happens in the DMN in normal and pathological aging, we have used the magnetoencephalography (MEG) with 60 healthy people and 70 mild cognitive impairment (MCI) subjects (30 with amnestic MCI, 30 with multidomain MCI) comparing a resting state condition with a mental arithmetic task with two levels of difficulty. To analyze the connectivity we have applied the Synchronization Likelihood to the MEG time series. Our results are in line with previous studies, finding differences in connectivity and task-induced deactivation, depending on the difficulty of the task, although with differences between the MCI and the control group, suggesting that the alteration of the DMN could be considered as an early marker of AD pathology.
Tu-63 - Frequency Specific Interactions of MEG resting state activity within and across brain networks as revealed by Multivariate Interaction Measure

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Resting state networks (RSNs) are sets of brain regions exhibiting temporally coherent activity fluctuations in the absence of imposed task. RSNs have been widely studied with functional Magnetic Resonance Imaging in the infra-slow frequency range (< 0.1 Hz), and their topography reflect stationary temporal correlation over minutes (1). However, neuronal communication occurs on a much faster time scale, at frequencies nominally in the range of 100 - 102 Hz.

We examined phase-shifted coherence estimated by the Multivariate Interaction Measure (MIM) (2) in the delta (2-4 Hz), theta (4-7 Hz), alpha (8-12 Hz) and beta (13-25 Hz) frequency bands of resting-state source space MEG signals between nodes of the dorsal attention network (DAN), one of the most robust RSNs, and between the DAN and other networks.

Interactions, as revealed by MIM, occurred between homologous left and right hemisphere regions of the DAN in the delta and alpha frequency bands. Even stronger coupling was detected between networks. Visual regions bilaterally showed interactions in the alpha band with regions of the DAN, while, bilateral somatomotor regions interacted with DAN nodes in the beta band. This study demonstrates the existence of consistent frequency specific interactions between cortical regions belonging to the same RSN, as well as between RSNs, on a millisecond time scale.


Figure 1. Seed based MIM map in the alpha band in one subject.

Tu-64 - Effects of continuous theta burst stimulation on human sensorimotor oscillatory activity

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Continuous theta burst stimulation (cTBS) is a repetitive transcranial magnetic stimulation protocol that can inhibit the excitability of the motor cortex (M1) and impair movement for 4-1 hour. In order to determine the effects of cTBS on motor function, we used magnetoencephalography (MEG) to characterise oscillatory dynamics in M1 before and after cTBS. The effect of 40-seconds of cTBS applied over left M1 on corticospinal excitability was measured using MEP amplitude in 16 participants. Inhibition (reduced MEP amplitude) was detected in 8 participants (responders). Three MEG recordings (275-channel CTF) were acquired (pre-cTBS, 10 mins post-cTBS and 30 mins post-cTBS) each consisting of 3 x 60-sec rest periods and 30 visually-cued abductions of the left and right index fingers. Bilateral M1 cortices were localised using a beamformer analysis of the post-movement beta rebound following the finger abductions. Virtual electrodes at these loci were used to reconstruct the oscillatory activity in the beta (15-30Hz) frequency range in the rest and movement conditions before and after cTBS. Our results demonstrate that cTBS increases spontaneous beta power in M1 in the stimulated hemisphere of responders, with no effect in M1 in the unstimulated hemisphere. Non-responders showed no beta power change in M1 of either hemisphere. Reaction times increased in the index finger contralateral to stimulated but not unstimulated hemisphere of responders. This effect was absent in the non-responders. We demonstrate that a specific window of pre-movement beta power is predictive of reaction time in the pre-stimulus recording. Using change-point analysis we demonstrate the relationship between pre-movement beta power, movement-related beta desynchronisation and reaction time, and describe the effects of cTBS on each of these components. These data provide insights into the electrophysiological mechanisms underlying...
Tu-65 - Statistical mapping of pathological slow activity in resting-state MEG data.

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Slowing is a typical feature of EEG signals recorded in a wide variety of neurological conditions. As pathological slow signals tend to have high amplitude, they dominate the EEG signal over much of the scalp, making it challenging to infer their sources. The ubiquity of slowing as a result of neural pathology makes it a sensitive indicator but not a specific one, reducing its diagnostic value. Localizing the generators of pathological slow activity greatly increases its utility, as it may reveal cortical dysfunction that is undetectable by structural imaging methods. Localization has been successfully accomplished by fitting single dipoles to the peaks of large-amplitude waves. However, this method uses only a small portion of the total dataset and may miss other meaningful features of the signal. We present an alternative procedure based on SAM beamforming. A beamformer is used to compute virtual signals on a regular grid of locations throughout the cortex. An advantage of this procedure is that any desired scalar quantity can be computed based on the signal, and therefore mapped in 3D space, allowing for extremely flexible signal processing choices. As an example, we estimated the power spectra of virtual signals on a 1cm³ grid throughout the brain, and computed the median frequency between 1-40 Hz. Pathological slowing is indicated by a downward shift of this quantity in damaged cortex relative to healthy tissue. The method is illustrated in aphasic stroke patients with left hemisphere lesions, who participated in an MEG study of language processing. In cases of cortical lesions, slowing is observed in the perilesional cortex. In subcortical stroke, we observed slowing in intact cortex that is deafferented due to underlying white matter damage. Beamformer-based mapping of pathological slowing appears to have the potential to reveal subtle dysfunction in structurally intact cortex, and may prove useful in the early diagnosis of dementia.

Tu-66 - A novel method for detection of phase shift of alpha rhythm in single trial

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Recent experimental studies have shown the influence of instantaneous phase and amplitude of ongoing oscillations in electroencephalogram (EEG) and magnetoencephalogram (MEG) on the performance of a variety of cognitive tasks. Hence, it is important to estimate precisely the instantaneous phase and amplitude of the ongoing oscillations. Moreover, the ongoing oscillations are synchronized and/or reset by external stimuli. These phenomena are caused by phase shifts of the ongoing oscillations. Therefore, it is important to detect the shifts. First, we develop a novel method that can be used to estimate the instantaneous phases and amplitudes of the ongoing oscillations with high accuracy by modeling the phase and amplitude as Markov random field (MRF) models (1). Using a belief propagation technique, we construct an exact-inference algorithm that can be used to estimate instantaneous phases and amplitudes. We generated simulated data that consist of oscillatory activities in the alpha frequency range and observation noise.
The simulated data are similar to experimental EEG data. The instantaneous phase and amplitude estimates obtained with our method have significantly greater accuracy than those obtained with Hilbert transform. Second, we developed a novel method for detecting phase shifts of the ongoing oscillations in a single trial based on the above mentioned method. Our method used the line process technique to detect shifts of the phase and amplitude of an ongoing oscillation. By using our method, we detected phase shifts of the alpha rhythm in flash EEG data after the flash stimulus onset. This result suggests that our method is useful to detect phase shifts of ongoing oscillations in a single trial.


Tu-67 - Monochromatic ultra slow oscillations in the human electroencephalogram

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Ultra slow electroencephalographic oscillations (< 0.1 Hz) have been extensively investigated in humans and animals and were shown to represent a fundamental mode of brain functioning. Despite the ample evidence for the presence of ultra slow oscillations in the human brain, little is known about their biological mechanisms. Here we report on the existence of monochromatic ultra slow oscillations (MUSO) in the human electroencephalogram (EEG). MUSO were present in 8 out of 10 subjects during the restful wakefulness. The striking signature of these oscillations is their almost monochromatic spectral profile, with a frequency band of 0.08-0.15 Hz, thus being restricted to a frequency range of merely 0.07 Hz. The topography of MUSO varied across subjects. Application of spatio-spectral decomposition revealed a presence of multiple MUSO components in a given subject. The oscillations were most pronounced after the application of spatial derivatives such as bipolar or Laplacian montages. In order to address the biological origin of these 0.1-Hz oscillations we performed simultaneous recordings with multi-channel EEG, near infrared spectroscopy (NIRS) and non-invasive continuous measurement of arterial blood pressure. While the peak frequency of NIRS and blood pressure was often similar across subjects, the peak frequencies of MUSO differed considerably from both NIRS and blood pressure oscillations. In some cases we observed coherence between MUSO and Oxy-Hb (NIRS)/arterial blood pressure. We hypothesize that MUSOs can occur due to the modulation of the blood-brain barrier DC potential by mechanical fluctuations related to hemodynamics or due to skin vasomotion. The discovery of such possibly extra-neuronal pronounced oscillations opens an avenue for studying hemodynamic responses with EEG and in addition poses a number of questions concerning the interpretation of previously recorded low-frequency neuronal oscillations in humans.

Tu-78 - EEG spectral topography and functional connectivity in patients with treatment resistant depression after DBS surgery

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Major depressive disorder (MDD) is an illness that affects 4% of the population in the industrialized world annually. Patients are usually treated with psychotherapy and medications, but up to 30% of those undergoing therapy do not achieve remission. Recently, deep brain stimulation (DBS) has been introduced as an experimental therapy for drug resistant MDD patients. While there have been encouraging results, about a third of those individuals also fail to achieve meaningful benefit. Although substantial progress has been made recently in understanding the neural circuitry that underlies MDD, the ability to characterize differences in brain dynamics between those who benefit from DBS and those who don’t is lacking. In this study we investigate EEG resting state data from 14 patients that have undergone DBS surgery, with the aim of establishing correlations between spectral power (SP) and functional connectivity (FC) measures on one hand and the Hamilton MDD rating scale (HAM-D-17) on the other. Two resting state datasets were recorded from each patient, with the DBS electrodes on or off. Our preliminary analysis on a subgroup of 10 patients with the electrodes off shows increased power in the beta band (12 to 20 Hz) correlating with the HAMD-17 score. In the low beta range (12 to 16 Hz) high power was distributed over the occipital and parietal regions, while in the high beta range (16 to 20 Hz) the power was predominantly focused in the parietal regions. FC analyses show that left-right synchronization asymmetry correlates with HAM-D-17 scores in the central and parietal-occipital channels, showing more synchronization in the left hemisphere in subjects with poor scores. We conclude that resting state dynamics recorded by EEG provide distinct information about SP and FC patterns that may provide insight into potential treatment efficacy. This preliminary analysis will be further extended to compare SP and FC with the electrodes on and off for all 14 patients.
Synchronization left-right asymmetry in the central (left) and parietal and occipital channels (right) as a function of HAMD-17 score. A HAMD-17 score < 8 indicates remission. Synchronization is calculated using phase lag index (PLI).

Tu-79 - EEG activity during blue and red light exposures in the early morning

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It is now well known that nighttime melatonin secretion in humans is effectively suppressed by short-wavelength (blue) light. However, more information is needed to elucidate the effects of light on alertness during the day and whether light can affect human alertness independent of melatonin suppression. The present study sought to examine how light affect human alertness during the morning after awakening, when melatonin levels would be naturally decreasing. We used two narrowband light sources, the short-wavelength (blue) light chosen for the study had been previously shown to reliably suppress nocturnal melatonin, whereas the long-wavelength (red) light did not. We measured EEG activity during exposure to each of these lights and during a dark condition in the early morning after awakening. Nine adults (five males and four females) participated in the study. All EEG sessions started at approximately 07:00 and ended approximately at 08:00. Darkness was maintained for the first 12 minutes, as an adaptation period. After the first 12 minutes, one of the three lighting experimental conditions (blue or red light, or no light) was presented for 48 minutes. During each session, EEG measurements were conducted in the last part of the dark adaptation period, repeated six times with 5.5 minutes intervals between them in the following period. The duration of each EEG recording interval was 150 seconds. Each EEG data was subjected to fast Fourier transform analysis. The results showed that EEG power in the alpha frequency range (8-13 Hz) was significantly reduced in the blue and red light conditions, compared to the dark condition, after approximately 30 minutes of light exposure. These results suggest that subjects' sleepiness was reduced by exposure to both blue and red lights in the morning. Moreover, the results suggest that the alerting effects of light in the early morning hours may be mediated by mechanisms independent of acute melatonin suppression.

Tu-100 - Changes of the electroencephalogram induced by repetitive transcranial magnetic stimulation: A comparison of different stimulation protocols in healthy subjects

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To optimise rTMS protocols of the left dorsolateral prefrontal cortex (DLPFC) for depression, we used EEG combined with rTMS as a tool to measure long-lasting modulation of brain activity by rTMS. Different protocols were tested: continuous Theta Burst Stimulation, intermittent Theta Burst Stimulation, 1 Hz, 10 Hz, and Sham as a control. For each protocol, we measured modulation of EEG power by comparing post-rTMS EEG with baseline recordings obtained before rTMS. 20 healthy subjects were recruited. Each subject received a total of 800 impulses in four trains during wakefulness with eyes-closed. Every session was divided into three fifteen-minute EEG recordings: baseline before the stimulation, time of stimulus and post-stimulus. EEG signals were recorded with 64 electrodes EEG-TMS cap (Brain Products). The signals were digitally band-pass filtered (1-45 Hz), artefacts were removed with visual and independent component analyses. Time-frequency analysis (Morlet wavelet) of cleaned EEG was computed and averaged within delta, theta, alpha and beta bands. Each period was cut into 144 epochs of 5 seconds duration, in which EEG power was time-averaged and entered into statistical designs as proposed in Statistical Parametric Mapping for EEG software (www.fil.ion.ucl.ac.uk/spm). On the subject level we performed two sample t-test between baseline
Tu-101 - Are behavioral and neuronal scaling laws correlated?

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Power-law scaling laws and fractal self-similarity are central characteristics of both psychophysical and neuronal dynamics [1, 2]. It has, nevertheless, remained unclear whether the behavioral scaling laws are causally related to those of underlying neuronal circuitry. To address this question, we performed simultaneous MEG/EEG recordings with subjects performing a continuous audio-visual threshold-stimulus detection task (TSĐT) where roughly half of weak constant-intensity stimuli were consciously perceived. Auditory and visual stimuli were temporally uncorrelated, and subjects were instructed to respond to all perceived visual or auditory (single-task conditions), or either stimulus (dual-task condition).

The detection rates in the single-task condition were significantly greater than those in the dual-task condition (39% and 29% of visual stimuli (p<0.001), 38% and 31% of auditory stimuli (p<0.05). Fractal properties of the detection rate time series were assessed by using detrended fluctuation analysis (3). The scaling exponents were significantly different from those of surrogate data for both auditory (0.72 ± 0.02, 0.74 ± 0.03, p<0.010) and visual (0.77 ± 0.02, 0.79 ± 0.03, p<0.001) stimuli in both single- and dual-task conditions, respectively. Interestingly, the exponents for auditory and visual modalities were significantly different (p<0.025) indicating that different brain systems exhibit distinct scaling laws at the behavioral level.

Psychophysical performance in an audio-visual TSĐT thus exhibits salient fractal-like dynamics. We will next use MEG/EEG and source reconstruction methods to quantify the scaling-laws of cortical oscillation amplitude fluctuations [2, 3] in resting-state and during task performance to test whether they predict individual behavioral scaling laws.


Tu-102 - Scale-free properties of MEG brain signals capture plasticity

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Most electrophysiological studies focus on evoked responses and oscillatory rhythms. However, ongoing activity and resting-state are relevant for cognitive functions and are more difficult to capture. Novel methodological techniques enable the description of the 1/f power spectrum in brain signals: in a first approach this consists of addressing scale-free properties (SFP) in the brain. Recent investigations coarsely contrasting conscious states (sleep vs. awake) have shown a change of 1/f power. Here, we hypothesized that refined perceptual discrimination during learning/plasticity could modulate the SFP of cortical responses. For this, we used MEG recordings acquired during a learning task.

Importantly, we capitalized on new analysis called the Wavelet Leader Based Multifractal Formalism (WLBMF) which robustly characterizes the SFP with two important measures: self-similarity (i.e. the amount of long memory or the slope of the log-power spectrum) and multifractality (local fluctuations). Self-similarity solely captures long memory on the second order statistics whereas multifractality probes how far the long memory lies from the Gaussian statistics. A visual learning task (5-12 min) was repeatedly alternated with a rest block (5 min, eyes open). The task consisted of discriminating the coherence of Random Dot Kinematograms (RDK). Additionally, all participants (n=12) passively viewed a RDK localizer at the end of session. Here, we report self-similarity in all sensors during learning, passive viewing and rest. Interestingly, learning blocks significantly differed from the rest blocks both in self-similarity and multifractality, however, no significant differences were found between the passive viewing and the rest blocks.

Our data suggests that SFP significantly differ from resting state when participants are engaged in a task. Crucially, measures of self-similarity over specific sensors exhibited a significant decrease after learning/plasticity.
Physiological basis of MEG and EEG signals

Tu-103 - Stimulus-specific adaptation measured in rodents using MEG

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Using a newly developed magnetoencephalograph (MEG) for small animals, we have measured cortical responses to onsets and sound transitions in guinea pig and gerbil using tone complexes. The small-animal MEG system has 9 magnetometers placed in an 8x8 mm square array. An additional set of 3 magnetometers and one accelerometer are used to measure and suppress environmental noise. Sound is delivered using Etymotics transducers in either closed- or free-field conditions. Using this system, we have characterised some basic properties of sound-evoked MEG responses in rodents. Auditory onset responses occur with a latency of approximately 50 ms and last 300-400 ms, roughly half that observed in humans, while offset responses are extremely weak. We have also observed MEG responses consistent with stimulus-specific adaptation (SSA). When short pips presented at a regular repetition rate were irregularly switched between two frequencies, a greater response was obtained for the first tone following a transition than for later tones. Consistent with previous physiology results, the underlying adaptation was extremely rapid and largely complete by the second pip in a sequence. We also report more sophisticated forms of adaptation, similar to those observed in humans, for example, guinea pigs show MEG responses to the unexpected omission of the second tone in a tone pair. In the long term, joint MEG and electrophysiology in the same animals will allow us to elucidate the neural basis of the MEG response, bridging the gap between human brain imaging and invasive animal electrophysiology.

Tu-104 - A modeling study of the neurophysiological response to transcranial magnetic stimulation in a simple rat head model

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Transcranial magnetic stimulation (TMS) is an established tool for non-invasive, painless brain stimulation. It acts via a time dependent magnetic field, generated by an external coil, inducing an electric field in the brain, which can interact with the neural system (Barker et al, 1985). Although TMS is a widely used technique for neurological and psychiatric disorders, such as depression, tinni-
tus and Parkinson’s disease, the underlying neurophysiological mechanism is still unclear. Therefore, we modulate this response to a 20mm figure-of-eight TMS coil (MagStim, UK) in a simple rat brain, see Figure 1. The rat head is modeled as 6 concentric ellipsoids representing the tissues scalp, bone, CSF, grey matter, white matter and thalamus. The nerve fibers are considered as straight radially-oriented bundles located in white matter connecting the thalamus with grey matter. The isotropic material properties are obtained from the 4-Cole-Cole model (Cole and Cole, 1941). The coil is positioned in the axial plane, perpendicular to the skull. We simulated the effect of a low-frequency (1Hz) and a high-frequency (10Hz) sinusoidal stimulation, both at 50% output on the Rapid2 stimulator.

The induced electric field is calculated using the recently developed independent impedance method (De Geeter et al, 2012). It affects the membrane potential of a nerve fiber as described by the passive cable equation (Roth and Basser, 1990). Studies have shown that straight nerves are primarily activated by the gradient of the component of the electric field along the nerves, the so-called activating function.

We simulated the spatio-temporal variation of the membrane potentials along a nerve bundle using the Crank-Nicholson method. Remark the differences in response between the 10Hz and 1Hz stimulation. This can most likely be associated with the depolarization or enhanced excitability and hyperpolarization or depressed excitability that occur at high- and low-frequency TMS respectively.

Fig.1: Axial and sagittal views of the modeled figure-of-eight TMS coil with coating and the rat head. The resulting membrane potentials in a nerve bundle for 10Hz and 1Hz stimulation respectively.

Tu-105 - Computational Neural Modeling of MEG Signals at the Cellular Level: Insights into Spontaneous and Evoked Sensory Signals

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Computational neural modeling is a powerful tool to non-invasively study the mechanisms and function of MEG measured human brain signals. We have developed a biophysically principled computational neural model to interpret the origin of MEG signals at the microscopic cellular level. In contrast to neural field models, our approach incorporates anatomical and physiological details of individual pyramidal and interneuron cell types across the cortical laminar, as well as exogenous synaptic drive into distinct layers. This approach allows us to directly compare units of measure (nano-ampere-meters) between model and MEG data estimated as primary current dipoles. Our method has led to novel predictions on the cellular and network level mechanisms of functionally relevant spontaneous rhythms from the somatosensory cortex containing alpha and beta components their impact sensory evoked responses and modulations with healthy aging in adults. Currently, we are expanding the applications of the models to study neural mechanisms regulating changes in cortical signals during development in infants and children. Here, we will describe current results that show close agreement between model and MEG data and initial in vivo electrophysiological recordings from rodents supporting model predictions.
Tu-106 - Theta phase reset in rat S1 upon tactile stimulation

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Theta oscillations are commonly seen in rat LFPs, most often in hippocampus during locomotion, or in sensorimotor cortex during whisking. In this study, we recorded epidural LFPs in adult (8-17 months) male Long-Evans rats over a large cortical area (6x7mm), including S1, S2, anterior auditory belt, and M1. We observed theta oscillations in primary sensory areas of rat macro- and micro- vibrissae, in the absence of both locomotion and whisking. Moreover, we found that tactile stimulation of the upper lip produces a phase reset in the theta oscillations, and subsequent phase locking to stimulus onset for more than 1 s after stimulation. The theta oscillation and its phase reset are robustly localised to S1, as is evident from current-source density reconstruction. In a subset of the animals, we simultaneously registered vibrissal motor activity to exclude whisking in response to the tactile stimulus. These phenomena were observed in awake unrestrained animals, but not during ketamine-anaesthesia. In sum, this study showed for the first time the existence of neocortically generated theta oscillations in the rat and its modulation by tactile stimulation.

Tu-107 - Gamma power in superficial layers is coupled to the phase of alpha oscillations in deeper layers in monkey visual cortex

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Recent MEG and EEG findings suggest that neural oscillatory activity in the alpha band (7-14 Hz) plays an important role in inhibiting task-irrelevant neuronal processing. Neuronal activity in the gamma band (30-120 Hz) is thought to reflect active cortical processing. Several EEG and MEG studies have shown an interaction between alpha and gamma activity in humans. We build on these findings by examining the cortical microcircuitry responsible for such a coupling. We recorded the laminar field potential from the primary visual cortex of two resting but awake monkeys. This approach allowed us to simultaneously evaluate the temporal and spatial characteristics of signals from all cortical layers, and thereby establish the relationship between the alpha and gamma field potentials. We discovered a strong coupling between the phase of spontaneous alpha oscillations in deeper layers and the gamma power in superficial layers, suggesting that the latter is entrained by the former. Furthermore, current source density (CSD) analysis aligned to isolated bursts of high gamma power revealed that the alpha oscillation phase-aligned to the gamma bursts has a source in the infragranular layers of the cortex. Adding to a growing body of evidence demonstrating that alpha activity directly modulates neuronal excitability in a phasic manner, these results demonstrate a clear laminar organization of this modulation within the cortical microcircuit. This modulation might serve as a mechanism for gain control of infragranular layers over corticocortical neuronal projections in the superficial layers. These findings help to explain EEG and MEG results in humans which show a direct influence of alpha phase on neuronal excitability and perception.
Tu-108 - Macroscopic high-frequency EEG responses reflect single neuronal spikes

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Low-frequency (<100 Hz) EEG/MEG responses are dominated by post-synaptic activity and sub-threshold membrane potential fluctuations with little contribution from supra-threshold (spiking) activity. In contrast, high-frequency EEG/MEG activity (≥400 Hz) has been linked to population spike bursts [1-3]. Recently, we have shown that the amplitude of these oscillations correlates with patterns of single neuron responses on a single-trial basis (4). Here, we study how high-frequency EEG/MEG signals could be explained by the direct contributions of single spikes. To this end, we combine extracellular recordings from single units with simultaneously recorded epidural EEG signals in awake macaque monkeys. To assess the single-spike contribution to the macroscopic surface EEG we calculate the spike-triggered EEG average. This measure contains a prominent, short-lived peak (<0.5 ms) with a peak-to-peak amplitude ∼100 nV. This estimate of a single-spike contribution is consistent with earlier modelling studies of extracellular fields related to spiking activity (5), and, in particular, it explains the amplitude of evoked high-frequency EEG oscillations. We therefore can conclude that high-frequency EEG/MEG provides an unique opportunity to study spiking dynamics non-invasively in humans.


Tu-110 - A neuronal network model for simulating the effects of repetitive transcranial magnetic stimulation on local field potential power spectra

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Complex interdependencies between stimulus duration, frequency and intensity obscure the exact effects of rTMS stimulation on neural activity in the cortex. To explain the effects of rTMS on neural activity, we define a random graph based asymmetric Hopfield network with synchronous updates. The simulation output is defined as the sum of the output Ei(t) of all neurons at time t which corresponds to macroscopic properties like the local field potential (LFP). The temporal resolution of the simulation was 1ms. We
assume that TMS stimulation acts on all cells of the network. The intensity was modeled by the factor I (4, 6, 8, and 10) which causes an additional increase of the postsynaptic membrane potential of 0.5 mV times I. The temporal distance between these artificial discharges was varied (factor F: 0.5, 1, 2, 5, 10 and 20 Hz). The activity of the neural network is simulated repeatedly and independently (20 independent model runs = $\geq$ 20 segments of 24 s length each). TMS stimulation starts for a period of 8 s, beginning at 8 s and lasting to 16 s of each segment.

For further analysis we selected two sections of 1 s length: the first section ending immediately before the onset of the TMS stimulation and the second section beginning immediately after the TMS stimulation (T: PRE, POST). The spectral power of the output is calculated using the Fast-Fourier-Transform (FFT) and averaged twice: over all segments (independent model runs) and within the common frequency bands (B: delta, theta, alpha, beta, gamma). We perform repeated measures ANOVA with 4 factors: T, F, I and B. As a main result, our simulation reveals that the effects of rTMS on the alpha, delta and theta band mainly depend on the applied stimulus intensity (Figure 1). Except for the stimulation frequency of 0.5 Hz, we do not observe any changes in the band power after stimulation at stimulus intensities of 4, 6 and 10. The model adequately explains experimentally observed effects of rTMS.

![Image: Graph showing mean band power POST vs PRE with standard deviation bars.]

### Tu-17 - The effect of 1/f fluctuation in inter-stimulus interval of flicker stimulus on flicker fusion threshold and visual evoked magnetic field

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This study focused on the effect of the exponent n of the fluctuation 1/fn in inter-stimulus interval (ISI) of visual stimulus on variation of flicker fusion threshold (FFT) and elicitation of visual evoked magnetic field (VEF). The FFT was defined as the frequency of an intermittent light stimulus that provoked a flickering sensation. ISI times were given by three types of fluctuation 1/f0, 1/f1, 1/f2, and with a fixed interval. Visual stimuli were presented to subjects with a light-emitting unit with a liquid crystal light valve. The FFTs were changed with the exponent n of the fluctuation 1/fn (F(3/21)=7.76, p=0.0001), as the FFT of 1/f0 was 111.9Hz, 1/f1 was 164.0Hz, 1/f2 was 81.5Hz, and the fixed interval was 46.5Hz on averaged data from eight subjects. The ratios of the flickering sensation detection with a individual threshold frequency of 1/f0 were also changed with the exponent n (F(3/21)=4.74, p=0.003), the ratio of 1/f0 was 80.0%, 1/f1 was 90.7%, 1/f2 was 65.9%, and the fixed interval was 3.0%. The off response of VEF was changed in reverse for the FFTs and the detection ratios with the exponent n of the fluctuation 1/fn (F(3/21)=3.46, p=0.035)(Fig.1).

The variations of the FFT, the detection ratio and the off response of VEF were supported by the simulation results of the effect of the exponent n of the fluctuation 1/fn in noise on detection of the subthreshold of signals by adding stochastic noise, as Stochastic...
Resonance in the FitzHugh-Nagumo neuronal model reported by Nozaki and Yamamoto (1997). The generation of minor informational order with stimulus from a random state enhanced the effect of the intensity of stimulus for the nervous system on the variation of the thresholds frequencies and the detection ratios, and inhibited elicitation of off response of VEF. The further magnification of informational order decreased the intensity effect of stimulus, arising from the increment of the exponent n of fluctuation 1/fn.

Fig. 1 showed the averaged wave forms of On and Off responses of visual evoked magnetic fields, elicited by 1/fn fluctuation in inter-stimulus interval of flicker stimulus, recorded in channels of occipital area at a maximum amplitude of P100m component.

**Tu-18 - Visual evoked magnetic fields elicited by checkerboard color-reversal stimulations.**

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Standard checkerboard pattern-reversal stimulation uses a black and white checkerboard pattern, with the pattern reversed every half cycle. Pattern-reversal stimulations evoke an achromatic sensation of motion because the subjects feel as if the white grid pattern is moving back and forth. Checkerboard color-reversal stimulation uses a static black and color checkerboard pattern, with the color grid alternated every half cycle, while maintaining the black grid in position. We used a 10 by 10 checkerboard color-reversal stimulation which alternated the color between red and green every 500 ms. Visual stimuli subtended an angle of 9 deg by 9 deg, and monocular left or right half visual field stimulations were presented to the right eye of six normal right-handed male subjects (mean age 22.5 ± 0.8). Visual evoked magnetic fields were measured with a 148 ch. magnetometer in a darkened magnetically shielded room. Unexpectedly, the evoked magnetic fields elicited by the checkerboard color-reversal stimulation showed waves similar to the triphasic N75-P100-N145 peaks elicited by checkerboard pattern-reversal stimulation. Source analysis with the single current dipole model identified two different sources: a peak at 106.0 ± 13.5 ms which originated in the left striate cortex (V1) indifferent to the stimulation side, and a peak at 166.8 ± 16.7 ms which originated in the ventral extrastriate cortex (V4) contralateral to the stimulation side (Fig. 1). This study found a peak similar to P100 was generated even for static (pattern-non-reversal) chromatic (color-reversal) stimulations, and a peak similar to N145 was generated through the wavelength sensitive ventral pathway, with simultaneous activations first in the left V1 at about 100 ms and then in the V4 contralateral to the stimulation at about 160 ms. The activation area for V4 was similar to the location estimated for N145 activities using the two dipole model. However, the direction of the current dipole in V4 was opposite.
Tu-19 - Temporal dynamics of spatial phase congruency sensitivity in human visual cortex

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Spatial phase information is important for visual perception. Features like edges and lines are perceived at locations where spatial frequencies across spatial scales are maximally in phase ( Morrone and Burr, 1988 ), i.e., at locations of maximal phase congruency (Kovesi, 1999). Recent functional magnetic resonance imaging (fMRI) studies have shown sensitivity to the spatial phase congruency in human visual cortex (Henriksson et al., 2009, Perne et al., 2008). However, due to the limited temporal resolution of fMRI, these studies have left open the question whether this sensitivity originates in the primary visual cortex (V1) or in a higher-level visual area.

In this magnetoencephalography (MEG) study, we aimed to clarify the temporal sequence of the phase congruency sensitivity in human visual cortex. The stimuli were compound grating patches, composed of five different spatial frequencies (f, 3f, 5f, 7f, 9f, where f = 0.4 cyc/deg) that were summed with either congruent or random phase alignments. The stimuli were shown in the left lower visual field quadrant at mean eccentricity of 7.6 deg. The data were analyzed with cortically-constrained L2 minimum-norm current estimates using the MNE software. For each individual, we also localized low-level retinotopic and higher-level object-selective visual areas with fMRI.

In V1, the activity was greater for the congruent phase stimuli than for the random phase stimuli already around 100 ms after the onset of the stimulus presentation ( Wilcoxon’s signed rank test across subjects, N=10, p < 0.05). The sensitivity to phase congruency in the higher-level visual areas emerged later. Within the object-selective posterior fusiform gyrus, this effect was observed around 190 ms after the stimulus onset.

These results indicate that phase congruency sensitivity emerges in V1 before higher-level visual areas. Early phase-sensitive pooling of frequencies across spatial scales would enable fast localization of natural broadband edges.

Tu-20 - Parietal Beta Activity Predicts Form/Motion Integration

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Synchronized activity of neuronal ensembles plays important functional roles in information processing. Crucially, activities in different frequency bands were previously reported to correlate with perceptual, cognitive or motor processes. Beta band activity has recently attracted growing interest, however, its functional role remains disputed as several studies related Beta to a variety of cognitive processes -perception, memory, attention, decision or motor preparation- raising vivid debates (Donner and Siegel 2011).

We report novel findings demonstrating MEG Beta activity in healthy humans provides a hallmark of the visual integration of elementary component motions into a whole moving figure. Our results reveal that Beta band activity provides a signature of perceptual integration. Beta modulation tightly correlates to the participants’ subjective rating and not to low-level stimulus characteristics or high level cognitive processes. As a matter of fact, we show that Beta modulation provides significant trial-by-trial predictions of perceptual states, thus providing a neural signature of perceptual form and motion integration. In contrast, Gamma oscillations do
not discriminate between perceptual states.
Overall, these new results support the view that Beta band activity underlies perceptual integrative processing while gamma oscillations reflect local encoding of low level features.

Tu-21 - Looking for the LOC with MEG using frequency-tagged natural objects

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Previous fMRI studies found that Lateral Occipital Complex (LOC) is preferentially activated by visual objects. Here, we used frequency-tagged 3D dot scans of natural objects, and their scrambled counterparts to localize with sources reconstruction in MEG cortical regions subtending object perception as the LOC, and characterize the dynamics of their sustained MEG responses. Object tagging, consisting of Rapid Sequential Visual Presentation (RSVP) of Objects, Scrambles or mix of Objects and Scramble at 2.5Hz rate was compared to feature tagging -dot renewal- with a single object at the same frequency. Localizer-defined ROIs from fMRI were also compared to, and used for, Magnetic Source Imaging. Results indicate that multiple object tagging reveals stronger activations in the temporal lobe than tagging with single object presentations. Contrasting responses to Objects and Scrambles revealed cortical sources activated between 150 and 350ms in regions comparable to those usually found with fMRI using the same -Object/Scramble- contrast. Contrasting mixture of Object and Scramble to Object or Scramble alone conditions revealed enhanced object-related activity for the mixed condition emerging around 150ms after each new stimulus onset. Cortical sources localized in the anterior temporal pole known to be involved in semantic processing were also activated. Altogether, the results indicate that frequency-tagging with MEG is well suited to uncover the localization and dynamics of perceptual processes underlying object processing.

Tu-22 - Temporal Dynamics Underlying Cognitive Processing of Referential Gaze

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Previous behavioral and neuroimaging studies suggest that eye contact modulates action generation and is supported by a brain network encompassing the medial prefrontal cortex, the anterior cingulate cortex and the inferior frontal gyrus. Besides pure directional information, gaze may also convey purposeful reference to objects and events. Despite its constitutive role for nonverbal communication this referential capacity of gaze is largely under-investigated. Often, referentially potent gaze stimuli entail directional information are contrasted with non-social stimuli or they entirely lack directional properties that build the basis for purposeful reference. To study the processing of referential gaze we employed a newly developed variant of a stimulus-response-compatibility paradigm that modulates the referential significance of gaze shifts serving as directional stimuli in a spatial action task by systematic variations of the preceding eye contact. In a first behavioral study, this task was administered to 27 healthy volunteers. Analyses of the response latencies suggest referentially charged gaze shifts to facilitate spatially congruent as compared to incongruent actions. The latency distributions revealed a constant influence of referential gaze with an onset before 300 ms. In a second study we will investigate the associated temporal dynamics of neuromagnetic correlates recorded in 24 volunteers using a 248 channel whole-head MEG system. We aim to examine the temporal dynamics of stereotypic brain responses using cross-trial phase statistics from decomposed MEG signals. Stimulus-locked neural activity will further be localized using magnetic field tomography. The implicated findings will be discussed on the background of our behavioral study and previous fMRI evidence suggesting a deep-seated neural mechanism for discerning the referential aspects of human gaze behavior.

Tu-23 - Investigating the neural correlates of the Stroop effect with the magnetoencephalography

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In the Stroop task, reporting the ink colour of a written word when the word itself is a colour name incongruent with ink colour (e.g. ’red’ printed in blue) induces a robust interference effect. Functional neuroimaging techniques have explored the neural correlates of the Stroop effect, but its underlying neuronal network is still a matter of debate. This study uses magnetoencephalography (MEG) with voxel-based analyses (SPM8) to investigate the timing and localization of brain regions implicated in the Stroop effect.
MEG (Elekta Oy, Finland) data were acquired in 12 right-handed healthy subjects (mean age 29.5 years) performing a colour-word Stroop task. Subjects were asked to respond as quickly as possible to congruent (C, 50% of stimuli) or incongruent (I) visual stimuli by pressing a button corresponding to the printed colour. Evoked magnetic fields (EMFs, -200 to 800 ms post-stimulus) were extracted for each subject and condition in SPM8 after preprocessing using the signal space separation (Taulu et al., 2004) method. Behavioural results revealed a significant interference effect (reaction times I ≥ C, p < 0.001). Analysis of EMFs in sensor space disclosed significant differences between conditions (I ≥ C) in a spatiotemporal cluster around 400-500 ms post-stimuli over the left temporo-parietal (paired t-test, p < 0.05 corrected) and mesial frontal (p < 0.001 uncorrected) sensors. Contrasts in source space (I ≥ C, paired t-test) within the identified time window (400-500 ms) disclosed significant differences in source activity in the left posterior parietal (PPC) and supplementary motor (SMC) cortices. No significant differences were observed in later time windows. This MEG study highlights the early involvement of left PPC and SMC in conflict monitoring. These data bring further evidence supporting the key role of SMC in interference cognitive control.

Tu-24 - Frequency-dependent topographical variations of visual steady-state responses recorded by MEG

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Studies of frequency tuning in the early visual system have shown resonant properties in the alpha and gamma band range (Rager & Singer, 1998) but a progressive slowing down of evoked response latencies (Bullier, 2001) suggests that resonant frequencies may shift along the cortical hierarchy. In others’ and our own previous fMRI work, we found that hemodynamic responses in different brain regions along the ventral visual stream indirectly indicated different tuning peaks when subjects viewed alternations of semantically meaningful stimuli at varying rates (Tong et al, 2007, Gauthier et al, in prep.). We launched an MEG study to obtain evidence that with slower stimulus alternations resonance phenomena extend into more anterior visual regions. Participants were instructed to passively maintain fixation while a face and a house periodically alternated at frame duration ranging from 50ms to 400ms. A functional localizer for face, house and object-responsive regions allowed us to obtain evoked related field (ERF) patterns which may serve as a proxy for functionally defined mid- and upper-tier visual brain responses. Preliminary data from a pilot subject show that power spectrum of the SSR show both fundamental and subharmonic frequency peaks for each of the frequency tested. The topographical map of tuning frequencies shows an occipital to frontal decrease of the tuning frequency for fundamental frequency SSR. Interestingly, the subharmonic tuning frequency map shows the highest tuning frequencies in both occipital and frontal poles. To assess tuning frequencies associated with the processing steps of visual hierarchy, we used spatial filter selector based on the following signals: occipital alpha (10.5Hz) topography for low-level, the M100 and M170 ERFs respectively for mid- and high-level visual cortex. We found the fundamental SSR tuning peak around 10Hz for low- and mid-level filtered data and different, and slower on average, tuning peaks for the high level.

Tu-25 - Abnormal oscillatory MEG brain activity in cirrhotic patients

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Patients diagnosed with liver cirrhosis and showing symptoms of hepatic encephalopathy (HE patients) have been characterized behaviourally by alterations of the visual critical flicker or fusion frequency, indirectly indicating cerebral dysfunction and impaired oscillatory processing. To attain a more direct and objective correlate of possible cerebral dysfunctions we conducted a combined electro- and magnetoencephalogram (60-channel EEG, 306 sensor MEG) study and compared HE patients with a normal control group. Resting, ongoing brain activity (OBA) and steady-state visually evoked fields (SSVEFs) in response to simple stimuli (checkerboards) and complex visual stimuli (showing familiar and unfamiliar objects) were analyzed. Spectral analysis of OBA revealed a significantly reduced individual alpha peak frequency in patients. Moreover, both groups showed significantly more SSVEF power for unfamiliar compared to familiar visual objects. However, this effect was reduced in HE patients. Further investigation of SSVEFs focused on independent component analysis of the 102 sensor magnetometer MEG data. This analysis revealed several distinct occipital independent components modeling the SSVEF response, specifically in normal controls. These task-specific independent components were largely absent in the patient sample. Taken together, the results indicate abnormal ongoing and event-related brain oscillations in HE patients. The SSVEF findings in particular suggest a lack of local cortical synchronization in response to visual stimuli.

Tu-33 - Categorizing faces and scenes in source space on the basis of oscillations
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There is converging evidence from functional imaging studies that some brain regions can be category-specific by showing different response amplitudes to different categories. Here, we took a different approach to investigating neural mechanisms underlying category-specificity and asked whether brain regions can distinguish categories in terms of temporal response patterns rather than response magnitudes. Ten healthy subjects were presented with pictures of Faces (male or female) and Scenes (indoor or outdoor) and they were asked to memorize the pictures. For this analysis beamforming (implemented at SPM8 toolbox) in conjunction with a single shell forward model was used to define the source space. A dimension reduced summary of the evoked (amplitude and phase) and induced (power) oscillatory (8-46 Hz) responses during first 1 sec after the onset of face and scene pictures were compared in source space using multivariate canonical variance analysis (Barnes, G.R., Litvak, V., Brookes, M.J., & Friston, K.J., Neuroimage, 2011, Soto J.L., Pantazis D., Jerbi K., Lachaux J.P., Garnero L., & Leahy R.M., Hum Brain Mapp, 2009). Those brain regions for which the evoked features best distinguished categories were right occipital cortex, right inferior temporal cortex and left dorsolateral prefrontal cortex. Conversely, those brain regions for which the induced power best distinguished categories were left occipital cortex, bilateral medial temporal lobe (peak in right), left inferior temporal cortex, and right medial prefrontal cortex. The statistical difference in a number of these regions were driven by a multivariate changes which would not have been visible in a standard univariate analysis. Thus our initial results indicate that category-specificity can be signalled within a single brain region through different combinations of temporal features.

Tu-34 - Minor structural abnormalities in the infant face disrupt neural processing: a unique window into early parental responses

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Both Darwin and Lorenz argued that infant faces play an important role in eliciting responsive care from adults. Infant faces have been shown to elicit early, specific activity in the orbitofrontal cortex (OFC), a key cortical region for reward and affective processing. A causal test of the relationship between infant facial configuration and early OFC activity is provided by naturally-occurring changes to the infant facial structure. One such change is cleft lip, which represents a relatively limited, localised abnormality, associated with disruption to early parenting. We investigated brain activity in response to briefly presented (300ms) infant faces with cleft lip and healthy infant and healthy adult faces using magnetoencephalography. We found OFC activity at 140ms in response to healthy infant faces but not to infant faces with cleft lip or adult faces. Activity in the fusiform face area was of similar magnitude for adult and healthy infant faces, but was substantially lower for infant faces with cleft lip. This is the first evidence that a minor change to the typical facial structure can disrupt the robust neural activity usually seen in response to infant faces. This may have implications for caregiving.
Tu-35 - Time evolution of the Steady State Visual Evoked Potentials

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Steady State Visual Evoked Potentials (SSVEP), observed in EEG over occipital areas of the scalp, are natural responses to flicker stimuli. Stimulation within 5-50 Hz induces oscillations at corresponding frequency and its harmonics in the EEG over visual areas of the scalp. This phenomenon is commonly used in Brain Computer Interfaces (BCI).

Designing efficient BCI system requires good knowledge of the behavior of the SSVEP on single trial EEG records. Meanwhile most studies concerning SSVEP focus on averaged EEG responses. In effect, BCIs are often designed on the basis of arbitrary assumptions.

In this study we present an analysis of stability of SSVEP in single trials and the habituation process to the flicker stimulus. This analysis was done using EEG signals recorded during the series of 30-second stimulation periods interleaved with 30-seconds rest periods, on a group of 10 volunteers at two stimulation frequencies with 50 repetitions of stimulation sequence.

Analysis of single trial EEG recordings is difficult due to the high content of noise in the signal. In this study, we applied an automatic method for calculating the optimal montage that maximizes the Signal to Noise Ratio (SNR). Then, the signal was filtered in the frequency domain using a narrow band-pass filter. The instantaneous power of such preprocessed signal was computed.

In most of trials we observed unequivocal decrease of SSVEP power during the first seconds of stimulation. The presence of habituation may disable BCI functioning. In such cases modification of paradigm is needed by interleaving stimulation periods with rest periods. Additionally, habituation rate varied significantly among subjects. Knowledge of this rate allows to personalize BCI classifier function for the user. Providing exact and complete SSVEP characteristics is undoubtedly beneficial as it will help to construct much more reliable BCI.

Tu-36 - Nonlinear processing in neural activity related to binocular interaction

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To investigate brain activity related to the binocular interaction in binocular viewing, we directly evaluated such activity using magnetoencephalography, a frequency-tagging approach, and binocular rivalry. Subjects responded to perceived color under the fusion and rivalry conditions: in the former, the orientations of left and right Gabor patches were the same, and in the latter, they were orthogonal. The results showed that the intermodulation components at the summed tagged frequency and at its harmonics were significantly greater for the fusion condition than for the rivalry condition. Because binocular interaction was stronger for the fusion condition
than for the rivalry condition, our result suggests that the intermodulation components, which must involve nonlinear processing, are related to the binocular interaction. We also show that the intermodulation components had different patterns in the topographies of the signal-to-noise ratios between the fusion and rivalry conditions. This difference suggests that the intermodulation components indicate a possible mechanism for monocular dominant perception and mixed perception. We conclude that the intermodulation components are related to the binocular interaction and are useful for investigating the visual system and visual awareness.

**Tu-37 - Facial color and inversion effects on N170 ERP component**

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It is known that faces are important for our social interaction as we can perceive a lot of information such as person’s race, age, and mood from faces. Recent studies have shown that both configural information (e.g. face shape, and inversion) and surface information (e.g. surface color and reflectance properties) are important for face perception (e.g. Sinha, 2002). Previous ERP studies showed that the N170 component of ERP reflects the neural processing of face and, inversion was reported to enhance and delay ERP component N170. In addition, our previous study reported that the N170 potential was larger in amplitude for atypical-colored (bluish color) faces than for natural-colored faces (Minami et al., 2011). This study aimed to examine the relation of facial color and inverted face affects the ERP, especially focusing on the N170 component. Stimuli consisted of natural and bluish-colored face. The faces were presented in both upright and upside down. ANOVA was used to analyze the N170 amplitudes and verify the effect of face color and inversion effect. In addition, we performed a current density analysis on ERPs to identify brain regions related to orientation and color sLORETA. Analysis of N170 amplitude revealed that the significant interactions between stimulus orientation and color. Subsequent analysis indicated that N170 was larger for bluish-colored faces than natural-colored faces, and N170 to natural-colored faces was larger in response to inverted stimulus as compared to upright stimulus. These results suggested that face color and face inversion effect are not additive but interacting on N170. Our sLORETA analysis showed that the sources of N170 response to face color effect was in the left fusiform gyrus, and to face inversion effect in the right superior temporal gyrus. Taken together, our study elucidated the temporal and spatial distribution of face inversion and color processing.

**Tu-38 - MEG evidence that contrast and colinearity speed up the brain**

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A study modelling the effects of V1 lateral interactions during fast apparent motion (Seriès et al., Vision Research, 2002, 42, 25, 2781-2798.) predicted that a low-contrast Gabor patch aligned to its motion path should appear much faster than the same high-contrast patch, a prediction we could verify in psychophysical experiments. In search of electrophysiological correlates of this
The relationship between behavioral timing and brain activity is essential for exploring the underlying mechanisms of visual perception. To account for the relationship between manual reaction time (RT) and MEG response evoked by the abrupt onset of coherent motion. For the gradual onset, we manipulated the rates of coherence increase. Subjects were asked to press a button immediately after they detected coherent motion. To reduce the effect of noise, hMT+ response, defined by the spatial pattern at the peak latency, was extracted by signal space projection (SSP). We assumed that stimulus is detected when temporally integrated hMT+ response crossed a certain threshold which is independent of stimulus type (both abrupt and gradual). Thus, we determined a threshold for integral hMT+ response and obtained the detection latencies of each coherent motion condition. By comparing the detection latencies and the RTs, we found that they are linearly correlated, which confirmed the validity of integrator model. We finally propose a new model suggesting a functional advantage of such speeding up in contour detection.

Tu-39 - Localisation of gamma oscillations induced by faces using phase scrambled control stimuli

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**Aims**

Intra-cranial recordings have revealed the presence of face-specific oscillatory activity in the gamma-band in human ventral temporal cortex [1,2]. Such effects should also be measurable in MEG, but contrasting time periods of face presentation with non-stimulus (e.g. blank screen or fixation) time periods produces images of relatively widespread gamma-band activity, presumably due to the fact that the low-level properties of face images stimulate many other regions of visual cortex in addition to face-specific areas. Here, we contrasted face images with scrambled images of the same stimuli in which the phase, but not the amplitude, of the Fourier spectrum had been randomised. By contrasting activity between faces and their phase scrambled counterparts we aimed to cancel out the effects of low-level image properties and localise the face-specific part of the gamma-band response.

**Methods**

Data were collected from participants using a 275-channel CTF MEG system while viewing face and phase scrambled control stimuli. Synthetic Aperture Magnetometry was used to localise induced gamma-band activity and the M170 evoked response.

**Results**

We found a difference between unscrambled and scrambled faces in right ventrolateral occipital cortex, close to the putative 'occipital face area'. The M170 evoked response was localised to a similar area. Interestingly we also found a reduction of both the gamma-band response and the M170 in medial occipital cortex, suggesting that faces may suppress activity in early visual areas.

**Conclusions**

The method we present here enables us to differentiate between face-specific gamma-band activity and activity generated by low-level aspects of faces. Thus, the use of phase scrambled images as a contrast for face presentation should enable future MEG studies to more precisely localise and test face-specific effects.

**References**

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Tu-40 - Estimation of visual perception timing for gradual onset of random-dots coherent motion

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The relationship between behavioral timing and brain activity is essential for exploring the underlying mechanisms of visual perception. To account for the relationship between manual reaction time (RT) and MEG response evoked by the abrupt onset of random-dots coherent motion (coherence level changes from 0% to certain value abruptly), Amano et al. (2006) proposed an integrator model assuming that subjects detect stimulus when temporally integrated MEG responses crossed a certain threshold. However, whether the integrator model is valid for visual stimulus with a gradual onset (coherence level changes from 0% to 100% gradually with certain rate) still remains unclear. In this study, we recorded MEG responses evoked by both abrupt and gradual onsets of coherent motion. For the gradual onset, we manipulated the rates of coherence increase. Subjects were asked to press a button immediately after they detected coherent motion. To reduce the effect of noise, hMT+ response, defined by the spatial pattern at the peak latency, was extracted by signal space projection (SSP). We assumed that stimulus is detected when temporally integrated hMT+ response crossed a certain threshold which is independent of stimulus type (both abrupt and gradual). Thus, we determined a threshold for integral hMT+ response and obtained the detection latencies of each coherent motion condition. By comparing the detection latencies and the RTs, we found that they are linearly correlated, which confirmed the validity of integrator model. This revealed that an accumulator in charge of the coherent motion detection might exist. Therefore we investigated the correlation between MEG signals and the integral hMT+ responses to find the neural areas involved in the integration of hMT+ signals. Brain activities around parietal region showed highly similar waveforms to integral hMT+ response, indicating that the parietal area might be the accumulator who receives input from hMT+ and integrates the response.

Tu-41 - The construction of form by the cerebral cortex
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Introduction: Ever since the discovery of orientation selective cells in the primary visual cortex, it has been supposed that they are the physiological building blocks for the elaboration of more complex forms in the brain, in hierarchical steps, though there has never been direct evidence for such a supposition. This hierarchical model supposes that more complex forms should cause stronger activation in V1 and in higher visual area and show longer latencies. We tested the spatial and temporal validity of this model.

Material and methods: Twelve healthy adult volunteers participated. They viewed three different forms of different levels of complexity in a scanner, lines, angles, and rhomboids. Lines and rhomboids represent simple and more complex forms respectively. These forms consisted of 16 lines and were projected onto the nasal lower quadrant of the field of view. To get good spatial and temporal resolutions, we used functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG).

Results: fMRI results showed that all forms activated the same visual areas equally. Rhomboids did not result in stronger activity in any of the visual areas along the form pathways. MEG did not show a difference in latencies between lines and rhomboids and source intensities were not stronger for rhomboids compared to lines.

Conclusion: We conclude that (a) if orientation selective cells are the basis for the construction of form, then this process is undertaken in parallel in at least three different visual areas known to contain them (V1, V2 and V3), (b) there is no evident temporal hierarchy in activation of these areas, as might have been expected from a hierarchical model in which the three areas are activated in sequence, (c) that, consequently, the construction of form by the cerebral cortex is undertaken by parallel processes in separate visual areas along the form pathways.

Tu-42 - Visual processing of self-attributed action effects

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Self-attributed action consequences are subject to sensory attenuation. A number of EEG/MEG studies on auditory attenuation consistently report reduced ERP/ERF components source localized to primary auditory cortex. Modulation of early visual processing under agency conditions has, however, remained controversial.

Here we report psychophysical and MEG data on visual processing of self-attributed action consequences in healthy adults. We gradually modulated the sense of causal control by variations in action-outcome causality and mapping. Participants performed a contrast discrimination task on Gabor patches, whose onset timing was either contingent on or independent of preceding actions. Crucially, stimulus orientation varied according to the prevalent action-outcome mapping, which was cued.

Preliminary behavioural analyses revealed a causality*mapping interaction consistent with sensory attenuation only under conditions of low discriminability. This behavioural effect was not associated with differences in ERF amplitude within the first 300ms after Gabor onset at source level. There was a symmetrical occipital dipole in response to the onset of the mapping cue before Gabor patch onset when comparing the dominant with the marginally less common action-outcome mapping in causal, but not in non-causal conditions. Possibly attributable to V1, this DC-shift exceeded an oddball effect as it maintained its sensor-level topography throughout the ~ 1.3s before Gabor patch onset.

We hypothesize that this effect represents a preparation of V1 for the uncommon action-outcome mapping under conditions of causal control. To test this, we are currently performing source- and time-frequency analyses of the DC-shift as well as a trial-by-trial correlation of the psychophysical and physiological data.

Tu-43 - Attentional modulation of the earliest visual neuromagnetic responses

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Recent EEG studies have shown attentional effect on the earliest C1 component (50-100 ms). There is, however, only one MEG study that reported very early attentional effects at the cortical level, in the V1, using a distributed source model. In this study, we used multiple current dipoles to model the earliest neuromagnetic responses in attended and non-attended conditions. Two types of top-down cuing were employed: trial-by-trial cuing with unpredictable attended location and sustained cuing with attention to a specific location during the whole block. The evoked visual responses were measured on 14 subjects using Elekta Neuromag 306-channel MEG system at the Biomagnetic Center in Jena. Standard stimulus was a Gabor patch presented in the upper left and lower right parafoveal locations for a duration of 100 ms. Target stimulus (P = 0.2) consisted of the standard Gabor pattern with a ring of reduced luminance. The task of the participants was to respond to targets presented at the cued location. In the control condition,
participants had to respond to targets presented at both locations. MEG data were analyzed using the MRIVIEW Calibrated Start Spatio-Temporal (CSST) multi-start inverse procedure for spatio-temporal source localization. Up to three sources were identified during the first 100 ms post-stimulus. Our preliminary results indicated differences in the dynamics of the occipital sources identified for the same stimulus when it was attended and non-attended during 70-100 ms. Both types of cueing caused attentional modulation. The results of our multi-dipole source localization analysis provide new evidence that even the earliest cortical visual neuromagnetic responses are modulated by attention.

Tu-44 - Steady-state visually evoked fields to positive and negative impression stimuli

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Steady-state visually evoked potentials (SSVEP) has been shown to be useful for many paradigms in cognitive (visual attention, working memory, and brain rhythms) and clinical neuroscience (aging, stress, and neurodegenerative disorders). The aim of this study was to examine the SSVEFs associated with the processing of positive and negative impression images. We used the International Affective Picture System (IAPS) which is increasingly used in brain imaging studies to examine emotional processes. Their images also allow valence to be systematically investigated. Seventy-five IAPS images of positive, neutral and negative valence assessed by subjects prior to the MEG measurement were used. The peripheral square, i.e., frame, of the image was flickered black and white at 15 Hz while the image was kept stationary. Those images were randomly presented for 2.0 s on screen set at 120 cm in front of the subject. The image size was 15 degree. Ten healthy subjects participated. MEG recordings were made with a 122-channel whole-head MEG system in a magnetically shielded room. The MEG signals were bandpass filtered from 0.03 to 100 Hz and sampled at 1000 Hz. At least 50 epochs were recorded for averaging. We made multi-dipole estimation of the averaged MEG signals and obtained the amplitude of source waveform in 15Hz component (using a bandpass filter at 14 - 16Hz) of SSVEF in occipital area. The amplitude of SSVEF in occipital area was larger in the negative impression images than the positive impression images between 1.0 and 1.5 s after the onset of the stimuli (p<0.05). This result suggests that the amplitude of SSVEF that originated from the surrounding field of visual object was modulated by the emotional object and that the SSVEF could be a measure of emotion of subjects.

Tu-45 - Interactions between Transient Auditory and Steady State Visual Stimuli

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Neuronal oscillations are considered crucial for information processing in the brain as they can potentially regulate information flow and dynamically bind different cortical regions. This MEG study investigated the interactions between a transient sound and a steady state visual signal. To induce steady state oscillations in the visual cortex, we presented subjects with a continuous visual signal that was luminance-modulated at 10Hz. The transient sounds were presented locked to four different equidistant phases of the periodic

The amplitude of SSVEF in the positive and the negative impression images (* indicate p<0.05).
In 3 subjects, averaged waveforms indicated a subtle but distinct component peaked in a very early latency initial rise latency. P45m is known. However its origin is still unclear. We investigated the origin of the very early latency components P45m of visual evoked neuromagnetic fields using moving equivalent current dipoles continuously estimated from P45m to N75m were localized first in the vicinity of contralateral lateral geniculate body and then rapidly moved along with the optic radiation then finally to the contralateral calcarine fissure.

In addition to the typical N75m component corresponding to the response of the primary visual cortex, an earlier latency component initially on a projected display every 2000 ms. The visual stimulation was delivered totally 1200 times at random intervals of 300 ms poststimulus, where activity was enhanced mainly for synchronous audiovisual trials (phase 0). Collectively, our results suggest that auditory transients and visual steady signals interact in a non-specific and in a phase-dependent fashion.

Tu-46 - Classifying perceived natural images from MEG data using multivariate methods

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Given the distributed nature of brain activity, neuroimaging data may best be analyzed using methods that take these distributed patterns into account. Multivariate analysis methods are sensitive to these distributed patterns and can be used to classify information present in brain signals.

In this study we attempted to decode from MEG data which class of natural images subjects were viewing. Subjects were presented with images depicting either faces, bodies, scenes or tools. Unlike the majority of previous decoding studies, which apply classification methods to fMRI data, we performed classification on MEG data, to include high-resolution time course information. Classification was done using the elastic net algorithm, which was trained and tested on whole brain data ranging from 0.1 to 0.3 seconds after stimulus onset using 10-fold cross-validation.

Using this method, we can reliably decode which image category the subject perceived, with maximum classifier accuracy over 90%. Classification performance is best when discriminating between faces and respectively scenes, tools, and bodies. For the other pairs classification performance is more variable, although occasionally rising well above chance level. These results are indicative of an early distinction in brain activity between different images, which is already present in the first few hundred milliseconds after stimulus onset. This distinction can be considered to be based on semantic information instead of differences in low-level features, as the images were normalized for both luminance and spatial frequency. This analysis shows strong involvement of occipital sensors in successful decoding of perceived image categories. Analyses currently in progress focus on classification based on time courses reconstructed in source space, which would allow us to pinpoint more exactly which brain regions are involved in the decoding of stimulus category and hence in categorical stimulus representation.

Tu-47 - Early latency components P45m-N75m of visual evoked neuromagnetic fields reflect neural conduction in the optic radiation

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In addition to the typical N75m component corresponding to the response of the primary visual cortex, an earlier latency component P45m is known. However its origin is still unclear. We investigated the origin of the very early latency components P45m of visual evoked neuromagnetic fields using moving equivalent current dipoles.

Four healthy volunteers participated in this study. Hemi-visual field white and black reversal visual stimuli were presented alternatively on a projected display every 2000 ms. The visual stimulation was delivered totally 1200 times at random intervals of 2000 ± 200 ms. Neuromagnetic data were measured using a 160-channel whole-head gradiometer at an sampling rate of 10 kHz.

In 3 subjects, averaged waveforms indicated a subtle but distinct component peaked in a very early latency 44.7 ± 2.1 ms (P45m, initial rise latency 36.8 ± 3.1 ms) followed by a typical prominent cortical component in 75 ms (N75m). Moving equivalent current dipoles continuously estimated from P45m to N75m were localized first in the vicinity of contralateral lateral geniculate body and then rapidly moved along with the optic radiation then finally to the contralateral calcarine fissure.

The initial rise latency of P45m is consistent with that of neuronal activities of the lateral geniculate body in macaque monkeys. There is only one human neuromagnetic study that reported delineation of the thalamocortical fiber instead of the optic fiber. This is the first report that demonstrated dynamic neural conduction of the optic fiber using neuromagnetic source imaging.
Tu-48 - Non-invasive measurement of long-range gamma synchronization in humans

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Non-human primate studies have shown modulations in gamma band power in early and extra-striate visual areas during visual stimulation (1). Recent evidence in macaque monkeys has suggested the existence of a strong phase-coherence in the gamma band between V1 and V4 (2). Based on these findings we set out to identify areas of the human brain with significant phase locking to the induced V1 gamma band oscillation, using previously collected MEG data (3). We used previously described methods to locate V1 response in 13 human participants. We then computed whole-brain measures of phase lag index (PLI) within a 20Hz band around the (subject-specific) peak gamma frequency at this location. For each participant we constructed a summary statistic image of the difference in mean PLI between two one second windows beginning 0.5 second after and one second before stimulus onset. We then determined whether any brain regions showed significantly greater PLI during stimulus presentation compared to baseline. Preliminary results show that during left visual field stimulation there was a robust inter-cortical phase relationship between V1 and the left fusiform gyrus (x=-38 y=-50 z=-14mm, MNI space) in addition to a region close to the frontal eye fields (x=+8 y=+60 z=+46mm), with whole-brain family wise error corrected significance p<0.021 and p<0.001, respectively. This provides evidence that long-range phase coupling in the gamma band can be reliably detected non-invasively in humans.


Tu-49 - Visual evoked magnetic fields to 4 Hz repetitive pattern-reversal stimulation

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PURPOSE
P100m of transient (TR) visual evoked magnetic fields (VEFs) is originated in the primary visual cortex (V1). However, neural generator(s) of steady-state (SS) VEFs has not been fully elucidated. We investigated the sources of equivalent current dipoles (ECDs) in each response using 4Hz repetitive pattern-reversal stimulation with a whole-head 306-channel magnetoencephalography.

METHODS
Ten healthy young adults were subjected to this study. A black and white checkerboard pattern (check size, 50 min, mean luminance, 30 cd/m\textsuperscript{2}, contrast, 97 \%) was phase-reversed at a rate of 4 Hz (duration, 1 s, interstimulus interval, 1.5 s) to stimulate each right and left visual half-field (field size, 8 deg). A total of 100 responses were averaged.

RESULTS
In this stimulus condition, TR-VEFs and SS-VEFs were simultaneously obtained in all subjects. In TR-VEFs, N75m and P100m were clearly evoked whereas N145m was not identified because of overlapping with SS-VEFs (Figure). The mean peak latency of P100m was 97.3 ms and its ECD was located in V1 around the calcarine fissure contralateral to the stimulated visual field. SS-VEFs were higher amplitude and quasi-sinusoidal responses compared with TR-VEFs and they were continuously observed from 150 ms after the stimulus onset to the end of stimulus offset. Fast Fourier analysis showed that second harmonic response (8 Hz) was the major component. In 8 of 10 subjects, the ECDs of SS-VEFs were widely spread in V1 contralateral to the stimulated visual field.

CONCLUSIONS
These results suggest that neural generators between TR- and SS-VEFs are differently located in V1. In addition, 4 Hz repetitive pattern-reversal stimulation can be a unique method to obtain TR- and SS-VEFs, simultaneously.
TR-VEFs and SS-VEFs were simultaneously obtained in all subjects. In TR-VEFs, N75m and P100m were clearly evoked whereas N145m was not identified because of overlapping with SS-VEFs.

We-101 - A matched filter to reduce MRI gradient induced artifacts: Application to filtering an ECG signal buried in noise

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Acquiring electrophysiological signals (EPS) during a MRI exam is of current research interest. EPS are useful for patient monitoring and image synchronization (1). However, changes in the magnetic fields, mainly due to the switching gradients, induce ‘contaminating’ voltages (IV) with amplitudes that are much higher than the acquired EPS. In a recent study (2), a parametric model, based on a sum of sinusoids, was proposed to model these artifacts. In this work, we propose the application of matched filters to extract the artifacts from the polluted signal, by cross-correlating the signal with the model proposed in (2).

Experiments were conducted in two steps on a 1.5T MRI system (GE Signa HDxt). The first step consisted on recording the IV signals on the surface of a gelatin phantom placed inside the MRI tunnel, according to the experimental protocol described in (2). The second step consisted on injecting a simulated EPS into the phantom, via a MR compatible transmitter, and collecting the contaminated signal.

An artifact pattern was obtained by averaging fifty epochs of the IV signal. The model’s parameters were estimated by a BFGS optimization. The filter was constructed as a linear time invariant (LTI) system whose impulse response equals the time-reverse of the input pattern in order to maximize the signal to noise ratio (SNR). The choice is backed up by the hypothesis that the gradients’ transfer functions may be approximated by LTI systems (1). We tested the matched filter on a contaminated ECG signal. The results are displayed in figure 1.

The matched filter is an optimal linear filter for maximizing the (SNR) in the presence of additive noise. Its main disadvantage lies in the fact that it requires a full knowledge of the signal.

(1) R. Abächerli et al. 2005 MAGMA (2) A. El-Tatar & O. Fokapu, EMBC 2011
We-102 - Examination of neuromagnetic signals after inhabitation in an ultra high static magnetic field with Magnetoencephalography

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As the static field strength of modern MR scanner is increasing, we set out to test whether an inhabitation of human subjects in an ultra high static magnetic field (≥7 Tesla, T) will effect subsequent MEG examinations. Three healthy male subjects with normal vision participated in a three step within-subject design. Subjects had to fulfill the criterion of being metal free and nonmagnetic (e.g., no dental fillings, no make-up, wearing paper clothes). Prior to participation, subjects must not been exposed to an MR scanner environment or participated in TMS experiments for at least 7 days. In the first step (MEG-0T), neuromagnetic field responses were recorded during a visual quadrant field stimulation. Vertical gratings changing their orientation from 90 to 45 in direction to the centre of the screen [1,2] using a 248 highly sensitive magnetometer whole head MEG system from 4D-Neuroimaging. The next step (9.4T MR), after a break for recovering, comprised a 10min exposure time in the isocenter of a 9,4 T esla MR-PET System (Siemens Healthcare). Here, subjects had to stay still with eyes open. In the final step (MEG-9.4T) the MEG experiment was repeated after 10 min of transportation and preparation. After artifact rejection applying independent component analysis (3) the MEG data were averaged based on the onset of stimulus (40 trials). Preliminary results revealed similar activations pattern in both MEG-0T and MEG-9.4T experiments. The source of the maximum V1 activation at around 80ms (M70) was found to be at the same location in both experiments. This study implies that for special circumstances MEG examinations of subjects which were exposed to ultra high magnetic fields lead to same results as without magnetic exposure.

(2) Duncan KK et al. 2010 Hum Brain Mapp. 2010 Jul,31(7):1003-16.

We-103 - Real time cardiac artifact reduction in Magnetoencephalography

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Real time MEG offers a great potential in providing new insights into ongoing electrophysiological brain processes during running MEG measurements. The analysis however is challenging, since noise and artifact rejection needs to be performed on single trial raw data before source localization is applied. Here we introduce a method capable for real time cardiac artifact rejection. The method is based on independent component analysis (ICA), a widely used method for separating a mixed data set in its underlying informal components. The measured MEG data originate from a mixture of brain activity, eye blinks/movements, heart beats and muscle activity. To optimize ICA for real time analysis we use the concept of constrained ICA (cICA), where prior knowledge of an underlying expected signal (e.g., the cardiac artifact) is used to optimize the internal cost-function of ICA. In general, when using the cumulative density function (cdf) of an
underlying source signal as the demixing cost-function within ICA, signal decomposition will be optimal with respect to the signal of interest. Therefore, an approximation of the cdf of the cardiac artifact signal was implemented in Infomax(1), referred to as cICA. The cdf of the cardiac activity was estimated using the signal from the electrocardiogram (ECG). For testing the above approach, an approximation of the cdf is determined from cardiac cycles in 6 subjects. MEG data were recorded using a 4D-Neuroimaging whole-head magnetometer system with 248 channels. For ICA estimation the data sets were chopped into segments of 10 seconds, which results in a data size of 248x10170.

Cardiac artifact rejection by means of an optimal cICA and Infomax filter was applied to neuromagnetic data from all subjects. On average the number of iterations to converge for Infomax and cICA was 10 and 2, respectively. For the above dimensionality this translates to a mean duration of $2.2 \pm 0.8$ seconds (on an Intel Core i5, 3.30 GHz).

(1)Bell & Sejnowski, 1995

We-104 - Weighted Subspace Filtering for MEG

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Signal-subspace projection methods are used in MEG analysis to extract signal components from noisy data. The reduced-rank extracted components have enhanced signal-to-noise ratio over the raw input measurements. Here we present a Wiener filter solution to the distributed-source MEG inverse problem, incorporating a variation on the SSP method to give a Weighted Subspace Fit of the data.

The WSF scales the reduced-rank SSP vectors to compensate for low SNR, and approaches the SSP solution as the limit at high SNR. In particular, the WSF estimate scales the unitary SSP weights using a regularisation parameter selected as the inverse of the effective rank of the whitened data covariance, this parameter represents the assumed SNR in whitened space. The rank of the WSF operator is determined by the signal covariance, this rank is estimated as the number of data covariance eigenvalues with values above the noise covariance threshold. The WSF-whiten signals closely correspond to the raw data signal amplitudes, demonstrating that it accounts for the adverse signal amplitude scaling which would otherwise be induced by the noise covariance operator correction for intrinsic correlations.

A Wiener filter (as a regularised generalised least squares estimator) is then applied to the WSF-whitened data to calculate source dipole amplitudes. The inverse operator is regularised to the same scale as the standard MNE operator to facilitate comparison when using identical SNR assumptions for the source-amplitude threshold. The WSF method provides more focal estimates of source activity than the standard MNE method. Testing on reduced-SNR data shows the WSF-whitened estimate of source dipoles is robust to poor signal quality. This improves on the dipole estimates from the standard MNE solution, which become more distributed for the same activation threshold at low SNR.
We-105 - Removing line-frequency, video, heart-beat, and vibration artifacts

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The magnetic fields generated by the brain are extremely weak and therefore are affected even by small artifacts from other sources. Some of these may be monitored in an independent way and therefore can be cleaned without affecting the actual brain activity derived magnetic fields, both in the time domain and in the frequency domain. Highly periodic artifacts, such as those generated by the main line supply, or by video equipment (cameras or projectors) may be cleaned in the following way:

1. Obtain a marker for every cycle of the source of artifact and record it through a ‘trigger channel’ with the MEG recordings.
2. For every channel to be cleaned compute the average shape around the marker over many repetitions.
3. Trim the edges by windowing and subtract its mean to assure a 0 DC component.
4. Subtract this average shape cycle by cycle from the signal on this channel.

Typically, the artifact cycle will not span an exact number of cycles. If the artifact is small and the sampling rate is high, the distance between two subsequent markers can be used as an estimate of the cycle length (in samples) for every cycle. If not the MEG data can be interpolated several fold. The cycle period can be smoothed and interpolated. These are then used for removing the artifacts and then the cleaned signal may be decimated back. This method assumes that the artifact size is fixed throughout the recording, or is changing slowly. In the latter case a ‘moving average’ can be computed.

Quasy periodic signals (such as heart beat artifacts), may be removed by the above method while splitting the average to groups of various sizes and computing a separate average for each size.

Building vibrations may have very complex shape. If stationary they can be removed in the following way:
1. Measure the acceleration of the recording hood in the X, Y, and Z directions and record concomitantly with the MEG.
2. Compute FFT of each of the accelerations at maximal possible frequency.

We-106 - ICA-based artefact rejection techniques improve spatial localization of beamformer algorithms in MEG

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Beamforming algorithms used for source reconstruction in magnetoencephalography (MEG) are often applied to unprocessed data assuming that the spatial filtering property of the beamformer prevents interference with brain activity. However, the beamformer’s capacity to block activity from sources outside regions of interest is hindered when strong sources such as eye movements are present. This in turn impacts the beamformer’s ability to detect and accurately localize weak/deep sources. The goal of our study was to characterize dynamics of deep structures (thalamus, hippocampus) and prefrontal areas as participants learned novel associations via trial and error. Fourteen healthy young adults (mean age: 22 ± 2yr sx) performed active learning and choice reaction time with no learning component. For learning, participants associated 4 scene-color pairs. For the control task, participants knew in advance that 2 out of 4 colors were correct and 4 scenes were presented randomly. MEG data was parsed into 150 trials per task with range -2.0 to 1.25 s relative to scene onset and filtered between 0.5-55 Hz. Next, we computed average global field power (GFP) for unprocessed sensor data to determine time intervals of interest. We observed multiple peaks for learning but source estimation was contaminated by task-correlated eye movements. We then removed ocular artefacts using ICA in order to improve GFP estimates. In source space, GFP contributing to the visual evoked field (100-200 ms) included large eye artefacts which decreased GFP magnitude slightly when removed. Other GFP peaks (560-700 ms, 840-900 ms) reflecting eye artefacts were absent in clean data. In cleaned learning data, we found early hippocampal (160-200 ms, Fig 1), bilateral thalamic, medial prefrontal (260-300ms) and anterior cingulate (840-900ms) activity which were not present in unprocessed data. In conclusion, better source localization using the vector beamformer was obtained for data with no eye artefacts.
We-107 - Suppression of uncorrelated sensor noise and artifacts: Demonstration with high frequency brain signals

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The recently developed method for suppression of uncorrelated sensor noise and artifacts from multichannel MEG data is expected to significantly improve the detectability and analysis of brain signals suffering from a low signal-to-noise ratio (SNR). Here we demonstrate the performance of this method by recording the high-frequency oscillations associated with somatosensory evoked responses (HFOs). Traditionally, the detection of these extremely weak MEG signals has required averaging of thousands of trials in order to achieve a reasonable SNR. This new pre-processing method reduces the overall sensor noise level in the frequency band of 400-800 Hz by factors of 4.5 and 2.1 for gradiometers and magnetometers, respectively. Thus, we expect to considerably reduce the number of trials needed for obtaining high-quality HFOs.

We measured SEFs from a healthy male subject, whose median nerve was stimulated electrically at the motor threshold (8.0 mA). A total of 4500 trials with a randomly varying ISI of 180-200 ms were recorded with a sampling rate of 5 kHz and frequency band of 0.03-1660 Hz.

The method for sensor noise suppression is based on the combination of the signal space separation (SSS) model and channel-specific features that allow estimation and subtraction of the sensor-specific uncorrelated signal from each channel separately. The multitaper time frequency representation (TFR) analysis clearly showed the benefit of the preprocessing. The number of trials needed to reach the SNR of 3 in the frequency band of interest was 4381 for raw gradiometer data and 487 for processed data, while 4381 averaged trials resulted SNR of 9.8 for processed signal.

In the high-frequency regime (≥ 100 Hz) uncorrelated sensor noise becomes the dominant noise source in MEG. Thus, the applied method effectively enhances the SNR of brain signals at these frequencies. Potentially this method can have high clinical relevance by revealing e.g. high-frequency epileptic signals.

We-108 - Extraction of infraslow motor signals by dynamic source separation

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Detection of slowly varying magnetic brain signals at frequencies below 0.1 Hz due to sustained finger movements was demonstrated before in an 8-layer magnetically shielded room (7 layers of mu-metal, 1 layer of aluminum). The weak shielding below 0.1 Hz of conventional 3-layer rooms (2 layers of mu-metal, 1 layer of copper: Ak3b Vacuumschmelze, Hanau) makes it very difficult to detect...
brain signals of this type. The separation of multichannel magnetoencephalographic recordings (MEG) into noise components and signals of interest can be done by the denoising source separation (DSS) method (1). Using an averaged stimulus response as bias function for DSS standard auditory evoked responses can be extracted.

To test DSS as a tool to extract slow magnetic brain signals seven subjects were measured using a whole head Yokoga-wa MEG system installed in a 3-layer shielded room. The subjects moved the fingers of one hand for 30 s followed by 30 s of rest and for a duration of 30 min. Beforehand the lower recording bandwidth limit was found to be below 0.01 Hz using the magnetic signal of a coil driven by a generator.

The measured subject data were analyzed using DSS and the time points of movement onset to calculate the averaged response as bias function. In 5 out of 7 subjects a DSS component was found, which was synchronous with the 30 s periods of finger movements and which had a top hat shape similar to the results obtained in the 8-layer room. This shows that the increase of signal-to-noise ratio due to DSS is sufficient to overcome some of the limitations of conventional shielded rooms at low frequencies.


![Fig. 1 DSS result for exemplary subject showing the component time series with activation during the finger movement window.](image-url)

**We-109 - Suppression of uncorrelated sensor noise and artifacts in multichannel MEG data**

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The main difficulty in MEG is that the magnetic interference is much larger than the signals of interest. So far, hardware- and software-related methods have been developed mainly to suppress interference, while the sensor-specific noise and artifacts have not been addressed to the same extent. These contributions may, ultimately, compromise the analysis of single-trial evoked responses or other low signal-to-noise ratio data. So far, random sensor noise has been handled with an estimated noise covariance matrix in source analysis, or by a cross-validation scheme where the correlated part of the signal of any MEG sensor is estimated from the signals of the near-by channels. Our novel method for suppressing sensor noise and artifacts is based on simultaneously modeling the correlated (brain + magnetic interference) and uncorrelated part (sensor noise and artifacts) of a multichannel MEG signal enabling a unique division of the measured signal into these components. Based on previous work, any MEG signal vector can be decomposed into an over-determined parametric model based on, e.g., harmonic basis fields of the signal space separation (SSS) method, or a regularized current dipole mesh. Here, we augment the SSS basis with additional channel-specific unit vectors representing the part of the signal that is uncorrelated with the other channels. When scanning through all the channels with this model (SSS + unit vector), the correlated part falls into the SSS basis while the uncorrelated, channel-specific signal component falls on the added unit vector. We thus get an estimate for the sensor noise and channel-specific artifacts to be subsequently subtracted from the data. The method decreases the white noise of the gradiometers and magnetometers by factors of 4 and 2, respectively, in our 306-channel MEG data. We also show examples of removal of sensor-specific artifacts and demonstrate how single-trial analysis is facilitated without adding bias to the source analysis.

**We-110 - Non invasive imaging of different cortical layers using magnetoencephalography (MEG)**

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The spatial resolution with which neuronal activity can be reconstructed using MEG is limited by a number of factors. Even when the underlying source covariance structure is known, noise remains due to both low signal to noise ratio (SNR) sensor data and errors in co-registration to anatomy.. In previous work we have shown that an inaccurate head model caused by co-registration error due to head movement can severely affect the source localisation(López et al., 2012). To solve this problem we have recently developed a
method to constrain head movement to sub-millimetre levels by producing a head cast made of nylon using 3D printing technology. The head cast is fitted to the individual subject’s head anatomy, thereby restricting movement during scanning. Co-registration error is reduced by using markers on the dewar/head cast and relating them to the subject’s structural MRI.

This gives us access to high SNR data (as measurements can be repeated) and more certainty about the location of the cortex (initial estimates suggest \( \sim 0.25\text{mm} \)). Given this accuracy we were interested whether it would be theoretically possible to distinguish between sources located within different cortical layers.

We simulated a number of sources on the cortical sheet, produced a new cortical manifold of increased or decreased relative size, and used the multiple sparse priors (MSP) algorithm to reconstruct the current distribution on this resized cortex. The algorithm returns an approximation to the log model evidence which can be used to quantify the (marginal) likelihood of any resized cortical model with respect to the original. Differences of greater than 3 mean that one model is 20 times more likely than another. Initial results suggest that, using only 2 simulated sources at 10dB SNR, we can distinguish between two cortical surfaces that differ in size by 7% (corresponding to a cortical thickness of \( \sim 5\text{mm} \)).

We-111 - A trial to reduce magnetic noise produced by tube earphones

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Magnetoencephalography (MEG) has been utilized to investigate auditory processing in the human brain. MEG is considered to be one of the best probes in this sensory modality because of its acoustic silence. Most MEG laboratories in Japan are using the tube earphones manufactured by Etymotic Research (Elk Grove Village, IL, USA) to deliver auditory stimulus to subjects’ ears. Because earphones of this type are not magnetically silent, the noise contamination from earphones is sometimes problematic. The aim of this paper is to identify the dominant noise source and to suggest how the earphones more suitable for MEG can be made.

There are several noise sources in this type of earphones, the electromagnetic miniature speaker (MS), lead wires, compensation circuit (CC), and feeder cable. To evaluate magnetic noise from the MS and CC, the CC was removed from the earphone body and replaced it in the output stage of the amplifier located outside of the magnetically shielded room (MSR). Magnetic noise introduced by driving current was measured before and after the CC removal using a whole head 306 channel magnetometer (Elekta Neuromag, Helsinki, Finland) in the MSR. 100-Hz and 1-kHz tone bursts with 100-ms duration were delivered to the ER-2 placed underneath the sensor unit 30 cm apart from the lowest edge of the dewar in a sitting position.

The noise produced by the transducer itself was approximately 1/36 (-31 dB) of that produced by the CC. When the frequency components of the auditory stimulus are well beyond the cutoff frequency of the antialias low pass filters of the MEG system, noise contamination is limited as transient onset/offset effects. Recent advances in the MEG system have been raising its sampling frequency and the risk of noise contamination passing through the antialias filters is getting higher. The result of this paper suggests that there is fortunately plenty of room for improvement of the earphones of this type as MEG equipment.

Dynamic noise produced by the earphone recorded by the representative SQUID sensor. Dashed lines indicate noise from the CC+MS, and solid lines indicate noise from the MS only. 100-Hz (A) and 1-kHz tone bursts (B) with 100-ms duration.
We examined the effects of aging on high-gamma synchronization during visual attention tasks. Fourteen young (age 18-25) and 37 elderly (age 60-75) healthy, right-handed subjects participated. Written informed consent was obtained from all subjects according to the guidelines of the local ethical committee and the Declaration of Helsinki (1991). Subjects participated in a 3-stimuli visual oddball task with a total of 260 stimuli (10% probability of target and 10% of distracter). Subjects pressed a button with the right index finger only when the target appeared. MEG recordings were carried out with a whole-head 200 channel MEG system (Yokogawa Electric Corp., Japan). Individual T1 structural images were obtained from a 3 T Philips MRI scanner.

In the analysis, virtual sensors were generated with 5mm voxels in MNI space. Event-related synchronization in the high-gamma band (52-100Hz) was calculated at the source level using optimal time-frequency beamformer (Dalal et al., 2008). Functional images were created with logarithmic conversion and spatial smoothing with a 20mm FWHM Gaussian kernel.

Firstly, second level analyses of the young and elderly were conducted using SPM8 (Wellcome Department of Imaging Neuroscience) with a statistical threshold of p<0.05 (FWE corrected). The contrast of [distracter-standard] identified the brain regions specific to the distracter, namely, the visual cortex, precuneus, and thalamus.

Secondly, the effects of aging were examined in each peak voxel. Results revealed that the young showed a greater high-gamma oscillatory increase compared to the elderly, from 0 to 100ms in the primary visual cortex and from 300 to 500ms in the visual associative cortex (Figure 1). Given that gamma synchronization in visual areas reflects the attention levels, our results suggested that a decrease of high-gamma synchronization during stimulus-driven attentive processes might underlie age-related changes in visual attention.

High-gamma power in the [distracter-standard] contrast in visual areas. A positive y value means high-gamma power was stronger for the distracter stimuli than the standard stimuli. Error bars show standard deviation.
We-129 - Neural mechanisms of feature attention revealed by frequency tagging in MEG

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We used a frequency tagging paradigm to study brain networks mediating feature attention. The stimuli were sequences of compound images of faces and houses flickering at different tagging frequencies. Our fMRI-guided analysis of the MEG/EEG signals revealed a network of areas in frontal and temporal cortex that closely followed the attended stimulus frequency at differential phase lags. We further analyzed interactions between the involved brain areas by means of neuronal synchrony and coherence across the spectrum, and we cross-validated the observed functional connectivity with each participants individual tractography. Our results imply that the inferior frontal gyrus provides attentional top-down signals to stimulus-tuned temporal areas by engaging into coherent oscillations.

We-130 - Neural correlates of conscious perception and exogenous attention during visual processing

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MEG (Wyart, 2008) and fMRI (Watanabe, 2011) studies had shown that endogenously triggered attention and consciousness are 2 distinct brain processes, however, it remains unknown if the same dissociation exists for exogenous attention. In the present study we explore the neural correlates of exogenous attention and consciousness during visual processing. Subjects were engaged in the detection and the discrimination of near-threshold stimuli presented in the peripheral visual field. A peripheral cue was presented for 50ms. After a 300ms delay, a circular grating was presented in one hemifield for 16ms. Subjects were asked to discriminate the grating orientation and to subjectively determine if the target was absent or present. Prior the recording session, the target was manipulated to estimate the threshold contrast for which the percentage of consciously perceived target was 50%. The cue position was not informative about the target location. MEG signal was recorded using a 306 sensors system (Elekta Neuromag).

Preliminary behavioral results from 8 subjects show that exogenous attention orienting increase the conscious perception of target stimuli. The first MEG analyses demonstrate a strong effect of consciousness access during target processing. Target stimuli acceding to conscious perception elicited a first specific activity between 200/300ms in posterior regions, following by a parieto-frontal response peaking around 380ms. Our first results confirmed the importance of exogenously triggered attention for the modulation of subjective visual experience. A large neuronal network seem to be involved in the access to consciousness during visual processing, starting around 200ms in the occipital regions and spreading to fronto-parietal regions after 300ms. Time-frequency and source analyses will determine more precisely the anatomy of this network and will allow us to evaluate if exogenous attention operate independently of consciousness at the neural level.

Experimental design and example of difference between seen and unseen target at the sensors level.
We-131 - Attention and emotion-related reduction of broadband gamma power in the default-mode and ventral attentional networks

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The functional significance of default mode network (DMN) deactivation remains largely debated and cannot be completely resolved without accessing its fine-scale temporal dynamics. Recent intracranial EEG studies have explored the electrophysiological underpinnings of the human DMN and the ventral attention networks (VAN) revealing high gamma power suppressions that are correlated with task complexity and subject performance on a trial-by-trial basis (1).

Here, we obtained intracranial EEG recordings from 11 epilepsy patients performing a high attention-demanding discrimination task and a low attention-demanding detection task. In particular, we aimed to compare task-related gamma deactivation networks for targets versus non-target stimuli in two contexts: an emotion discrimination task (target: fearful faces) and a simple pop-out detection task (target: red dot detection). In addition to finding strong brain-wide high gamma (60-140 Hz) power suppression maps (Figure 1A) that closely match the gamma suppression pattern we previously reported in a visuo-spatial search task (1), our results also confirm the relationship between the dynamics of power decreases and task difficulty. But we also found that the power suppression was more pronounced for the target facial expression (fear) in the emotion discrimination task, and that, in the color detection task, it was only significant for the target stimuli (Figure 1B).

Our results provide novel insights into the electrophysiology of DMN and VAN deactivation and fine-tune our understanding of their functional role in terms of global attention engagement to external stimuli, detection of task-relevant stimuli and involvement in goal-directed behavior. Analysis of MEG recordings with the same tasks is underway and will provide direct comparison between the spatio-spectral network properties observed invasively and non-invasively.

(1) Ossandon et al. J Neurosci. 2011

A: Anatomical distribution of gamma-band suppression
B: Example of time course of deactivation (medial prefrontal cortex) for the color detection task (green) and the emotion discrimination task (blue). In both tasks, target stimuli (dotted line) elicit

We-132 - Cholinergic enhancement of visual attention and neural oscillations

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Cognitive processes such as visual perception and selective attention induce specific patterns of brain oscillations. The neurochemical basis of these orchestrated spectral changes in neural activity remains unknown, but neuromodulators are thought to regulate processing. The cholinergic system is linked to attentional function in vivo, while separate in-vitro studies found cholinergic agonists induce high-frequency oscillations in slice-preparations, leading to theoretical proposals that cholinergic enhancement of visual attention might operate via gamma oscillations in visual cortex. Here we applied a cholinergic agonist (physostigmine) during a spatial visual attention task in humans, while recording cortical oscillations. The cholinergic agonist enhanced attentional lateralization
of low-frequency alpha/beta oscillations in visual cortex. This related closely to the drug-induced enhancement of performance. By contrast, the cholinergic agonist did not alter high-frequency gamma oscillations in visual cortex. This observed dissociation between high- and low-frequency oscillations may relate to a recent proposal that lower-frequency oscillations are generated by feedback pathways within visual cortex suggesting that cholinergic neuromodulation in the context of visual attention affects the latter pathways. Our findings show that cholinergic neuromodulation enhances attentional selection via an impact on oscillatory synchrony in visual cortex, but for low- rather than high-frequencies.

**We-133 - Top-down controlled alpha power and phase protect working memory against distracting information**

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It has been proposed that optimal performance in attention and working memory (WM) operations is crucially dependent on the ability to eliminate task-irrelevant information. In particular, if distracting information can be anticipated in time, the efficiency of such inhibition can be even more optimal. In this experiment, we tested whether neuronal oscillations can adjust in phase to suppress anticipated distracting information. We applied a modified Sternberg WM task in which predictable distracters (weak, i.e. a symbol, or strong, i.e. a letter, in different blocks) were presented in the retention interval to human subjects, while we recorded the ongoing brain activity using magnetoencephalography. In addition to an adjustment of alpha power (∼10Hz), the data revealed an adjustment of the phase of alpha activity in anticipation of strong distracters, which was significantly stronger than before weak distracters. Further, in trials with strong phase adjustment, response times to the memory probe were reduced. This was assessed by a significantly different alpha phases for slow and fast trials. Finally, we found that alpha phase modulates gamma power (40Hz). The gamma power was lower at the trough of alpha activity, which indicates a lower excitability at this phase. When the activity triggered by the distracter reached the temporal cortex (∼50 ms after distracter onset), the excitability of this area was then low.

Our findings show that the ‘doors of perception’ close at the time when a distracter is expected (see figure illustrating the key findings). This mechanism is implemented by means of alpha activity which is under top-down control. The anticipatory phase adjustment improves performance and adds to the computational versatility of the neuronal oscillations, since it allows for adjusting the processing capabilities on a fine temporal scale.

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**We-146 - Gamma-band steady-state visual evoked responses reflect distinct sources in visual cortex that are enhanced by attention**

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Schematic illustration of the key findings. The alpha activity adjusted in phase just prior to the onset of the distracter (compare the phases ta and tb). The excitability is lower during the trough of alpha activity than during the peak.
Gamma-band oscillations are believed to facilitate binding of visual information into coherent representations, and are enhanced by attention. Previous EEG and MEG studies have shown that selective spatial attention enhances neural responses to a visual stimulus. This enhancement effect can be measured in the increase of synchronization in EEG and/or MEG by making use of steady-state visual evoked responses (SSVEP/F) paradigms. Previous studies showed attention enhances theta and alpha band SSVEP/F distributed over occipital, parietal to frontal regions. We have carried out an experiment with the SSVEP/F paradigm using gamma band frequencies (20 and 30 Hz) using concurrently recorded EEG (128 channels) and MEG (102 magnetometers, 204 planar gradiometers). The gamma-band steady-state responses are observed mostly over the occipital areas, and the phase distributions of the SSVEP/F each strongly suggest a single generator. However, we observe a difference in phase distribution between the concurrent EEG and MEG, indicating that possibly distinct but spatially close sources. To localize these sources, we constructed head tissue volume conduction models from anatomical MRI scans for each of our 6 subjects, using symmetric Boundary Element Methods (OpenMEEG). For the inverse procedure we implemented both minimum L2 norm and minimum L1 norm solutions. Inverse solutions obtained separately for EEG and MEG shows sources regions primarily in V1 and V2 of the contralateral visual cortex, as identified by retinotopic maps in a separate fMRI study. Attention modulation has a significant effect on magnitude of both EEG and MEG evoked responses at the fundamental frequencies, but the spatial localization result is largely unaffected by attention. The response at the harmonic frequency (40 Hz) exhibited a complex pattern of phase suggesting a cortical resonance with a more complex source distribution.

We-147 - How does the brain represent vibrotactile temporal structure? An SEF study

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Temporal structure is one of important factors in object recognition. Touching objects with different surface roughness cause distinct perception in different timing of successive vibrotactile inputs. To date, however, electrophysiological signature for the perception of temporal structure has not been fully understood. In this study, we measured SEFs to vibrotactile train stimuli with two different temporal sequences: regular train stimuli with constant frequency of 20 Hz and irregular train stimuli with their frequency centered at 20 Hz. The lengths of the train stimuli were 1500 ms, and the two different trains were presented in a random sequence with intervals of 1200-1600 ms. The stimuli were delivered to the right index finger, and approximately 100 responses were averaged for each train. The experiment was performed in two conditions. In the attended condition, subjects discriminated the train stimuli. In the unattended condition, they watched a silent movie to distract attention. Source localization was performed by beamformer. We initially identified transient response (TR) for both regular and irregular trains and 20 Hz steady-state response for the regular train, but these responses were not significantly different between the conditions. Activated areas corresponding to those two components were localized to SI. Interestingly, there was an additional component, which was characterized by sustained response (SR) of over 1000 ms in duration following TR that was observed within 250 ms. SRs were evoked bilaterally, and amplitudes were significantly higher in the attended condition. Estimated sources for SRs were localized to the opercular regions, including SII. Although SII is involved in higher order functions such as sensorimotor integration, a few studies lend credence to the idea that it is involved in roughness discrimination. Therefore, we suggest that SRs reflect at least in part the perception of temporal structure in vibrotactile processing.

We-148 - Alpha activity reflects individual abilities to adapt to the environment

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Recent findings suggest that alpha activity (8-13Hz) is directly responsible for functional inhibition of sensory regions thus allowing filtering of incoming information (reviewed in Jansen&Mazaheri, 2010). For instance, posterior alpha activity is lateralized with respect to the direction of covert attention, with a decrease in the task-relevant contralateral hemisphere and a relative increase in the task-irrelevant ipsilateral hemisphere (Woorden et al., 2000). Recent work showed that this lateralization is modulated by cue reliability, suggesting it to be under top-down control and influenced by the environmental statistics (Haegens et al., 2011, Gould et al., 2011). We conducted an attention switching study in which subjects had to covertly attend to a square in one hemifield and report its color. They had to switch sides when the square-color in the unattended hemifield changed (Fig. A). The likelihood of a target at the unattended side increased with number of trials since the last switch (inter-switch trial number, ISTN, Fig. B). While switch trial likelihood increased with ISTN, there was no effect on the switch rate (trend analysis, p>0.05, Fig. C). We computed the alpha modulation index (AMI) by contrasting attention left and attention right trials per ISTN. There was no significant effect of ISTN in the grand average (p>0.09, Fig. D). However, there were strong individual differences by which subjects utilized the switch trial likelihood. We found a significant negative correlation between the regression slope of the AMI and the switch rate.
over ISTN (p<0.01, Fig. E). Subjects with a stronger decrease in the AMI with increasing ISTN are also those subjects that became better at the unattended square with increasing ISTN. These findings strengthen the claim that alpha activity reflects functional inhibition and show that subjects who adjust their alpha activity to the statistics of the environment benefit behaviorally.

We-149 - Dynamic imaging of oscillatory networks contributing to voluntary and involuntary auditory attention shifting

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Voluntary auditory attention shifting is constantly needed in our daily lives, for example, when a listener switches focus between speakers in a chattering crowd. In such situations, auditory attention may also be involuntarily oriented towards unrelated sounds, such as a fire alarm going off in the room. Here, we used magnetoencephalography/electroencephalography (MEG/EEG) and functional MRI (fMRI) to investigate neuronal mechanisms of voluntary and involuntary auditory attention shifting. Stimulus trials consisting of an orienting cue that predicted the location of a target sound were presented, embedded within streams of dichotically presented non-target standard sounds. Subjects were instructed to shift attention to the cued ear and detected the targets as quick as possible. Occasionally, an unexpected novel sound occurred opposite to the cued ear, to trigger involuntary orienting. Our results suggested that endogenous anticipation and implementation of voluntary attention shifting is associated with 'induced' beta band (13-34 Hz) oscillations. Goal-driven engagement of attention to the cued location, occurring after the initial orienting process, was reflected by sustained frontocingular/temporal gamma (35-100 Hz) activity that correlated with behavioral target detection. Indices of increased endogenous activity were also found after the task-irrelevant novel sounds, as reflected by increased beta/gamma activity, potentially reflecting suppression of involuntary attention shifting and boosting of attention to the relevant sound stream. Our MEG/EEG/fMRI results revealed distinct but mutually interacting voluntary and involuntary auditory attention shifting processes.

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We-150 - Influence of Dopamin on Gamma synchronization during self reflection

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It was previously shown (1) that the degree of self reference was positively correlated to the synchronization in a paralimbic net-
Methods: Fifteen participants were presented with either a non-specific 200ms visual alerting cue or no cue followed by a lateralised discrimination tasks. Cortical oscillations associated with the exogenous cue in advantage measured behaviourally for both target detection and discrimination tasks.

Introduction: In the study reported here, we examined brain activity in response to phasic alerting to elucidate the complex roles of 3-4 brain regions in the 30-100 ms time interval, including bilateral superior temporal gyrus (STG), prefrontal (PF) and parietal (PA) regions. Targeting attention toward the second tone enhanced the M50 amplitude of the bilateral STG responses to the repeated stimulus S2. These results demonstrate that voluntary attention can modulate the gating out phenomenon opening a possibility of using attention control as a potentially efficient mechanism for reducing the gating disorders in some pathological conditions.

We-151 - Attentional modulation of the M50 cortical network underlying the auditory gating out phenomenon

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Spatial-temporal identification of the cortical network underlying the suppression of the M50 auditory response after a repeated stimulation, a process conceptualized as the gating out mechanism, may advance understanding of the neural ability to inhibit redundant information, since a disruption of this ability is often associated with pathological conditions. This study challenges the accepted model of the M50 gating as a preattentive, automatic inhibitory process by investigating whether a voluntary attention directed at the second tone of a pair could affect the gating out phenomenon at the cortical level. MEG recordings (Elekta 306-channel and magnetically shielded room at the Biomagnetic Center in Jena, Germany) and the multi-dipole Calibrated Start Spatio-Temporal method were used to identify the M50 cortical network evoked by the paired-click paradigm in 19 healthy young subjects (21-38 years). Two consecutive (ISI=500 ms) identical short tones (S1 and S2, duration=20ms, f=1200Hz, ITI=8 ± 1 s) were used to evoke standard gating cortical responses. In the second condition, the task was to direct attention toward the second tone and to respond to a rarely presented non-identical second tone of the pair (R=1300Hz, p(S1R) = 0.3) . Preliminary results indicated the activation of 3-4 brain regions in the 30-100 ms time interval, including bilateral superior temporal gyrus (STG), prefrontal (PF) and parietal (PA) regions. Targeting attention toward the second tone enhanced the M50 amplitude of the bilateral STG responses to the repeated stimulus S2. These results demonstrate that voluntary attention can modulate the gating out phenomenon opening a possibility of using attention control as a potentially efficient mechanism for reducing the gating disorders in some pathological conditions.

We-186 - Cortical oscillations in phasic alerting revealed by magnetoencephalography

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Introduction: In the study reported here, we examined brain activity in response to phasic alerting to elucidate the complex roles of cortical oscillations associated with the exogenous cueing advantage measured behaviourally for both target detection and discrimination tasks.

Methods: Fifteen participants were presented with either a non-specific 200ms visual alerting cue or no cue followed by a lateralised square-wave grating (3.5 c/d) subtending 2 degrees of visual angle, 0.1 degrees below midline. For task one, participants responded when they detected the presence of a grating whereas a second task measured discrimination responses to grating orientation. MEG data were acquired using a 275 channel whole head system. Synthetic aperture magnetometry (SAM) was used to localise stimulus related activity.

Results: Participant reaction times to target stimuli in both the detection and discrimination tasks were significantly reduced in cued trials. Analysis of group gamma frequency patterns showed significant power increases for the right and left laterally positioned gratings localized to corresponding contralateral extrastriate regions. Within each corresponding region, gamma power related to target gratings was significantly greater when preceded by an alerting cue compared to non-cued trials. There was no direct relationship between gamma power changes and behavioural responses.

Conclusions: Results show gamma oscillations in response to visual targets are modulated by non-specific visual alerting cues regardless of task criteria. While the alerting cue does modulate sensory processing related to target stimuli, the sensory changes do
not correspond to behavioural responses. Therefore, local changes in gamma activity do not appear to directly modulate response related activity. Further analysis of oscillatory activity in lower frequencies may however identify the mechanism linking sensory and behavioural responses.

We-187 - Differential sensitivity to effects of masked semantic priming in MEG/EEG and fMRI

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This study examines the locus of masked semantic priming effects using MEG/EEG and fMRI. Although MEG/EEG and fMRI semantic priming studies have demonstrated priming suppression (unrelated ≥ related) in left temporal and inferior frontal regions when there is a reasonable lag between prime and target, it is not clear that the same should hold for masked semantic priming, which has been argued to engage more automatic processing. Several masked repetition priming fMRI studies have shown an enhancement of the BOLD response for repeated relative to novel targets, contrasting with the shorter reaction times and reduced electrophysiological response typically seen to repeated targets. We investigated whether masking also differentially impacts fMRI and MEG/EEG responses to semantic priming. Related, indirectly-related, and unrelated pairs were visually presented to the same participants across one fMRI and one MEG/EEG session. Pairs were presented with 100ms SOA and included both forward and backward masking of the prime. To encourage semantic processing, participants were asked to press the button when they detected a probe from a given semantic category on filler trials. ERPs showed a significant N400 facilitation effect (unrelated ≥ related) between 300-500ms. MNE dSPM source estimates of the MEG response localized this priming effect to left anterior temporal cortex. However, in fMRI the most prominent differences between conditions were effects of enhancement (related ≥ unrelated), particularly in bilateral inferior frontal cortices. These results suggest that fMRI and MEG/EEG may be most sensitive to different processes engaged during masked priming, while MEG/EEG in the N400 time-window appears to reflect automatically facilitated processing of a related target. fMRI may reflect memory processes invoked by prime-target relatedness or increased activation in a related target due to overlap between the prime and target representations.

We-188 - A MEG study into the Modulation of Attentional Networks by Task-relevance

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Using fMRI, we have shown that children with ADHD show a raised motivational threshold at which stimuli induce event-related modulation of attentional networks 1, suggesting abnormal motivational modulation of mechanisms implicated in switching between networks. Magnetoencephalography (MEG) offers the potential to study the millisecond-by-millisecond evolution of brain networks and their temporal dependency in response to stimuli 2. We present results from an MEG study utilising a human model of ADHD. A sample of healthy young adults undertook a visual target-detection task in an MEG scanner, in which stimuli varied in task-relevance. Beam-forming was used to translate signals from sensor space to voxel space, and a novel application of Independent Component Analysis (ICA) was used to identify distributed functional networks analogous to those seen in fMRI, allowing the fine-grained temporal relationships between brain networks and their modulation by task-relevance to be delineated. Results (see figure) indicate theta and gamma band synchronisation across networks coupled with extensive beta-band desynchronisation, the onsets of an initial theta burst being temporally staggered across networks from the primary visual networks to networks implicated in attention. Stimuli to which there was a motivational incentive to attend were associated with greater and more sustained beta desynchronisation in primary sensory networks, and greater beta synchronisation in attentional networks. We conclude that MEG offers an informative imaging modality in which to study modulation of networks by motivation in ADHD.

References:
Signal magnitude (normalised deviation from the mean) at each of four frequency bands: 6 Hz (theta), 20 Hz (beta), 60 Hz (gamma) in each of four networks: Primary visual (V1), extrastriate visual, Bilateral Insula, Dorsal Attention Network (DAN). Horizon

**We-189 - Color-based attention and visual awareness rely on independent neural mechanisms**

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There is converging evidence that electrophysiological responses over posterior cortical regions in the 200-300 ms range distinguish between physically identical stimuli that reach consciousness or remain unseen. Here, we attempt at determining the sources of this awareness-related activity using MEG. Fourteen subjects were presented with faint colored gratings at threshold for contrast reported on each trial the grating presence or absence. Subjects were primed with a color cue that could be congruent or incongruent with the grating’s color, to probe to what extent two co-localized features (color and orientation) would be bound in consciousness. The contrast between neural responses to seen and unseen physically identical gratings revealed a sustained posterior difference between 190 and 350 ms, thereby replicating prior studies. We further show that the main sources of the awareness-related activity were localized bilaterally on the lateral convexity of the occipito-temporal region, in the lateral occipital (LO) complex, as well as in the right posterior infero-temporal region. No activity differentiating seen and unseen trials could be observed in frontal or parietal regions in this latency range, even at lower threshold. Color congruency did not improve gratings’ detection, and the awareness-related activity was independent from color congruency. However, at the neural level, color congruency was processed differently in grating-present and grating-absent trials. The pattern of results suggests the existence of a neural process of color congruency engaging left parietal regions that is affected by the mere presence of another feature, whether this feature reaches consciousness or not. Altogether, our results reveal an occipital source of visual awareness insensitive to color congruency, and a simultaneous parietal source not engaged in visual awareness, but sensitive to the manipulation of co-localized features.

**We-190 - Passive time processing: a high-density event-related potential study**

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How we compute time is not fully understood yet. A main question is whether exists an automatic ‘core’ cognitive mechanism engaged in passively monitoring the sensory environment in order to track and process temporal regularities of events as well as which the neural correlates are of such mechanism. To investigate these issues, a passive time processing task was specifically designed, during which high-density event-related potentials were recorded. Participants were presented pairs of visual stimuli (S1 and S2), interspaced by an empty interval (ISI). In the standard condition (70% of trials) the ISI was 1500-ms long, whereas in the two deviant conditions (15% each) it was 2500- and 3000-ms long respectively. Although neither attention nor behavioural responses were required, the passive over-exposition to the standard ISI condition drove participants to automatically create an implicit temporal expectation of S2 onset (i.e., after 1500 ms from S1 offset). This temporal expectation was reflected by the time-course of the deviant-ISI contingent negative variation (CNV), which peaked in correspondence to the point of S2 maximum
temporal expectation regardless the actual duration of the ongoing ISI, and afterwards inverted in polarity towards the baseline. Brain source analysis revealed the activation of two main cortical regions associated with ISI processing, that are the supplementary motor area (SMA) and the right dorsolateral pre-frontal cortex (r-DLPFC). Our data furnish support to the existence of a basic twofold mechanism whenever our brain is requested to passively process time. This mechanism implies: a) the ability to automatically track time durations through a pacemaker-accumulator system, associated with the involvement a network entailing the SMA, and b) the automatic storing, retrieval and comparison in memory of time intervals, associated with the involvement of r-DLPFC.

We-191 - Modulation of visual awareness in- and out-of-time with rhythmic apparent motion

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Sensory entrainment to rhythmic events has been shown to increase cortical excitability and enhance the perception of stimuli. In the visual domain, this has been demonstrated with stationary stimuli (in a single location). Two identical objects presented in sequence at different locations can be perceived as a single moving continuous stimulus (apparent motion). Here, we investigate using MEG the sensory entrainment induced by such rhythmic apparent motion and how it affects the perception of targets presented in and out of time.

The entraining stimuli were two identical flashing white squares in the upper and lower right hemifields, with alternating frequency of 7.5415 Khz. The target is presented between them, either in or out of time with the entraining rhythm. Behavioral results show that targets presented in-time have a small perceptual advantage compared to out-of-time targets, as do subsequent congruent targets (in-time, in-time, and out-time, out-time). These results indicate two types of perceptual enhancement: one due to the presentation of the target in-time with the apparent motion time-course, and another due to habituation to the timing of the target relative to the apparent motion phase in both in-time and out-of-time cases.

Initial MEG data analysis in the time-frequency domain shows a strong entrained alpha oscillation consistent with the apparent motion over occipital areas in all subjects, with each subject showing an individual peak alpha frequency. In addition to primary visual cortex, the left area MT shows the same entrained alpha power. Target presentation suppresses the alpha power in the contralateral primary visual areas and MT while it enhances alpha power in the ipsilateral visual areas. Further in this work, the mechanisms underlying such perceptual enhancements are investigated in the time and frequency domains at both the sensor and source levels.

We-192 - Heart-brain interactions in conscious visual perception

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Consciously perceiving a visual stimulus requires taking a first-person perspective and therefore some minimal concept of the self, that could be based on the neural representation of the internal state of the body and central modulation of homeostatic regulations. Here, we experimentally test the hypothesis that episodes of visual awareness and episodes of unawareness are associated with different states of brain-heart interactions.

We presented 12 subjects with weakly contrasted Gabor stimuli at threshold for conscious detection and recorded MEG signals, electro-cardiogram (EKG) data, blood pressure and eye movements. We sorted trials according to subjects’ reports (stimuli seen or unseen) and studied heart-brain interactions prior to stimulus onset, when subjects are preparing to detect the faint stimulus. Basic cardiac parameters (mean RR interval, R-T variability) were identical in seen and unseen trials. We next examined brain responses to heartbeat, known as the heart-evoked response (HER), that is obtained by averaging MEG data with respect to the R peak of the EKG. This response corresponds to a mixture of cardiac muscle activity picked up by the MEG sensors (the cardiac artifact) and of the neural response to heartbeats, attributed to afferent signals from heart and aortic arch relayed to cortical structures through vagus nerve and brainstem. A cluster permutation test of HER revealed significant differences between seen and unseen trials. Those differences in HER are likely to be of neural origin since they precede any difference between seen and unseen trials in the EKG signal itself. This pattern of results could suggest that during episodes of enhanced sensitivity to external visual events, the brain is also differentially sensitive to internal events such as heartbeats. Additional control analysis disentangling cardiac artifact from neural responses are needed to strengthen this conclusion.

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Recently, there has been increased interest in understanding brain networks and their connectivity, especially regarding structural and functional connectivity at the cortical level. Functional connectivity dynamics and particularly thalamo-cortical interactions are as yet insufficiently integrated with our knowledge of large-scale connectivity and regional function.

An important question, yet to be answered in detail, is how cognitive functions and consciousness are temporally generated across the entire brain space. The challenge in current dynamic brain imaging is to analyze the detailed communication or connectivity dynamics across five dimensions, namely within 3D space across oscillatory frequency and time, and to describe in detail the relation of these dynamics to cognition and consciousness.

Over the past two decades, MEG/EEG work has been reported on the dynamics of functional connectivity, particularly emphasizing that synchronization of neuronal oscillations both within and between brain regions is an important mechanism mediating formation and communication within distributed neural networks. In particular, there is a large and accumulating body of evidence that task-dependent gamma-band activations and connectivity across frequency and time play a vital role in most cognitive brain functions and represent a critical component to the biological basis of consciousness.

We present a conceptual overview of oscillatory network dynamics and its implications for how brain imaging technologies can be further used to probe fully intact functional and temporal connectivity in thalamo-cortical, cortico-cortical, and cortico-thalamic circuits to better understand typical and atypical cognition and consciousness.

We-194 - Effect of stressful conditions on central and autonomic nervous system responses during simulated driving: MEG and EDA relationship.

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We recorded both magnetoencephalographic (MEG) and electrodermal activities (EDA) during standard and stressful driving conditions. We aimed to test the extent to which central and autonomic nervous system (ANS) activities were impacted, with potential detrimental effects on driving behavior. Six men drove a driving simulator in MEG and stopped at the traffic lights when changing from green to orange. They were confronted to stressful conditions (SC) or standard driving (SD), considered the reference. During SC, several scenarios were given to elicit high strain, particularly with time pressure. We processed MEG signal from the motor cortex in the beta band, as well as from the occipital and prefrontal cortices (PFC) in the beta band. We performed SAM analyzes to compare [0s-1s] time-window following light change with [-5s-4s] control time-window. Then, we determined virtual sensors to process power variations between [0s-1s] and [-5s-4s] time-windows. EDA and heart rate were the ANS dependent variables, reaction time (RT) to light change and rate of light violation were those from behavior. RT increased under SC as compared to SD, and 4 drivers exhibited higher rate of light violation. The variation of power in the left motor cortex increases simultaneously with the rate of light violation, by comparison with SD. We observed a decrease in the left motor cortex beta activity in drivers who did not respect the red light (probably due to lower braking). EDA response duration decreased along with the increased rate of light violation. Furthermore, the bradycardia preceding light perception was larger under SC than under SD, suggesting that drivers better focused their attention toward environment changes. Finally, we observed a negative relationship between ANS and left-brain activity, especially in the left anterior cingulate cortex. This is in accordance with previous studies reporting that the left hemisphere is involved in the inhibition of ANS responses.

We-195 - EEG markers of attention in patients with disorders of consciousness

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Assessing preserved cognitive functions in noncommunicating patients with disorders of consciousness remains a major medical and neuro-scientific challenge. Recent studies have provided important neuroimaging tests for detecting high-functioning conscious patients that cannot be detected using only clinical examination. But we still lack more sensitive neuroimaging tests that can detect patients who, despite not being fully conscious, have the potential of regaining consciousness.

Since the attentional system plays a central role in conscious processing, we designed an EEG test to assess the preservation of
both basic and advanced functions of this system in noncommunicating patients. This test is a variant of the classical Posner cueing paradigm. The patient hears an auditory stimulus (own name, other name or non-vocal sound) to their right or to their left, followed by a test sound (a ‘beep’) on the same or opposite side. If attention is mobilized by the first sound, this can be read out from the potentials evoked by the test sound. In different blocks of trials, the first sound is either predictive of the second, yielding anticipatory responses typical of endogenous attention, or not predictive at all, yielding only exogenous orienting.

On 15 healthy volunteers we confirmed that this EEG test provides robust individual markers of exogenous and endogenous attention. We tested 16 patients. The EEG markers of exogenous attention were present in minimally conscious patients (n=9), but not in vegetative patients (n=7), suggesting that the first clinical signs of consciousness co vary with the basic functioning of the attentional system. Furthermore, the only two patients who also showed endogenous anticipatory responses actually regained consciousness within a few days. In conclusion, consciousness in these patients seems to co vary with the functioning of the attentional system. This EEG paradigm could thus provide an important and sensitive test to assist diagnosis.

We-196 - Does fMRI-guided Thetaburst Stimulation of Frontal Eye Fields Disrupt Top-Down Modulation of Posterior Alpha Rhythms?

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The human frontal eye field (FEF) is a key node in the frontoparietal attention network, which controls covert spatial attention in a top-down manner, possibly through the lateralisation of posterior alpha oscillations. Previous research indicates a right-hemisphere dominance of this network: Damage to right but not left parietal cortex can lead to spatial hemineglect. Furthermore, Transcranial Magnetic Stimulation (TMS) of right FEF has been shown to have perceptual consequences for both hemispheres, while left FEF TMS affects only the contralateral hemisphere.

These findings are commensurate with a model in which right FEF modulates alpha in both hemispheres, whereas the left FEF modulates alpha only in the left hemisphere. Accordingly, when right FEF is disrupted, the influence of left FEF should no longer be counterbalanced, resulting in a dysfunctional shift of attention to the right hemifield reminiscent of hemineglect. In contrast, disruption of left FEF should not result in a neglect, but should reduce the capability to direct attention to either visual hemifield.

To test this model, we will inhibit either right FEF, left FEF, or vertex (control site) with continuous theta-burst TMS (cTBS), and assess its consequences on posterior alpha by recording magnetoencephalography (MEG) data whilst participants perform a cued visual spatial attention task. Individual FEFs will be located by an fMRI localiser based on shifts of covert spatial attention.

So far we have demonstrated that the FEF can be reliably localized and disrupted using our paradigm. We are currently investigating whether right FEF cTBS causes a lateralisation bias of alpha towards the right hemisphere (leading to perceptual impairment in the left hemifield), whereas left FEF cTBS disrupts the ability to lateralise alpha (reducing the spatial cueing effect). We will use functional connectivity measures to determine whether long-range coupling between frontal- and visual- cortex is disrupted by cTBS.

We-197 - Effects of Low-Frequency Repetitive Transcranial Magnetic Stimulation of the Supramarginal Gyrus on Event-related Potentials

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The aim of this study was to investigate the effects of repetitive transcranial magnetic stimulation (rTMS) on brain activity. We investigated the effects of rTMS on P300 latencies as measured by electroencephalography (EEG) by stimulating the supramarginal gyrus (SMG), which is considered to be the area of origin of the P300. As the frequency-dependence of low-frequency rTMS has not been previously investigated in detail, we evaluated the effects of rTMS at frequencies of 1, 0.75, 0.5 or 0.25 Hz on P300 latencies. The odd-ball task was used to elicit P300s before and shortly after the scalp was stimulated by rTMS. Magnetic stimulation was performed over 100 pulses. The stimulus intensity was 80% of each subject’s motor threshold. EEG measurements were collected on the Fz, Cz and Pz line of the international ten-twenty system.

Fig.1 shows event-related potentials (ERPs) at the Cz both before and after rTMS of the left SMG at 1, 0.75, 0.5 and 0.25 Hz. At 1 Hz, P300 latencies after rTMS were shorter than P300 latencies before rTMS. The latencies were shortened by approximately 25 ms at the Fz. At 0.5 Hz, P300 latencies were longer after rTMS. The latencies were lengthened by approximately 26 ms at the Fz. In contrast, at 0.75 or 0.25 Hz, no change in P300 latencies was observed after rTMS. Furthermore, following rTMS stimulation of the right SMG, there were no significant differences in P300 latencies compared with before the rTMS.

The results of this study show that changes in P300 latencies depend upon the frequency of rTMS when the left SMG is stimulated. However, there were no significant differences between pre- and post-rTMS regardless of the stimulation frequency when rTMS was applied to the right SMG. Thus, the results of this study demonstrate that rTMS over the right SMG is not frequency-dependent.
We-198 - High-risk perceptual decisions modulate frontal gamma-band activity

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Bridging perception to action in coordinated behavior often involves a bottleneck, namely decision making. Neuroimaging studies have highlighted brain regions involved in this process, but a thorough understanding of the neuronal mechanisms underlying our subjective choices and their impact on behavioral outcome is still lacking. Here we show with MEG recordings the rhythmic human brain activity reflecting perceptual decision making and behavioral performance in a task involving stimulus change detection near detection threshold. In this experimental context subjective reports indicating a ‘stimulus change’ carry intrinsically more risk than ‘no stimulus change’ reports. We found that the power of a frontal gamma-band response prior to report reflects the subjective content of perceptual choices, independent of the external stimulus configuration. We also observed that frontal and occipital gamma activity uniquely predicted performance prior to report. In addition, alpha-band power suppressions centered at occipital-parietal regions with the same choice-predictive response pattern as frontal gamma-band activity extended before and after the behavioral response but were unable to predict performance. Finally, throughout the task subjects showed a clear response bias towards reports carrying minimal risk (no-change detection report). Because frontal gamma-band activity was source-localized into anterior cingulated cortex, a region known to play an important role in action selection and response conflict, and that this neuronal oscillatory activity showed relative increases for high-risk decisions (change detection report), we suggest these findings to show an important link between cognitive control processing and underlying oscillatory neuronal activity.

We-199 - Gating of information to downstream visual areas by alpha activity: a simultaneous EEG-fMRI study

Johanna Zumer¹, René Scheeringa¹, David Norris¹, Jan-Mathijs Schoffelen¹, Ole Jensen¹

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Increased alpha power has been proposed to gate information by selectively inhibiting task-irrelevant regions. We here ask if the alpha shifting with spatial attention in visual regions gates the information to, thus modulating activity in, downstream regions. We test this with simultaneous EEG-fMRI using faces and scenes, which are known to selectively increase BOLD activity in ventral stream FFA and PPA.

Multi-echo fMRI (3T) and 64 channel EEG were recorded in 7 healthy subjects. The task required left/right cued attention to faces or scenes: within each trial, a left or right cue appeared, followed by a face and scene on either side. Maintaining central fixation, the subject must remember the cued image during a 10s delay and respond if the cued image on the next trial is an exact match (14% matches). EPI data were collected with 4 successive volumes then a 4s gap during which MR-artifact-free EEG data were recorded. BCG artifacts were removed with DSS component rejection. An fMRI localizer task was used to create FFA and PPA.
ROIs. Leave-1-out classification within each modality was used to compute optimal weighting of posterior EEG channels and ROI voxels (using main fMRI task), accuracies were 72% (EEG) and 94% (fMRI) (50% chance).

Both the alpha lateralization index (Fig 1A) and the BOLD within FFA and PPA (Fig 1B) were significantly modulated with spatial attention ($p < 0.005$). The correlation between classifier-weighted EEG channels and classifier-weighted fMRI voxels over trials was 0.09 ($p < 0.01$, over subjects). For example in an attend-left-face trial, greater left-minus-right alpha correlated with greater FFA-minus-PPA BOLD. Classification of the 4 trial types using both alpha and BOLD was 71% (25% chance).

In conclusion, alpha modulation in visual areas correlates with category-specific ventral stream BOLD modulation. This provides direct support for the hypothesis that alpha activity gates information flow.

**Wednesday, August 29th, 2012, 13:30-15:00 Room 8**

**Decoding & BCI**

**We-18 - Real-time MEG with OpenViBE, an open-source software platform for brain-computer interfaces**

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Electroencephalographic (EEG) is generally favoured in Brain Computer Interface (BCI) applications, simply because it is cheap and portable but also because it samples brain activity with high temporal resolution and non-invasively. However, Magnetoeencephalography (MEG) offers the same performance, but with higher spatial precision, due to a much lower sensitivity to the blurring effect of the skull. This also makes easier to monitor brain activity at higher frequencies. Although it is obviously not mobile, MEG provides a fine and whole head coverage in a minimum preparation time. Finally, it has been shown that MEG could be used online and proved useful for a certain type of BCI [1, 2]. We have developed a system to read out and process MEG signals in real-time. This interface connects our whole-head MEG system comprising 275 first-order gradiometers (VSM-CTF Omega 275) with the OpenViBE software platform. The OpenViBE graphical user interface is simple to access and easy to use to create new BCI scenarios (3).

The platform’s main advantages are modularity, portability, flexibility and compatibility with virtual reality technologies. It offers different tools and levels of access for different types of users (programmers, researchers and clinicians). It also comes with many 2D and 3D visualization tools to extract and display brain activity in real time (Fig. 1). Finally, it is compatible with Matlab and thus enables electrophysiologists to incorporate existing methods from advanced software in the field [4, 5]. Real-time MEG opens up
new possibilities for the study of brain functions. Potential applications include neurofeedback training to promote neuroplasticity and brain state monitoring for either basic research or clinical applications in different pathologies.

1 Mellinger et al, NeuroImage 2007
2 Sudre et al, Comput Intell Neurosci 2011
3 Renard et al, Presence: Teleop Virt 2010
4 www.fil.ion.ucl.ac.uk/spm/software/
5 fieldtrip.fcdonders.nl

Figure 1. The OpenViBE designer and its graphical user interface

We-19 - The analysis of objective recognition free from stimulus modality

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Conceptual recognition has significant role in higher-order brain functions. Although several fMRI studies using picture, word or auditory stimuli have reported category-specific brain activities, neural substrates independent of task types remains unclear.

The aim of this study is to investigate the brain function of conceptual recognition by measuring the brain activities for the picture and word of animals/tools using magnetoencephalography (MEG) with varying the familiarity.

For analyzing the MEG data, we proposed new analytical techniques, combining several existed methods such as the beamformer localization, decoding analysis with support vector machine (SVM), and searchlight decoding analysis. To be concrete, decoding across modalities with SVM was considered to be suitable for our purpose. SVM was trained to decode familiarity or category (animals/tools) from the MEG evoked by pictures. The decoder was applied to predict familiarly or category from the MEG evoked by words.

To find the brain regions involved in object categorization, before the decoding analysis, we converted sensor domain MEG data to fMRI like source domain data by applying beamformer method.

The analysis, conducted with varying the latency and frequency of interest, revealed that the activity common across pictures and words exists at gamma band activity in some regions reported in previous fMRI studies. It also suggests that there might be common neural substrates between sensory and semantic categorization. Furthermore, using this methodology make enable to localize the brain activity from MEG datasets, with keeping its temporal resolution.

We-20 - Single Trial Classification by Simultaneous MEG/EEG Source Imaging

Minkyu Ahn¹, Jun Hee Hong¹, Hohyun Cho¹, Sung Chan Jun¹

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(Introduction & Methods)

In brain computer interface field (BCI), EEG is widely used rather than MEG because of its convenience/portability and economic cost. However, inherent heavy noise on EEG makes BCI system unreliable. MEG and EEG measure different physical parameters deeply related with brain dynamics, so effective combining strategies of two modalities are beneficial. Ko and Jun (1) proposed
simultaneous beamforming source imaging of MEG and EEG, which yielded improved performance in localization. In this study, as preliminary work, we investigate 399 single trial data of median nerve stimulation and classify them into right or left hand stimulation. Beamforming source imaging is used to reconstruct source activation power and averaged powers over pre-defined voxels in left and right hemispheres are used as features. Each of two modalities (MEG or EEG) and their combined modality (MEEG) are compared in terms of classification accuracy.

(Results & Discussions)
In event related potential (ERP) data (averaged), MEEG localized reasonably well for both left and right stimulation as reported in (1). In single trial data (unaveraged), we observed the classification accuracy of MEG was the best and MEEG performed between EEG and MEG. MEEG showed mild synergy effect in improving classification, but its improvement did not surpass MEG single modality. It is expected that power average feature in predefined area is very simple and hard to contain different information obtained from each single modality. Anyway, MEG may be useful as supplementary information to EEG. It is under investigation how combining MEG and EEG can improve their synergy effect in BCI classification.

(Acknowledgement)
This work was supported by an NRF grant (NRF-2010-0006135).

(Figure)
(a) Pre-defined area for each hemisphere and (b) classification accuracy over three different modalities (MEG, EEG, MEEG).

(Reference)
(1) S. Ko and S. C. Jun, J Appl. Phys. 2010

We-21 - Continuous tracking of covert visual spatial attention in 2D
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Covert visual spatial attention, which is called in short `covert attention’, is a well studied psychological process that has its unique brain signature. Humans can voluntarily deploy attention to locations in visual space without moving their eyes. Covert attention has been shown to be characterized by changes in the alpha band (8-12 Hz) over the visual cortex. From various studies, we know that the modulation in alpha band activity by covert attention is not limited to only the left and right visual hemifields. Using MEG recordings, we have previously shown that we can decode the direction and the eccentricity of covert attention. In this work, we aim at combining the previous results to decode the location of covert attention in a 2-dimensional space while recording MEG data. The goal is to identify the location of moving objects that subjects are tracking by covert attention in a 2D space. The obtained topographies in the alpha band are modulated by the location of the attended object. Currently we are developing the tools to classify the location of the attended object based on alpha activity, however, gamma (35-75 Hz) band activity seems to be also informative. The result of this experiment will provide new insight about the mechanism of continuous tracking of covert attention and could be of practical use in BCI setups.

References:

BIOMAG 2012 - August 26-30, 2012 - Paris, France
We-22 - Random field theory for functional images of unknown topology

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The problem of correcting for multiple statistical comparisons of volumetric imaging data has been comprehensively addressed through the use of random field theory (1). The Euler characteristic (number of blobs-number of holes) of a smooth random (statistical) field can be predicted through measures of its intrinsic volume or Lipschitz-Killing curvature. Crucially, in order to compute this local smoothness some topological assumptions are necessary. Typically, in SPMs testing for effects in fMRI and PET, this topology is simply that of Euclidean space and hence only local spatial gradients need be estimated. In MEG however, the Euclidean distance between two sources is not necessarily a good predictor of their statistical dependence (e.g., correlation) or ‘closeness’. This is because the lead fields determining MEG sensitivity depend in a nonlinear way on source orientation. In this work we attempt a principled characterisation of high dimensional random fields in MEG data. We use persistent homology - a method for defining the topology and dimensionality of any arbitrary field (2). We first demonstrate that - using methods based on persistent homology - we obtain the same result as classical random field theory, when the topology is known. We go then on to show that when the topology is incorrect (when nearest neighbours are not the most correlated) our generalised method outperforms classical methods. Moreover, it furnishes an estimate of the true dimensionality and statistical topology of the underlying data.

Figure shows the achieved against the required false positive (FP) rate for a t-test on the evoked response for sources on the cortical surface based on random field theory with standard topological assumptions (squares) and based on a topology estimated from the data (circles).


We-23 - Online Brain-Computer Interface - Performance Comparison among Various Feature Extraction Methods

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To achieve an robust online brain-computer interface (BCI), we recently proposed a variant of Common Spatial Pattern (CSP) (1) by
combining the Common Spatio-Spectral Pattern (CSSP) (2) and the invariant Common Spatial Pattern (iCSP) (3), which is called 'invariant CSSP' (4). In this work, we investigated the BCI performance of iCSSP in online session. For selected motor imagery (MI) data acquired from 10 subjects (4), we trained 4 filters (CSP, iCSP, CSSP and iCSSP) and 4 LDA classifiers (1) with half trials for each subject. We artificially created the online simulation data by randomly concatenating remaining trials (left/right hand MI trials) into a long combined signal. Classification accuracy was estimated with classification results between 0 and 4 sec after onset. We investigated BCI classification performance over various temporal window for training ([0, 0.5 ~ 4] sec after onset) and test data block size (as Figure (B)). For the fixed test data block size (1 sec long), comparative online BCI classification performance of 4 different filters was done to see optimal discriminative temporal window for training. Figure (A) shows that iCSSP method yielded best overall performance and the filter using temporal window [0, 2.625] sec after onset gave the reasonable discriminative result. In addition, with the filter trained with temporal window [0, 4] sec, 5 kinds of different test data block sizes were tested. Figure (B) shows that iCSSP yielded classification result (≥ 70%) for test data block size of 1 or 2 sec long. Our findings tell that the invariant property on spatio-spectral features provides more robust classification than iCSP and CSSP in even online processing.

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**We-25 - Finding a needle in the electrophysiological haystack: analysis techniques for weak brain activity.**

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The activity of interesting sources is often buried in a background of competing brain sources and noise. I review a suite of methods that can extract sources that are extremely weak (e.g. SNR=10⁻⁸) based on their repeatability, spectral content, contrast between conditions, etc. Similar in spirit to Independent Component Analysis, these methods capitalize on the correlation structure of multichannel data by optimizing the criterion of interest directly, rather than indirectly by maximizing a measure of independence. The leverage offered by multidimensional data is further enhanced by (a) applying time shifts (so that the linear solution space includes spatio-temporal finite impulse response filters), (b) forming instantaneous cross-products (so as to capture quadratic structure such as induced activity), (c) performing non-stationary analysis (to steer the solutions according to the underlying time-varying spatio-temporal correlation structure). The methods are illustrated with synthetic data, as well as with real data from a variety of MEG, EEG, multielectrode LFP, and optical recording systems and tasks. Extremely weak sources can be revealed using these methods, including brain sources with evoked, induced and oscillatory activity. These methods are part of an ongoing effort to produce tools to unravel the complex mixtures produced by multichannel electrophysiological techniques.

**We-26 - Brain Atlas based Region of Interest Selection for Real-Time Source Localization using K-Means Lead Field Clustering and RAP-MUSIC**

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Real-Time source localization from single trial electroencephalography (EEG) / magnetoencephalography (MEG) has recently been brought into focus of neuroscience to clarify brain functionality, identify mental states and to improve online applications such as brain-computer interface (BCI) systems. To succeed with real-time single trial localization two major challenges have to be solved: first, handling the low signal-to-noise ratio (SNR) and second, managing the computational effort. We aim to address both by reducing the lead field through clustering the lead field dipoles. With low SNR the possible source localization resolution of single trial measurements is much lower compared to averaged signals, meaning, it is not possible to distinguish as many sources. Due to that circumstance we are clustering similar lead field dipoles, which we are likely not able to differentiate by a localization algorithm. In order to maintain the position information of the resulting clusters, the clustering is done region of interest (ROI) wise. The ROIs are defined by the Destrieux atlas. To keep a high variance we cluster the lead field dipoles of each sensor separately. The clustering is accomplished using a k-means approach, which encapsulates a ROI in n clusters depending on their size. To localize correlated activated ROIs we are using the RAP-MUSIC scanning approach. The localization shows a high accuracy up to a SNR of -20dB in simulations, e.g. the correct or neighbored ROI is localized. We use cluster sizes depending on the given SNR, which results in lead field reductions of 40 to 80 times. This reduction leads to a large amount of calculation steps saved, e.g. a lead field reduction from 8195 to 174 dipoles provides calculation savings by 2206 times, which allows real-time ROI localization with a computationally intensive scanning approach. In a second processing step a localization based on selected ROIs using the high resolution lead field can be applied.
We-27 - Monitoring attention in a simulated driving scenario using EEG-based connectivity measures

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Monitoring the mental state of a human operator can be essential in safety critical applications such as driving, where emergency situations can be caused by distraction or lapses of attention. Here, we aim at the classification of focused and divided attention in a simulated driving scenario based on the measured EEG of the driver. In contrast to previous studies concentrating on band power, we employed measures of functional connectivity.

We conducted an EEG study in a realistic driving simulator with 13 subjects, each experiment lasting three times 45 minutes. The driver had to convoy a preceding computer controlled car, where abrupt brakes of the leading car were randomly induced forcing the subject to sustain attention to the driving task. Every three minutes, phases of normal driving alternated with phases of driving with an auditory secondary task, wherein subjects additionally performed a word detection task while listening to an audio book. For the extraction of features based on connectivity measures, the continuous data of the drive was divided into blocks of ten seconds length where coherence was evaluated between all pairs of the 58 EEG electrodes.

As a result, cross-validation with a regularized LDA classifier trained to differentiate between the two driving phases yielded a classification error below 25% for the majority of subjects. Compared to classification based on conventional power features, the results are similar for subjects with low classification error. If the classification error for a subject is high, the results obtained with coherence features are better than the results obtained with power features. Concluding, the phase information contained in the coherence measure allows for the dissociation of different modalities of attention. We hypothesize that the classification is physiologically based on altering connection strengths we observed between most frontal and occipital sensors.

We-28 - A new dual-frequency stimulation method to increase the number of visual stimuli for multi-class SSVEP-based brain-computer interface (BCI)

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In the present study, we introduce a new dual-frequency stimulation method that can produce more visual stimuli with limited stimulation frequencies for use in steady-state visual evoked potential (SSVEP)-based brain computer interface (BCI) systems. The methods for increasing the number of visual stimuli is necessary, particularly for the implementation of multi-class SSVEP-based...
BCI, as available stimulation frequencies are generally limited especially when visual stimuli are presented through a computer monitor. The new stimulation method for generating visual stimuli was based on a conventional black-white checkerboard pattern, however, unlike the conventional approach, ten visual stimuli eliciting different SSVEP responses could be generated by combining only four different stimulation frequencies. Through the offline experiments conducted with eleven participants, we confirmed that all the visual stimuli could evoke distinct and discriminable single SSVEP peaks, of which the signal-to-noise ratios were sufficient for applications in practical SSVEP-based BCI systems. In order to demonstrate the possibility of the practical use of the proposed method, a mental keypad system was designed using the new method and additional online experiments were conducted with four participants. We achieved the average information transfer rate of 26.69 bits per minute with the average accuracy of 88.26%, and all four participants succeeded in calling their mobile phones using the BCI system, demonstrating the possibility of the proposed dual-frequency stimulation method.

![Schematic diagram to elucidate a proposed pattern reversal checkerboard stimulus: (a) pattern 1 stimulus flickering at F1, (b) pattern 2 stimulus flickering at F2, (c) checkerboard reversing at F1 & F2 (identical or may be different)](image)

We-33 - Iterative phase-interpolated averaging supports the evoked model for MEG generation

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Phase-interpolated averaging [1, 2] can separately extract evoked, amplitude-modulated, and phase-modulated components of EEG/MEG. The accuracy of separation depends on estimation of instantaneous phases. If the evoked component is relatively large, a bias occurs along the real axis and aggravates the estimation. Iterative uses of phase-interpolated averaging would overcome the bias problem. We analyzed the MEG of a behavioral experiment, which was a selective response task for visual stimuli, with this technique. First, signal source activities were estimated with sLORETA (3). Second, signal sources that showed conspicuous activities (including e.g., vision, Go, and NoGo responses) were picked up. Frequency-band limited instantaneous phases of the sources were estimated with the Hilbert transform. Finally, iterative phase-interpolated averaging was performed. As a result, the evoked component was dominant. If a single use of phase-interpolated was instead performed, the phase-modulated component was dominant. Note that phase-interpolated averaging is somewhat fail-safe for the evoked component, and hence does not generate artifacts of the evoked component. Therefore, these facts imply that the evoked component was actually dominant and the phase-modulated component was mostly generated by the bias problem.

We-34 - Proposal of a variance stabilization transformation for averaging evoked MEG/EEG responses

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The mismatch negativity (MMN) in MEG/EEG studies is calculated by subtracting responses to different stimulus conditions. This procedure ideally requires homoscedasticity, which is hardly ever the case. For the auditory M100, we observed a nearly linear growth of the arithmetic standard deviation with the arithmetic mean, which is a distinctive mark of a multiplicative model (Psychophysiology 48, 1069-1082, 2011). Consequently, the signals for different stimulus conditions, subjects and hemispheres predominantly differ by scaling factors. This multiplicative behavior follows from the nature of the neural sources generating the M100 and other components, and the physical principles involved in the measuring technique.

To achieve homoscedasticity, variance stabilization transformations (VSTs) must be applied before arithmetic averaging and subtraction. With a purely multiplicative behavior, as found for the M100 peak, a simple log-transform suffices to achieve homoscedasticity. However, to achieve homoscedasticity over the entire waveform, necessary for proper calculation of a MMN, a more general approach is required. Here, we propose a VST based on a mixed model that merges the additive and multiplicative models. Its application results in a variance that is independent of the mean. Averaging the transformed data arithmetically and, subsequently, applying the inverse transform enables correct comparisons.

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We-35 - Intracranial BCI implant localization using MEG pre-surgical evaluation

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Brain Computer Interface (BCI) provides non-muscular communication channels for subjects suffering from severe disabilities. The most successful are invasive BCI systems, such as intracortical (microelectrode arrays) and intracranial (matrix of EEG electrodes). Their drawback is that invasive systems require a surgical intervention. The pre-surgical noninvasive optimization of the BCI implant placement for a particular patient is necessary in order to minimize surgery related risks, as well as to maximize the efficiency of control of effectors.

The problem of noninvasive task-related brain activity localization and classification was discussed in a number of papers, based mainly on the source analysis and a single sensor processing. We propose an efficient method of localization of brain activation at the level of EEG-based implant placement (cortex surface). Statistical approach combines different MEG-sensors and frequency-bands, resulting in higher correlation values and better localization of imaginary and real motion-related brain activation. Moreover, it is able to combine data from different experiments in a 'virtual' one, allowing emphasizing the motion-related brain activity and suppressing spurious signals, in particular the brain activation related to stimuli, generally used in BCI experiments.

The results of analyses in the MEG sensor space are projected into cortex surface in stereotactic coordinates frame. The difference of the algorithm from the traditional source-localization approach is a direct helmet-to-brain mapping according to spatial resolution of MEG-sensors. This allows fast approximation of the cortical localization and excludes mathematical difficulties of inverse problem, such as non-uniqueness of solution.

Validation of our methods was performed on MEG/EEG signals recorded in healthy subjects performing a set of imaginary and real motor tasks. A set of imaginary movements was considered as simulated BCI tasks.

We-36 - Principal component method : algorithm of magnetocardiogram signal analysis

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The algorithm was developed to analyze the results of magnetocardiographic measurements (MCG) on the phase of the study of averaged cardiocomplexes. The magnetic map of MCG signal at any arbitrary timepoint of cardiocycle represented as a linear algebraic combination of magnetic maps for the Q principal component of MCG signal (the value of Q is ranged from 1 to N, N - number of MCG measurement points).

Schemes of calculations of principal components, correspondent magnetic maps and matrixes of the transformation coefficients are given for the algorithm of MCG investigations, that suggest the frequency of 1 kHz readout signal in each of the 36 grid nodes of measurement having a step of 4040 mm in mutually perpendicular axes. At the final stage of the calculations error between measured and calculated values of the MCG signal is estimated (in percentage).

As an example, the figure shows measured magnetic map, values of the coefficients and magnetic maps for the three principal components, as well - the value of the error and found after computing the magnetic maps for each step (only one component, Q = 1,
while two or three components, \( Q = 2 \) and \( Q = 3 \).
The developed algorithm is used for the analysis of the results of solving the inverse problem of magnetostatics, if the source of biomagnetic signal is a 2D layer current, distributed in a plane which is secant to the heart and parallel to the plane of measurement. The algorithm was applied for data processing for real MCG records: 105 healthy volunteers and 164 patients with different heart diseases. Estimations of the number of principal components, sufficient for description of measured data with set level of validity, are obtained. The possibilities of the developed algorithm for reducing of the amount of stored information and for magnetic noise filtering are shown. We found a decision rule for classifying of groups of patients, which includes one parameter and provides a discrimination of these groups with

\[ \text{Example of data transformation for real MCG record} \]

**We-37 - How to use Independent Component Analysis in a Bayesian Inverse Solution**

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We present some new results about the MEG inverse problem using independent component analysis, which can be used to separate MEG data into statistically independent components. The idea of using independent component analysis in solving the MEG inverse problem has been a known topic for at least more than a decade, but the known results have been justified heuristically, and their relationships are not understood properly. Here we show how to obtain a Bayesian posterior for a spatial source distribution, by using an ICA demixing matrix as an input. The posterior allows us to rederive and reinterpret the previously known methods, and also implies some new methods. We demonstrate our new methods with both a simple artificial forward model and a real MEG forward model.

**We-38 - Spatiotemporal Source Complexity Imaging**

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We have developed a spatiotemporal imaging method for MEG that measures source waveform complexity. Signal complexity is estimated using a new symbolic entropy algorithm, 'rank vector entropy' (RVE). The source time-series for each specified coordinate is estimated using a scalar LCMV beamformer (SAM). The RVE algorithm is then applied to this, as follows. For each time step a group of subsamples (a word) is selected at specified lag spacing. The rank values of these samples form a rank vector that is interpreted as a symbol in state space. Advancing the word one sample at a time generates new symbols and the frequency of occurrence of each new symbol is accumulated in a histogram using 'leaky' integration. The Shannon entropy is then computed from the distribution of states in the histogram. The normalized entropy value is updated for successive samples and mapped to the corresponding voxel and time sample. RVE is a measure of signal complexity and is independent of source amplitude. RVE is
independent of signal amplitude and can measure changes in waveform morphology that are not accompanied by changes in source power. For words of 5 subsamples there are 5! or 120 possible states. RVE imaging can be applied to resting and event-related MEG data.

In the example shown in the figure, 250 seconds of resting MEG (eyes opened) were acquired at 600 Hz from a CTF 275-channel instrument and processed using an RVE of length 5 in a 4 4 150 Hz bandpass. We choose a wide bandwidth in order to measure complexity, there is no complexity in signals of very narrow bandwidth. The lags are defined according to the lowpass cutoff so as to avoid aliasing. At the specified lowpass and sample rate, the lags are spaced at 2 sample intervals. A 3D+time image was assembled at 5 mm resolution and 50 ms intervals, and displayed using AFNI. For the example resting data we observe locations where there are transient decreases in entropy and slower increases.

We-39 - P300 Evoked Changes in Rank Vector Entropy

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The rank vector entropy (RVE) time series of resting MEG exhibits fluctuations above and below its statistical mode. In this study, we examined the direction of entropy change relative to activation in the averaged evoked response to frequent and rare tones. MEG was in measured normal subjects using an auditory P300 protocol. Data were acquired continuously (CTF 275-channel MEG, DC 4 150 Hz bandpass, 600 Hz sample rate). There were 200 and 50 presentations of a frequent tone rare tone, respectively with an ISI of 1.5 4 2.0 seconds. Subjects responded by button press to the rare tones. Spatiotemporal images of RVE (4 4 150 Hz) for the frequent, rare, and combined tones were computed using the procedure outlined in the accompanying abstract, ‘Spatiotemporal Source Complexity Imaging’. The T-value of the average change in entropy relative to the pre-stimulus baseline was mapped at 5 ms intervals from -0.2 to 0.8 seconds.

The question as to whether ‘activation’ corresponds to an increase or decrease in entropy was only partially answered. A decrease in entropy at the time of the N100m was localized to the primary auditory cortex, mainly on the left (see figure). For frequent tones, the entropy increased following the N100m but remained negative to the trial end. By contrast, the rare tone resulted in a large increase in entropy following the decrease at the N100m. Early focal increases in entropy in prefrontal cortex were also observed for the rare tones (not shown). There was no clear pre-stimulus baseline for either frequent or combined tones, where entropy declined smoothly from -0.2 up to 0.1 seconds. This appears to be due to the prolonged late increase in entropy of the rare tones, averaged in from preceding trials. This entropy increase did not correspond to any waveforms appearing in the averaged evoked response. It remains unclear whether entropy increase is a consequence of recovery from a refractory state or represents activation relative to the baseline.
Spatiotemporal distribution of rank vector entropy for P300 data. The N100m latency corresponds to a decrease in entropy. The rare tones evoke a slow prolonged increase in entropy that is not evident in the averaged signal.

**We-40 - The usefulness of prefrontal area for classifying pre-movement ECoG signals.**

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**Objective:** Recently, earlier neural signals have been focused to shorten the delay time between subject’s action and brain-computer interface (BCI) response, which is one of prominent weaknesses of the current form of BCI. Although prefrontal area has been recognized to generate pre-movement signals reflecting motor intention or preparation such as readiness potential (RP) and event-related desynchronization (ERD), most studies of BCI have interests on the motor related area. Here we aimed to determine whether prefrontal area is as useful in the classification of motor intentions or preparations as motor related or parietal area.

**Method:** Six patients with intractable epilepsy performed a self-paced hand grasping and elbow flexion while electrocorticography (ECoG) was recorded. A classifier, support vector machine (SVM), was trained using a power of the specific frequency band showing clear difference between hand grasping and elbow flexion from 2.0 s before to the movement onset. In order to assess classification performance, we used 5-fold cross validation.

**Results:** The average accuracy rate of the prediction was 74% on average (range, 55.4 to 99.3%) across six subjects. On five of them, prefrontal area was where the electrodes differentiating hand grasping and elbow flexion were located. The frequency band was mostly in the beta band (13-30Hz).

**Conclusions:** Our results suggest that the beta band is the most informative in classification using pre-movement signals. Also our results show that prefrontal area could be at least as useful in prediction of movement intentions or preparations as motor related or parietal area, and implicate that our approach could be an alternative for a BCI system in neurological rehabilitation for patients with motor cortex injury.

**We-41 - Revealing the time-course of experimental effects in multivariate time-series data using a supervised leave-one-out procedure**

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Multi-sensor technologies such as EEG, MEG, and ECoG result in very high-dimensional data sets. Whatever the scientific question, the objective of data analysis is to extract the answer to that question from a set of multi-variate time series, each labeled according to experimental condition. Given the high temporal resolution of such techniques, scientific questions very often focus on the time-course of experimental effects. But how is one to choose which sensor(s) to subject to analysis? Inverse source estimation techniques offer one solution by projecting the data onto probable sources in the brain. However, a given experimental effect may involve more than one source at any given time and may traverse multiple sources over the time-course of a trial. Other solutions, such as...
single-sensor or ROI analyses fail to make full use of the distribution of activity across sensor space. We introduce a method for reducing experimental effects in multi-variate time series data to one dimension plus time. The method involves iteratively replacing each frame of each trial with its projection onto a spatial filter derived based on all other trials for a simple technique borrowed from machine learning, and similar to the jackknife procedure in statistics. The resulting set of surrogate trials can be used to reveal the time-course of an experimental effect, which distinguishes this method from techniques that reveal the time-course of an anatomical source or region of interest. The method can be used to address any question that can be answered in the form of a set of coefficients across sensors (e.g. the difference between condition A and condition B). We demonstrate the effectiveness of the method in dramatically improving the signal-to-noise ratio and the quality of single-trial data. Most importantly, very many sensors are reduced to one dimension plus time, while making use of all potential information present in the data.

Application of the method to an MEG data set from a published study (Marti et al, NeuroImage 2011)

**We-42 - Phase template analysis for decoding steady-state visual-evoked responses**

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This study proposes a new analysis method for steady-state visual-evoked responses using phase template matching. Steady-state visual-evoked potential/field (SSVEP/SSVEF) is oscillatory brain activity evoked by flickering visual stimuli (Regan, 1982, Herrmann, 2001), and has been applied to many Brain Computer Interfaces (BCIs) (Middendorf et al., 2000, Allison et al., 2008) and basic cognitive sciences (Muller et al., 1998, Okamoto & Nakagawa, 2011). Since many previous analysis methods focused on the power of the target frequency band, we developed a new method using phase information which locks to the onset of target stimuli. Checkerboard pattern reversal images flickering at 15, 20 and 30 Hz were employed as visual stimuli, and represented as onset stimuli of flickering with two seconds duration. Event-related SSVEFs triggered by the onsets were recorded using magnetoencephalography (Magnes 2500WH, 4-D Neuroimaging). The acquired data were processed by continuous wavelet transform, and normalized with the power of each frequency and time point. The set of averaged complex values among trials whose real part corresponded to phase locking index (PLI) was used as a phase template of the target frequency and phase shift. Each template was applied to single trial, and evaluated the discrimination performance among several frequencies and phase shifts. Correct rates among one hundred single trials resulted higher than 0.95, suggesting good discrimination performance both for frequencies and phase shifts. These results enable us to decode single trial data of SSVEP/SSVEFs with high temporal resolution. The discrimination of phase shifts could be possible to improve the performance of BCIs based on SSVEP/SSVEFs and, furthermore, useful in basic cognitive sciences (e.g. ambiguous image or binocular rivalry) by the equalized visual condition.

**We-43 - Classification of unilateral upper limb movements using MEG**

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A brain machine interface (BMI) provides the possibility of controlling such external devices as prosthetic arms for patients with severe motor dysfunction using their own brain signals. However, there have been few studies investigating the decoding accuracy for multiclasses of useful unilateral upper limb movements using non-invasive measurements. We investigated the decoding accuracy for classifying three types of unilateral upper limb movements using single-trial magnetoencephalography (MEG) signals. Neuro-magnetic activities were recorded in 9 healthy subjects performing 3 types of right upper limb movements: hand grasping, pinching, and elbow flexion. A support vector machine was used to classify the single-trial MEG signals. The movement types were predicted with an average accuracy of 66 ± 10% (chance level: 33.3%) using neuromagnetic activity during a 400-ms interval (-200 ms to 200 ms from movement onsets). To explore the time-dependency of the decoding accuracy, we also examined the time course of decoding accuracy in 50-ms sliding windows from -500 ms to 500 ms. Decoding accuracy significantly increased prior to movement and peaked twice after movement onsets. These three peaks were observed in all subjects. Significant variability in the decoding features in the first peak was evident in the channels over the parietal area and in the second and third peaks in the channels over the sensorimotor area. In source analysis, cortical sources were shown at the parietal area before movements and at the sensorimotor area after movement onset in each movement. Our results indicate that the three types of unilateral upper limb movement can be inferred with high accuracy by detecting differences in movement-related brain activity in the parietal and sensorimotor areas.

We-44 - Sensorimotor Signal Separation

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Neuromagnetic signal sum the activity of many sources. Each sensor is mainly influenced by proximal brain regions, but is also affected by distant brain regions. At any activity where there is a motor response to a sensory stimulus, the measured signal is a mixture of the neuronal motor and sensory responses. The asynchronies between the motor response and the sensory stimulus allow us to determine the time delay between the overlapping motor and sensory neuronal activities. Based on these delays, a separation of the recorded signal into two components can be achieved.

Assuming that the sensory response is time locked to the stimulus and the motor response to a button press, we can write the recorded response as a set of linear equations:

\[ Y(i,k) = s(i,k) + m(i+d,k) \]

Where \( y(i,k) \) is the measured neuromagnetic signal for trial \( k \) at the \( i \)th sample. \( s(i,k) \) represents the sensory component of the signal and \( m(i+d,k) \) represents the motor component of the signal shifted according to the delay \( d \) between the motor response and the sensory stimulus for that trial. If there is enough variability in the asynchronies, we can solve such over-determined system by linear least squares.

We tested the effectiveness of this method by a simulation and got a good recovery of the pure sensory and motor components of the signal even when introducing various degrees of noise, taken from actual MEG measurements.

MEG recordings were performed during a tapping paradigm in which the subject was asked to tap in synchrony with a rhythmic auditory stimulus. In order to verify that we are getting an auditory and a motor component of the signal, we used Synthetic Aperture Magnetometry (SAM) beamforming on the signals after the separation. Figure 1a shows the original measured signal, the auditory and the motor components. The peak activity of the auditory component was localized at Heschl’s gyrus (b) and the peak activity of the motor component was localized at the left precentral gyrus (c).
We-45 - Phase-locked PCA: a subspace method enhancing the signal-to-noise ratio of event-related activity

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Brain activity that is phase-locked to an event tends to be masked by noise and background brain activity. As a consequence, neuroscience researchers typically resort to the event-related potential (ERP) that is obtained by averaging across all repetitions of an event. However, the ERP obliterates the study of single-trial dynamics and single-trial classification. Here, the ERP is used to enhance single-trial analysis of event-related EEG. Principal components analysis (PCA) on the ERP covariance matrix yields the principal subspace of phase-locked activity. The method is validated using simulated and real EEG data. Results show that the projection of the original data onto the phase-locked subspace and subsequent backprojection successfully increases signal-to-noise ratio by attenuating noise while preserving phase-locked activity. Other applications of phase-locked PCA such as artifact attenuation and feature selection for brain-computer interfaces are discussed.

We-46 - Movement estimation from delta wave of MEG signals

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Introduction:
Previous BMI studies focused on indirect methods selecting a choice among limited options. It implies that the subject might imagine movements different from real ones. In contrast, recent BMI studies have evolved to control prosthetic devices with movement intention only which is called a direct BMI, since it is more convenient and intuitive. However, there have been few non-invasive BMI studies for a direct BMI, compared with invasive BMI studies. Here, we aimed to estimate the 3-dimensional movement from non-invasive MEG signals.

Methods:
Nine healthy right-handed subjects participated in this experiment. Subjects were instructed to move their arm in 3-dimensional space according to stereographic images (Fig. 1a). One session of the experiment consisted of 30 trials for each direction. For each subject, 2 sessions were performed. The brain signals were measured with a 306 channel whole-head MEG system. To record the movement trajectory, a 3-axis accelerometer was used. 68 gradiometer channels covering motor areas were used for decoding. Signals from the 68 channels were band-pass filtered with 5 sub frequency band 0.5-4, 4-8, 9-22, 25-40, 57-87Hz based on the results of time-frequency analysis. After filtering, the signals were downsampled with 20ms intervals. To estimate present fingertip position, past 200ms MEG signals were used. The x, y, z position of movement trajectory was estimated with a multiple linear regression method.
Results:
Delta wave (0.5-4Hz) was the best for estimating the movement trajectory, while other four other frequency band signals cannot decode the trajectory. Fig. 1b describes real movement trajectories and the estimated results from MEG signals for 1 session of one subject. Mean correlation coefficient was 0.615, 0.638 and 0.604 on x, y, z-axis.

Conclusions:
Our results demonstrate that 3-dimensional movements could be estimated from delta frequency signals recorded from non-invasive MEG measurement.

Figure 1. a) Timeline of visual stimuli and instructed behaviors b) Real movement trajectory and Estimated movement trajectory from MEG signals for 1 session of one subject c) Sample results of estimation on X, Y, Z axis for each direction.

We-47 - Accelerated brain-state segmentation using Laplacian Eigenspace Operator

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The temporal syntax of brain state dynamic is suggested to be a sensitive measure of variations of mental activity in different cognitive and pathological states, and greatly influences the processing of incoming information. In theory, these brain states reflect different momentary electrophysiological topographies of brain activity. A given topography remains stable for about 80 ms to 120 ms, indicating a highly coherent global brain state in sub-second range. However, one main drawback of this approach, is its computational complexity, which increases with the number of sensors. This problem can be handled by applying a recently proposed adaptive spatial harmonics analysis using Laplacian Eigenspace functions. This approach leads to an information reduction, which allows to consider only low spatial frequency basis functions that can be derived from the sensor configuration. The harmonic Eigenspace decomposition can be performed online on standard computer hardware since it requires only the multiplication of the incoming data with a pre-computed transformation matrix. Since brain states often manifest themselves as dipolar quasi-static topographic configurations, it seems feasible to identify brain states by solely investigating low spatial harmonic frequencies. This approximation allows spatial low pass filtering and thus fast spatial denoising of EEG as well as MEG data, which is indispensable for online applications. We have compared brain-state segmentation results using multi-channel (58 sensors) EEG data as well as segmentation based on data transformed using Laplacian Eigenspace Operator and which were reduced to less than the 10th order. The results in temporal segmentation were found to be identical, whereas the computational effort for the transformed data was approximately 3 times lower.
We-48 - Decoding movement intentions from brain oscillations using intracranial EEG

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Monkey studies have shown that movement parameters such as direction or speed can be inferred not only from unit activity in primary motor cortex but also from local field potentials (LFPs) in motor, premotor and parietal cortices. Intracranial EEG (iEEG) recordings in epilepsy patients have shown that movement execution leads to power modulations in multiple frequency components of the LFP in motor cortex (e.g. Crone et al. Brain, 1998). More recently, a number of invasive studies report that iEEG recordings from the human motor cortex show directional tuning (Leuthardt et al. J Neural Eng, 2004, Mehring et al. J Physiol Paris, 2004, Schalk et al. J Neural Eng 2007, Ball et al. J Neural Eng 2009). We explore the feasibility of classifying motor intentions from depth recordings in multiple brain regions. Several patients performed delayed motor or oculomotor tasks, in which the first cue indicated the target of the movement to be performed while the second cue instructed the subjects to perform the prepared movement. Beyond classifying movement directions during the execution phase, the main objective was to decode the direction of the intended limb movement or intended saccade during the delay period. We compared the performance of several classifiers including linear-discriminant analysis (LDA), Support Vector Machine (SVM), K-Nearest Neighbor (KNN) and Neural Network classifiers. In addition to successful discrimination of movement execution vs rest and of movement preparation vs rest by recordings in multiple brain regions, some electrodes contained spectral properties that allowed for decoding movement directions (Left vs Right or Up vs Down) not only during actual execution but also during the delay period prior to execution. Moreover, the decoding accuracy achieved by the different frequency components of the iEEG signal suggests that the discriminant features were most prominent in the low-frequencies (< 10 Hz) and in the high gamma band (approx. 60-140 Hz).

We-49 - Decoding stimulus modalities from MEG: Different ways of using spectral information

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We built five logistic regression classifiers (C1-C5) to investigate whether, spectrospatial information present in MEG data is useful in separating different, stimulus categories from each other. Nine healthy adults were exposed to 6-33-s blocks of auditory, visual and tactile stimuli that were interspersed with rest blocks. The 12-min sessions were repeated once.

We first applied short-time Fourier transform to the MEG traces and then independent component analysis (ICA) of the time-frequency decompositions. Each spectral epoch was labelled as 1 = visual, 2 = auditory, 3 = tactile or 4 = rest. We estimated 64 independent components (ICs, frequency range from 5 to 30 Hz). We trained our classifiers using windows from the first session and evaluated the classifier performance with data from the second session.

Our reference classifier (C1) used the total energies of the 64 ICs as features and thus did not utilize spectral information. C2 utilized unspecific spectral information by using the standard deviations of the spectra of the ICs as features. C3 was trained by utilizing more detailed spectrospatial information by treating each window as a matrix. With C4 and C5, we estimated frequency coefficients for each IC prior to classification using principal component analysis and Fisher’s linear discriminant analysis, respectively.

The (min/mean/max) classification accuracies for the 9 subjects were (0.24/0.40/0.63) for C1, (0.25/0.43/0.68) for C2, (0.31/0.50/0.70) for C3, (0.35/0.51/0.64) for C4, and (0.47/0.57/0.70) to C5. Thus, the mean accuracy was clearly above a chance level (0.25) for each classifier. The results of classifiers C3-C5 were significantly higher when compared with the reference C1 (paired t-test, p < 0.01, uncorrected), suggesting that detailed spectral information is useful in decoding. Our new method which uses class information in finding the optimal spectral filters (C5) gave the best results.
We-50 - Processing of local and global auditory regularities in infants

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Many cognitive functions are already present in young infants. Are young infants able to perform conscious top-down processing of sensory information? If so, at what age this capacity emerges? We aimed to address these questions using an auditory rule-extraction test with 2-month-old infants. This test comprises two levels of auditory violation. The local violation is similar to the classical mismatch paradigm and corresponds to local deviant sounds (e.g. $<u\geq Y<u\geq$), whereas the global level corresponds to the violation of the global structure of the stimuli (e.g. $<u\geq x<u\geq Y$). In adults, local auditory violations lead to a fast and automatic mismatch response (MMN). However, the detection of global auditory violations needs consciousness and is associated to a later response (P3b). To identify these two levels of auditory processing in infants, we recorded high density EEG responses to a series of four repetitions of /a/ and /i/ vowels. The fourth vowel in each trial was the crucial sound which could be local standard or local deviant and, regarding the global regularity of the stimuli, it could be frequent or rare. The results showed an early mismatch response to the local auditory violation at around 300 ms after the onset of the local deviant sound. This effect is characterized by a positive response over frontal region and a negative response over posterior regions (Figure A). Concerning the violation of the global regularity, we observed an early component at the same latency as the local effect with a significant positive left-lateralized topography (figure B, left). Interestingly, the global violation led to a significant late negative response in frontal region (figure B, right). These results suggest that 2-month-old infants could perform conscious processing of sensory information and extract the global regularity of the auditory stimuli.

We-53 - Functional connectivity of resting state networks in children

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Abstract

The dynamics of resting state functional connectivity were studied in 29 children. Signal power was analyzed across different frequency bands. Coherence and a new index for functional connectivity, the Weighted Phase-Lag Index (WPLI) were employed for estimating synchronization between a seed region identified in the central occipital area from the power plot and all other channels outside the seed region. Results show that WPLI provides a more articulated connectivity mapping than coherence. Moreover, co-
herence and WPLI were used as measures for calculating the graph theory parameter $L$ as a parameter for global interconnectedness in the different frequency bands.

**Introduction**

A constantly growing number of studies on resting state networks has outlined the importance of such functional aggregates in the understanding of brain states. However, Resting State Networks (RSNs) remain poorly understood, in particular in the pre-adult age.

**Methods**

Twenty-nine children between the age of 9 and 10 years participated in the current study. Data was recorded using a 275-sensor whole head system. Children were asked to sit quietly and relaxed with their eyes closed for 4 min. Power detection was performed within the range 0.5 to 30 Hz. A cluster of sensors in the occipital part of the helmet was identified as seed region for the connectivity study. The cluster comprised 29 channels. The mean signal across the sensor in this area was employed as a seed to calculate WPLI and coherence measures with the remaining sensors. Moreover, the global interconnectedness of the network was evaluated employing both WPLI and coherence.

**Results**

While coherence coincides well with power, WPLI provides a more articulated connectivity map in the alpha range (Fig. 1). Furthermore, global path length $L$ results show that WPLI provides shorter path lengths than coherence in every frequency band with the exception of the delta band.

WPLI proves to be a valuable tool for connectivity analysis.

**FIG. 1**: Comparison of FFT power, mean coherence and mean WPLI from/to each sensor to the occipital FFT power cluster for the 3 to 10 Hz range.

**We-54 - Magnetoencephalography reveals relationships among neonatal pain, functional cortical activity and school-age cognitive outcome in children born preterm**

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**Background:** Children born very preterm (less than 33 weeks) display cognitive difficulties at school-age in the absence of major intellectual impairment. Neonatal pain has been proposed as one factor contributing to altered brain function due to the vulnerability of the developing brain. MEG was employed to investigate relations among neonatal pain, functional brain activity and cognitive outcome in school-age children born very preterm.

**Methods:** Subjects: 22 extremely low gestational age (ELGA) children (born 24-28 wks, mean age 7.74 years), 32 very low gestational age (VLGA) children (born 28-32 wks, mean age 7.72 years), 25 full-term children (mean age 7.61 years). Exclusions: major neurological or sensory/motor/cognitive impairment, current ADHD medication. Spontaneous MEG activity was recorded using a 151-channel CTF system and cognitive ability was assessed (WISC-IV). Medical variables including neonatal pain (number
of skin-breaking procedures from birth to term-equivalent age) were obtained by chart review.

Results: The ratio of gamma-band (30-46 Hz) to alpha-band (8-14 Hz) activity was higher in the ELGA children (0.033) than the VLGA (0.23, p = 0.008) and full-term (0.23, p = 0.007) groups. Gamma/alpha ratio was negatively correlated with Working Memory Index (r = -0.43, p = 0.046) and Visual Processing Index (r = -0.46, p = 0.033) in ELGA children. Gamma/alpha was positively correlated with neonatal pain (r = 0.27, p = 0.01) in ELGA, but not VLGA children. These associations persisted after controlling for medical confounders.

Conclusion: Atypical spectral structure of background MEG in ELGA children, and its association with both neonatal pain and cognitive outcome in this group, suggests that developing thalamocortical systems underlying brain oscillations critical for cognitive function may be selectively vulnerable to procedural pain during the gestational epoch corresponding to ELGA birth.

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We-55 - Altered gamma oscillations associated with motor impairment in childhood epilepsy

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Background: Childhood epilepsy is associated with a host of functional impairments. High frequency oscillations (HFOs) and abnormal brain synchrony have also been associated with epilepsy, and these processes are known to play a critical role in the generation of cognition and behaviour. Relations between abnormal oscillations, neural synchrony and functional impairment in epilepsy, however, remain poorly understood. In this study, we focus on motor deficits and examine their relation to altered gamma oscillations.

Methods: MEG pre-surgical functional mapping data from 8 children undergoing median nerve stimulation were analyzed. Equivalent current dipoles fitted to the second peak of the cortical response were used to localize primary motor cortex. Event related beamformer analysis was employed to reconstruct motor cortex activity and the Hilbert transform was applied to band-pass filtered data to obtain envelope amplitude and instantaneous phase information. Phase locking values (PLVs) were used to measure interhemispheric synchrony. Hand grip strength, an indicator of motor function, was evaluated with a dynamometer.

Results: Children with motor impairments exhibited higher amplitude gamma responses in motor cortex contralateral to the stimulated arm (p = 0.039). The amplitude of gamma motor cortex response in the hemisphere contralateral to stimulation was negatively correlated with motor function (grip strength) in the contralateral hand (r = -0.73, p = 0.04). Interhemispheric gamma synchronization between motor cortices was correlated with motor function (grip strength) in the hand contralateral to stimulation (r = -0.88, p = 0.004).

Conclusion: Elevated high-frequency functional responses of motor cortex are associated with motor difficulties in children with epilepsy. These results suggest that invasion of eloquent cortical regions by epileptogenic high-frequency activity may interfere with functional networks and cause impairments.

We-56 - Fetal auditory evoked responses to different modulation rates. A fetal magnetoencephalography (fMEG) study

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Studies of our group, using fMEG method, demonstrated the ability of the fetus to respond to sinusoidal tone-bursts and to frequency differences between tone-bursts presented in 'odd-ball' sequences. In a short time after birth, the newborns demonstrate auditory cognitive abilities and react to preferential sounds (maternal, parents voices), differently then to stranger's voices. It could suggest that fetuses can differentiate spectral sound features and probably temporal features too. We extend our paradigms, involving auditory stimuli with complex sensory temporal structures (amplitude modulated tones 4 AM). In this study, we used tones in a constant pitch frequency but modulated in different modulation rates. We assume that the late transient auditory evoked response (AER) to the stimulus onset could reflect the fetal brain reaction to rapid and slow temporal onset changes in sounds. The aim of the study is to investigate if the fetuses are able to recognize and to respond differently to differences at the stimulus onset rise, which corresponds to different modulation rates. Fifty pregnant women between 31 and 40 weeks were measured by the fMEG. The stimuli were separated in 5 conditions, a sinusoidal tone was modulated by frequency of 2 or 4 Hz (slow modulation rates), 8 Hz (middle) and 27, 42, 78, 91 Hz (fast). The results showed that there was a significant decrease of the response latencies of AERs to the high and middle modulation rates in comparison to the slow modulation rates (Fig.). The highest response rate was assessed by modulation rates of 8, 27 and 78 Hz (80%, 100%, and 78%, respectively). These results were in line with a previous report, that the newborn brain is sensitive to the temporal structure of the auditory input. The differences between response latencies to slow, middle and fast
modulation rates were interpreted to reflect the different reaction of the fetal brain to temporal speech structure like phoneme and prosody.

AM stimuli (upper graphs) and the corresponding fetal AERs to different modulation rates

We-57 - Artemis 123: Development of a whole-head infant MEG system

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Background: Whole-head MEG systems to date have been optimized for adults. Because magnetic field strength produced by neuronal currents decreases as a function of \(1/distance^2\) and because toddlers and infants have the smaller head sizes (and thus an increased brain-to-sensor distance), present whole-head MEG systems do not provide optimal signal-to-noise in these younger individuals. Developed in 2005, the 76 channel babySQUID® showed the advantage of placing the head closer to the sensors in infants and children. This spurred development of a whole-head infant MEG system, the Artemis 123®. This poster describes the design of this system.

Methods: 123 first-order gradiometers (15mm coil diameter and 60 mm baseline) are housed within a realistically shaped helmet, with whole-head coverage optimized for a typical three-year-old (i.e., 50cm circumference). Using a coil-in-vacuum configuration, distance from the sensor to outer surface is as little as 6mm and less than 9mm throughout, with noise performance better than 10 fT/Hz. Twelve reference channels (two sets of triaxial magnetometers and 6 axial gradiometers displaced from the measuring coils) provide reduction of common mode noise. Using 24 bit A/D hardware, MEG data can be collected up to 5KHz. Data is acquired using LabView® and analyzed using BESA®. The accompanying figure shows the table, helmet, and electronics cabinet. Details of the data acquisition hardware are provided in the poster.

Conclusions: The Artemis 123® will allow rapid and efficient recording of high-quality whole-head MEG in infants three years and younger. Future use of this system in clinical and research studies will demonstrate the strength of the system as well as where enhancements can be made.
We-58 - Tablet disintegration assessed by AMR-ACB array with 36 magnetometers

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Disintegration of tablets is an important quality parameter and it is strongly influenced by several pharmaceutical properties. Disintegration is rate determining of drug release, and various technologies have been developed to evaluate the physical principles that govern this process. AMR-ACB is a novel biomagnetic system that combines the spatial resolution of the anisotropic magnetoresistive sensors (AMR) with the alternating current (AC) excitation. The aim of this study was to employ the AMR-ACB system to monitor the disintegration process of tablets in vitro by acquiring magnetic images. AMR-ACB consists of two identical pickup coils connected directly in series with 36 magnetometers arranged in a 6x6 array. Sensing and reference sensors are axially aligned and separated by a fixed baseline. Output signal was connected to a PC by an analog-to-digital board. Magnetic tablets (ø=11mm, n=6) were obtained by direct compression (30 kN) of 1.0 g of ferrite powder (75?m 4 ø 90?m) and 0.1 g of excipients. The tablets were placed in a square glass vessel containing 900 mL of phosphate buffer (pH 6.8) kept at 37 ± 0.5°C. The signals were continuously monitored by the AMR-ACB system with sample rate at 7 Hz/channel. Magnetic images were obtained and processed to quantify imaging areas at pre-determined time intervals. From the imaging area time curves, it was calculated the parameter t50 (time to obtain 50% of variation). The results showed that AMR-ACB system was feasible to obtain magnetic images to evaluate the disintegration process of tablets. Disintegration was monitored in real-time and was characterized by transition between a magnetic marker, when the particles were concentrated, to a magnetic tracer representing the spreading of the ferrite. The time to obtain 50% of variation (t50) was 47 ± 1.5s. AMR-ACB associated with conventional analytical tools may be employed as a tool for pharmaceutical quality control.

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We-59 - Synthesis and Quantitative FMR Measurements of Magnetic Iron Oxide Nanoparticles

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Magnetic nanoparticles (NPs), functionalized or not, are used in different medical and biomedical applications such as contrast agents for magnetic resonance imaging (MRI), heating mediators for cancer therapy (hyperthermia) and in magnetic immunoassays (MIA). In these applications, the aggregates of these NPs can be formed depending mainly on the magnetic properties, temperature and size distribution. Associated with these parameters, magnetic NPs may exhibit unique magnetic properties such as high coercivity, low Curie temperature, high magnetic susceptibility, strong superparamagnetism and have a free behavior of paramagnetic
particles in solution without attracting each other. In this work, we prepared magnetic iron oxide NPs and show the possibility of to use ferromagnetic resonance (FMR) to quantify these NPs. Moreover, we study the possibility to use FMR to characterize Curie temperature. The prepared magnetic iron oxide NPs were characterized by transmission electron microscopy and dynamic light scattering, showing sizes between ~30 to 200 nm depending on the synthesis conditions. FMR measurements were performed in a JEOL FA200 X-Band spectrometer using only 3 ?L solution samples in a standard cylindrical cavity. To quantify the magnetic NPs, the FMR spectra of water solutions containing different proportions of NPs, were acquired. Mass percentages were varied from 100% down to 0.01%. Improvement that we are able to detect FMR signals of the magnetic nanoparticles in solution 0.01% (~10 nanograms), and improvements can be made in the instrumentation by using a loop gap resonator with larger sensitivity, that can handle smaller volumes than the standard cylindrical cavity. The possibility of FMR utilization can be an interesting alternative to other methods as SQUID magnetometry, which requires expensive liquid helium.

**We-60 - Complementing visual cues assist children with APD in listening in background noise - an EEG/MEG study**

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Children with auditory processing disorders (APD) are characterized as having listening difficulties in noise in presence of normal hearing. Current management strategies for the APD population include addition of visual cues to assist in listening though there is little objective evidence for any benefits. This research aims to investigate the effect of additional visual cues on auditory evoked potentials and fields when listening in background noise in school-aged children with APD.

Two groups of children (aged 7-12) participated in this study (12 controls and 10 children diagnosed with APD). EEG and MEG data were recorded concurrently to the natural speech token /ba/ presented as auditory, visual or audiovisual stimulation imbedded in 8-talker babble at +10 and +3dB SNR.

Independent component analysis (ICA) was performed on the EEG data through the EEGLAB toolbox (EEGLAB, San Diego, CA) under the public GNU license (Delorme and Makeig, 2004). IC activations with <15% residual variance were retained for further analysis, and source waveforms were estimated by k-means clustering of the retained IC activations. MEG data was pre-processed and exported using BESA v.5.3. Cortically constrained source estimates of the EEG and MEG activity were then conducted using the sLORETA algorithm (implemented in Brainstorm v3.1, Tadel et al., 2011) assuming a generalized Boundary Element Model (BEM) (OpenMEEG, Gramfort et al, 2010, Kybic et al, 2005).

Preliminary results suggest greater activation in the anterior cingulate gyrus for the control group compared to the APD group in the auditory only conditions. This difference was reduced in the audiovisual condition. Activation in the anterior cingulate gyrus was also found in all conditions which may be indicative of active attendance to the stimulus. Further analysis is being undertaken to determine the differences between how listening in noise occurs in populations with APD and how visual cues assist in adverse listening situations.

**We-63 - Abnormal Neurodynamics of Face Processing in Autism**

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Autism spectrum disorders (ASD) are neurodevelopmental syndromes characterized by impairments in social interaction, including an apparent failure to make eye contact. The neural mechanisms underlying this behavioral abnormality are not understood. We conducted a magnetoencephalography study to investigate the spatiotemporal dynamics of brain activation during neutral and emotional face processing in high-functioning young adults with ASD and neurotypical controls (NT). In the majority of our autistic participants, we observed an abnormally early activation of the ventral occipitotemporal, face-specific, cortex at ~110 ms, rather than the NT response peak at ~170 ms. We employed phase-locking analysis (Lachaux et al., 1999) to examine the strength of communication between the primary visual cortex (V1), the fusiform face area (FFA), and the posterior superior temporal sulcus (pSTS), a region involved in processing dynamic and emotion information in faces. We found increased alpha-band (8-13 Hz) phase-locking for the autistic, but not neurotypical, participants between V1 and FFA. Conversely, there was strong beta-band (13-30 Hz) phase-locking for the NT, but not ASD, participants between FFA and pSTS. These effects were stronger for emotional, rather than neutral, faces. Given the proposed role of alpha-band activity in gating the engagement of neural regions for particular tasks (e.g., Jensen and Mazaheri, 2010), our findings suggest that there may be a disengagement of key face-processing nodes (FFA, pSTS) in individuals.
with autism in the early stages of face processing. The FFA blocking by alpha-band activity may interfere with FFA-pSTS communication integrating dynamic face features (pSTS) with configural face processing (FFA). This can explain impaired processing of emotional face cues in ASD. We conclude that abnormal alpha- and beta-band phase-locking patterns in the face-processing network could be developed for use as a biomarker of autism.

**We-64 - Expanding the conventional somatosensory evoked response evaluation in newborns from the primary to the secondary somatosensory cortex with MEG**

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Traditionally, clinical neonatal somatosensory evoked response evaluation has concentrated on the early responses. Our objective was to characterize the somatosensory evoked magnetic fields (SEFs) from both the primary (SI) and secondary (SII) somatosensory cortices in healthy newborns in attempt to create a clinically relevant method for detection of abnormalities in somatosensory processing. We recorded SEFs to stimulation of the contralateral index finger in 46 healthy fullterm newborns (19 females, 27 males) and analyzed the magnetic responses with equivalent current dipoles. The interhemispheric differences as well as the effect of post-menstrual age (PMA), height, and gender on SEFs were evaluated. Activity from both the SI and SII was consistently detectable in the contralateral hemisphere of the newborns, the SII responses being detected more reliably during quiet than active sleep. No significant interhemispheric differences existed either in SI or SII responses in the eight individuals that had recordings from both hemispheres. SI and SII response peak latency or source strength were not significantly affected by PMA, height, or gender within the neonatal period. We conclude that activity from SI and SII can be reliably evaluated with MEG in the fullterm neonatal period (PMA 37 to 44 weeks) during quiet sleep. No corrections for PMA, height, or gender are necessary for interpreting the results, but the evaluation of SII activity should be conducted in quiet sleep. Extending the interpretation to SII responses may bring about new information of higher level somatosensory processing.

**We-65 - Relations between cognitive functioning test score and MEG power spectral density of healthy 2-5-year-old children**

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We conducted Magnetoencephalogram (MEG) as a brain functioning measurement, Kaufman Assessment Battery for Children (K-ABC) as a cognitive skills’ measurement with one hundred healthy 2-5-year-old children during 2009-2011. We analyzed them to explore relations between MEG power spectral density and cognitive/behavioral indices which may suggest developmental achievement of young children. We focused on the conducted durations of MEG acquisition with eye-closed state using our special MEG customized for young children. In seventy two children (thirty three males and thirty nine females) of right handed, using the multiple regression analysis, there were significant relations between conducted durations and, Sequential Processing scores of the cognitive test and alpha power spectral density on upper occipital area. Also, there were significant relations between conducted durations and, Sequential Processing scores of the cognitive test and theta power spectral density on lower occipital area. In the analysis, we rejected MEG channels of frontal area because the distance form MEG sensors was different in each child. MEG data strongly depends on the distance between the head surface and sensor channels. Also we rejected the channels of temporal area because some studies show the sex differences of brain functions on the temporal area. Channels on central and occipital areas of head were selected. In general, domestic power spectral density shifts from theta band to alpha band along with children’s chronological development. But there was no significant effect of month-ages of children in the analysis concerning the conducted durations of eye-closed state. Our results show that increasing alpha and Sequential Processing scores indicate long duration for keeping eye-close condition, increasing theta and decreasing Sequential Processing scores indicate short duration for keeping eye-close condition.

**We-66 - Absence of SEFs in the secondary somatosensory cortex at term is associated with adverse neurodevelopment in infants born 28 weeks**

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Very preterm birth is associated with brain injury caused by primary ischemic/hemorrhagic insults and secondary maturational and trophic disturbances. The most common type of brain damage in preterm infants is diffuse white matter injury that may cause abnormal development of corticocortical and corticosubcortical connectivity which is thought to lead to the diverse developmental impairments seen in preterm survivors. Though cranial ultrasonography (US) and magnetic resonance imaging (MRI) predict outcome to some extent, new methods are needed for early recognition of the infants with normal imaging findings but adverse developmental outcome.

We recorded somatosensory evoked magnetic fields (SEFs) to tactile stimulation of the index finger at term equivalent age in 39 preterm infants born before the 28th gestational week and 46 control infants born at term. Responses from the primary somatosensory cortex (SI) were detected in all infants of both groups and there were no differences between SI peak latencies or source strengths. Secondary somatosensory cortex (SII) responses were absent significantly more often in the preterm infants than in the control infants (right hemisphere p=0.01, left hemisphere p=0.04). The preterm infants with SII response absent to both contralateral and ipsilateral stimulation in either hemisphere had significantly worse developmental quotients and locomotor subscales (Griffiths Mental Developmental Scales) at 2 years corrected age than preterm infants with SII responses present (p<0.01). On the contrary, findings in US or MRI did not correlate with outcome.

Our results indicate that studying brain function in addition to neuroimaging provides complementary information on brain development and may also have clinical implications. The lacking SII response may reflect either injury or delayed maturation of the somatomotor networks. In addition, it may represent a more widespread abnormality of corticocortical connectivity.

We-67 - Contamination of Electrophysiological Signals during High MRI Resolution: An in-vitro Study

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New developments in MRI techniques create sources of artifacts that ‘pollute’ the simultaneously acquired electrophysiological signals (EPS), used to monitor patients and/or synchronize images (1).

We developed a device to allow a deep study of the contamination mechanism, which would assist in elaborating new tools to obtain higher quality EPS. The system consists of three main modules: (i) a signal transmission system composed of an EPS generator and a transmission box, which transmits the EPS to a MR-compatible receiver inside the tunnel, (ii) an electro-conductive tissue-mimicking phantom (ε = 0.27 S/m) in which the EPS is injected, (iii) a signal collection module composed of a MR compatible amplifier-transmitter that emits, via an optical cable, the collected signal to a receiver box placed outside the MRI room. The receiver box comprises 20 channels distributed into four frequency bands (40, 80, 160, and 350 Hz).

The measurements were performed on a 1.5 T MRI. Fast spin echo and cine gradient echo images sequences were applied. An algorithm to extract and analyze the ‘reference noise’ Nref was developed. The contaminated ECG is decomposed into 5 frequency sub-bands (15.63, 31.25, 62.5, 125, 250 and 500 Hz) using the classical discrete wavelet transform. Nref was obtained by adding detail signals corresponding to the [62.5-250 Hz] sub-band. Statistical analysis (mean, standard deviation, and correlation) to characterize Nref was performed with respect to the wavelet and imaging sequence.

This works aimed to assess the disturbance level of the EPS, when using larger bandwidth amplifiers. Wavelet analysis is a very efficient tool applied to signal noise reduction (2). Characterizing detail signals, which represents the global noise, reveals relevant information with respect to the given wavelet and imaging sequence, which will be used to develop robust and efficient noise reduction algorithms.

(1) R. Abächerli et al. 2005 MAGMA (2) AbiAbdallah et al. 2007 ABME
We-68 - Development of auditory cortical activation in the child brain

Tiina Parviainen

The development of the cortical auditory system is poorly understood in the child brain. Previous EEG-studies show dramatic changes in the timing and morphology of the auditory evoked response during childhood, that are likely to reflect maturational changes of the underlying auditory system. For a more reliable description of the age-related changes in the auditory system it is necessary to include information about the spatial characteristics of activation. We studied the sequence of activation evoked by passive presentation of 1-kHz, 50-ms sine-wave tones (ISI 0.8-1.2 s) in four age groups (6-7, 9-10, 12-13 years old children and adults) using magnetoencephalography (Elekta Neuromag). The activated brain areas were modeled using equivalent current dipoles (ECD’s) that represent the mean location of an active cortical patch and the activation strength and direction of current flow in that area. In line with previous research, adults showed weak upward current at $\sim 50\text{ms}$ ($P50\text{m}$) followed by prominent downward current at 100 ms ($N100\text{m}$). In the youngest age group the earliest response detected at $\sim 100\text{ms}$ reflected an upward current flow, similar to the adult $P50\text{m}$, in both left (detected in 90% of the subjects) and right (70%) hemispheres. This response was followed by strong long-lasting activation peaking at $\sim 250\text{ms}$, with the current flow directed downwards in all children. In the two older child groups majority of the subjects showed upward current at $\sim 100\text{ms}$ in the left hemisphere (70%/65%), but a downward current at the same time window in the right hemisphere (70%/65%). The strong downward current at $\sim 250\text{ms}$ was detected in both hemispheres in all child groups but not in adults. The results indicate that developmentally specific auditory activation at $\sim 250\text{ms}$ is clearly present still at the age of 13 years. Moreover, the rightward emergence of the $N100\text{m}$ type of response in older children indicates a maturational lag in the left-hemisphere auditory cortex.

We-69 - Fetal auditory evoked cortical responses development by fetal MEG measurements: influences on the responses latency by the gestational age, behavioral states and steroids treatment.

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Objective:
The effects on the higher cortical function induced by different behavioral states and steroids have been studied during the maturation of the fetuses with gestational ages between 26 and 41 weeks.

Methods:
A group of 167 fetuses underwent fetal MEG to study auditory evoked cortical responses (fAECR) (ARGOS 200, AtB, stimulus 100 dB, ISI 800 ms, standard 500 Hz, 50 ms, deviant 750 Hz, 50 ms, pseudo-random 75/25 %). Reliable fAECR were identified in 141
fetuses (1). Group 1 consisted of 128 normal controls whereas 13 were exposed to antenatal steroids (GC) on average 1 week prior to examination (5-11 d) for symptoms of threatened preterm labor (Group 2).

Results:
The two major statistically significant fAECR components that were identified were deliberately named P1 and P2 (1). In the Group 1, P1 were identified in 61 and P2 in 55 cases and in Group 2 P1 in 10 and P2 in 12 cases. Levels of activity were estimated according to characteristic heart rate patterns in active (n=77) and quiet state (n=17).

(1) A reliable decrease of latency of fAECR components P1 and P2 as a function of maturation can be observed. (2) There are no significant differences of latency of the components between different fetal activity levels. (3) We observe a tendency of a reduction in latency of P1 in the GC compared to the controls around 30 weeks of gestational age.

Conclusion:
Reliable responses could be elucidated by advanced signal processing methods (1) in around 50 % of the cases. Latency of the responses decreases with gestational age. In this large sample, we were not able to elucidate significant latency differences between different fetal states of activity. Previous steroid exposure about one week ago prior to 30 weeks GA seems to result in a latency reduction of the early component of the fAECR.


We-70 - Predominance of bottom-up functional interactions between posterior and frontal regions during reading

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The study investigated functional associations between occipitotemporal, temporoparietal, and inferior frontal regions in the left hemisphere during oral reading in 58 school aged children with typical reading skills (aged 10.4 ± 1.6, range 7.5-12.5 years). Participants were tested on an oral pseudoword reading task, involving three-letter pronounceable non-words. Event-related neuro-magnetic data acquired with a whole-head, first-order gradiometer system (4-D Neuroimaging, Magnes WH3600) were used to compute source-current density waveforms using a minimum norm algorithm during the first 800 ms post-stimulus onset. Temporally-constrained contributions (cross-correlations) were established for four ROIs (STG, SMG, ANG, and IFG) by controlling for the autoregressive effects of activity in each ROI. Unique contributions made by activity in one ROI to subsequent activity in a second ROI were assessed through multiple regression analyses. Forward associations between lateral (LOC) and ventral occipitotemporal cortices (fusiform gyrus) to each of the four main ROIs were also examined.

The data corroborate previous findings for a regular progression of activation peaks between occipitotemporal, temporoparietal, and inferior frontal regions, in the left hemisphere, among typical readers. The earliest significant contributions to SMG and ANG activation (at 200-250 ms) were made by preceding activity in the fusiform gyrus. At all latencies, degree of activity in IFG appeared to be determined by earlier activity in ANG and STG. These cross-correlational data support the pre-eminence of ‘feed-forward’ (bottom-up) signalling. Feedback (top-down) inputs may take place but may not be sufficient (in intensity or spatial spread) to modulate the average activity in a given ROI.

Schematic rendering of significant regression coefficients for pairs of ROIs. The beginning of each line represents activity at an earlier time bin in a given ROI predicting degree of activity at a subsequent time bin in a different ROI.

We-71 - Increased temporo-parietal connectivity in children with ADHD and CSWS

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Attention-Deficit hyperactivity disorder (ADHD) is one of the most common neuropsychiatric conditions in childhood. It is characterized by inappropriate expression of impulsivity, inattention and hyperactivity. A percentage of children with ADHD appear to have continuous spikes and waves during their sleep—a condition most often called Continuous spike and waves during slow sleep (CSWS). One of the hypotheses used to explain the affected cognitive functioning of those children concerns changes in resting-state connectivity. In this framework, we studied the functional and effective brain connectivity in children with ADHD and CSWS, focusing on the resting state network with Electroencephalographic recordings. Twenty-four-hour recordings including wakefulness and sleep of children admitted to the National Centre for Epilepsy at Oslo University Hospital were analyzed and compared with controls of the same age group without ADHD. Directed transfer function (DTF) was used to measure the effective connectivity between brain areas, in the theta and gamma frequency bands. The analysis have shown an increased temporo-parietal connectivity of the ADHD children, when compared to the control group ($p<0.035$), most prominently in the left hemisphere. Parietal to frontal connections were also significantly different between patients and controls for both frequency bands. The time dynamics of these most active connections have shown increased values of connectivity during the day compared to sleep. This may be related to arousal impairment in children with ADHD.
We-72 - An Efficient Liquid Helium Circulation System for MEG and its Performance

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We have developed efficient systems to collect evaporated helium gas, to cool it down to liquid and to return it into dewars using GM cryocoolers without delivering any disturbing noises to applying devices such as MEGs (Magnetoencephalographys) and low temperature physics devices (MPMS or PPMS). The key idea is not to use liquid helium directly to keep the dewars cooled down, but to utilize relatively high temperature helium gas (about 40K) cooled by the first stage of the GM cryocoolers to get rid of invading heat to the dewars. The gas is fed at the neck tubes of the dewars. The evaporated helium gas in the dewars is collected swiftly while it is in the low temperature (about 8K) and is returned to liquid helium without using much energy.

The systems use transfer tubes specially designed for each devices that pass the liquid helium, the low temperature helium gas (about 8K) and the relatively high temperature helium gas with very low heat invasion (lower than 0.1W/m). They also use a refiner to collect the contamination gases such as oxygen and nitrogen effectively by freezing the gases. It has an electric heater to remove the frozen contamination in the form of gases into the air. This time, a special VTF valve, which could be operated electrically in low temperature with very low leakage, is developed and used to ensure proper operation. The vibrational and acoustic noises are attenuated to be low enough for measurements. The systems have been confirmed to be able to liquefy above 10 litters/D of liquid helium from evaporated helium gas. A helium circulation system for a commercialised MEG (Yokokawa Inc., PQ1160C) has been used about a year.

Multi-pipe TT of the HCS installed on the commercialized MEG (PQ1160C, Yokokawa Electric Cor. Inc., Japan). As the TT has 1/2 inch insert tube, there was no need to modify the MEG to install the HCS. TT is twisted twice to use the ventilation hole located

We-73 - Graph theoretical analysis of neuromagnetic data during a motor task in infants and young children

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During infancy and early childhood, the brain is involved in large functional and structural changes. The investigation of the functional changes occurring in the sensorimotor cortex has important clinical implications since a deviation from normal development can be a symptom of developmental disorders. Complex network measures have been recently proposed to characterize the brain development in children in terms of changes of connectivity patterns within the default-mode network. Based on these findings and on the evidence that the dominant feature characterizing the sensorimotor cortex is the movement-related synchronization/desynchronization of the mu-rhythm, we used graph theoretical concepts to examine functional changes in the sensorimotor network supporting mu desynchronization during prehension as a function of age in infants and young children.

Neuromagnetic data were acquired over the left hemisphere in infants and young children (<5 years) using a pediatric magnetoencephalography (MEG) system. A group of adults was used as control. The subjects were involved in a paradigm where periods of ‘rest’ (RE) were alternated with ‘prehension’ (PR) tasks during which a pipette was squeezed with the right hand. For each subject...
and for each condition, a synchronization likelihood-weighted graph was calculated in the mu band. A subject-specific frequency range was considered in order to take into account the age-dependent differences observed in the mu frequency peak (Berchicci et al., 2011). Network clustering coefficient and characteristic path length were calculated to evaluate the network organization during the RE and PR conditions. The results showed that, from infants to adults, the functional brain development is characterized by a shift from more random to more organized topology in the RE condition, whereas an opposite trend describes the evolution of brain topology in the PR condition.

Berchicci M et al. 2011 Developmental Neuroscience 33(2):130-43

We-74 - Localizing the N400m in preschool children: A lexical access study

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Using a picture-word matching task, MEG was used to identify the source of the magnetic N400 in preschool children. Previous ERP studies have found that N400 are elicited in children as young as 19 months old, using pictures that are incongruent with the linguistic input. This effect is clearest in centro-parietal sites in children, as in adults. However, ERP studies are not very informative about the anatomical sources of the cognitive processes that underlie the N400 reflects. Using MEG, we investigate the brain structures that are activated in children in response to language, to see if these are the same as those activated in adults. MEG signals from preschool children (N= 13, Mean= 53 months, SD= 6 months) were recorded using a 64-channel whole-head paediatric MEG system. The task was picture-word matching, children saw the picture of a common object, followed by a matching or non-matching word. Children were instructed to press one button for correct trials, and another one for incorrect trials. An eyetracker was used to ensure fixation on the pictures. Generators were localized using an iterative classical LORETA analysis. Incongruent words elicited significantly larger responses in the left middle temporal gyrus (Fig. 1). Activity in bilateral temporal lobes was evident from the onset of the spoken word, with a stronger and larger source over the left hemisphere between 350 and 550 ms. This source is consistent with locations reported in adults with intracranial EEG studies and MEG studies. We conclude that the posterior middle temporal sources of the N400m in preschool children can be resolved using a paediatric MEG.
Figure 1: Source analysis between 350-550 msec after onset of spoken word. Stronger bilateral activation for the mismatch condition is evident over the middle and superior temporal lobes (top panel). Statistical comparison between conditions showed a

We-75 - MEG Characterization of Aversive Trace Conditioning in FASD

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Prenatal exposure to alcohol is the leading preventable cause of mental retardation in the US and is also implicated in a wide range of behavioral and social deficits. Brain regions particularly impacted by exposure to alcohol in utero include medial frontal cortical structures, hippocampus and cerebellum. Predictive capability and plasticity are characteristic features of cortico-cerebellar circuits. We utilized an aversive trace conditioning paradigm to probe for differences in brain dynamics in children 12-19 years of age with fetal alcohol spectrum disorder (FASD) and typically developing age- and sex-matched controls. Data were recorded with a 306-channel MEG array following 1) visual (CS+) stimuli followed after a delay by aversive (US) sounds, 2) identical CS+ stimuli unpaired with US and 3) a different set of visual stimuli (CS-) which were never paired with US. Source analysis of the data utilized individual MR images, followed by projection onto a standard Colin27 brain (BrainStorm: wMNE). Spatio-temporal activation patterns were examined for significant differences between FASD and controls. We found adolescents with FASD exhibited reduced activation of frontal and parietal cortex following the CS. Responses in anterior cingulate were muted throughout the conditioning trials. In FASD, enhanced activation was observed following US in auditory cortex, amygdala and insula, consistent with a decrease in the predictive power of the CS+. Differential activation was observed also in hippocampus and cerebellum. Adolescence is a period of significant functional reorganization and behavioral vulnerability for this patient population. Elucidation of differences in the developmental trajectories of cortico-cerebellar network dynamics throughout adolescence could facilitate the development of interventions for FASD appropriate to this age range.

We-76 - Abnormal Auditory Evoked Responses to Standard and Novel Stimuli in Adolescents with Fetal Alcohol Spectrum Disorder (FASD): A Magnetoencephalographic (MEG) Study

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Prenatal exposure to alcohol is the leading preventable cause of mental retardation in the US. Affected brain regions include medial frontal cortex, hippocampus and cerebellum. Predictive capability and plasticity are characteristic features of cortico-cerebellar circuits. We utilized an auditory oddball paradigm to probe auditory processing in 12 adolescents (12-19 years) with FASD and 12 age- and sex-matched controls. Data were recorded with a 306-channel MEG array. Subjects were presented with randomly intermixed standard stimuli (80%), novel stimuli (10%) and also target stimuli that cued motor responses (10%). BrainStorm (Tadel et al. 2011) was used to extract individual spatio-temporal patterns of activation and to project these results onto the Colin27 brain for comparison between groups. There was no evidence for differential onset, peak latency or amplitude of the P50m response to standard stimuli. Activity was significantly enhanced in temporal, parietal and frontal cortex between P50m and N100m for standards in FASD but not in controls. The amplitude of N100m in right auditory cortex (BA41) for standard and for novel stimuli in FASD was similar to
the N100m amplitude for novel stimuli in controls. Evoked responses to standards in STS at 100ms was enhanced in left hemisphere but reduced in right hemisphere. Interestingly, left Crus I of cerebellum displayed a 120ms response to standard stimuli in controls but not FASD. The P50m and N100m differences observed in FASD are in contrast to auditory responses characteristic of Down Syndrome (Pekkonen et al. 2007). The curious cortico-cerebellar response to the standards following P50m in FASD suggests that lateral cerebellum contributes to the development of a template for repeated (standard) stimuli and that this function is impacted in FASD. Impaired ability to predict non-novel stimuli may contribute to attentional difficulties that can be found in this patient population.

We-77 - Neurophysiological Processes in the Learning of Novel Object’s Functions in Children

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This study investigates the neurophysiological correlate underpinning the learning of functions and usage of novel objects in semantic memory in children. Continuous MEG data were recorded using a whole-scalp 306 channels MEG (Elekta Oy, Finland) in 11 healthy children (mean age 10.21 years) during a picture-definition task. Two MEG sessions (S1 and S2) were administered, separated by a behavioral verbal learning session during which children learned short definitions about the ‘magical’ usage of 50 unknown chimeric objects. Additionally, 50 other chimeric objects for which no definition were learned and 50 familiar real objects were presented in both sessions. MEG data preprocessing (signal space separation - head movement correction - subjects realignment in the same sensor space - band-pass filtering 0.5-40 Hz - epoching -200:1100 ms - baseline correction -200:0 ms 4 downsampling 250 Hz - artifact rejection: gradiometer ≥2000 fT/cm, magnetometer ≥ 4000 fT, EOG ≥ 150 , EMG ≥ 300 ) and analyses were performed using SPM8. Behavioral results showed that all children successfully learned at least 75% of the new definitions. Evoked responses (ER) in sensor and source space (temporally windowed on the timing of significant effects observed in sensor space) were entered in a factorial design with Session (S1 vs. S2) and Object type (learned chimeric [LC], unknown chimeric [UC] and real familiar [RF]) as within-subject factors. The comparison between ER for LC at S1 vs. S2, masked exclusively by between-sessions repetition effect for UC, revealed learning-related neuronal activity modulations developing 550 to 800 ms post-stimulus onset in bilateral orbito-frontal, right parietal (530-690 ms) and right temporal (700-760 ms) regions. Altogether, these results suggested that these late ERs components changes may support, in children, the challenging task of rapidly creating novel semantic representations about objects functionalities and usage.

We-78 - Investigating inhibition in adults and adolescents with and without ASD

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Autism spectrum disorders (ASD) are a set of neurodevelopmental disorders that encompass deficits in communication, social interaction and restricted/repetitive behaviour. Impairments in inhibition, defined as the ability to withhold a prepotent response, may underlie symptoms falling under two of these categories: social deficits and repetitive behaviours/restricted interests. Thus, socially inappropriate or perseverant behaviours commonly observed in individuals with ASD may reflect deficits in inhibition. As the neurobiology and development of inhibition is not well understood, we examined this cognitive construct using MEG. Whole-head MEG data were acquired from 24 adults (12 ASD) and 30 teenagers (15 ASD) with age- and sex-matched controls. Participants performed a visual go/no-go task in which they rapidly responded to ‘go’ stimuli or withheld their response if an ‘x’ was overlaid on the visual stimulus (‘no-go’). The inhibition condition consisted of 33% no-go trials to generate a prepotent tendency to respond, whereas the baseline condition consisted of 67% no-go trials. Greater global field power (GFP) was seen for controls than ASD in both adult and adolescent groups. Beamformer analyses revealed activation in the right inferior/middle frontal gyri between 200-300 ms in the adult controls, whereas this was not seen in adults with ASD. Typically developing adolescents also showed right inferior/middle frontal gyri activation, but this was diminished in adolescents with autism. The similarities between control adolescents and adults suggest that typically developing teenagers are employing the appropriate functional network for inhibition. The unusual neural activity in both ASD groups concur with behavioural observations of inhibitory dysfunction. The atypical pattern of neural responses in the ASD groups, compared to controls, suggest a latent impairment that can be quantified with MEG.
We-79 - Assessment of Spatial and Spectral Signatures of Word Recognition in the Developing Brain using Accumulated Virtual Spectrograms

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Introduction: High-frequency oscillations (HFOs) in the brain open a new window for the studies of language development in humans. The objective of this study is to determine the spatiotemporal and frequency signatures of word processing in healthy children.

Methods: Sixty healthy children aged 6-18 years were studied with a whole-cortex magnetoencephalography (MEG) system. One hundred stimuli consisted of matched words in which the seen and heard words were identical, twenty stimuli consisted of mismatched words in which the word seen was different from the word heard. All the auditory and visual words were presented simultaneously. The spatial and frequency signatures of neuromagnetic activation associated with word-processing were assessed with wavelet-based beamformer analyses at source levels.

Results: The source imaging data have shown a clear lateralization in terms of source activation in 70-120 Hz in children over the age range of 6 to 13 years of age (p=0.001). Males and females showed different developmental trajectories over the age range of 9 to 13 years of age. The activation in 30-50 Hz was localized to diffused areas which included frontal and parietal regions. However, it was overlapped on the areas localized by signals in 70-120 Hz in 48 children (80%, 48/60). The activation in 13-30 Hz was localized to much wider regions including the occipital-temporal cortices. However, the location of activation in 13-30 was overlapped on the area localized by signals in 70-120 Hz in 39 children (65%, 39/60). The correlations between magnetic source imaging and conventional waveform have revealed that the latency of brain activation around 250 millisecond decreased with age (p<0.05).

Conclusion: These findings suggest that left-hemisphere language processing emerges from early bilateral brain areas with gender optimal neural networks.

We-100 - Boys and girls show different developmental trajectories on a MEG language lateralization task

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It is well known that cognition and language development differ between boys and girls, though the timing and neural representations remain poorly understood. While evidence from clinical and neuroimaging studies have indicated that language function is typically lateralized to the left hemisphere in the mature brain, the issue of language-related sex differences is still under debate. In this study, MEG was used to investigate the developmental trajectory of language lateralization as a function of age and sex. Eighty-six typically developing children (48 females), aged 4 to 18 years participated in an overt verb generation task to visually presented picture stimuli. In each subject, low-beta event-related desynchrony was analyzed using differential beamformer analyses [1,2] in four active time windows: 300-500, 400-600, 500-700, 600-800 ms compared to a 200 ms pre-stimulus baseline. The region of interest was set to exclude occipital areas and images were thresholded at 95% activation using a bootstrap statistical procedure (3). Laterality indices using a power-weighted average of supra-threshold voxels were computed. A significant correlation between age and left hemisphere lateralization was found for girls only. Boys demonstrated a more bilateral pattern across childhood. This is the first neuroimaging evidence of language-related sex differences in childhood. Girls exhibited more adult-typical, left-sided patterns, while boys showed bilateral brain involvement. These different patterns could be attributed to maturational differences in functional neuroanatomy between girls and boys, alternatively, girls and boys may have utilized different strategies during the verb generation task.

We-1 - Multi-source minimum variance localizers for dual state scenarios

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Multiple constrained minimum variance (MCMV) beamformers allow for the spatial localization and reconstruction of correlated neural activity. In particular, MCMV source localizers derived recently (Moiseev et al., NeuroImage, 2011) provide unbiased estimates of positions and orientations of multiple arbitrarily correlated sources for the case of a single-state beamformer that is, when only one brain condition is studied.

In many cases a dual state beamformer which images the differences between two conditions proved to be more powerful. Each condition is characterized by its own set of active sources. Typically, extrema in the spatial distributions of certain differential statistics are used to identify the emerging sources in each condition, despite the unbiased property of the measures (e.g. pseudo-T, pseudo-F statistics) not being proven.

To address this problem, in this work the MCMV localizers mentioned above are generalized to a dual state case. Given brain conditions 1 and 2, three scenarios are considered.

A) In condition 2, new sources are added to those existing in condition 1, but they are uncorrelated with the old ones (this is a typical active/control state scenario)

B) In condition 2, some sources disappear. The remaining sources are not correlated with the vanished ones

C) Sources may both emerge and disappear between the conditions. No constrains on the correlations are imposed

We prove that generalized localizers are unbiased in a dual state case, namely: in scenario A), a global maximum of the localizer is reached when the beamformer probes match the new sources in condition 2, in scenario B) a global minimum is reached when the disappeared sources are located, in the general case (C), a stationary point is attained when all the sources that changed their parameters are identified. This stationary point can be a maximum or a minimum or neither of the two depending on the source parameters and their correlations.

We-2 - Brain source localization with Champagne on real and simulated EEG data

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We performed a head-to-head comparison of different methods for brain source localization with EEG data. On real and simulated data we compared Champagne (1) to sLORETA (2), eLORETA (3), LORETA (4), LAURA (5), CLARA (6) and eigenspace vector beamforming (7).

We simulated EEG data from four correlated sources. Real EEG noise samples were remontaged to the same 33 channel standard configuration and added with different signal-to-noise ratios. Lead fields were created in a standard brain (8) with a 5 mm resolution. Champagne is the only method that can resolve the location of all four correlated sources, even under poor signal-to-noise conditions.

Our conclusions from real data sets of epileptic spikes and auditory evoked potentials are not as definite as for our simulations. While for rolandic spikes Champagne showed multiple discrete sources within the rolandic regions, for an occipital spike it showed appropriate onset and peak sources but also additional sources were found that appeared to compensate for misspecification errors in the head model.

We-3 - MEG analytical method - possibility of a group analysis -

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In addition to the equivalent current dipole model (ECD) typically used for MEG analysis, another method of analysis, the spatial filter method, has recently come into use. In this study, we considered whether the group analytical method used in fMRI can be applied to MEG analyses. Fourteen healthy, young adults, ages 18 to 22 (mean = 20.7, 9 males), were recruited from Tohoku University. Written informed consent was obtained from all subjects according to the guidelines of the local ethical committee and the Declaration of Helsinki (1991). In our experiment, subjects performed the visual oddball task, a motor task, and a sensory task. MEG recordings were carried out with a whole-head 200 channel MEG system (Yokogawa Electric Corp., Japan) and individual T1 structural images were obtained from a 3 T Philips MRI scanner. In the analysis, virtual sensors were generated with 5mm voxels in the MNI space. Event-related synchronization was calculated at the source level using an optimal time-frequency beamformer. Functional images were created with logarithmic conversion and spatial smoothing with a 20mm PWHM Gaussian kernel. In the oddball task, activity was seen in the prefrontal cortex (PFC), temporo-parietal association area, temporo-parietal junction, precuneus, and visual cortex. Activity in the motor task was seen in the motor cortex and supplementary motor area. In the sensory task, only the sensory area showed activity. It is difficult to record activity of the PFC only by personal data. However, the group analysis enables a record. The shape of the helmet of MEG system has it for the factor that cannot record activity of the PFC. Furthermore, a noise is easy to get mixed with activity of the PFC. The group analysis is effective technique to improve the S/N ratio. On the other hand, there is a possibility that active region became large because the time width that is necessary for frequency analysis is wide as for the activity of the sensor-motor area.

We-4 - Spatio-temporal Regularization in Linear Distributed Source Reconstruction from EEG/MEG A Critical Evaluation

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The high temporal resolution of EEG/MEG data offers a way to improve source reconstruction estimates which provide insight into the spatio-temporal involvement of neuronal sources in the human brain. In this work, we investigated the performance of spatio-temporal regularization (STR, see Schmitt et al., IEEE Trans Med Imag, 2001) in a current density approach using a systematic comparison to simple ad hoc or post hoc filtering of the data or of the reconstructed current density, respectively. For the used STR approach we implemented a frequency-specific constraint to penalize solutions outside a narrow frequency band of interest. The widely used sLORETA algorithm (Pascual Marqui et al., Meth Find in Exp Clin Pharmacol, 2002) was adapted for STR and generally used for source reconstruction. STR and filtering approaches were evaluated with respect to spatial localization error and temporal correlation between original and reconstructed source time courses in single source and two source scenarios with fixed source locations and oscillating source waveforms. We used extensive computer simulations and tested all algorithms with different parameter settings (noise levels and regularization parameters) for EEG data. To verify our results, we also used data from MEG phantom measurements. For the investigated scenarios, we did not find any evidence that STR-based methods outperform purely spatial algorithms applied to temporally filtered data. Furthermore, the results show very clearly that the performance of STR depends very much on the choice of regularization parameters. As an example, see figure for the localization error of a single thalamic source, reconstructed using classical sLORETA, sLORETA applied to filtered data and STR based on sLORETA, depending on the choice of spatial and temporal regularization parameters.
Localization error for a single thalamic source pointing in dorsal direction (averaged over 100 trials with SNR=2 and 61 time steps per trial), showing the dependence on the regularization parameters (lambda - spatial, mu - temporal).

We-5 - MEG/EEG brain imaging based on Beamforming and sparse anatomical priors

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The use of Multiple Sparse Priors (MSP) for solving the MEG/EEG inverse problem provides a flexible mechanism to select between different combinations of priors in the form of discrete patches of active cortex. The main disadvantage of this technique is that the size and location of the patches must be selected a priori. Many of them will be placed in un-interesting regions of solution space and simply add to the computational burden and potentially under-sample interesting regions. In this work we use a Beamformer solution to augment this set of fixed anatomical priors.

We propose a two-step reconstruction: first we use a Beamforming prior to solve the inverse problem within the Bayesian framework, and the indices of the most active sources are recorded. Then an MSP reconstruction is performed over the original set of patches distributed over the cortical surface in addition to patches centred at locations defined by the Beamforming solution. This methodology adds a new degree of flexibility to the MSP, by proposing locations based on functional assumptions (no correlated sources) without imposing hard constraints.

Simulations demonstrate how the algorithm effectively uses the Beamforming prior only when it improves the solution, reducing the localisation error caused by the fixed set of priors in the MSP. Figure 1(a) shows an MSP reconstruction of a single source with an error of 9.77 mm caused by lack of patches in that location, Figure 1(b) shows the solution of the new algorithm exhibiting zero localisation error because the Beamforming prior was able to locate the source. Figure 1(c) shows how Beamformer fails to recover two synchronous sources, one of them completely disappeared, Figure 1(d) shows the solution of the proposed algorithm, where the MSP ignored Beamformers solution in favour of patches from the original set.
Source localization in magnetoencephalography (MEG) is an ill-posed inverse problem. In order to be able to obtain a unique solution, it is therefore necessary to constrain the space of possible solutions by using additional information. Location and orientation constraints are commonly used: the source currents are restricted to lie on the neocortex with their orientations perpendicular to the cortical mantle. In distributed source models, which simultaneously estimate the current magnitudes for several thousands of dipoles, it is necessary to use additional regularization, as the source localization problem amounts to solving a highly underdetermined regression problem. Commonly used are minimum l2-norm and minimum l1-norm regularizations, which promote diffuse and sparse current distributions, respectively.

In our work, we explore the use of additional constraints for distributed source localization methods, with the goal of obtaining physiologically more plausible current distributions. Specifically, we build on results from recent animal studies which indicate that the maximum current density on the cortical surface is relatively constant for different brain regions and species. We combine the maximum current density constraint with l1-norm regularization, resulting in a source localization method which leads to solutions where the magnitude of each of the few active dipoles is below a maximum value. We use an efficient quasi-Newton interior point optimization method to solve the source localization problem for high resolution source spaces with over 300 000 current dipoles on the cortical surface, each corresponding to approximately 0.65 square millimeters of tissue. We show results for both simulated data and data from an auditory experiment. From our simulation with an extended source on the somatosensory cortex we found that our approach produces a more faithful estimate along the wall of the fissure than the standard l1-norm regularization.
We-7 - Localization of epileptogenic zones in secondary generalized epilepsy using frequency domain source imaging of intracranial electroencephalography (iEEG) high gamma oscillations

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Although intracranial electroencephalography (iEEG) has been widely used to localize epileptogenic zones in epilepsy, visual inspection of iEEG recordings does not always result in a favorable surgical outcome, especially in secondary generalized epilepsy such as Lennox-Gastaut syndrome (LGS). Various computational iEEG analysis methods have recently been introduced to confirm the visual inspection results. Of these methods, high frequency oscillation in iEEG has attracted great interest because a series of studies have reported a close relationship between epileptogenic zones and cortical areas with high frequency oscillation. Meanwhile, frequency domain source imaging of EEG and MEG oscillations has proven to be a useful auxiliary tool for identifying rough locations of epileptogenic zones. To the best of our knowledge, however, frequency domain source imaging of high frequency iEEG oscillations has not been studied. In the present study, we investigated whether the iEEG-based frequency domain source imaging of high frequency oscillation (high gamma band, 60-100 Hz) would be a useful supplementary tool for identifying epileptogenic zones in patients with secondary generalized epilepsy. The method was applied to three successfully operated LGS patients, whose iEEG contained some ictal events with distinct high gamma oscillations before seizure onset. The resultant cortical source distributions were compared with surgical resection areas and with high frequency spectral power distributions on the intracranial sensor plane. While the results of the sensor-level analyses contained many spurious activities, the results of frequency domain source imaging coincided better with the surgical resection areas, suggesting that the frequency domain source imaging of iEEG high gamma oscillations might help enhance the accuracy of pre-surgical evaluations of patients with secondary generalized epilepsy.
We-8 - Accurate skull modeling from MRI for EEG source localization

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In EEG source localization, the skull plays an important role due to its low conductivity compared to other tissues in the model and due to its inhomogeneity as thickness and conductivity varies throughout its structure. While MRI is the most used imaging modality for the visualization of the head structure, it does not allow an exact distinction of the skull and its tissue types. Conversely, CT is the modality that can accurately describe the geometry of the skull but is not commonly performed on patients due to ionizing radiation. We investigated the effect of using MR-based models for the skull as opposed to a ground truth CT-based skull model. A head model with an accurately segmented skull from CT, including compact and spongy bones as well as air cavities, was used as reference. To analyze the influence of using MR-based skulls, 4 models were constructed with skull geometry and air cavities segmented from MRI using SPM toolbox: M1 isotropic inhomogeneous, the spongy bone was modeled as eroded compact, M2 4 anisotropic homogeneous, M3 4 hybrid, isotropic inhomogeneous in the vault (as M1) and anisotropic in the base (as M2), M4 4 isotropic homogeneous.

The forward problem was solved through FDM with Reciprocity using 128 electrodes. The estimated dipole parameters were chosen as the ones that best fitted the surface potential. Large errors in the temporo-basal region were seen in Figs. 1(a) and 1(d) where the difference in shape between MR and CT-based skulls is particularly noticeable. In Fig. 1(b), the errors were smaller in the basal region but more distributed in the whole volume. The hybrid model, Fig. 1(c), showed overall lower errors. When the geometry of the skull cannot be accurately segmented, the isotropic inhomogeneous model (M1) can better model the cranial vault but anisotropic conductivity (M2) is appropriate in regions such as the skull base. Then, for a patient-specific MR-based head model, the skull will be better modeled as M3 (Fig. 1(e)).
Localization errors for models 1 to 4

We-9 - Resolution of MEG inverse problem via Reweighted l1 Minimization Algorithm

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The MEG inverse problem is heavily ill posed, since many solutions are possible from the same set of measurements. In practice, current density can be discretized by current dipoles in a fixed position, thus a linear system is obtained, though ill conditioned and a regularization scheme must be adopted to invert lead field matrix. Under suitable conditions (e.g. during a task), we can suppose that the recorded signal is due to the contribution of few brain regions which can be modeled by a sparse representation of the current dipole distribution. In this work, we present a novel approach to solve the MEG inverse problem under the hypothesis of a sparse solution.

The algorithm (1) consists in solving a recursive sequence of constrained weighted l1-minimization problems, where the weights used for the next iteration are computed from the values of the current solution. This approach, de facto, acts as an ‘auto-regularization’ of the problem that improves the accuracy of the source estimate.

We tested the proposed method on extensive simulations and on real MEG data recorded during non painful stimulation of right median nerve. The results of the inverse problem solution via reweighted l1-minimum norm are compared with sLORETA (2), and standard l1-minimum norm approaches. Figure 1 shows the normalized amplitude for the sources active at 35 ms after stimulation. Although none of the methods mislocalizes the source, reweighted l1-minimum norm solution is less sensitive to spurious brain activity.

(1) Candès et al., J Fourier Anal Appl (2008),pp. 877-905
In recent times, there has been an explosion in development of novel source reconstruction algorithms, including powerful sparse Bayesian methods. Statistical analyses of such source reconstruction images from M/EEG imaging typically proceed with voxel-level inference above a pre-defined threshold criteria. Many nonparametric resampling techniques have however been designed for this purpose and have also been successfully applied to M/EEG reconstructions with minimum-norm estimation (MNE) methods. However, these methods are yet to fully developed and tested for sparse reconstruction methods. In this work, we seek to answer three questions. First, can traditional nonparametric statistical thresholding methods be applied to the inverse solution obtained from sparse algorithms to remove spurious peaks? Second, can nonparametric statistical thresholding reject spurious peaks obtained by sparse algorithms? And third, can brain images obtained from non-sparse algorithms resemble the sparse maps through stringent thresholding? We developed a nonparametric method for thresholding the source reconstructions obtained from M/EEG and tested on four source construction algorithms - two 'diffuse' methods (minimum-variance adaptive beamforming (MVAB) and s-LORETA (SL)) and two sparse methods (Champagne and minimum-current estimation (MCE)). We generate surrogate data sets by resampling the pre-stimulus period, which protects against signal leakage. We apply the maximal statistic procedure to the surrogate reconstructions and derive threshold that are corrected for multiple comparisons. The method is applied to three real data sets, somatosensory-evoked field (SEF), auditory-evoked field (AEF) and audio-visual (AV) integration task. We find that for all three data sets, spurious peaks are removed from Champagne’s reconstructions. The proposed method provides a more balanced approach to thresholding of sparse images and can be applied individual subjects data.
Somatosensory (SEF) data: The unthresholded post-stimulus power values in the window from 40ms to 80ms are shown in the first column (coronal slice). The power is thresholded with the maximal statistic at \( \alpha = 1\% \), \( \alpha = 5\% \) and \( \alpha = 10\% \). For Champagne, MCE, and MCE, we present an extensive performance evaluation of our recently published source localization algorithm called Champagne. Champagne is an empirical Bayesian inference algorithm that yields sparse solutions to the MEG inverse problem. It is robust to correlated sources and learns the statistics of non-stimulus-evoked activity to suppress the effect of noise and interfering brain activity. Here, we test Champagne on a variety of simulations and real MEG data, including single-trial data from various cognitive tasks and spontaneous epilepsy datasets. We examine the robustness to the noise model, and correlated source influences. We demonstrate the superiority of Champagne for reconstructing correlated sources in many distinct and functionally relevant brain areas with real MEG and EEG data when compared to benchmark algorithms such as SLORETA, minimum-variance adaptive beamformers (MVAB) and minimum-current estimation (MCE).

**We-12 - An explicit method for MEG inverse problem with the equivalent current dipoles and quadrupoles source model**

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Objective:
The equivalent current dipoles and quadrupoles (ECDQ) source model for MEG inverse problem has attracted attention (1) since it can parametrically represent the current source with spatial extent. Jerbi et al. showed that the center of spatially distributed source can be estimated more accurately when using ECDQ model than when using the conventional equivalent current dipoles (ECD) model with the nonlinear least squares algorithm (1). The aim of this paper is to develop an explicit algorithm that can reconstruct the number, positions, and moments of ECDQ directly from MEG data without requiring an initial parameter estimate or iterative computation of the forward solution.

Theory:
We derive the simultaneous second degree equations for the coefficients of the Nth degree equation whose roots are N positions of the ECDQs projected on the xy-plane. The second degree equations are the extension of the linear equations for ECD model derived in (2).

Verification with numerical simulations:
To model dipoles on cerebral convolutions, we assumed that 30 dipoles were placed on a half cylinder (Figure) with the moments...
perpendicular to the cylinder surface. The total dipole moment was almost parallel to the radial direction so that the source was regarded to be oppositely-directed two equivalent dipoles. The forward solution was computed with the Sarvas equation to which 5% Gaussian noise was added. 361 radial sensors were assumed.

When assuming ECD model, the two dipoles (blue dots in Figure) were estimated, which were far from the side walls of the cylinder. In contrast, when assuming ECDQ model, a single dipole-quadrupole (black dot) was well estimated at the center of the cylinder. This suggests that our algorithm with ECDQ model can well localize the oppositely-directed adjacent dipoles on the cerebral convolutions.


The proposed algorithm with ECDQ model can accurately estimate the center of the distributed dipoles on a cylinder surface (black dot), while, with ECD model, the two dipoles are estimated far from the side walls of the cylinder (blue dots).

We-13 - Beamforming with vector spherical harmonic lead fields

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Signal space separation (SSS) is a signal processing method that uniquely decomposes M time-dependent MEG signals into amplitude waveforms of N harmonic basis functions (N << M) (1). SSS multipole expansion for magnetic field B(r) generated by electric currents inside of the sensor array can be formulated in terms of vector spherical harmonic (VSH) functions (Eq 1). Conventional dipole lead fields (2), linking primary currents to MEG signals the M sensors, have a significant overlap. On the contrary, the VSH lead fields (Eqs 2-3), associating neural currents to the N multipole amplitudes, constitute an orthogonal basis.

Previously, we combined SSS and beamformers (3). For beamformer outputs which depend on power normalized by the projected noise, the spatial resolution of the SSS beamformer is significantly better than that of the conventional beamformers if the sources are deeper, and about the same as that of the conventional beamformer when the sources are superficial. In (3) we first computed the conventional dipole lead fields and transformed them into the multipole basis for beamforming. In the current work we utilize the direct VSH formulation in Eq 3.

The VSH lead field for each dipole location needs to be evaluated for the N multipole amplitudes, instead of the conventional lead field for the M sensors and P integration points. For example, the scalar beamformer Z-score for a dipole at voxel k (Eq 4) requires only 80 VSH lead field computations of the multipole amplitudes corresponding to the expansion order L=8, in contrast to the conventional lead field computation at total of 2550 integration points for 306 Elekta Neuromag sensors. The VSH lead field beamformer provides the same advantages as the transformed-SSS beamformer but with very significantly shorter computation time.

Eqs 1-4. $Y_{lm}$ are the spherical harmonic functions and $\sigma$ are the covariances for the SSS multipole amplitudes and noises. See (1) and (3) for further details.

We-14 - Whole cortex parcellation combining analysis of MEG forward problem, structural connectivity and Brodmann atlas

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Functional cortex parcellation is one of the most important ways to understand the link between structure and function in the brain. Brodmann’s atlas remains a fundamental pillar to understand this relationship because its areas are defined by similar cytoarchitecture and functional imaging notably had revealed that they correspond, entirely or in part, to functional areas. So, its integration to diffusion MRI (dMRI) data is pertinent, dMRI being the only non invasive and in-vivo imaging modality able to have access to a detailed geometric description of the anatomical connectivity between brain areas. This is why our method proposes to define a new connectivity profile of cortical sources based on the Brodmann’s atlas. After its registration to T1 and diffusion weighted images of the same subject, we reconstructed the brain surfaces and considered the cortical sources to be the vertices of the white matter/grey matter boundary mesh. We performed a probabilistic tractography taking each cortical sources as seeds and the Brodmann’s areas as targets. Thus, we obtained the connectivity profile of a cortical source: a vector of size where is the degree of connectivity of the source to the Brodmann’s area. Then, we developed a cortical parcellation method jointly analyzing the MEG forward problem and the connectivity profiles based on Brodmann’s atlas of cortical sources. We computed the leadfield matrix that relates the sources to the MEG sensors. We applied a k-means algorithm to the leadfield matrix to cluster sources having a close magnetic field to the MEG sensors. Then, in each leadfield-based cluster, we clustered sources via their connectivity profile based on Brodmann’s atlas. The figure presents results of this method applied on the whole brain of a subject with simulated sensors and shows suitable clusters. This automatic parcellation is an efficient preprocessing to compute a MEG inverse problem on functional data informed by its structural connectivity.
In yellow, blue, green and cyan, 4 leadfield-based clusters. Framed by its corresponding color, each cluster is parcellated by connectivity profiles of its sources based on the connectivity to Brodmann’s areas.

**We-15 - A GPU accelerated finite volume method for EEG forward and inverse modelling**

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Successful concurrent EEG/MEG inverse modelling requires an accurate EEG forward model (1). The finite volume method (FVM) is a flexible means of calculating forward solutions for EEG inverse modelling based on MRI data (2), but due to computational demands is inaccessible to many researchers. We demonstrate implementation of a novel FVM approach exploiting the capabilities of a CUDA enabled Graphics Processing Unit (GPU) and demonstrate the feasibility of a concurrent EEG/MEG beamformer.

**Methods:**

Three subjects performed a finger-tapping task (32 x 10s trials). EEG and MEG data were acquired simultaneously using a MEG compatible 64 channel system, and a 275 channel MEG system. T1/T2 anatomical images were collected using a 3T MR scanner. The FVM for EEG was implemented in C++ with CUDA using a linear system $Ax=b$ ($A$=conductivity information, $b$=current sources, $x$=unknown potentials) solved using the BiCGStab algorithm. T1/T2 images were segmented and conductivity values assigned. EEG/MEG data were frequency filtered (13-30Hz) and beamforming was implemented using the FVM for EEG and a dipole forward model for MEG. Pseudo-T ($\Psi$) comparisons between active (0-4.5s) and rest (5-9.5s) times were performed for MEG, EEG and combined EEG/MEG.

**Results:**

Source localisation for the FVM beamformer was comparable to the MEG alone. The concurrent EEG/MEG beamformer performed as well as the MEG alone indicating that the EEG had not had any negative effects on the inverse solution (Fig 1). The processing time for a single dipole for the GPU was 0.96s compared to 6.72s for the CPU implementation, a 7-fold improvement.

**Discussion:**

We have shown the FVM to be an efficient method of accurate forward modelling and EEG source reconstruction and ideal for use in concurrent EEG/MEG inverse modelling. Concurrent EEG and MEG will be advantageous for deep and radially orientated sources.

1. Brookes et al 2008 NeuroIm 40, 3, 1090-1104
2. Witwer et al 1972 Ieee TBE 19, 352-365
The dura layer which covers the brain is less conductive than the CSF (cerebrospinal fluid) and therefore, could significantly influence the computer simulations of scalp EEGs and MEGs. This was examined with a 3-D finite element method (FEM) model of an adult subject constructed from 192 segmented axial MR slices with 256x256 pixel resolution. The voxel resolution was 1.1 mm. The model included the dura layer. In addition, other major tissues were also identified. These included: scalp, fat, muscle, CSF, cerebellum, gray and white matter, and hard and soft skull bone. The electrical conductivities of various tissues were obtained from the literature. The conductivities of dura and CSF were 0.001 S/m and 0.0179 S/m, respectively. The electrical activity of the cortex was represented by 144,000 distributed dipolar sources with orientations normal to the local cortical surface. The dipolar intensity was in the range of 0.0 to 0.4 mA meter with a uniform random distribution. Scalp potentials and magnetic fields were simulated for two head models with an adaptive finite element solver. One model had the dura layer and in the other model, dura layer was replaced with the CSF. The MEG sensor coils were assumed to be on a curved surface, 1.0 cm above the scalp. The magnetic fields at the sensor locations were computed by use of Biot-Savart law. Spatial contour plots of potentials on the scalp surface and magnetic fields on the sensor surface were made and are shown in the attached figure. The left column of plots is for the full model where the dural layer was included, the middle column of plots is for the model where the dural layer was replaced with CSF and the right column of plots shows the differences between the two models. With the inclusion of the dura layer, scalp potentials decrease by about 20% and magnetic fields decrease by about 2%. This suggests that dura layer should be included for modeling of scalp potentials and EEGs.
Effect of dura layer on scalp potentials and magnetic fields. Last column shows that inclusion of dura layer changes scalp potentials by about 20% and magnetic fields by about 2%.

We-17 - Task-Specific Source Localization

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A key problem in brain research is to identify and reconstruct active neuronal sources from extracranially collected electrophysiological data. This problem of projecting signals measured in sensor space back to source space is often tackled by inverting a biophysically realistic forward model together with the use of particular prior assumptions for the sources. To date, however, most source localization algorithms have not directly taken into account the modulation of source activations induced by certain experimental manipulations. In this work, we introduce a new source localization technique which incorporates the experimental design in the source localization procedure. We show that by starting from the standard solutions to source localization, and by adding the constraint that the estimated sources should explain the experimental condition, we arrive at the solutions for task-specific source localization. We show that this improves source reconstruction for simulated data as well as for an empirical data-set.

In experimental source analysis with magnetoencephalography (MEG), the most common realistically-shaped head models are the single-shell and three-shell models. In the 1-shell model, only the inner skull surface is modelled, assuming the skull perfect insulator. In the 3-shell model, also the skull and scalp are modelled. In this study, we assess the error due to omitting the outer shells of the head and compare it to the differences between different 3-shell models.

An anatomical head model was generated from T1 and FLASH MR images: the brain was segmented with FreeSurfer, and volume conductor models were constructed with MNE-Suite, Curry, and FieldTrip programs. In segmentation, MNE-Suite used both MR sets, while other programs used the T1 set only. The resulting meshes were co-registered with the sensor surface of the 306-channel Elekta MEG system. 3- and 1-shell models were built using the Quick Galerkin boundary-element method, and lead field matrices (LFM) were constructed.

MNE-Suite produced the smoothest anatomical model that also had the most regular triangulation. The FieldTrip model added some detail. The Curry model had thinner skull that was in some regions farther away from the sources, and the head was truncated below the brain. Comparing different 3-shell models, mean relative morphological differences (RDM) and field magnitude ratios (MAG) were between 0.13-0.18 and 0.96-1.07, respectively. Corresponding figures between 3- and 1-shell models were between 0.17-0.37 and 0.99-1.11. The largest differences were obtained in the temporal lobe and sylvian fissure. In cross-comparison between the programs, Curry-based LFMs produced the largest differences.

The results show that the differences between 3-shell models produced by different segmentation tools are considerably smaller than the errors due to the 1-shell simplification. As the effort of constructing 3-and 1-shell models is comparable, we recommend the use of the more realistic 3-shell model.
We-30 - On performance of linear estimators in MEG/EEG source analysis

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In bioelectromagnetic inverse problem, sources that give rise to measured signals are estimated. To render the solution unique, various constraints are used. The effects of these constraints on linear estimators can be studied using point-spread and cross-talk functions (PSF, CTF). Resolution metrics characterise features of the PSF and CTF, such as localisation error and spatial spread (Molins et al. 2008, Hauk et al. 2011). In this work, we evaluated minimum-norm (MN), dSPM, and sLORETA estimators in MEG and MEG+EEG setups.

A 3-shell realistic boundary-element model and cortical source model were built and co-registered with the Elekta MEG/EEG system using FreeSurfer and MNE-Suite software. PSFs and CTFs were computed and characterised using several intuitive and well-defined metrics.

The ability to localise a point-like source was studied using the dipole-localisation error (DLE) measure. In MEG, dSPM performed better than MN with deep sources, and worse elsewhere. Adding EEG to MEG had small effects on DLE: with MN, DLE decreased for some sources, and with dSPM, the overall DLE increased slightly. By definition, sLORETA has zero DLE.

The spatial spread was studied with several metrics that all pointed in the same direction: with all estimators, the MEG+EEG had smaller spread than MEG. With any modality, MN had generally the smallest spread, while dSPM and sLORETA had approximately the same performance.

In the quest for new linear estimators, the weight has been on the localisation error. Optimising the localisation, however, may increase the spatial spread of the estimates (Hauk et al. 2011, Grave de Perlta et al. 2009). For all estimators tested here, adding EEG to MEG decreased the spread and thus increased resolution. Comparing the estimators, MN had the smallest spatial spread, while the sLORETA had the smallest DLE. Visualisation of resolution metrics and PSFs/CTFs will help experimenters to choose the optimal estimator for their specific purposes.
We-31 - Modified Source Stability Index for improved accuracy of evoked source localization using spatial filters

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Recent work has demonstrated the viability of a novel method of localizing evoked responses in MEG using the Source Stability Index (SSI) \cite{1,2}, which uses spatial filters and a repartitioning and correlation scheme to quantify the strength of the evoked response at a particular location. Here we demonstrate a modification of this method (mSSI) employing calculation of a t-statistic on the covariance of each repartition. This is shown to be no more computationally expensive than the original formulation of the SSI, whilst having greatly improved signal to noise characteristics (Fig 1). We further compare the performance of the mSSI against another proposed method for localizing evoked responses through a spatial filter, Event-related beamforming \cite{3}, along with a jackknifed t-statistic generated from this event-related beamformer with a similar computational burden to mSSI. In addition we generate surrogate data by applying a single random phase angle shift to all frequencies in the frequency domain for each epoch of data, hence destroying the evoked response while retaining phase relationships between adjacent frequency bins in that epoch. This allows robust statistical testing against a non-parametric null distribution without the need of a baseline period for comparison.


We-32 - Complementary sensitivity of EEG and MEG depending on source depth and orientation

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Simultaneous EEG and MEG recordings of neuronal activity from epileptic patients revealed situations where both modalities showed different sensitivities to interictal spikes. In a previous study we showed that for superficial focal sources EEG and MEG show different sensitivity depending on the orientation of the source. Here we extend this work to deep focal sources and extended patch

\begin{figure}
\centering
\includegraphics[width=\textwidth]{comparison.png}
\caption{Comparison between SSI and mSSI localization (in one spatial dimension) of a synthetic evoked source embedded in real brain noise.}
\end{figure}
sources. Altogether 5600 focal and 4600 extended sources were distributed on the segmented cortical surfaces of two volunteers. The source location ranged from 20 mm to 60 mm below the skin surface. The extended patch sources covered an area of approximately 20 mm² and were modeled by a set of dipoles with equal strengths. The source wave forms were adopted from a measured spike. Background activity was modeled by approximately 30000 single dipoles distributed in the cortex, where the wave forms emulated resting activity with the help of filtered white noise. A three compartment boundary element model was used for the forward computation. The signal to noise ratio (SNR) was evaluated in 128 EEG and 102 MEG channels.

For superficial focal and superficial extended sources, EEG showed higher SNRs for radial orientations and MEG for tangential orientations. For deep locations, focal and extended sources exhibited a different behavior. Deep focal sources generated higher SNRs in EEG compared to MEG for all source orientations. In contrast, deep extended patch sources induced higher SNRs in EEG for radial orientations and in MEG for tangential orientations. However, these differences were less pronounced compared with superficial sources. In addition, for the given patch sizes, the SNRs of deep sources were presumably too small to visually detect spikes under normal measurement conditions. There were no systematic differences in the SNRs for different brain regions.

For improved spike detection likelihood, the complementarity of both modalities should be utilized.

We-112 - Spatiotemporal patterns of the resting state: a virtual brain study

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Over the past years the ongoing human brain activity at rest came into focus, emphasizing the role of the rest-state activity for brain functions such as planning and perception in both healthy and diseased brains. For instance, it has been shown that the alpha rhythm during rest can be affected (e.g., resetting, entrainment) using stimulations such as sensory or Transcranial Magnetic Stimulations (TMS). However, the origin and the mechanisms underlying the rest-state activity are not yet well understood.

In addition to our sister study 'Brain Dynamics during rest-state: a combined TMS-EEG study' (see abstract poster presented at the BIOMAG), we focus here on the propagation of large-scale brain responses to stimulations such as TMS to identify sub-networks involved in the rest-state.

Using The Virtual Brain (www.thevirtualbrain.org) we model the dynamics of the human cortex as a network of 16,384 neural masses (NMs), each representing nearly 16 mm² of the cortical surface. A sub-threshold Hopf oscillator with a Van der Pol term describes the temporal behavior of each NM and a Gaussian kernel defines the spatial interactions among NMs. We also consider the connections through the white matter extracted from a combination of diffusion spectrum MRI tractography and the CoCoMac database.

We systematically stimulate different brain areas and analyze the spatiotemporal responses of the model, using Principal Component Analysis.

The preliminary results show that the stimulation in the Medial Prefrontal Cortex (MPFC) induces a stronger propagation (larger amplitude, longer transient) compared to the stimulation of the Primary Motor Area (M1) due to a higher number of activated NMs. Our results indicate that resting state networks involving MPFC are more critical (closer to the destabilization boundary) than networks involving M1, which is consistent with experimental studies and recent hypotheses upon the mechanisms generating resting state activity (Deco et al. (2011)).

We-113 - A fully Bayesian variational approach to brain source localization

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We present a novel approach for inferring the location, orientation, and magnitude of multiple, possibly correlated, brain sources from MEG and EEG sensor data.

Other recently published methods [Friston 2008, Wipf 2010] infer a type-II maximum likelihood estimate (also called Empirical Bayes) and therefore suffer from over-fitting under realistic noise conditions and model mismatch. To avoid over-fitting, we rely on approximate variational inference.

We assume normally distributed source currents and zero-mean sensor noise. The covariance of the sensor noise can be inferred from the sensor baseline and the sensor data using stimulus evoked partitioned factor analysis [Zumer 2007]. The precision of the source current distributions are hyperparameters for which we chose a non-informative conjugate prior, which is a Wishart distribution.

Given the sensor data, we approximate the joint distribution over both the source currents and the hyperparameters by a product of a distribution over the source currents on the one hand and a distribution over the hyperparameters on the other hand which minimizes the Kullback-Leibler divergence to the true distribution.

Finally, we propose an algorithm for fast computation. Since the solution cannot be found analytically, we developed an iterative method for approximation. We optimized the per iteration cost such that it is now comparable to Champagne [Wipf 2010], a method praised for its low computational effort.

**We-114 - Modeling the dependence of current dipole moment on synaptic input patterns**

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The sources of magneto- and electroencephalography (MEG, EEG) signals in the cerebral cortex can be represented by current dipoles. We used computational modeling to examine the current dipole moment resulting from different patterns of synaptic inputs within realistically-shaped passive-membrane dendritic trees of pyramidal cells. The spatial pattern of synaptic inputs affected the magnitude, direction, and timing of the current dipole. In several cases, qualitative differences between the dipole moment and the somatic potential were found. Excitatory inputs always resulted in depolarization of the soma, whereas the direction of the current dipole depended on the location of the input. Inclusion of shunting type inhibitory inputs influenced the response in the somatic potential more than in the current dipole. The response latency was shorter for the current dipole than for the somatic potential. Increased asynchrony among the excitatory inputs reduced the peak amplitude of the responses, but increased their time integral. Relating the properties of the macroscopic current dipoles to the patterns of underlying dendritic currents could help to better interpret MEG and EEG data in terms of neural processing.

**We-115 - Predicting resting state MEG data using a biophysical network model**

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Recent advances have shown that widely distributed brain networks display highly coherent spontaneous activity during rest in the absence of stimuli, tasks, or overt responses [Deco 2011]. Investigation of the underlying neurobiological determinants governing the emergence of this spatiotemporally organized intrinsic activity is fundamental to understanding computation and dynamics in the brain.

In this work, a realistic large scale network model of (∼ 90) brain regions in the resting state is used to simulate spontaneous MEG activity. The model combines key aspects of brain anatomy and physiology by using a biophysical model for node dynamics with neurobiologically realistic network parameters, and is based on the model used in Dynamic Causal Modelling (DCM). Key ingredients include empirically based network topology, time delays, and background (white) noise. Previous work used Kuramoto oscillators in place of DCM [Cabral 2011], and an initial aim is to see if a more biologically based model has similar characteristics. We explore the effect of changing the global scaling of node-node coupling strength, and observe that at moderately weak coupling strengths, metastable oscillatory states (or transient synchronizations) occur, due to fluctuations in the synchrony degree. This results from a stochastically driven exploration of different state space positions around the network’s equilibrium state, indicative of self-organized criticality, where the system operates at the edge of chaos with perturbations leading to regions of high meta-stability (persistent attractors in state spaces).

In particular, it is found that when the network is operating in the metastable regime, it produces slow neural activity fluctuations in the alpha and beta bands. This is consistent with evidence of spontaneous activity in MEG, and matches the findings in [Cabral 2011], though using a more biological model.

Deco et al. Nat Rev Neurosci (2011)
Cabral et al. SFN (2011)

**We-116 - Localization of true brain interacting sources and their interactions from EEG and MEG data using Self-Consistent MUSIC and modified beamformers**

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Localization of interacting brain sources is a problematic issue in inverse calculations on EEG and MEG data due to the artifacts of volume conduction. Non-interacting brain sources do not contribute systematically, i.e. apart from random fluctuations around zero, to the imaginary part of the Cross-Spectrum (CS) calculated from EEG/ MEG data. These measures are therefore ideal quantities...
to study functional brain connectivity. The Multiple Signal Classification (MUSIC) algorithm is a standard method based on the subspace of the covariance matrix of the data. In one of its variants, called RAP-MUSIC, sequential projections were proposed to properly identify local maxima of the gain function as origins of true sources. The purpose of this research is twofold a) to extend the RAP-MUSIC approach to a fully recursive algorithm called Self-Consistent MUSIC (SC-MUSIC) and localize the interacting sources through replacing the covariance matrix by the imaginary part of the CS of the data in order to define the subspace, and b) to estimate which of the found sources is interacting with which other source. We applied a modified version of the LCMV beamformer to the data to estimate the activity of each source and each grid point and estimated the imaginary part of coherency between each reference and each grid point in the direction which resulted in the maximum imaginary coherency between those two points.

We show the results of the methods for three and four simulated interacting sources in the presence of high noise signal as well as real data. Four interacting sources localized using RAP-MUSIC are not fully separated while the results of SC-MUSIC show a full separation of the sources resulting in accurate source location estimates. Localization of odd number of interacting sources is more problematic, since the dimension of the subspace collapses in this case. While this leads to substantial misestimations in RAP-MUSC, SC-MUSIC in general results in accurate estimates.

We-117 - CUDA-ification of the BEM forward solution for the EEG and MEG.

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Recently, a symmetric BEM formulation for the EEG/MEG was put forth which increases the accuracy of the classical BEM solution that is presently being used in the EEG/MEG community, particularly for sources close to the interface. However, the speed of this BEM computation is still an issue as the compute time can run into several minutes to hours depending on the size of the problem. CUDA is the parallel computing platform developed by NVIDIA to harness the processing power of the GPU. The aim of this study was to investigate the utility of a CUDA based parallelized approach to improve the speed of the symmetric BEM formulation. We present the strategy for formulating the BEM solution on the GPU and also present some of the limitation of such an approach. The results are compared with those of the OpenMEEG package, which provides a CPU solution. The symmetric BEM solution has three main components: the head matrix assembly, its inversion and the source matrix assembly. The matrix assembly phase constitutes a significant portion of the compute time. For example, for the test case of three-shell head model with approximately 700 vertices per surface and 16000 dipoles, the CPU based solution, requires approximately 460 seconds and 150 seconds for a single threaded and OpenMP based multithreaded solution respectively. The CUDA solution computes the solution in only 2 seconds, thereby providing speedups by a factor of 230 and 75 when compared to the single threaded and multithreaded CPU solution respectively. We also compare and report the results of the GPU solution versus the CPU solution for larger head meshes and larger number of dipole locations. The GPU based parallelization provides dramatic speedups and a cost-effective approach to obtain an accelerated forward solution on a common desktop workstation. The source code for the CUDA-BEM solution will be released under an open-source license.

We-118 - Improved Accuracy in MEG Source Localization using a 3D Laser Scanner

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Precision in localizing underlying anatomy based on magnetoencephalography (MEG) data requires accuracy in both digitizing anatomical landmarks prior to the scan and co-registering to anatomical magnetic resonance images (MRI). We compared the surface and source localization accuracy of two head digitization systems - a laser scanner and the current standard electromagnetic digitization system (Polhemus) - using a calibrated phantom. The accuracy of MEG-MRI co-registration was also investigated using human digitization and MRI data. The calibrated phantom data showed that digitizing with the laser scanner improved surface and source localization accuracy over digitizing with the Polhemus by 141% and 132%, respectively. When compared to the Polhemus, laser digitization reduced MEG source localization error by 1.38mm on average. In human participants, the laser scanner generated a 1000-fold more points per unit time than the Polhemus head digitization. Structures on the face (i.e. nose, forehead, ears, eyes, and cheeks) that offer ideal landmarks for MEG-MRI co-registration were easily identified in the high-resolution laser scan. Further, MEG-MRI co-registration accuracy improved with automated surface alignment of the laser scanner data to the MRI-based scalp surface, as compared to the equivalent manual procedure. In simulations, we also showed that the coverage of the laser scan necessary to maintain high co-registration accuracy could be reduced to an area around the eyes only. This result suggests that laser digitization acquisition time can be substantially reduced. In conclusion, our study shows that head digitization based on the laser scanner technology can reduce MEG setup time and improve localization accuracy, in comparison to the Polhemus digitization system.

We-119 - Soft Anatomical Constraints for Source Localization
In EEG/MEG inverse problems, it is common practice to build the head model based on magnetic resonance images (MRI). Usually, the MRIs are used to obtain a cortical surface to model the cortex gray matter. The primary current or source of electromagnetic activity is then restricted to this cortical surface, with its orientation constrained to be normal to the surface. In this way the set of possible source locations is reduced using anatomical information, alleviating the inverse problem complexity. However, the requirement of normal orientation may lead to localization errors in the inverse problem, since the cortical surface is an approximation of the cortex gray matter and the organization of the pyramidal neurons may not be exactly normal to it. To overcome this, we propose a set of possible sources with soft or probabilistic anatomical restrictions.

We start from a probabilistic image of the gray matter, based on the MRI, and compute the gradient of the gray matter probability in the image voxels. At each voxel we define three possible orthogonal directions for the primary current and assign a probability to each one by performing a singular value decomposition of the set of gradients in a neighborhood of the voxel. The number of possible sources is then extremely large, so the last step is to group the sources that produce similar forward problem results. The groups are assembled so that the energy of the difference of the forward problem results of any pair of sources in a group is below a given threshold. Thus, we obtain a set of volumetric sources that incorporate anatomical information by giving higher probability to more likely source positions and orientations, without precluding other orientations. We show that the adoption of the cortical surface model may lead to localization errors even in a noise-free single source problem. This probabilistic model could be used as an anatomical prior in different inverse problem algorithms.

Gray matter probability map (top left), and probability maps of each of the orthogonal orientations. The main orientation (top right) is aligned with the mean gradient direction in a neighborhood.

**We-120 - A mesoscopic biophysical model for multimodal brain activity data**

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Neuroimaging techniques have considerably improved over the past decades allowing for simultaneous multimodal recording of brain activity, both under normal and pathological conditions. However, the interpretation of multimodal data (EEG, MEG, depth-EEG, fMRI) in terms of underlying neuronal, metabolic and hemodynamic activity remains an unmet challenge.

We address this issue through the development of a computational mesoscopic model of the neuro-glio-vascular coupling. In contrast with already existing models, the novelty is to describe the main interactions between neuronal (pyramidal cells and interneurons) populations, an astrocytic population, the local vascular system and the extracellular space (five compartments). These interactions include excitatory/inhibitory processes among neurons, glutamate and GABA cycles, glucose/lactate exchanges and tissue respiration. The hemodynamic response is obtained from the classical Balloon model. We first established a highly detailed and refined...
model using biophysical models defined at the cellular level. Our proposed model was progressively simplified from cellular to mesoscopic level in order to reach a trade-off between simplicity (without oversimplification) and physiological relevance. A particular attention was paid to the balance between measurable and hidden variables in order to facilitate subsequent parameter identification issues.

The model is currently being used in the context of epilepsy. In particular the joint time-course of multimodal variables was qualitatively analyzed during the generation of sporadic epileptic spikes. Relevant variations could be observed such as that of glutamate in the extracellular space as compared with glutamate-sensing fluorescent reporter. Future work includes quantitative analysis and comparison with multimodal (MUA, LFPs, CBF, O2) data recorded in the rat neocortex under epileptic activity induced by bicuculline local perfusion. Acknow: ANR Blanc MULTIMODEL 2010-13.

**We-121 - The adjoint method of OpenMEEG for EEG or MEG forward problem resolution**

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In Electro- or Magneto-Encephalography, a leadfield is defined as the linear operator which associates unitary dipolar source to the resulting set of measurements on the corresponding sensors. It is an essential ingredient in inverse source localization problems. An accurate computation of the leadfield requires the use of an appropriate physiological (conductivity) model, and a pertinent numerical method, this implies realistic geometries and thus numerical methods such as the FDM, FEM or BEM. In order to build the leadfield in the traditional approach, a forward problem needs to be solved for each source, which can amount to more than 10 000 dipoles in practise, which sometimes causes memory problems.

The reciprocity principle considers the forward problem from the viewpoint of sensors instead of sources: this drops down the number of linear systems to solve to a few hundred (number of sensors), i.e. by two orders of magnitude. The reciprocity principle for EEG and MEG leadfields has already been proposed and implemented in the context of Finite Element Methods, but, to our knowledge, had never been proposed for Boundary Element Methods.

In this work, we present the adjoint method for the symmetric BEM, which has been implemented within the OpenMEEG software library and has been made available in the latest release.

We demonstrate the computational savings provided by this new approach in terms of memory consumption. The time consumption is also reduced with the adjoint method, especially when computing only one of EEG or MEG leadfields.

The adjoint method provides exactly the same leadfield as the traditional method, and its benefits come for free, since in practise the commands are not more complicated to launch.

**We-122 - A GPU-accelerated Performance Optimized RAP-MUSIC Algorithm for Real-Time Source Localization**

*Christoph Dinh¹, Johannes Ruehle², Steffen Bollmann³, Jens Haueisen¹, Daniel Güllmar⁴*

⁴BIOMAG 2012 - August 26-30, 2012 - Paris, France
Up to now source localizations using scanning approaches, such as Recursively Applied and Projected Multiple Signal Classification (RAP-MUSIC), were hardly able to deliver real-time results due to their computational effort. RAP-MUSIC is a scalable source localization algorithm, which is predestined to be computed on a many-core processor such as a graphics processing unit (GPU). By utilizing the GPU and NVIDIA's Compute Unified Device Architecture (CUDA), we developed a high performance optimized RAP-MUSIC algorithm. The computational costs are reduced about 50 percent by modifying and pre-calculating components of the subspace correlation. These modifications together with Powell’s Conjugate Gradient Method highly optimize the search process, which now allow the application for online source localizations. We proved the robustness of the localization accuracy with the help of simulations, where we analyze the influence of the SNR and different regularization parameters on the localization accuracy and calculation time. The presented algorithm provides the ability to obtain up to ten localizations per second with just one GPU (Tesla C2050) on a typically sized lead field matrix (10000 dipoles).

Localization accuracy of the correlated dipole pairs for different SNRs

We-123 - A Functio-Anatomical Inspired Source Covariance Estimate for Linear Reconstruction of EEG and MEG Generators

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Common approaches for distributed source reconstruction are the minimum norm (MN), weighted MN (WMN) and LORcETA method. While MN weights sources equally, WMN gives more impact to deep sources, which implies an assumption about source variances. LORcETA additionally imposes source covariance using a Laplacian operator as a smoothness criterion. We propose a new method, LineLORETA, that allows incorporating individual functio-anatomical information with the Laplacian, e. g. functional borders, leading to a functio-anatomically inspired source covariance estimate. Such priors can be taken from general functio-anatomical knowledge applied to the individual cortical sheet, or from similarity measures as derived from, e.g., fMRI. In LineLORETA, the Laplacian is modified by cutting the geometrical neighborhood at functio-anatomical boundaries. A valid source covariance estimate is achieved by applying normalization to the inverted Laplacian. A regularization parameter controls the impact of the smoothness constraint on the solution. We show a method that balances the impact between maximal and minimal smoothness.

First, we evaluated LineLORETA using simulations on the folded cortical surface. We defined patches and simulated activation inside and outside these regions. LineLORETA was able to reconstruct both, individually and simultaneously activated patches. Activation outside patches produced source patterns in contradiction to the priors, as expected. Second, we analyzed real experimental data, expecting activation in Heschl’s Gyri. In spite of poor signal quality, we could reconstruct activation in Heschl’s Gyri by giving high impact to prior smoothness information in the source covariance estimate. This was not possible with any other method.
Summarizing, the combination of functio-anatomical priors with a general smoothness assumption leads to an individual source covariance estimate. By giving different weights to it, one can verify priors in the light of the data.

**We-124 - Sensitivity of MEG and EEG for Extended Cortical Activity**

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In a simulation study we compared the sensitivity of MEG magnetometers, planar gradiometers (102 sensors each), an extended EEG 10/20 montage (81 electrodes), and the combined modalities for extended cortical sources. A common realistically shaped Boundary Element Method (BEM) head model with three compartments (6685 nodes overall) was used and extended sources on the folded cortical surface (30381 nodes) with up to 60mm diameter were investigated.

With increasing patch size cancellation of tangentially oriented sources on opposing sulcal walls leads to a more and more radial effective overall orientation. Due to the different sensitivities of MEG for radial and tangential current components as compared to the more homogeneous orientational sensitivity of EEG increasing source sizes have a larger effect on MEG than on EEG. Combining both modalities has advantages because of the orientational specificity of MEG and the more homogeneous sensitivity of EEG and depends on the number of sensors used and their Signal-to-Noise Ratio (SNR). However, comparing both modalities can exhibit virtual signal phase shifts between MEG and EEG when e.g. propagation or growing extension of an epileptic zone is observed.

Furthermore, fitting single dipoles to extended cortical activity can result in misleading dipole orientations and positions due to cancellation (MEG and EEG) and invisible radial components (MEG).

![Normalized sensitivities of MEG and EEG for extended cortical patches. The colored cortical surfaces display top, bottom, and left views for source diameters of 0, 15, and 50mm. The diagram shows the relative sensitivities for EEG, MEG, and both (All).](image)

**We-125 - Localization using beamfomer based on Wavelet-based time-frequency analysis with Magnetoencephalography in Epilepsy**

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In clinical aspect, the MEG data analysis has been relied on single equivalent current dipole (ECD) source modeling for inverse solution. For the forward solution, inside a sphere located within the skull and estimates the possible fields produced by these sources. This method has been shown its usefulness on epilepsy surgery as one of the non-invasive method. However, there have been pointed the limitations with this method and have suggestions of new extent analysis methodologies (i.e., multi-dipole ECD, current distributed analysis) as well as using realistic head model. The last phase of surgical decision is still depending on the intracranial EEG (iEEG) with seizure onset zone (SOZ). Recent studies with iEEG have been showing that the fact activities, especially high frequency oscillations, well-correlated with SOZ ictally/interictally. In this retrospective studies, we hypothesize that interictal MEG oscillatory with various phenomena (i.e. bilateral discharges, generalized discharges) may be able to provide the useful information for surgical
planning with combined newer analysis technique. We analyzed 10 patients who had either diffuse bilateral discharges or generalized discharges interictal during MEG recording as their presurgical evaluation. First wavelet based time-frequency analysis (TFA) was applied to each single discharges without averaging in order to reveal fast oscillations which superimposed epileptic spikes. Second, the realistic head models were created using the patient’s own MR image to co-registered to MEG fiducials. Third, after discretize the brain volume into 5 mm resolution, the beamformer technique were applied to the estimated power in the frequencies revealed by the wavelet TFA. Finally, these MEG analysis results were compared with iEEG result and surgical outcome. We found that the combined analysis with wavelet TFA and beamformer technique were more useful especially for bilateral or generalized or generalized discharges.

We-126 - Beamformer based on Matching Pursuit and application to Auditory Evoked Fields

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We have incorporated the Topographic Matching Pursuit (TMP) signal-decomposition method in the beamformer source localization technique (TMP-Beamformer). We apply it to auditory evoked fields (AEF) using individual boundary element models (BEM). Beamforming relates measured data H(t) via a weight matrix W to the time course q(t) of a dipole with given position and orientation. The weights W of linearly constrained minimum variance beamformers involve a lead field L and the inverse of the covariance matrix of the measured data inv(Cd).

Our proposed method calculates different weight matrices Wc for separate components of a dataset. The TMP signal decomposition method calculates these components in form of multi-channel Gabor-atoms g, such that each multi-channel Gabor-atom g represents a different component of the measured signal H(t). The Gabor-atoms differ in their time-frequency parameters. The channels of one Gabor-atom possess identical time-frequency properties and only differ in terms of amplitude and phase. Gabor-atoms model sinusoidal components singling them out from noise.

A weight matrix Wc contains the inverted covariance matrix inv(Cg), which is calculated from the respective Gabor-atom. We invert the degenerated covariance matrix Cg by single value decomposition and eliminated unwanted elements (Cg'). The weight matrix Wc is defined as:

\[ Wc = \frac{(\text{inv}(Cg')*L)}{(L^T*\text{inv}(Cd)*L)} \]

We apply the TMP-Beamformer on the averaged AEF of one subject (MEG/275chans/142 trials). We find the maximum auditory activity close to the cortical region of Brodmann area 42.

The introduced TMP-Beamformer localizes components of measured signals and yields time/frequency estimates for the localized components.

We-127 - Bayesian preconditioned CGLS for source separation in MEG time slices

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It has been shown that MEG can be useful in locating the foci of the onset of epileptic seizures. This information is particularly helpful in surgery planning for patients that suffer from drug-resistant epilepsy. Detecting these focal sources of interest is quite difficult due to the high noise levels in MEG data. In particular, it is well known that MEG data are contaminated with biological noise which is correlated in space and time. Our goal is to develop an algorithm which will be able to localize focal sources in the presence of biological noise.

We take the novel approach of solving the MEG inverse problem using an iterative solver, specifically CGLS. In addition, we add left and right statistically inspired preconditioners to the CGLS algorithm. The left preconditioner is related to the covariance structure of the biological noise, while the right preconditioner is used to impose our prior beliefs about the statistical properties of the unknown focal sources. The combination of CGLS with left and right preconditioners significantly improves localization.
We-159 - An MEG compatible system for the measurement of orofacial kinematics: The MASK system

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The control of speech, swallowing, and other oromotor activities involves the rapid and precise coordination of many muscle groups. How the brain coordinates these movements remains relatively unknown. Combining MEG recordings with orofacial kinematics presents a unique opportunity to understand the underlying neural mechanisms of oromotor functions. We have developed an MEG-compatible tracking system, dubbed MASK (Magnetoarticulography for the Assessment of Speech Kinematics) for five-dimensional tracking of movements of the tongue, lips and facial muscles. The MASK system uses similar principles to MEG head tracking systems and can be integrated into existing MEG systems with the low-cost addition of coils, driving electronics and software for tracking coils with high temporal and spatial resolution. A MASK coil comprises of a small light-weight inductor soldered to thin twisted-pair wires. Up to twelve coils can be tracked simultaneously, driven by electronic circuitry placed outside the magnetically shielded room using sinusoidal signals ranging from 150-930Hz at low current levels (0.1-1mA) and electrically isolated for patient safety. MASK electronics are controlled by custom software running on a desktop computer. The coils generate magnetic signals that are directly measured by the MEG detectors, but are outside the frequency range of interest for neural activity. The MASK system tracks the coils for movement rates up to 50 cm/s with less than 1 mm relative position error. The positions and orientations of the coils are displayed in real time. We will show preliminary data demonstrating the ability to measure the 3-dimensional motion of lips, jaw and tongue and their related brain signals. These new measures provide a novel approach to the study of neural activity accompanying speech production and other oromotor functions in relation to the dynamics of individual movements and their coordination patterns.

Movement trajectories of the lip during utterances of /epi/ and /pa/

We-160 - MEG Correlates of Single-Session Learning Using a Visuomotor Task

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Assessment of learning-related changes in neural activity provides important information related to mechanisms that coordinate and
control learning. To facilitate such an assessment, it is necessary to have an experimental paradigm that modulates both behaviour and the neural activity that underlies it. Motor learning is an ideal paradigm for this application as motor performance engages multiple brain regions comprising the sensorimotor network. In this study, we investigated a visuomotor task to determine its ability to induce i) motor learning over a single scan session, and ii) learning-related changes in neural activity as measured using magnetoencephalography (MEG). A cohort of healthy control subjects performed a visuomotor task that required a precise combination of bilateral grip force to accurately move a cursor towards a target. We assessed motor learning by comparing behavioural measures (accuracy and error magnitude) and neural activity in specific regions of interest (ROIs) using MEG pre- and post-training. A beamformer spatial filter was used to estimate source activity at anatomically prescribed ROIs. The source activity was analyzed for learning-related changes in event-related synchronization and desynchronization of cortical oscillations. Behavioral results showed a training-related improvement in performance based on increased accuracy ($p < 0.05$) and decreased error magnitude ($p < 0.05$) from pre- to post-training. Thus, the use of this visuomotor task allows for the occurrence of single-session motor learning. Preliminary inspection of MEG source activity shows learning-related changes in brain areas associated with motor performance. We present results pertaining to the correspondence of changes in neural activity and these learning-related changes. Establishing the ability of the visuomotor task to generate learning-related changes in brain responses will facilitate future studies examining the modulation of sensorimotor neural networks.

**We-161 - Modulation of cortex-muscle coherence by observation of another person’s hand movements**

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**INTRODUCTION:** During steady contraction of hand muscles, \(\sim 20 - H_z\) oscillations of the contralateral primary motor cortex (M1) are coherent with surface electromyogram (EMG). This cortex-muscle coherence (CMC) likely reflects population-level modulation of the motoneuron pool. Here we used CMC as an index of the motor-cortex state during observation of another person’s movements.

**METHODS:** We recorded CMC between cortical signals, measured with 306-channel MEG (Elekta Oy, Finland) and the right first dorsal interosseous EMG from 14 healthy subjects who viewed an experimenter performing transient index-thumb flexions against a load cell once every 3-6 s, the experimenter was sitting 2 m in front of the subject, only his hand visible. Measurements were carried out at the MEG Core of the Aalto University, Finland.

CMC was first evaluated over the whole experiment to identify the gradiometer displaying the strongest coherence in the 10-30 Hz range. Five subjects lacking significant coherence were removed from the further analysis, and thus results are based on the data of 9 subjects (mean age 29 yrs, range 22-35, 4 f, 5 m). Time-frequency power and coherence maps from -3000 to 3000 ms time-locked to experimenter’s movement onsets were computed for the selected gradiometer and averaged across subjects.

**RESULTS:** The group-level coherence map revealed a significant coherence increase at \(\sim 18 H_z\) about 500 ms after the movement onset, \(\sim 7 - H_z\) and \(\sim 15 - H_z\) signals were suppressed around 400 ms.

**DISCUSSION:** The viewer’s M1 cortex is activated during action observation, as is evident from the suppression of the rolandic 20-Hz rhythm. Nevertheless a healthy viewer does not automatically imitate the seen action. The current findings of increased CMC following the observed action can be interpreted to indicate improved stabilization of the motor-cortex output, thereby contributing to the prevention of automatic imitation.

**We-162 - SMA activity coherent with hand muscle activity during a precision grip task revealed by DICS analysis of MEG data**

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A recent human EEG/EMG study performed in our team revealed coherence between intrinsic hand muscle activity and electrodes lying not only over the contralateral primary sensorimotor area but also over the supplementary motor area (SMA) during a precision grip task (Chen et al., 2012, submitted). Although these results suggest that corticospinal projections from SMA are involved in manual precision tasks, source localization of corticomuscular coherence (e.g., Guggisberg et al. 2011) is difficult with EEG data. Therefore, in the present study, we performed simultaneous MEG/EMG recordings in order to precisely localize the cortical sources that activity is coherent with EMG activity during a precision grip task.

Right-handed subjects performed a visuomotor tracking task involving thumb-index grip of their right hand. According to the force applied on a device mounted with a force sensor, the subject controlled the vertical position of a cursor and adapted it according to a force curve pattern continuously presented and moving from right to left on a computer screen. The coherence analysis was performed using FieldTrip, an open-source Matlab toolbox for neurophysiological data analysis (Oostenveld et al., 2011). The localization of coherent sources with the muscle activity was performed using Dynamic Imaging Coherent Source method (DICS) (Gross...
et al. 2001).

We obtained corticomuscular coherence topographies at the sensor level showing coherent activity over contralateral cortex with EMG recordings (Fig. 1B). The localization results clearly revealed that not only left primary motor cortex activity (M1) is coherent with the muscle activity but also SMA activity (Fig. 1A). We conclude that direct communication between SMA and the muscles via corticospinal projections play a functional role during precise manual motor tasks.

![Figure 1. Results for one subject. A. Source localization of coherent sources with right hand muscle (First Dorsal Interosseous). B. Corresponding corticomuscular coherence topography at the sensor-level.](image)

**We-163 - HR-EEG imaging of post-stroke brain recovery induced by VR-augmented rehabilitation performed with a passive robotic device**

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Current knowledge on post-stroke brain recovery has given rise to an increasing interest in new approaches focused on the use of virtual reality (VR) for a more efficient neuro-motor rehabilitation. We present a high resolution electroencephalography (HR-EEG) study on functional brain recovery induced by VR-augmented rehabilitation using a passive robotic device (Trackhold, PERCRO, Pisa, Italy) and dedicated VR applications. The Trackhold records the kinematic data of limb movements while providing real-time control on VR applications used to train the patients in activities of daily living or abstract visuo-motor coordination tasks. Five virtual environments (VE) were realized for upper limb rehabilitation in 2D and 3D movements. Stroke patients with motor deficits in one upper limb were recruited in the sub-acute stage (< 3 months after the cerebrovascular event). In addition to conventional therapy, they performed 30-min VR-rehabilitation sessions for 4 weeks (3 sessions per week). HR-EEG (128 electrodes, EBNeuro, Florence, Italy) was synchronously recorded in multiple sessions during rehabilitation. Ocular and muscular artefacts were removed using Independent Component Analysis. Data were then filtered (0.1-200 Hz) and epoched on the basis of the time course of selected kinematic parameters. After surface-matching coregistration of EEG data on patient’s structural MRIs, inverse reconstruction was performed using the multiple sparse priors (MSP) algorithm. The results of inverse reconstruction were summarized as 3D images using SPM8 (http://www.fil.ion.ucl.ac.uk/spm). Source maps showed an initial over-recruitment of the patients’ motor control area and a decreased recruitment as the rehabilitation proceeds over time. The proposed novel rehabilitation system based on the conjoint use of VR and a passive robotic device has been proven to be feasible for the neuro-motor recovery of sub-acute stroke patients.

**We-164 - A novel multimodal functional neuroimaging approach for non-invasive mapping of the primary sensorimotor cortex**

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PURPOSE. Non-invasive functional mapping of the primary sensorimotor hand area (SM1ha) usually relies on functional MRI (fMRI) or MEG. In some patients with brain disorders, this unimodal approach may lack reliability. We introduce a novel multimodal approach for SM1ha mapping by integrating information from fMRI and multiple MEG indicators.

METHODS
We studied ten right-handed healthy subjects (19-33 years, 5 females, 5 males) and four patients (24-64 years, 2 females, 2 males) suffering from space-occupying brain lesion (3 tumors, 1 cavernoma) close to the central sulcus. Functional SM1ha indicators were obtained from block-design motor fMRI (1-2 Hz flexion-extensions of fingers), and six MEG indicators: somatosensory evoked fields to electrical median-nerve stimulation, mu-rhythm suppression (10 Hz and 20 Hz), corticomuscular coherence, and corticokinematic coherence with and without finger contacts. Coordinates were obtained for equivalent current dipoles and for parametric-map local maxima. The degree of functional indicators spreading was assessed with an ellipsoid computed by principal component analysis of functional indicators coordinates relative to their center of gravity.

RESULTS
In all participants, five to seven functional indicators were available and the fitted ellipsoid was located at anatomical SM1ha. In control subjects, $80 \pm 19\%$ (mean $\pm$ SD, range 50-100$\%$) of functional indicators were located at less than 10 mm from ellipsoid center (volume $145 \pm 91\,\text{mm}^3$, major axis $6.1 \pm 1.8\,\text{mm}$). In patients, $49 \pm 39\%$ (range 17-100$\%$) of functional indicators were located at less than 10 mm from ellipsoid center (volume $304 \pm 256\,\text{mm}^3$, major axis $7.8 \pm 1.8\,\text{mm}$).

CONCLUSION
This multimodal approach showed co-localization between the ellipsoid and anatomical SM1ha in all subjects. Spreading of SM1ha functional indicators in patients with brain disorders highlights the potential benefit of the proposed multimodal approach for a reliable non-invasive SM1ha mapping.

This figure illustrates the location of the different SM1ha functional indicators and the fitted ellipsoid in healthy subjects (Top) and patients (Middle).

We-165 - Motor command inhibition during motor imagery after spinal cord injury: A MEG study.

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Motor imagery (MI) is the mental representation of an action without its actual execution. There is now compelling evidence that MI and actual performance of the same movement share common neural substrates, but how the motor command is suppressed during...
MI remains debated. Recent studies suggest weakened motor inhibition in deafferented and de-efferented patients when they performed MI. Using magnetoencephalography (MEG), we recorded the cortical activity in patients with spinal cord injury (SCI) to study motor inhibition during MI. Four SCI patients mentally and actually attempted to perform thumb abduction (i.e., a movement involving paralyzed muscles, which could thus not be actually performed). They also imagined and physically performed wrist extension (which remained possible due to residual upper limb motor functions) with their dominant arm. As control condition, participants were instructed to remain motionless. Experimental conditions were randomly performed with a total of 30 trials each. MEG data were recorded using a whole head CTF-MEG system including 275 radial gradiometers over the scalp and 33 reference channels for ambient field correction. While the amplitude of neural desynchronization in M1 in the beta-band (15-35 Hz) was higher during actual wrist extension as compared to MI, the attempt to perform thumb abduction elicited similar M1 desynchronization to that during MI. Interestingly, reduced M1 activation during MI of wrıst extension came together with increased involvement of the SMA and S1. These findings support selective weakening of motor command inhibition during MI after SCI. Deafferented and deafferented areas might be primarily affected, while inhibitory processes would remain active during imagination of motor skills involving effectors that retain voluntary motor control. These findings are congruent with previous data showing that both the SMA and S1 might play a critical role in motor suppression during MI.

**We-166 - Movement-related cortical oscillations and Parkinson’s disease**

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Current measures of clinical state and motor improvement in Parkinson’s disease are hampered by subjective evaluation and insensitive scales. We sought to determine whether MEG may provide a biomarker of clinical state and medication response.

Eighteen veterans with Parkinson’s disease were recruited at the Philadelphia VA Medical Center (PV AMC). Parkinson’s Disease Research, Education, and Clinical Center (PADRECC) and underwent a Unified Parkinson’s Disease Rating Scale (UPDRS) motor subscore examination and a MEG in the off- and on-medication states. MEG recordings were obtained using a VSM 275 channel MEG (1250 Hz AD) during self-paced motor task involving separate button press responses of the right and left index fingers.

The mean age of the all-male cohort was 69 (SD 7.4). The mean UPDRS motor score off medications was 20.2 (SD 9.1), and on medications was 14.4 (SD 6.4). The time of onset (and thus duration) of significant pre-motor task beta-band event-related desynchronization (Beta-ERD) in the motor cortex was inversely related to the UPDRS upper extremity motor subscore (p=0.018), as was, to a lesser degree, the intensity of Beta-ERD. In approximately half of the cohort, the pre-motor task Beta-ERD present while off-medication disappeared when on-medication (p<0.05). In the remaining patients, the Beta-ERD remained stable or was even enhanced. This difference did not correlate with the change in UPDRS from off- to on-medication state. While baseline UPDRS status showed a tendency to be associated with off-medication right hand finger button-press gamma ERS (p<0.1), post-medication improvement in UPDRS (≥ 2 pts) was significantly associated with increase in motor gamma-band ERS (chi-squared, p<0.05).

MEG assessment of brain activity demonstrates clear differences in Beta-ERD and Gamma-ERS characteristics from the off to on-medication state, and thus represent potential biomarkers of clinical state and medication response.

**We-167 - Does early change in hand usage influence language lateralization? 4 A twin case study**

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It is known that forced switching of hand-usage in childhood leads to changes of sensorimotor cortex in the brain (Kloppel et al. 2010). There is also evidence that brain injuries affecting the dominant hemisphere can cause reorganisation of language in favour of the contralateral side (Pataria et al. 2004). However, little is known about the switch of hand usage and its long term impact on speech dominance (Auer et al. 2009). We investigated cortical language representation in a pair of 29 year old female homoygous twins. Twin II suffered an injury of the right hand with remaining motor impairment at the age of two and had to convert to left hand usage. We measured activation of language-specific cortex with a 248 channel MEG system and used 1 expressive and 2 receptive language tasks: a verb generation task, a word recognition task and a paradigm in which both subjects were asked to generate antonyms to visually presented words. Analyses of data revealed left lateralized language dominance in twin I and bilateral language representation in twin II. We conclude that conversion of hand usage does not only lead to changes of sensorimotor representations in the brain, but might also lead in part to a reorganisation of language lateralization. Our case study indicates a close bidirectional relationship between hand usage and cortical language representation.
We-168 - The long latency motor response in the upper limbs muscle evoked by transcranial magnetic stimulation on the cerebellum

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Background and Purpose: We have found the long latency electromyographic (EMG) response in the both sides of lower limbs soleus muscles evoked by transcranial magnetic stimulation (TMS) at the cerebellum level and also this EMG response was conducted through the vestibulospinal tract in the previous studies (Sakihara K et al. Neurosci Res 2003, NeuroReport 2004, NeuroReport 2007). Based on these findings, we examined whether cerebellum-related EMG response appears in the upper limbs muscle and aimed to develop the quantitative clinical examination of cerebellum-related motor system.

Methods: We used a transcranial magnetic stimulation device made in Magstim company for healthy volunteers in this study. We stimulated to one side cerebellum of the volunteers with a double coil with averaging method. We recorded EMG response evoked by magnetic stimulation at the extensor carpi radialis muscle with mild sustained contraction which had the most stable response in the preliminary studies at each muscles of upper limb.

Result: When we performed the magnetic stimulation to one side of the cerebellum, we obtained a reproducible long latency EMG response in the both sides extensor carpi radialis muscles. The latency of the response evoked by cerebellar TMS changed when movement loading to cerebellum with the finger to nose test.

Discussion: Similar EMG responses were recognized by TMS at other cerebral areas. But cerebellar TMS showed different manner from other cerebral areas during changing strength of the stimulation. We showed this response evoked by cerebellar TMS was cerebellar-specific.

Conclusion: We obtained cerebellum-related long latency EMG response in the both sides extensor carpi radialis muscles evoked by cerebellar TMS.

We-169 - Neuromagnetic Correlates of Cortical Thickness Changes in Children Receiving Therapy for Motor Speech Disorders

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Motor Speech Disorders (MSDs) are characterized by deficits in planning and/or executing the movements necessary for accurate and fluent speech. Children with MSD show poor articulation, and as a consequence, may be reluctant to engage in discourse. Childhood MSD does not resolve spontaneously, but may be amenable to targeted early interventions. One effective treatment, known as PROMPT (Prompts for Restructuring Oral Muscular Phonetic Targets), involves multi-sensory training with direct tactile-kinesthetic input provided by the therapist (Chumpelik, 1984, Grigos, Hayden, & Eigen, 2010). In this study, we investigate the structural and functional correlates of oral-motor control and speech production in a group of children with MSD (n = 12, ages 4-6 years) receiving 8-weeks of PROMPT therapy. Participants were studied at the Hospital for Sick Children and the Speech and Stuttering Institute in Toronto, Canada, before and after the intervention. At each visit, participants completed standardized neuropsychological and speech-language assessments, high-resolution MRI, and MEG (151-channel whole-head CTF system). In the MEG, participants performed a mouth-opening task, and spoke ‘pa’ and ‘pa-ta-ka’ to presentation with visual cues. All participants demonstrated improvement in speech quality following PROMPT therapy. Cortical thickness analyses revealed a significant decrease in the left posterior superior temporal gyrus (Wernicke’s area) associated with successful intervention (Kadis, Goshulak, Pukonen, et al., 2012). For this report, we characterize changes in neuromagnetic correlates of oral-motor control and speech production. We interrogate the region showing decreased cortical thickness using virtual sensors in beamformer analyses. To our knowledge, this is the first study to combine quantitative MRI and MEG to characterize neuroplasticity in a group of children receiving brief intensive therapy for speech disorders.
We-170 - Impact of hand movement rate on corticokinematic coherence

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Introduction
Corticokinematic coherence (CKC) has been so far used to evaluate the coupling between cortical magnetoencephalographic (MEG) signals and the kinematics of fast (3 Hz) voluntary repetitive hand movements (Bourguignon et al., NeuroImage 2011). However, the effect of hand-movement rate on CKC is still unknown.

Methods
CKC was evaluated in ten right-handed healthy adults performing flexion-extension of right-hand fingers at three different movement rate: slow (∼ 1 Hz for 11 min), medium (∼ 2 Hz for 5 min), and fast (∼ 3 Hz for 3 min). Fingers did not touch the thumb during the movements. Before each condition, subjects were trained for 1 min to move at each rate by listening to pacing tones. Neuromagnetic signals were recorded with a whole-scalp covering MEG (Elekta Neuromag) and index-finger acceleration was monitored with a 3-axis accelerometer. CKC sources were computed on the basis of cross-correlograms and modeled with equivalent current dipoles.

Results
Significant coherence was found at movement frequency (1 Hz: 9 subjects, 2 Hz: 10 subjects, 3 Hz: 10 subjects) and its first harmonics (1 Hz: 9 subjects, 2 Hz: 8 subjects, 3 Hz: 10 subjects). No effect of movement rate was found on coherence level as assessed by one-way repeated measures ANOVA. CKC sources (goodness of fit ≥ 80%) were located in the primary sensorimotor (SM1) hand area, contralateral to hand movements, with no consistent differences between the movement rates.

Conclusion
We demonstrated that CKC can be elicited equally well with movement rates from 1 to 3 Hz, with no systematic effects on source locations. These data further reinforce our previous hypothesis (Piitulainen et al, submitted) that CKC directly reflects task-related parameters rather than an intrinsic central rhythm. The possibility to record CKC at slow hand movement rates may be of interest in patients struggling to perform fast repetitive hand movements.
We-171 - Age-related differences in post-movement mu rhythm modulation after motor learning

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Post-movement modulations of mu rhythm in alpha (≈ 10 Hz) and beta (≈ 20 Hz) bands reflect changes in neural activity within the primary sensorimotor cortex. Here we investigated how prior motor sequence learning changes post-movement mu rhythm modulation and whether this effect evolves with age.

MEG signals (Vectorview, Elekta) were recorded in 15 right-handed young (18-30 years) and 5 elderly (65-75 years) healthy subjects while they were performing auditory-cued key presses using all four left fingers simultaneously (index to little finger) every 5 seconds during two separated MEG sessions (100 trials). The first MEG session was followed by learning of a sequential finger-tapping task involving the four fingers of the left hand (sequence: little finger, index, ring, middle, little finger), to be reproduced as fast and as accurately as possible (140 trials). This learning was followed by an inactivity period of 10-20 min before the second MEG session. Mu power from -1000 to 4000 msec peristimulus (auditory cue) onset was averaged across 18 gradiometers over the right sensorimotor region (Kim & Chung, 2007) and compared before and after learning in alpha and beta bands separately.

No significant difference before and after learning was found for mu power decrease. In young subjects, post-movement rebound was enhanced after motor sequence learning both in alpha and beta bands (Figure, Wilcoxon signed-rank test: p < 0.01), whereas it was not the case in elderly subjects (Figure, p ≥ 0.3). A permutation test disclosed age-related differences in alpha power rebound, 2500-4000 msec after movement initiation (p < 0.01), with enhanced rebound after learning in young as compared to elderly subjects.

These preliminary findings suggest that prior motor sequence learning enhances post-movement mu rhythm rebound during a simple motor task in young subjects, but that this post-training modulatory effect disappears with age.

Post-movement mu rhythm modulation (alpha and beta bands) before vs after motor sequence learning in young and aged participants

We-172 - Cortical activation of the tenodesis grasp after C6 quadriplegia: a MEG control case study

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Background: Human prehensile movement is dramatically disturbed after cervical spinal cord injury. Indeed, persons sustaining C6-quadruplegia lose the ability of active grasp. However, a compensatory passive prehension remains possible using the tenodesis grasp: wrist extension elicits passive fingers closure. So far, little is known about the pattern of cortical activity mediating the tenodesis grasp. Using magnetoencephalography (MEG), motor tasks can be studied within the 13-35 Hz beta band using the beta rebound occurring right after movement end.

Objective: This study investigated cortical activations in a C6-quadruplegic participant and a control participant performing repetitive wrist extension movements.

Participants: A chronic stable stage C6-quadruplegic participant 24-aged and a healthy age-matched control participant were included in this study after the local ethics committee has given its approval (CPP 2009-051 B). Both participants were right-handed. The C6-quadruplegic participant had a normal muscular strength of the wrist extensor muscles.

Methods: Both participants were requested to perform a set of 30 wrist extensions while MEG data were recorded. Inverse modelisation of the cortical activation sources within the 13-35 Hz beta band were used to determine the location and amplitude of maximal activation when comparing time-windows during and after movement.

Results: Preliminary results showed a significant increase of the beta rebound within the left contralateral motor cortex in the C6-quadruplegic participant as compared to the control participant, suggesting an enlarged cortical activation of motor areas involved in wrist extension movements.

Conclusion: This activation pattern does not correspond to an increasing of the wrist extensors muscular strength which was similar for both participants. It could reflect the motor cerebral plasticity induced by the repetitive wrist extension movements performed during the tenodesis grasp learning.

**We-173 - Motivational modulation of motor beta de-synchronization during effort preparation**

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Introduction
The brain shows robust oscillatory activity during motor execution, with a decrease in the beta band power (13-30Hz) over the motor cortex (Feige 1996). This beta event-related de-synchronization (ERD) mirrors the event-related readiness potential, as it progressively builds up before movement onset. Puzzlingly, no motor parameter is known to impact the beta ERD amplitude, except movement direction uncertainty (Tzagarakis 2010). Here, we address whether this preparatory ERD could represent a marker of incentive motivation.

Methods
In every trial, subjects (n=19) had 30 seconds to win as much money as possible by squeezing a handgrip. The payoff was proportional to the time spent above a target force level and to a monetary incentive (10, 20, 50 cents) announced before each trial. Subjects freely alternated rest and effort periods while MEG data were recorded (151-channel CTF system). We computed a wavelet analysis, using FieldTrip, in a 4s time window centered on effort onset. Power in the beta band was z-scored with respect to a 2s baseline rest period preceding the trial.

Results
Higher incentives shortened rest periods, such that total effort duration and hence monetary payoff were enhanced. The a priori wide beta band (13-30Hz) showed a typical preparatory ERD over central sensors. During the 1.5s preceding effort onset, beta z-score parametrically decreased with incentive levels. This effect was driven by the low (13-15Hz) and high (≥23Hz) beta, and survived the inclusion of rest duration as a confound factor in partial correlations. Additionally, incentive effects on beta ERD and rest duration were significantly correlated across subjects.

Conclusions
Beta ERD amplitude during motor preparation reflected incentive motivation, since it was higher for higher incentives and in subjects exhibiting stronger motivational effects. More generally, it supports that beta rhythm could be involved in top-down regulation of motor processes (Wang 2010).
We-174 - rTMS and tDCS to the motor cortex modulate event related desynchronization of mu wave

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In our study, we studied the effects of repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) to the event related desynchronization (ERD). Mu wave is traditionally defined as an 8-12Hz wave recorded over sensorimotor cortex. The power of mu wave decreases with imagination of movement. ERD describes the short lasting and regional localized amplitude attenuation or blocking of oscillations that occurs in direct relation to an event. Both rTMS and tDCS can modulate cortical excitability. The aim of this study is to investigate the rTMS and tDCS effects on the ERD of mu wave, when rTMS and tDCS induce the facilitation or inhibition of cortical excitability. EEGs were measured before and after stimulation. At one measurement, subjects were given 1Hz 600pulses 90% resting motor threshold (RMT) rTMS, 1Hz 600pulses 110% RMT rTMS, 1mA 10min anodal tDCS or 1mA 10min cathodal tDCS over the motor area of the thumb in the left hemisphere. The reference electrode of tDCS was fixed at the forehead of the right hemisphere. During the measurement of EEG, subjects were required to either relax, or image grasping the right hand, or actually grasp the right hand for 4seconds during every 4seconds interval as indicated by the word cues ‘Relax’, ‘Imagery’ or ‘Movement’, which were displayed on the monitor. Each task was repeated ten times at one measurement. To investigate the differences between the effects of real stimuli and noise, sham rTMS and sham tDCS conditions were added in this experiment. We analyzed the amount of difference ERD according to imagery or according to movement between before the stimulation and after the stimulation. Fig.1 shows the amount of power difference ERD. Using paired t-test analysis, it was found that the anodal tDCS which produces facilitation, significantly increased the ERD and 1Hz 110% RMT rTMS and the cathodal tDCS which produces inhibition, significantly decreased the ERD.

We-175 - Action understanding: top-down effects

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It is commonly accepted that the perception of others actions results from the activation of a feedforward hierarchy of areas, leading to increasingly complex representations: the observed actions initially processed in the occipital lobe are encoded in Superior Temporal Sulcus region and subsequently transformed into a motor format in the parietal and premotor areas. This transformation is done via the mirror mechanism (1) allowing the observer to understand the goal of the observed motor acts at a level of generalization that cannot be achieved at a mere visual level.
It is unclear, however, how understanding of action goal is related to the visual description of the observed actions. Here we present evidence for a fundamental role in action perception of backward projections to the occipital lobe. The evidence is based on two studies. In the first one, using high-density EEG, we showed that during action observation there is a first (stimulus related) activation of occipital, parietal and premotor areas followed by a second (top-down) late activations of the occipital cortex, occurring approximately 220 ms following stimulus presentation. In the second study, using TMS, we found that participants show a clear impairment in the accuracy of action recognition following occipital lobe stimulation applied in correspondence of the late wave. Thus, combining EEG and TMS techniques we were able to demonstrate that the visual areas are activated by a top-down mechanism and that this activation plays a fundamental role for the perception of action details. Top-down projections 'bind' the understanding of the goal of an action with the pictorial descriptions of the same action. This binding allows what we call full perception of the observed actions as a joint function of visual and motor areas.


**We-176 - Interactions between sensory and motor areas during action recognition.**

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Several studies have shown the importance of temporal, parieto-occipital, and sensorimotor areas when observing action movements, but far less is known on their interaction during this process. Here, we used MEG to study the interactions between sensory and motor areas when differentiating between point-light displays of biological (e.g. walking) and non-biological movements (random configuration of dots). We were particularly interested in coupling of oscillatory activity between areas.

Pooled over both conditions, stimuli evoked sustained power suppression in the alpha and beta band over bilateral temporal, parieto-occipital, and sensorimotor areas, and a sustained power increase in gamma over bilateral parieto-occipital areas. Additionally, an increase in high alpha power was observed over sensorimotor areas.

When assessing differences between the conditions, a significant increase for biological movements was observed in gamma (55-75 Hz) power between 0.5-0.8 s in parieto-occipital areas, followed by a beta (20-35 Hz) increase in sensorimotor areas (0.7-1.2 s), and an alpha (9-13 Hz) power increase between 0.9-1.3 s in left temporal areas. In addition, gamma (50-80 Hz) power decreased in right temporal areas between 1.3-1.6 s followed by an alpha/beta (10-22 Hz) power decrease in parieto-occipital areas (1.6-2.0 s).

Between these significant clusters, we observed a positive trial-by-trial correlation between sensorimotor beta and parieto-occipital gamma power as well as left temporal alpha for the biological condition. Non-biological motion revealed a significant positive correlation between parieto-occipital beta and right temporal gamma power and a negative correlation between sensorimotor beta and parieto-occipital beta.

The results provide new insights in the role of neuronal oscillations for the recognition of different actions. The power correlations accentuate the importance of interaction between sensory and motor areas during action recognition.

**We-177 - Coherence between MEG and peripheral motor-action-related signals**

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Velocity and acceleration of hand movements are coherent with magnetoencephalography (MEG) signals recorded from the contralateral primary sensorimotor (SM1) cortex [1,2]. We compared coherence between MEG and four different motor-action-related signals (acceleration, force, pressure, and EMG of flexor carpi radialis muscle). Fifteen subjects performed for 3.5 min three continuous self-paced motor tasks, each at about 3 Hz: (T1) flexions/extensions of right-hand with thumb touching the other fingers (acceleration, EMG), (T2) dynamic index-thumb pinches against an elastic rubber ball attached to a pneumatic pressure sensor (pressure, EMG), and (T3) brief isometric index finger-thumb pinches against a rigid load cell (force, EMG).

Coherence between MEG and all peripheral measures peaked at movement frequency (F0), range 1.8-5.0 Hz and its first harmonic (F1). Coherence was stronger (p < 0.05) with respect to pressure (mean ± SEM 0.45 ± 0.04 in T2) and force (0.37 ± 0.04 in T3) than acceleration (0.28 ± 0.04 in T1) and EMG (0.23 ± 0.03 in T1, 0.31 ± 0.04 in T2, and 0.31 ± 0.04 in T3) at both F0 and F1. In all tasks, the cortical sources (equivalent current dipoles) of cross-correlograms were located at the contralateral hand SM1 cortex, with less than 6 mm difference in their mean coordinates.

As novel findings, we observed that the SM1 cortex is strongly coherent at F0 and F1 with kinetic pressure and force signals, in addition to the previously demonstrated kinematic and EMG signals. These measures are potential tools for functional mapping of the SM1 cortex.

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We-178 - Localization of cortical motor areas in humans using a magnetoencephalography

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The study aimed at localization of the hand area of primary motor cortex using magnetoencephalography (MEG). Based to the literature (Shibasaki and Hallett, 2006), we expected that the source of averaged magnetic fields in the peak of the 'readiness field' (RF) component of the motor evoked response will be localized in the hand area of primary motor cortex M1 ('omega-like' part of the central gyrus) contralaterally to the moving finger.

We evaluated cortical sources of the evoked magnetic field preceding the onset of voluntary lifting of the index finger in seventeen healthy subjects. For the movement onset detection we used automatic detection procedure based on a moving window-based computation of variance of the accelerometer signal. For each subject, at least 150 epochs were averaged. The sources of averaged magnetic fields in RF peak were fitted with a single dipole model. Only estimates with a goodness of fit above 85% were analyzed.

Results showed that at the group level the magnetic fields source localization in RF peak agreed well with the existing finding of the location of the primary motor hand area. However, at the inter-individual level the sources of the RF peak spread widely across the sensorimotor complex, being localized in the primary motor or sensory or premotor cortical areas of the contralateral hemisphere. These findings indicate the presence of the simultaneous multiple sources of the magnetic field at the time immediately preceding the movement onset. Our data are in a good agreement with animal literature suggesting the involvement of neural populations of the somatosensory and premotor cortex into the movement preparation (Donoghue and Wise 1982, Murphy, Wong et al. 1985, Widener and Cheney 1997).

Our results point to an inadequacy of the single dipole modelling for sources localization of motor readiness field. This conclusion is important for application of MEG-based cortical motor mapping in clinical settings.

We-179 - Revealing covert brain activity from MEG measurements

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In such stimulus-response tasks as Go/NoGo tasks, brain activities related to attention, recognition, or decision making might occur. Such brain activities are not considered to be time-locked to externally observable events and are referred to as covert brain activities.
Conventional averaging procedures cannot extract covert brain activities because of their unknown delays. Recently, we proposed a method that can extract covert brain activities (Takeda et al., 2010). The main advantage of our method is its ability to estimate waveforms without hypotheses about their shapes even if their delays are variable and unknown. Therefore, our method allows us to reveal covert brain activities in a data-driven way. Our study has two purposes: (1) to extract covert brain activities from MEG epochs during the Go trials of a visual Go/NoGo task by using this method and (2) to infer the functional roles of the extracted activities. For (1), we extracted waveforms time-locked to neither stimulus nor motor response onsets (unlocked waveforms) from the MEG epochs. The unlocked waveforms have large oscillatory components at the alpha band (8–10 Hz) around the temporal areas. For (2), we compared the results of the Go condition with those of other conditions: the NoGo condition, a passive viewing (Passive) task, and a simple reaction time (SRT) task. Compared to the Passive and SRT tasks, more cognitive functions, such as attention and decision making, are needed for the Go/NoGo task. Based on detailed analysis and comparisons among the various conditions, we conclude that the unlocked waveforms of the Go condition may reflect the attentional modulation of the task-irrelevant brain regions, which are not directly involved in the execution of the Go/NoGo task.

We-180 - Neuromagnetic imaging of movement-related cortical activity: development of rolandic rhythms with age

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Neural activity of pericentral cortex during voluntary movements exhibits oscillatory behavior detected as amplitude changes in the rolandic mu and beta bands. In the healthy adult brain, voluntary movements are mainly associated with two event-related desynchronization and synchronization (ERD/ERS) patterns on scalp neuro-electrical/magnetic measures: contralateral dominant mu and beta ERD right before and during the movement, and a subsequent contralateral dominant beta rebound (beta ERS) after movement-offset. Relatively little is known about how these measures are affected by aging. Whereas most of the works examining the developmental changes in neural rhythms with aging were focused on the default-mode (i.e. idle) rhythms, we propose to use the evolution of movement-related fluctuations of mu and beta rhythm as markers of the development of brain sensorimotor function. Pediatric MEG data were acquired over the left hemisphere in infants and young children (<5 years). A group of adults was used as control. The subjects were involved in a paradigm where periods of ‘rest’ (RE) were alternated with ‘prehension’ (PR) tasks during which a pipette was squeezed with the right hand. MEG signals were preprocessed using Independent Component Analysis in order to remove environmental and biological (e.g. ocular, muscular) artifacts. The resulting time series were analyzed in the time-frequency (TF) domain by convolution with complex Morlet wavelets having a frequency range from 1 to 50 Hz in 0.5 Hz steps. The time window of PR epochs was set from 6 s before the PR onset to 4 s after the PR termination. In order to compare stimulus-locked and spontaneous rhythm fluctuations, TF analysis was performed also on RE epochs selected anywhere during rest. The resulting TF maps revealed a shift of the frequency range of mu ERD toward higher values as age increases, whereas no clear post-movement beta-rebound is visible in infants and children, especially at early ages.
We-181 - Primary motor area as main direct target of somatosensory projections.

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Introduction: Identifying essential features of primary motor area’s (M1) function not only can help understand the general organization of human motor control, but also promises to provide indicators of processing dysfunction, essential to establish or improve rehabilitation procedures of the motor system after an insult.

Objectives: to show that neuronal activity originating within a section of M1 that is devoted to hand control (M1-h) can be extracted from the general response of the cortex to an external galvanic stimulation (of the median nerve in our case).

Methods: Left rolandic activity was recorded with magnetoencephalography (MEG) in 8 right-handed healthy volunteers during stimulation of the right median nerve and during non-fatiguing weak isometric gripping under visual feedback. M1 and S1 sources (FS_{M1} and FS_{S1}) were identified by the Functional Source Separation procedure (FSS). FS_{M1fS1} was the FS obtained by maximizing the responsiveness to the median nerve stimulation at around 30 ms in the channel space subtracted by the contribution of FS_{S1}.

Results: FS_{M1} and FS_{M1fS1} did not differ each other, while both differed with respect to FS_{S1}, for position, direction, responsiveness to median nerve stimulation (higher at 30 ms than 20, while the opposite was the case for FS_{S1}) and coherence with thumb opponent electromyography during the isometric gripping.

Conclusion: The new FS_{M1fS1} identifies the activity of M1’s region devoted to hand control by simply acquiring the response to contra-lateral median nerve stimulation. Remarkably, once provided with the source activity and weights exploiting the functional constraint active in a short time interval (median nerve stimulation in this case), the source can be investigated in other conditions of interest. Here, although we identified M1 only exploiting its responsiveness to the galvanic median nerve stimulation, we can study its behaviour during a voluntary movement.

We-182 - Movement induced uncoupling of primary sensory and motor areas in focal task-specific hand dystonia.

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Objective. Due to growing evidence of sensorimotor integration impairment in focal task-specific hand dystonia, we aimed at describing primary sensory (S1) and primary motor (M1) cortex source activities and their functional cross-talk during a non-dystonia-inducing sensorimotor task free of biases generated by the interfering occurrence of dystonic movements.

Method. Magnetoencephalographic brain signals and opponens pollicis electromyographic activities were acquired at rest and during a simple isometric contraction performed either alone or in combination with median nerve stimulation. The task was performed separately with the right and left hand by 8 patients suffering from focal-task-specific-hand-dystonia and by 8 healthy volunteers. Through an ad-hoc procedure (Functional Source Separation), distinct sources were identified in S1 (FS_{S1}) and M1 (FS_{M1}) devoted to hand control. Spectral properties and functional coupling (coherence) between the two sources were assessed in alpha[8, 13]Hz, beta[14, 32]Hz and gamma[33, 45]Hz frequency bands.

Results. No differences were found between spectral properties of patients and controls for either FS_{M1} or FS_{S1} cerebral sources. Functional coupling between FS_{M1} and FS_{S1} (gamma band coherence), while comparable between dystonic patients and healthy controls at rest, was selectively reduced in patients during movement. All findings were present in both hemispheres.

Interpretation. Because previous literature has shown that gamma-band sensorimotor synchronisation reflects an efficiency index of sensory-motor integration, our data demonstrate that, in dystonic patients, uncoupling replaces the functional coupling required for efficient sensory-motor control during motor exertion. The presence of bihemispheric abnormalities in unilateral hand dystonia supports the presence of an endophenotypic trait.
We-183 - Simultaneous EEG, fMRI and NIRS in healthy subjects and myoclonic patients during unilateral hand movement

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Human brain mapping by multimodality approaches has been proposed as an integrated methodology that can improve the knowledge of the cortical mechanisms underlying the neural activations following specific stimuli. We carried out simultaneous EEG-fMRI and EEG-NIRS recordings in 9 patients with progressive myoclonus epilepsy (PME) and in 10 healthy subjects (HS). Subjects performed repetitive hand movement in a block-designed protocol.

To investigate the functional activation of cortical areas involved in the movement execution, we used ERD/ERS analysis on ?- and ?-bands. [Oxy-Hb] and [deoxy-Hb] changes in the cortical motor region were also estimated. We extracted the fMRI time-series with an assumption-free approach. To obtain fMRI and fNIRS activation maps, we analysed signals by General Linear Models (GLM) using the event function from EMG as regressor.

In all subjects 4 and ?-ERD were observed on the contralateral central area. The ?-ERD time course was similar in the two groups although during the movement execution patients presented a lower mean value of desynchronization than controls. In the beta band, patients showed a more reduced ERD/ERS pattern than HS: the ?-ERS was significantly smaller in patients than in controls (6.7±23.4 vs. 81.2±4.4%, p=0.004). The mean amplitude of the haemodynamic response on activated area was on average smaller in PME than in HS (3.9±1.1 vs. 6.0±1.5, p=0.007). Also [oxy-Hb] change was significantly reduced in patients (0.02±0.02 vs. 0.07±0.05, p=0.010). fMRI and fNIRS activation maps obtained with GLM analysis didn’t show significant differences between PME and HS.

Different neuroimaging techniques can be simultaneously applied with consistent topographic results. ERD/ERS and haemodynamic time-series analyses revealed a different PME behaviour. Our data suggested that NIRS could be a useful technique aimed at studying patients with movement disorders being able to disclose changes in haemodynamic not revealed by fMRI.

We-184 - Response inhibition mechanism during ongoing rapid reaction: An MEG study

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Purpose
Response inhibition is an important property of motor executive functions, depends on posterior parietal lobe, prefrontal area etc. We investigate generators of reaction for suspending rapid repetitive movement to clarify the mechanism of motor inhibition.

Methods
Ten normal right-handed subjects participated in this study.

Stimulus: Two kinds of binaural tone burst (1 kHz and 2 kHz) were used and were randomly presented in conventional oddball manner with their probabilities of 80/20% (Frequent/ Rare). Assignment of two kinds of tones were changed for each subject. The stimulus onset asynchrony of the tones was fixed to 850 ms.

Motor task: Subjects were asked to make brisk right thumb opposition in response to frequent tones (Go) and had to inhibit the movement when rare tones appeared (NoGo).

Control task: Subjects listen quietly the same sequence of auditory stimuli.

Recordings: Magnetoencephalography with 204 planar gradiometers was used and the responses were averaged from -100 to +850 ms with respect to the tone onset. Electrooculogram and electromyogram of thenar muscles were simultaneously recorded. Source analysis with multiple equivalent current dipoles (ECD) were conducted and the resultant estimated sources were superimposed onto subjects’ own MRI.

Results
The mean success rate of motor response was 95%, and reaction time for Go trials in each individual ranged from 147 to 267 ms. In the motor task, when the subjects inhibited the movement in NoGo trial, the first MEG response peaked at about 100 ms bilaterally, and their generators estimated by ECD analysis were in the temporal auditory cortices. The following responses were found at 170 ms-210 ms around the left central area, and 185 ms-235 ms around the right central area. Those sources were estimated in the left premotor and in the right premotor cortices, respectively.

Conclusion
Ipsilateral motor-related cortices play roles in interrupting ongoing rapid movements.
We-185 - MEG frequency modulation in motor cortical network during active and passive ankle dorsiflexion

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This study investigates cortical involvement during ankle joint passive mobilization in healthy subjects. Magnetoencephalographic (MEG) signals were collected from twelve subjects by means of a 165-channel device. Electromyographic activity from right tibialis anterior (TA) muscle was also recorded. Rest periods were intermingled by right passive ankle dorsiflexion (passive movement, PM), imparted through a non-magnetic device, and by active TA isometric contraction (AIC).

MEG data analysis was performed by means of a recent approach developed by our group [Mantini et al., Brain Connectivity 2011] for estimating the time evolution of brain source activity. This approach relies on Independent Component Analysis (ICA) for decomposing MEG signals with the aim of rejecting artifacts and improving the MEG inverse problem accuracy at the same time. The time evolution of each brain voxel was estimated by linearly combining the IC time courses after source space projection. In the source space, Event Related Desynchronization (ERD) was evaluated for each brain voxel in alpha (8-13 Hz) and beta (15-25 Hz) bands in the period following the onset of PM and AIC. Similar patterns of band power modulation in alpha and beta band were found for AIC and PM in the contralateral primary sensory and motor areas. A greater ERD in beta band was found during AIC compared to PM in supplementary motor area and premotor area. PM ERD in alpha band was greater in bilateral secondary somatosensory areas than for AIC, probably resulting from an increased sensory integration during PM.

These results may have clinical implications given that passive mobilization of the ankle joint could provide beneficial stimulation of the sensorimotor areas during the functional recovery period.

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We-136 - Modulation of somatosensory evoked fields by intensity of interfering stimuli in human primary and secondary somatosensory cortices

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The present study aimed to investigate the effect of interfering stimuli with different levels of intensity on somatosensory evoked fields in human primary (S1) and secondary (S2) somatosensory cortices. We hypothesized that cortical response to a physically identical test stimulus (TS) would be altered according to the levels of interfering stimuli intensity. In the control condition, strong TS was delivered to the left median nerve with an interstimulus interval (ISI) of 3 to 4 s. In the three interference conditions, interfering median nerve stimuli with three different levels of intensity from weak (WI), which the subject felt clear tactile sensation without any motor movement, through moderate (MI), which elicited a visible twitch of the abductor pollicis brevis muscle, and finally to strong (SI), which is below the subjective pain threshold, were interspersed among the TS in each condition. The ISI between the interfering stimuli varied from 0.5 to 1.5 s. The cortical responses to the TS were modeled with equivalent current dipoles in the contralateral S1 and bilateral S2 cortices from 17 subjects. At the S1, the dipole strength for N20m was not changed by any interfering stimuli, whereas that for P35m was reduced by MI stimulus. The dipole strengths for the P60m in the MI-TS and SI-TS condition were significantly smaller than control and the WI-TS condition. The dipole strength for the bilateral S2 response was significantly reduced by the WI and MI stimuli, but further reduction by the SI stimulus was not observed. These results indicated that somatosensory cortical activation in the S1 (P35m and P60m) and S2 are modulated by the intensity level of the previous somatosensory input. Our findings of greater gating effect on the bilateral S2 than contralateral S1 indicate that S2 may play an important role in temporal integration of different intensity levels of somatosensory inputs.

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We-137 - Evaluation of lip sensory disturbance by somatosensory evoked magnetic fields following lip stimulation

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BIOMAG 2012 - August 26-30, 2012 - Paris, France
We-138 - Lowered frequency and altered stimulus-induced modulation of S1 alpha activity in hepatic encephalopathy

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Hepatic encephalopathy (HE), a frequent, neuropsychiatric complication of liver cirrhosis, is associated with a slowing of oscillatory activity in the motor and visual system (Kahlbrock et al., 2012 NeuroImage, Timmermann et al., 2008 Clin Neurophys). Here, we examined somatosensory alpha activity and its modulation by somatosensory stimulation in patients with varying degrees of HE. 21 patients with liver cirrhosis and 7 healthy, age-matched controls received electrical stimulation of the right median nerve while brain activity was recorded using magnetoencephalography. To quantify the degree of HE, a clinical and neuropsychometric assessment was performed. In addition, the critical flicker frequency (CFF) was measured, a reliable indicator of HE severity that decreases with worsening HE (Kircheis et al., 2002 Hepatology). Using a virtual sensor analysis, source waveforms in the primary somatosensory cortex (S1) contralateral to stimulation were individually reconstructed and (time) frequency analyses performed. A fast Fourier transform of the obtained stimulus-evoked source waveforms revealed a correlation between the individual alpha peak frequency and the CFF (r = .46, p < .01). Thus, the frequency of S1 alpha activity decreased with increasing disease severity. Time frequency analyses showed that S1 alpha activity was first suppressed by median nerve stimulation and then rebounded. Cluster-based randomization statistics of alpha activity in individually adjusted frequency bands revealed a delay and increase of this rebound in patients with clinically overt symptoms of HE compared to healthy controls (p < .01).

Quantitative evaluation of the lip sensory disturbances is important in oral surgery. To evaluate disabled sensory function of the lip, somatosensory evoked magnetic fields (SEFs) were measured following electrical lip stimulation in 6 patients and 10 healthy volunteers for control. The patients had unilateral (3 right-side) lip sensory disturbance due to inferior alveolar nerve injury during minor oral surgeries. Unilateral lip stimulation (2 cm lateral to the midline) was employed for both sides. Biphasic square pulses of current (0.5 ms duration) were applied at 1 Hz. The stimulus intensity of 3 times the sensory threshold in the healthy-side was used for both sides in patients. For healthy volunteers, the intensity was set to 3 times the sensory threshold for each side. MEG signals recorded by 204-channel planar gradiometers were used for analysis. The band pass was 0.1 to 990 Hz, and the sampling rate was 2997 Hz. Six-hundred times were averaged for each session. The group-averaged data of 2 reproducible sessions were used for analysis. For healthy subjects, the earliest consistent response around 25 ms (P25m) was detected only over the hemisphere contralateral to the stimulation, and at least one of three following components (P45m, P60m, P80m) were observed over the bilateral hemispheres, 23-33, 42-50, 56-67, and 72-98 ms for the right-side stimulation and 23-34, 46-49, 52-68, and 71-90 ms for the left-side, respectively. For patients, the stimulation induced responses around 24-34 ms (P25m) for the healthy-side but not for the affected-side. The affected-side stimulation evoked only traceable responses in 5 out of 6 patients. Their peak latencies were 57, 89, 65, 53, and 54 ms. The present findings suggest that the P25m component of lip SEFs can serve as an effective parameter to assess sensory abnormality of the lip.

We-139 - Neuromagnetic detection of laryngeal area: Sensory evoked fields to air-puff stimulation

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Understanding the sensory information processing of oral cavity, pharynx and larynx is crucial to assure safe deglutition. Regarding with pharynx and larynx, physiological implications of visceral afferents of glossopharyngeal and vagus nerves that project into the solitary tract nucleus have been well studied. Although several studies have reported the somatotopy of the pharynx using brain imaging techniques, little is known about somatotopy of larynx due to the restriction of the current non-invasive brain measurements. Therefore, this study aimed to elucidate the characteristics of laryngeal SEFs (LSEFs) using MEG. Five healthy volunteers participated in this study. In order to stimulate the mucosa of arytenoid region, an elastic tube was inserted for air-puff stimulation and the position of a tube tip was placed in hypopharynx by confirming with the endoscope. In order to assure the locations of major LSEF components, the right buccal mucosa and the right index finger to tactile air-puff stimulation were also recorded in the same session. Prior to the experiment, the subjects were trained to inhibit their swallowing. We also performed video monitoring and the causes of the motion artifacts were carefully fed back to each subject. MNE was performed to best differentiate the objective activations from non-task related ones. A ROI was drawn around the caudolateral central sulcus. The peak latency of LSEFs was approximately 100 ms in most cases both in sensor channel and activation curves within the ROIs. A peak activation corresponding to the LSEFs was located at the caudolateral region of the primary somatosensory area (S1) with acceptable reproducibility. Although the reproducibility and the accuracy of source localization must be established with refining the technique in the future study, our results clearly demonstrated the usefulness of the detection of LSEFs using MEG. The present results also suggest the existence of laryngeal visceral afferent inputs to the S1.

The main peak latency of LSEFs was approximately 100 ms in most cases both in sensor channel and activation curves within the ROIs. A peak activation corresponding to the LSEFs was located at the caudolateral region of the primary somatosensory area (S1)

We-140 - Buildup of a perceptual internal reference during tactile frequency discrimination: a MEG study.

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We studied the neural correlates of perceptual decisions in a two-alternative forced choice paradigm. Task consisted in tactile frequency discrimination of electrical stimulations. The first stimulation was a reference frequency that had to be retained and compared to a second inconsistent stimulus. Participants (N=20) remained unaware of the consistency of the reference stimulation. At the behavioral level, subjects became significantly more accurate and faster over time. This suggested a strategy shift in the experiment that we split into (Fig.1A):

(i) a learning part where performance increased (3 first sessions),
(ii) and a plateau where accuracy and reaction time remained stable (3 last sessions).

We identified several MEG correlates of this effect (Fig.1B).

First, the amplitude of the steady-state response evoked by the reference stimulation, which was source-localized in the primary somatosensory cortex, correlated positively with discrimination performance, in the first but not the second part of the experiment. Second, the amplitude of the transient ipsilateral evoked response to the reference stimulation, around 200ms, which was source-localized in the second somatosensory cortex, was significantly higher for correct than incorrect trials, in the first part only.

We argue that this might reflect the learning of the reference stimulation and the fact that its precise trial-specific encoding is no more crucial in the second part of the experiment.

In addition, alpha power over occipital areas increased in the delay period and correlated negatively with behavioral performance. This activity does not reflect visual sensory inhibition but rather a drop in alertness due to task automation.

These results seem to reflect implicit mechanisms involved in the buildup of an internal perceptual reference. The absence of effect in the second part of the experiment might reflect the shift from a comparison to a classification strategy(1).

1.Nahum et al. JNeuro, 2010
We-141 - Physiological aging impacts the hemispheric balances of resting state primary somatosensory activities

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To hone knowledge of sensorimotor cerebral organization changes with physiological aging, we focused on the primary somatosensory cortical area (S1).

S1 neuronal pools (FS₁) were identified by the Functional Source Separation (FSS) algorithm applied to magnetoencephalographic (MEG) recordings during median nerve stimulation. Age dependence of FS₁ was then studied at rest separately in the left and right hemispheres of 26 healthy, right handed subjects between the ages of 24 and 95 years. Possible sex dependences were considered.

The resting state FS₁ spectral features changed with increasing age: 1. alpha activity slowed down and became asymmetric (right ≥ left), 2. gamma band power increased bilaterally, 3. powers in delta and beta increased in the right hemisphere only, becoming asymmetric, 4. right ≥ left interhemispheric asymmetry increased in the whole spectrum, 5. S1 spectral entropy increased in the left hemisphere. Resting state FS₁ also depended on sex, females, with respect to males, showed: 1. faster individual alpha activity, 2. lower whole spectrum power, 3. higher spectral entropy.

The present FSS-enriched electrophysiological procedure provided measures of resting state hand representation area sensitive to changes with age. Alterations were stronger in the right hemisphere, and interhemispheric unbalances emerged with age, possibly due to asymmetric impairments of bilateral spontaneous firing rates and of local inhibitory-excitatory networks, as well as an increased excitability within the right thalamo-cortical circuit.

We-142 - Directionality of the coupling between somatosensory areas revealed by neuromagnetic sources of the vibro-tactile steady-state response

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This study focuses on the processing hierarchy within the human somatosensory system. We used the notion of complexity of brain signals and dynamic changes in measures of signal variability as an indicator of the exchange of information between brain signals, and developed a data-driven pipeline of nonlinear analysis of neuromagnetic source activity. Human magnetoencephalographic (MEG) data were collected in 10 young healthy adults during 23-Hz vibro-tactile stimulation of the right hand index finger. The dynamics of MEG source activity was reconstructed with a linearly-constrained minimum-variance beamformer. Single trial virtual sensor data were obtained for sources on a 5-mm grid across the brain volume. In our previous study, we applied complexity-based tools to identify brain areas with dynamic patterns that remain regular across repeated stimulus presentations. Activation in the primary somato-sensory area SI in the hemisphere contralateral to the stimulated hand was characterized as a source with the highest regularity, equivalent to having the lowest complexity of neuromagnetic activity. In the current study, we applied information-theoretic tools, specifically, a measure of transfer entropy, to quantify an asymmetry in the information transfer between SI and other
brain areas. The analysis identified a pattern of coupling, leading from SI to a source in the secondary somato-sensory area SII and a thalamic source, in both cases contralateral to the stimuli. Our results demonstrate that exploring the asymmetry in mutual interdependencies between neuromagnetic activities at the nodes of a functional network is a powerful method for understanding of the information exchange between co-activated brain regions. For central processing of sensory information, our results are in accordance with previously reported empirical evidence that the functional coupling between SI and SII involves cortico-thalamic connections rather than a thalamus-SI-SII hierarchy.

**We-143 - Anticipation improves tactile perception via increased ipsilateral stimulus processing**

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Stimulus anticipation improves perception. To investigate the neurophysiological mechanisms that underlie this improvement, we recorded magnetoencephalography in 19 humans while they performed a cued somatosensory discrimination task in which unilateral tactile stimuli occurred at various intervals between 0 and 1000 ms following a symbolic attentional cue. Because anticipatory processes require some time to develop, this manipulation of the cue-target interval allowed us to investigate the processing of the target as a function of the degree of anticipation. To our surprise, we observed that anticipation increases the response originating from ipsilateral primary somatosensory cortex (S1). This response concerns the suppression of beta-band oscillations and occurs 300-600 ms post-target. The time course of this effect (i.e. its dependence on the cue-target interval) matches the time courses of two related phenomena: (1) the anticipatory alpha- and beta-band suppression in contralateral S1, and (2) the improvement in tactile accuracy. We hypothesize that increased distributed processing of sensory information across bilateral primary sensory cortices constitutes an important mechanism underlying the improvement in perception following stimulus anticipation.

**We-144 - The effect of median nerve stimulation on evoked responses and beta band power loss in human somatosensory cortex**

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Introduction: We have previously studied the modulation of event related beta band (13-30Hz) oscillations in somatosensory cortex in response to paired pulse median nerve stimulation (MNS). We found that stimulus induced beta power loss was not modulated by inter stimulus interval (ISI), whereas the evoked response P35m was (1). Here, multiple pulse MNS is used to investigate the modulation of beta power and evoked responses.

Methods: In 8 subjects, non-painful MNS was applied. 10 pulses were applied at intervals of 0.5s. MEG data were recorded using a 275 channel CTF system at a sample rate of 600Hz. Spatial localization was achieved using Synthetic Aperture Magnetometry (SAM) by comparison of an active window (0-0.5s following each pulse) to a control window of the same duration centered in the rest period (6.5s < t < 11.5s). Timecourses of electrical activity were extracted from peaks of activity in the SAM images. These were averaged to derive evoked responses and filtered and Hilbert transformed to derive timecourses of oscillatory amplitude fluctuation.

Results: Fig. 1A shows the location of beta power loss in the brain. The timecourse of evoked responses from the contralateral somatosensory cortex shows the P35m amplitude decrease down the pulse train (Fig. 1B). This decrease, relative to the first pulse, reaches significance (Wilcoxon sign rank test) at the third pulse (p=0.008) and for all subsequent pulses (p<0.05). However, no significant modulation of the beta power loss following stimulation was observed (Fig. 1C).

Discussion: The evoked response P35m is increasingly attenuated as more pulses are applied. However, beta power loss does not change with the number of pulses, consistent with its putative gating role (1). This finding suggests that the evoked responses and beta oscillations are modulated by different mechanism in the somatosensory cortex.

(1) Stevenson et al., Neuroimage 59(3), 2722-2732, 2012
**We-145 - Comparison of auditory and somatosensory evoked fields measured with whole-head magnetometer, planar and axial gradiometer systems**

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Magnetoencephalography (MEG) has been available for over 30 years, and has been proven to be of clinical utility, enabling improved patient management in the evaluation of epilepsy as well as the presurgical functional mapping of visual, auditory, somatosensory and language areas. To confirm inter-machine consistency, we compared somatosensory (SEF) and auditory evoked magnetic fields (AEF) recorded from the same participants, using the two MEG machines: PQM160C (Yokogawa Electric Corporation, Tokyo, Japan) and VectorView (Elekta Neuromag, Helsinki, Finland).

In SEF measurement, a rectangular current pulse with 0.2-ms duration at 1.2 times motor threshold was delivered to the median nerve at the wrist of the left hand of the participants. Stimulus onset asynchrony (SOA) was randomized in a range of 0.6 Hz ± 50%. Two hundred responses were averaged for the SEF measurement. In AEF measurement, a 1-kHz tone burst with 100-ms duration (including 10-ms rise/fall) was presented to the left ear of the participants via the tube earphone ER-2 (Etymotic Research, Elk Grove Village, IL, USA) at the interstimulus intervals of 0.5-1.5 s. Intensity was set at 60 dB SL for each participant. A hundred responses were averaged for the AEF measurement.

The magnetic signals were lowpass filtered at 330 Hz and 260 Hz in YG and EN, respectively, and sampled at 2,000 Hz and 1,000 Hz in YG and EN, respectively. After measurement, the SEF and AEF data were lowpass filtered at 200 Hz and 40 Hz, respectively, and the averages in the period of 5-10 ms and -100-0 ms were used as in both YG and EN.

**We-152 - Successful functional integration of the transplanted hand heralded by the dynamics of reemergence of somatosensory responses**

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Human hand allotransplantation represents an exclusive model for studying brain plasticity. Embodiment of the new limb requires substantial reorganization of the somatosensory system in response to the transplant, and better understanding of the underlying mechanisms might lead to improvements in transplant medicine and particularly rehabilitation strategies.

We recorded whole-scalp neuromagnetic signals from a 24-year old right mid-forearm hand allotransplant recipient longitudinally...
over 12 months. Only somatosensory evoked fields (SEFs) to mechanical stimulation of his palms are presented here. The palm was stimulated by a hand-held tapping device, the recording pass band was 0.1-330 Hz, and 150-200 responses were averaged per session. Standard methods of signal preprocessing and source identification (equivalent current dipole modeling) were used. The patient’s structural brain MRI was used to display the sources of SEFs, while diffusion tensor images (DTIs) and fractional anisotropy (FA) maps were used to evaluate the fiber tracts structures.

For the native hand, SEFs peaked at the contralateral primary somatosensory cortex SI at 56 ± 1 ms. The first reliable SEFs to stimulation of the transplanted hand occurred 6 mo after the transplantation in the contralateral SI with a latency 39 ms longer than for the native hand. These latencies shortened by about 1 ms per month for the rest of the first-year follow-up. A considerable change was evident in the structure and directionality of the contralateral fiber tracts from 4 to 6 months after the operation. Patient’s sensory (and motor) recovery, paralleled the MEG and DTI/FA changes.

Recurrence of the contralateral SEFs 6 mo after the transplantation and the associated DTI/FA changes were in line with the expected speed of peripheral nerve regeneration, and they coincided with the onset of the tactile sensation. Shortening of the SEF latencies was paralleled by improved sensory performance.

**We-153 - Increasing neural synchrony parallels successful embodiment of the transplanted hand**


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Hand transplantation creates a unique model for studying brain reorganization in response to the transplant. Successful functional integration of the transplanted hand relies on extensive reorganization of the somatosensory system, and improved understanding of its basic mechanisms might lead to improvements in transplantation and rehabilitation strategies. We recorded whole-scalp neuromagnetic signals from a 24-year-old right mid-forearm hand transplant recipient (RHTR) and a 35-year-old right mid-forearm and left above-the-elbow double hand transplant recipient (DHTR) over 12 and 24 months, respectively. Here we report the analysis of oscillatory MEG responses to mechanical stimulation of their palms using a hand-held tapping device. We focused on the signals from the gradiometers of the Elekta Vectorview sensor helmet and estimated sensor-level synchrony in different frequency bands (1-50 Hz) by quantifying phase locking between the MEG signals and the stimulus onset.

Preliminary results show an increase in stimulus-induced phase locking of neuromagnetic signals in sensors over the contralateral sensorimotor area to both hands evolved in a fashion similar to the pattern of the sensorimotor area in frequencies 30-50 Hz. Over the longitudinal recordings, the phase-locking pattern of RHTR approached the patterns of the transplanted hand of DHTR.

The phase-locking results correlated with the improving sensorimotor hand-function recovery in both transplant recipients. Future research should investigate whether the increased stimulus-related synchrony mainly reflects improved synchrony of the sensory afferent volley or whether the synchronous oscillations in the somatosensory networks also play a role in neural plasticity subtending successful recovery following a hand transplant.

**We-154 - Evolving connectivity pattern during successful functional integration of the transplanted hand**


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Hand transplantation creates an exceptional model for studying brain reorganization in response to the transplant. Full functional integration of the transplant relies on broad restructuring of the somatosensory system, and improved understanding of its basic mechanisms might lead to improvements in transplantation and rehabilitation strategies. Whole-scalp neuromagnetic signals were recorded from a 24-year-old right mid-forearm hand transplant recipient over 12 months, during resting and palms stimulation by a hand-held tapping device. The recording band pass was 0.1-330 Hz, 150-200 responses were averaged, data was TSSS-filtered and trials for palm stimulation lasted from -500 ms to 500 ms. Using magnetometers data, analysis was performed at sensor and source level, for beta band and entire spectral content. Estimates of sources were calculated...
using the Beamforming-LCMV algorithm and connectivity patterns were computed by means of mutual information and characterized with different topological measures based on graph theory. When stimulating the transplanted palm, the strength of the long-range (principally interhemispheric) connections in the beta band is higher than when the native palm is stimulated, where a more local connectivity pattern emerged and remained stable throughout the study. However, during the transplanted palm stimulation, we observed a decrease in the long-range connections in sensor and source space during the first year of recovery. Overall, the observed network reorganization appears to involve a reduction of inter-hemispheric connections ensuing several months after transplantation as clinical improvement became evident. Observed connectivity patterns changes during the first year of recovery may suggest initial reliance on the long-range connections and a shift away from them as the functional recovery of the transplanted hand progresses. Future studies should explore if these findings reflect subtending patterns of neural plasticity.

**We-155 - Audiotactile interactions and defensive responses in the perihead space: an MEG study**

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'Peripersonal space' is defined as the portion of space within the reach of individual’s limbs, whose neuronal representation is based on the integration of various types of sensory information. Among the multiple purposes a body is required to pursue, there is its own protection from external threads. The present study aims to assess the mechanisms involved in the processing of potentially threatening stimuli presented within the peri-head space of humans. Magnetic fields evoked by air-puffs presented at the peri-oral area of fifteen participants were recorded by using magnetoencephalography (MEG). Crucially, each air puff was preceded by a sound, which could be either perceived as looming, stationary and close to the body (i.e., within the peri-head space) or stationary and far from the body (i.e., extrapersonal space). The comparison of the time courses of the global field power (GFP) indicated a significant difference in the time window ranging from 70 to 170 msec between the conditions. When the air puff was preceded by a stationary sound located far from the head stronger somatosensory activity was evoked as compared to the conditions where the sounds were located close to the head. No difference could be shown for the looming and the stationary prime stimulus close to the head. Source localization was performed assuming a pair of symmetric dipoles in a spherical head model that was fitted to the MRI images of the individual participants. Results showed sources in primary and secondary somatosensory cortex. Source activities in secondary somatosensory cortex differed between the three conditions, with larger effects evoked by the looming sounds and smaller effects evoked by the far stationary sounds, and the close stationary sounds evoking intermediate effects. Overall, these findings suggest the existence of a system involved in the detection of approaching objects and protecting the body from collisions in humans.

**We-157 - Sensitivity of low-noise EEG and MEG systems at 1 kHz**

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Ultra-fast electro-/magnetoencephalographic signals, having frequencies above 500 Hz, can be observed in somatosensory evoked potential/field measurements. Usually, these recordings have a low signal-to-noise ratio (SNR) because weak responses are overlaid by intrinsic and/or extrinsic noise of higher amplitude, e.g., generated by biological sources (such as EMG) or the recording system. Recently, using a dedicated low-noise amplifier made in-house (voltage noise $4.7 nV/\sqrt{Hz}$, FET inputs), we demonstrated the detectability of weak components (tens of nV) up to and above 1 kHz. Here, we combined this low-noise EEG with single-channel low-noise MEG (1.9 fT/\sqrt{Hz} at 1 kHz). Resting state measurements are used as a reference baseline for SNR calculation. EEG revealed three spectrally distinct components: N20 (< 100 Hz), sigma-burst (450-750 Hz), and kappa-burst (850-1200 Hz). The MEG system detected the evoked averaged sigma-burst, albeit with a SNR lower than the EEG, yet missed the higher spectral response components: Sigma SNR (peak-to-peak) reaches 15 in the EEG and 5 in the MEG, for the kappa band EEG SNR decreases to 4 while MEG has no longer significant activity above its noise level. Thus, state-of-the-art low-noise EEG systems enable the noninvasive detection of evoked activity at 1 kHz, i.e., in the frequency range housing spike-related multi-unit activity in intracortical recordings, while there is still a motivation for improving high-frequency low-noise MEG technology.

**We-158 - Cross-modal gating of sensorimotor networks revealed by magnetoencephalography**
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Research on the neural processes underlying cross-modal cortical activation suggests that sensory divergence can occur at very early processing stages across different levels of neural hierarchy. We utilized whole-head magnetoencephalography recordings combined with beamformer source reconstruction to investigate the neural correlates of rhythmic auditory processing for stimulation rates from 0.75Hz to 1.75Hz. Time-frequency analysis verified the modulation of source-level oscillatory (induced) activity and principal components analysis was used for spatiotemporal decomposition of volumetric whole-brain evoked responses. The results provide evidence of extensive and spatiotemporally patterned cortical activation as a consequence of passive listening to rhythmic auditory stimulation, revealing a dual pathway for auditory cortical processing. Furthermore, evoked cortical dynamics were modulated by the rate of stimulation with specific sensorimotor networks displaying gating effects with increases in rate. The rate effects in this study correspond to a critical range of rates also found to affect the behavioral stability of certain sensorimotor coordination tasks thought to rely on attentional resources. Thus, cross-modal gating may be implicated when temporal constraints on information processing restrict sensorimotor coordination.

Wednesday, August 29th, 2012, 13:30-15:00 Room 8

Ultra-low field MRI

We-51 - Highly multi-channel SQUID system for ultra-low-field MRI and MEG

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Magnetoencephalography (MEG) outperforms functional magnetic resonance imaging (fMRI) in temporal resolution and electroencephalography (EEG) in spatial accuracy. However, the spatial accuracy is limited by coregistration of the MEG sensors with a structural image based on anatomical landmarks and MEG head-position measurements. Additional errors are caused by slight changes in the shape of the brain depending on orientation. Even with perfect coregistration, the structural image would still require a separate session and MRI scanner. A hybrid MEG-MRI system is a natural approach to addressing these issues. State-of-the-art MRI with its multi-tesla magnets and restricted geometries is incompatible with MEG. However, in an emerging approach, called ultra-low-field (ULF) MRI, signals are detected by superconducting quantum interference devices (SQUIDs) in a magnetic field on the order of 0.1 mT. Moreover, SQUID sensors designed for ULF MRI can be used also for MEG, making hybrid MEG-MRI feasible.

We have designed and constructed a multi-channel hybrid MEG and ULF-MRI system, incorporating a helmet-bottom liquid-He cryostat and other components from a commercial MEG device. The system includes two planar sets of MRI coils to produce the main magnetic field and gradients. The main challenge of ULF MRI, low image signal-to-noise ratio, is addressed by prepolarizing the target in a mT-range field before each MR acquisition. As the prepolarizing coil, we use a non-dissipative superconducting Nb coil in contrast to high-power Cu coils seen in typical ULF-MRI systems. The coil also features self-shielding to reduce eddy currents in the surrounding magnetically shielded room walls.

We will present developed techniques as well as ULF-MRI and MEG of a subject. With tailored high-precision amplifiers for the MRI coils and on the order of 100 sensors, hybrid MEG-MRI allows accurate source localization and coregistration of the coordinate systems of the two imaging modalities.
We-52 - Dynamic shielding: A novel method for reducing eddy currents in ultra-low-field MRI

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While the state of the art of magnetic resonance imaging (MRI) has developed towards using multi-tesla magnetic fields, another approach has emerged, where the signal is detected by SQUIDs in a magnetic field on the order of 100 nT. Such ultra-low-field (ULF) MRI has many promising characteristics, including safety, silent operation, low cost, and compatibility with other sensitive technology. However, ULF MRI has not yet reached its breakthrough, as the image signal-to-noise ratio (SNR) and field of view (FOV) are still insufficient for most applications.

In ULF MRI, the signal is proportional to the polarizing field, which is applied before each signal acquisition using a separate coil. The SNR and FOV can be improved by increasing the polarizing field and the polarizing coil size, respectively. These changes, however, directly lead also to larger unwanted eddy currents induced in the conducting walls of the magnetically shielded room (MSR), which screens the system from external magnetic interference. The eddy currents are a superposition of spatial current density patterns that decay exponentially at their individual time constants. The currents further generate a field transient at the target, seriously hampering both the SQUID measurement and the magnetic resonance. One solution is to use, in series with the polarizing coil, a shielding coil, which cancels most of the polarizing field at the MSR walls. However, the method may be inadequate or difficult to implement because of geometric constraints or requirements in power supply or cooling.

We introduce a novel method, dynamic shielding, where a shielding coil is pulsed with current waveforms designed to kill specific spatiotemporal components of the transient. In simulations, eddy-current modes were eliminated with an accuracy limited by numerical precision. Dynamic shielding provides efficient software-tunable eddy-current reduction, and can relax requirements in coil design, cooling, and power supply.
An example of a dynamic shielding pulse for a polarizing pulse. At the end of the pulse, features at different timescales couple to eddy-current modes with different time constants. The pulse eliminates 11 longest time constants in a model system.

We-80 - SQUID-based system for interleaved ULF MRI and MEG of the occipital region of human head

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Magnetic resonance imaging at ultra-low magnetic fields (ULF MRI) combined with magnetoencephalography (MEG) appears to be a promising technique for investigation of dynamics in the human brain by achieving both the necessary spatial and temporal resolution of neural activity for clinical relevance. In this paper we propose the first SQUID-based system for interleaved ULF MRI and MEG of the occipital region of human head. The area is covered by 16 MRI and 64 MEG channels located in a Neuromag cryostat. Each MRI channel employs a Superconducting Quantum Interference Device (SQUID) sensor CE2Blue with cryogenic switch and 40 mm diameter pick-up coil. Each MEG channels is an 8 by 8 mm squared SQUID-based magnetometer. To perform magnetic resonance imaging a special MRI coil setup is implemented. It consists of coil system to generate measurement field BM (~ 230uT), three sets of gradient coils wound on square forms with symmetry axes along the x, y, and z directions, and two small coils placed orthogonal to BM to generate spin-flip pulses. In addition a liquid nitrogen cooled coil with inductance 0.2 H and resistance 0.4 Ohm is placed around the dewar in upper area of a subject's head to generate the pre-polarizing field BP applied for ~ 2s and then ramped down adiabatically before the detection of NMR echoes. The spatial resolution of MRI detection is 336 mm³ and the voxel SNR is limited by dewar thermal noise.
We-81 - Toward neuronal current spectroscopy at Ultra-Low field NMR

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The functional significance of different frequency bands of the electroencephalography (EEG), Local Field Potential (LFP) and Multi-Unit-Activity (MUA), is the goal of many studies for the comprehension of the brain activity and for the assessment of non-invasive monitoring of its electrical activity. The recent possibility to perform nuclear magnetic resonance (NMR) and imaging (MRI) at Larmor frequencies below 2kHz (ULF-NMR, Ultra-Low field NMR), together with the possibility to modulate the Larmor field during the acquisition of the free precession decay (FPD), could open the route toward neuronal current spectroscopy, by selectively tuning the Larmor field within the band of the neuronal activity of interest. In this paper we illustrate phantom studies for the real-time acquisition of NMR signals with Larmor frequencies tuned in the wide range 100Hz-2kHz, i.e in a spectral band of the MUA activity and high-frequency LFP. The Larmor frequency is piloted by an external signal, monitor of the brain activity. We used a dipolar phantom inserted in a solution reproducing physiological parameters (relaxation times and electrical conductivity) to mime the neuronal sources and real microelectrode recordings waveforms to simulate the timing of the neuronal currents with high temporal resolution. Electrodes mounted within the phantom mimed epidural EEG electrodes, and the recorded signals were used to tune the Larmor frequency. We focused on NMR over the MUA band ($\geq 500$Hz) to illustrate the properties and the performances of the system. The setup is conceived in view of the full implementation of the Resonant mechanism (RM) in in-vivo acquisitions using simultaneous EEG recordings. Temporal resolution, stability and possible applications are discussed in detail. This work could open new directions in ULF-NMR, like the simultaneous recording of EEG-NMR and the neuronal current spectroscopy at ULF-NMR.

We-82 - Phase Imaging at Ultra-Low Field MRI

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Imaging using nuclear magnetic resonance (NMR), i.e. Larmor fields comparable or even smaller to the earth magnetic field ($\sim 50$), is possible, and it has been widely demonstrated so far using precession frequencies above 1kHz. Recently, it has been shown that imaging is also possible at Larmor frequencies below 1 kHz, i.e. in the spectral band of the neuronal activity in the brain.
Up to now, published ultra low field NMR images (ULF-MRI) were reconstructed using the magnitude of the FFT transform of the recorded NMR signals, but it is not well know that at the ULF regimes the phase contrast could also provide important or complementary information. This work addressed the topic of phase imaging at ULF-MRI, i.e. images reconstructed using the phase of the FFT transform and it aims at comparing their properties in comparison with the standard magnitude MRI images. A comparison between the two reconstruction modalities (phase and magnitude) at ULF-MRI is reported with the indication of similarities, differences and future perspective for medical applications like the direct neuronal imaging.

We-83 - Magnetic resonance electrical impedance tomography at ultra-low fields
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Electrical Impedance Tomography (EIT) of tissue provides information for a range of biomedical applications such as detection of cancer. EIT also provides conductivity information required for forward models to localize brain sources measured with MEG or EEG, and prediction of exogenously applied current paths such as in Transcranial Direct Current Stimulation. Impedance measurements may also provide a new modality of functional neuroimaging, reflecting both slow hemodynamic changes similar to fMRI, and fast changes in neural tissue impedance linked directly to polarization and depolarization of synchronous neuronal populations measured by EEG and MEG.

EIT estimates of brain tissue conductivity are limited by the resistive structure of the skull. In bounded EIT (bEIT) the conductivity of multiple head and brain tissue compartments has been estimated with EIT performed by an inexpensive dense array EEG (dEEG) system and reconstruction bounded by tissue geometry obtained from MRI or X-ray CT. MRI also allows direct in situ measurement of local magnetic field perturbations produced by applied currents producing high spatial resolution images of electrical conductivity (MREIT) without the ill-posed problem in traditional EIT. Traditional MRI is performed at fields ≥ 1 T, but we have shown that MRI can be performed at ultra-low fields (ULF) 1 - 500 μT offering important advantages including novel pulse sequences, flexible magnetic field configurations, compatibility with imaging methods such as MEG, and the ability to use resonance to probe physiological processes at Larmor frequencies from Hz-kHz (rather than MHz). We recently combined bEIT and dEEG with ULF MRI methods to demonstrate ULF MREIT. Here we present a proof-of-concept demonstration in water-filled current phantoms, showing measurements of both phase shift and resonant effects of applied DC and AC current at 5-10 mA using an MRI read-out of 94 μT. Data, methods, and possible applications are discussed.

We-84 - Toward Dynamic, Multi-modality Imaging of Human Brain Function in a Single Instrument
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We have previously demonstrated the feasibility and value of strategies for dynamic mapping of neural activation, integrating MEG with anatomical and functional MRI. However, these methods have been limited to studies in which stereotypical patterns of activity can be reliably reproduced. The development of ultra low field (ULF) MRI techniques in principle allows the converge of these technologies, and the development of combined dense detector arrays for MEG and ULF MRI, described elsewhere at this meeting provides the basis of a capable integrated instrument. But ULF MRI is not well-suited for functional neuroimaging exploiting commonly used techniques such as BOLD, based on paramagnetic susceptibility contrast of oxy- versus deoxy-hemoglobin. ULF MRI may have important advantages for direct in situ imaging of neural currents, but this remains an attractive but elusive goal. In order to enable functional neuroimaging with ULF MRI, we have implemented imaging sequences such as FAIR that can exploit changes in blood flow which also accompany neural activation. We are developing and exploring strategies for magnetic resonance tomography of brain electrical impedance, which shows promise for mapping of activated neural tissue based on the underlying changes in neuronal conductivity. This approach also has important implications for more accurate forward modeling of the biophysical processes that produce MEG and EEG signals at the head surface. Finally, we are developing and applying methods for the reconstruction of spatiotemporal brain activity, which may enable mapping of the dynamic, transient patterns of brain activity that are characteristic of cognitive function.
We-85 - Low Field set-up for Magnetic Resonance Imaging

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A couple of modalities are proposed at low magnetic fields below 1 mT. Namely direct neuronal current detection and T1-contrast at low magnetic fields. Both offer new perspectives in particular in combination with spatial resolved information. To this end we developed a SQUID based MRI system enabling a Larmor frequency range below 1 kHz.

The measurement system consists of three main components. The magnetic sensor is realized by using a superconducting quantum interference device. To apply all the required magnetic fields and field gradients a coil set-up is placed inclusive current sources. And, a PXI based data acquisition and timing completes the set-up. Each measurement starts with a pre-polarizing of sample volume by applying up to 50 mT. To get the spatial information phase and frequency encoding is used. After the polarization the phase gradient is applied for adjustable time. Then the applied frequency gradient and detection field are reversed repetitively according to the phase time. So, echo signals of samples T2 decrease can be measured.

Starting with phantom studies we prepare three plastic bottles filled with tap water, copper sulphate-solution and hydro ethyl cellulose-solution. They differ in their T1 relaxation time 2.7s, 220 ms and 190 ms, respectively. Here, we present 2D images of our phantoms with a resolution of 1.8mm x 1.4mm taken at Larmor frequencies of 731 Hz and 100 Hz, respectively. By using a fixed polarization time the observable intensities in measurement signal of each sample reflect the different T1-time constants what enables their differentiation in the image.

Phantom measurements with T1 times in the range of human tissue show that imaging at ultra low magnetic fields is possible. Next step is extension of the measurement set-up to perform 3D-imaging and an increase in sensitivity to realize in vivo studies at ultra low magnetic fields.

We-86 - Low Field MRI at 10mT with Mixed Sensors

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Working with very low-field magnetic resonance imaging has several important advantages. Requirements concerning the static field's strength and homogeneity allow the use of a light setup free from any superconductive coils. Moreover, it has been demonstrated that some new contrasts appears at low frequencies which could lead to new diseases diagnosis in the future (1).

However, low-field MRI requires sensitive magnetometers for the detection of corresponding very weak magnetic signals. Mixed sensors (2), based on spin electronics principle, are good candidates for this type of experiment. Comprising a Giant Magneto-Resistance coupled to a superconductive loop, they offer a good sensitivity of several \(\frac{fT}{\sqrt{Hz}}\) and are robust against external static fields and radio-frequency pulses.

A functional setup, adapted for volume of 5x5x5 cm, has been built to test sensors and sequences with fields varying between 1mT and 10 mT, which offers a good compromise between signal strength and contrast detection. All static and gradient fields are generated by copper coils and no dedicated shielded room is used. We obtain an homogeneity of 10 ppm in our detection zone with gradient’s strength of 300Hz/cm. A mobile cryogenic environment has been designed specifically incorporating 6 mixed sensors able to perform parallel acquisition. The signal is collected by a flux transformer in copper Litz wire which is coupled to the mixed sensor superconductive loop.

In this configuration, we have developed several MRI sequences adapted to our setup to image different type of samples. Spin Echo, Gradient Echo and Inversion Recovery Echo have been applied to achieve Proton Density/T1/T2 weighted images in three dimensions with a resolution of 1mm\(^3\).

We will present the setup and results highlighting the possibilities of our approach for mT field MRI.

\begin{itemize}
\item (1) S. K. Lee et al, Magnetic Resonance in Medicine, 53: 9-14, (2005).
\end{itemize}
We-87 - NMR experiments of the asymmetry spin echo technique for ultra low-field functional magnetic resonance imaging (ULF-fMRI)

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Ultra low-field magnetic resonance imaging with SQUIDs has become accomplished technology. In further application, it has a potential to obtain functional information of a human brain (ULF-fMRI). This new-type fMRI is principally different to conventional high-field fMRI. The difference between the two systems is that whilst the conventional fMRI is imaging mainly changes in blood flow, the ULF-fMRI is directly imaging neural activity. We estimated the strength of the magnetic field generated by brain activities by using MEG data. The result shows a current dipole of 50 nAm which is slightly smaller than a brain activity generates a field of about 200 pT near the dipole. This field is large enough to modulate nuclear magnetic resonance (NMR) signals if the measurement field is lower than 1uT. A problem is that the frequency of the NMR signal becomes extremely low and this causes difficulties to reconstruct images. In this paper, we propose a method to transform such extremely low frequency to more practical frequency by using a spin echo technique. The principle of this method is that the first measurement field after pre-polarization is set to lower than 1uT and then a reversed higher field is applied to form a spin echo with a higher frequency. The timing of stimuli to a human subject is adjusted so as to cause brain activities within the first period. This echo signal is affected by the phase shift in the first field due to brain activities. We performed simple NMR experiments using a multiple coil for the NMR sensor and a Helmholts coil for the measurement field. The figure shows a result of the experiments to demonstrate the asymmetry spin echo technique as mentioned above. The first measurement field was about 20uT and the second reversed field was about 44uT. We observed clear echo signal in the second field, and found that the peak frequency was different from the first one. The results indicated the proposed method works properly.
Demonstration of the asymmetry spin echo technique

We-88 - Heart Magnetic Resonance

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The high sensitivity of the SQUID magnetometer makes it possible to measure weak magnetic resonance free induction decay signals even for the low Larmor frequency at micro-Tesla static field. The ultra-low field nuclear magnetic resonance (NMR) technique is one of the most challenging applications based on superconducting quantum interference device (SQUID) technology. Measuring the NMR signals at such a low field gives a good advantage such as direct measurement of low frequency electrophysiological activity. Here, I suggest a novel idea, heart magnetic resonance (HMR), to be applied to development of a medical instrument localizing an abnormal myocardial excitation in hearts. In the treatment of arrhythmia like atrial fibrillation or flutter, it is a very important and difficult process to find the focus of the abnormal excitation. Generally, such abnormal excitation has rhythmic activity and its own characteristic frequency. The main idea of HMR is to match the proton magnetic resonance frequency to the specific frequency of the abnormal heart activity so that we could find the position of the reentry current by using the magnetic field gradient spatial coding method in the conventional magnetic resonance imaging. In this presentation, the feasibility of this new idea has been demonstrated by conducting a numerical simulation based on a realistic heart model and experimental parameters in SQUID-based micro-Tesla NMR. Here, I introduce an experimental trick to decouple the NMR signal from the direct measurement of the reentry magnetic fields. That is a non-adiabatic change of the Bm field strength and the trick provides a extremely low detection bandwidth, as well.
We-89 - Toward a novel brain functional connectivity visualization tool by direct imaging of coherent brain waves: Brain Magnetic Resonance

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We also used an effective approach, namely the extrema circle, whose diameter is defined as the distance between the maximum and the minimum of measured magnetic signals in magnetocardiograms. With this approach, the measurement error at the boundary of the measurement plane can be excluded to improve the accuracy of sources reconstruction. The numerical experiments have shown that the x and y coordinates of most of the stronger current dipole sources which were reconstructed are just located within the extrema circle in a measurement plane over the human heart. In addition, source-moment components were also obtained. The future work is addressed to statistically analyze the diagnosis results of the ischemic heart disease (IHD), which were obtained by the approach mentioned above.
We-90 - Development of optically pumped atomic magnetometers toward ultra-low field multimodal MRI systems

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Optically pumped atomic magnetometers (OPAMs) using alkali metal vapors contained in glass cells are capable of measuring extremely small magnetic fields. In recent years, OPAMs operating under spin-exchange relaxation-free (SERF) conditions have reached sensitivities comparable to and even surpassing those of superconducting quantum interference devices (SQUIDs). The most sensitive atomic magnetometer has sensitivity in the subfemtotesla range. In addition, OPAMs have the intrinsic advantage of not requiring cryogenic cooling. Therefore, OPAMs are currently expected to overtake SQUIDs, and the possibilities for using OPAMs for biomagnetic field measurements and MRI have been demonstrated.

We have been developing a highly sensitive OPAM as a magnetic sensor to measure both magnetoencephalography (MEG) and magnetic resonance (MR) signals. Recently, an ultra-low field (ULF) MRI system with an OPAM has been proposed. Since OPAM does not require cryogenic cooling, it allows easily to measure extremely small magnetic fields. Here, we describe the principle of atomic magnetometers and results of biomagnetic field measurements. To test the performance of our newly developed atomic magnetometer, we made a phantom that models neuronal currents in the brain and measured tiny magnetic fields. We demonstrated measurements of magnetic field distributions with the phantom scanning two-dimensionally above the magnetometer. Finally, we describe the feasibility of atomic magnetometers as magnetic sensors for measuring MEG and MRI signals simultaneously toward ULF multimodal MRI systems.

We-91 - On the prospects of direct neuronal current detection by SQUID based low field NMR: a phantom study

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Today’s neuroscience and neurological diagnostics may benefit from the precise knowledge of the temporal and spatial distribution of neuronal currents. As the possibility to detect neuronal currents by high field NMR techniques directly remains controversial, low field NMR promises to be an alternative. In low field MRI the utilization of a resonant and a direct current (DC) mechanism has been proposed. The DC effect relies on the superposition of the neuronal field (hundreds of pT) and the detection field (∼). This might lead to a detectable alteration of the NMR signal of the brain region around the active neurons. DC-MEG measurements of brain activity elicited by repetitive electric stimulation of the median nerve show that a sustained activity is generated which can be modelled by an equivalent current dipole with a typical strength of around 15 nAm.

In order to demonstrate the DC effect we emulated the sustained neuronal activity by means of a single dipolar source in a physical phantom. The phantom consisted of a hollow sphere made of PVC filled with an aqueous solution of NaCl and CuSO4. By adjusting the concentration of CuSO4 the nuclear relaxation times could be tuned to the value for brain matter (∼100 ms). Inside the sphere an electric current dipole was mounted, which was made from two insulated twisted copper wires with non-insulated platinum endings. Initial measurements with polarization fields of up to 5 mT showed that the minimal detectable evoked current dipole moments in the phantom were up to 2 orders of magnitude higher than the physiologically observed values.

We present measures which were undertaken in order to increase the signal to noise ratio. These include the design and construction of a low noise dewar and the implementation of hardware enabling the application of polarizing fields of up to 50 mT. With this improved system the detection of neuronal currents in vivo via low field NMR appears feasible.

We-92 - Atomic magnetometers for MRX-mapping of SPIONs

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Superparamagnetic nanoparticles (SPIONs) have a large number of applications in biomedical research, ranging from drug delivery, MRI contrast enhancement, hyperthermic therapy, to imaging. Our research interest focuses on imaging applications using the method of magneto-relaxometry (MRX), for which we deploy two distinct systems based on laser driven atomic magnetometers. MRX measurements record the time-dependence of the magnetic field produced by a SPION sample following its magnetization by an external magnetic field pulse. Particles in a liquid environment show a fast (sub-ms) Brownian relaxation of the magnetic field, while for particles embedded in a solid or bound to its surface, relaxation times of several 10 seconds are observed. When applied to functionalized particles 4 designed to bind to spe-cific biological entities (cells, organs, tumors) 4 a mapping of the spatial
distribution of MRX-determined relaxation rates offers new ways for biomedical imaging. We use an array of 19 atomic magnetometers, the signal of each being the magnetic field value averaged over a 30 mm diameter sphere for mapping structures of several 10 cm². The magnetometers are based on the method of optically-detected magnetic resonance in a vapour of alkali atoms. We report on ongoing work towards SPION imaging with all 19 sensors. In parallel we develop a ‘magnetic field imaging camera’ system for imaging small-scale (mm²) SPION structures. The method uses Cs atoms contained in a cubic glass cell with an inert buffer gas, and a laser-based pump-probe scheme that prepares and detects coherent population trapping (CPT) resonances. The polarimetric detection of the large diameter probe beam by a CCD camera yields on each pixel a signal that contains magnetometric information. We anticipate a detection limit of 10 pT with sub-mm spatial resolution. The results of first studies with this prototype system will be reported.

We-93 - Magnetic Imaging with Dynamic Nuclear Polarization by using Ultra-low-field NMR

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Microtesla magnetic resonance imaging (MRI) technique is a challenging applications based on superconducting quantum interference device (SQUID) technology. The high sensitivity of the SQUID magnetometer enables measurement of very weak nuclear magnetic resonance (NMR) signals even for the low Larmor frequency in microtesla fields. But the microtesla level static field is not strong enough to polarize the spins. Therefore, strong pre-polarization field is usually applied during the SQUID based ultra-low-field (ULF)-NMR/MRI experiments. However this method restricts the spatial degree of freedom of the NMR/MRI system and causes troublesome electromagnetic interference in the sensitive SQUID sensor. One substantial way to increase the polarization is to utilize the dynamic nuclear polarization (DNP) approach based on the Overhauser double-resonance effect. Since this approach can enhance the nuclear polarization by saturating the electron spin resonance, the enhanced signal can be measured with rf field and pre-polarization fields of a few mT. We obtained DNP image of a phantom in fields of a few microtesla.

We-94 - Ultra-low-field MRI noise suppression using a data consistency constraint

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Compared to high-field MRI, ultra-low-field (ULF) MRI with B0 in the order or 100 µT has the advantages of 1) compatibility with metal objects, 2) system of a lighter weight and a lower cost, 3) higher T1 contrast, and 4) possibility to measure MRI and magnetoencephalography (MEG) simultaneously. Yet the most significant challenge of ULF MRI is the low SNR. Since a SQUID...
array with up to hundreds of sensors can be used in a ULF-MRI system for signal detection, we propose to use the collection of all spatially localized measurements from all SQUID sensors to suppress noise that deteriorates the theoretical data consistency (DC) across coils.

Mathematically, such DC relationship is described as $x = Gx$, where $x$ denotes the concatenation of $k$-space data from all coils and $G$ is a convolution kernel. Practically, given the data across coils in the $i$th iteration, we first estimated the convolution kernel: $x_i G_i$ and then reconstructed images $G x_i x_{i+1}$. This process was repeated until convergence $x_i = x_{i+1}$.

Note that our method did not discard any data point in the $k$-space for accelerated acquisitions. Instead, the reconstruction algorithm kept the same amount of the data and adjusted the dependency within the data. Our method is different from signal-space projection (SSP) and signal-space separation (SSS) methods in MEG processing, both of which are spatial filtering methods to separate measurements into signal and noise components and to remove the latter. The DC constraint is a unique $k$-space property in MRI, while MEG does not have a similar spatial encoding. However, we expect that this DC constraint can be integrated with SSP and SSS to further suppress noise and thus to improve the quality of ULF MRI.

**We-95 - Flow-based microtesla magnetic resonance imaging of phantoms**

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Recent progress in multi-modal microtesla, or ultra-low field (ULF), magnetic resonance imaging (MRI) has demonstrated the possibility of performing interleaved ULF MRI and magnetoencephalography (MEG). Even with recent enhancements in pre-polarization and super-sensitive detectors to enhance the signal-to-noise ratio, the resolution of ULF MRI does not compete with conventional anatomical MRI, but it achieves resolution comparable to typical functional MRI (fMRI). There are significant benefits to performing MEG and fMRI in a single system. For example, MEG can employ anatomical and functional constraints to solve the ill-posed inverse problem. We propose to expand the application of the ULF MRI/MEG system to incorporate hemodynamic functional MRI to provide inputs for MEG source localization. Since the low fields in ULF MRI result in a negligible change in susceptibility between oxygenated and de-oxygenated hemoglobin, a flow-based spin-labeling technique must be implemented instead of the commonly used blood-oxygen-level dependent (BOLD) method at conventional fields. One challenge to the approach is to understand the implications of shorter T1 relaxation times for blood and tissue at ULF. We have implemented the FAIR (flow-sensitive alternating inversion recovery) method to image a phantom with both static and flowing water. The method uses adiabatic spin-inversion pulses to flip the spins within a slice or within the whole sample, and the two images are subtracted to show the flow within a certain slice. We will present FAIR images of our flow-phantom to show the potential for functional ULF MRI in vivo.
We-96 - Development of a SQUID-Based LF-MRI System for small animals

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In the case of most physiological tissues, longitudinal relaxation time (T1) depends on the applied magnetic field strength, and the T1-contrast between different types of tissues can be enhanced at low magnetic fields. Prepolarized SQUID-based MRI could be used to perform T1-weighted imaging at low fields. We aimed to develop a low-field MRI system that can provide clear T1-weighted images. In this paper, we describe the setup of our MRI system and report basic imaging experiments. Our MRI system consists of five coil sets: a pair of circular coils that generates the polarizing field, and four sets of shielded planer coils that generates the measurement field and the 3D gradient fields. These coil sets were designed and manufactured in desktop size (350 x 350 x 188 mm$^3$) which corresponds to the size of our biomagnetic measurement system for small animals. The coil patterns were designed using the target field method so that the homogeneities of the measurement field and the gradient field are below $\pm0.5\%$ over 40 mm DSV (diameter sphere volume). A first-order LTS SQUID gradiometer was used as the magnetic field detector with a multi-integrator type flux-locked loop electronics. For the imaging experiment, we used 2.3 ml of NiCl$_2$ aqueous solution (1x10$^{-3}$ mol/L), located in the center of the coil sets. A clear MRI signal was observed, with a pre-polarizing field of 13 mT, a measurement field of 33 uT and an appropriate gradient magnetic fields: $G_x = 38\ nT/mm$, $G_y = 7.2\ nT/mm$, $G_z = 38\ nT/mm$. The MR image was obtained with a resolution of 3.8 mm/pixel.

We-97 - Three-dimensional current-density and conductivity imaging with ultra-low-field MRI

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Accurate interpretation of magnetoencephalography (MEG) or electroencephalography (EEG) data requires a precise forward model. The geometry of the brain structures needed for the model can be obtained with magnetic resonance imaging (MRI). In addition, also the conductivities of the different brain compartments have to be known. Ultra-low-field (ULF) MRI, where MR signals are acquired in microtesla-range fields using superconducting quantum interference devices (SQUIDs), permits three-dimensional imaging of current density and conductivity. Moreover, ULF MRI and MEG can now be performed with a single device comprising an array of SQUIDs. We present a novel ULF-MRI sequence, which can be used to image the conductivity of an object without the need to rotate it. By supplying an electric current through electrodes to the sample, a current density, which depends on the conductivity distribution, is produced. This current density generates a magnetic field within the object. We show that this magnetic field can be imaged using adiabatic switching of MRI fields. First, the object is prepolarized, and the magnetization is let to align along the local magnetic field produced by the current density. Then, this alignment is imaged, which provides means to reconstruct the magnetic field inside the sample. From the measured magnetic field, the current density can be computed. Furthermore, by applying the sequence for two different current densities, the conductivity distribution can be calculated. If imaging of brain conductivity with ULF MRI becomes possible, MEG and EEG source reconstruction can be improved dramatically. In that case, the available conductivity information would favor the combination of ULF MRI and MEG into a single device. However, it is still an open questions whether the available signal-to-noise ratios are sufficient to measure current densities that are acceptable in human investigations.

We-98 - Temperature dependence of T1 relaxation in ultra-low magnetic fields

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In ultra-low-field MRI (ULF MRI), images of human anatomy are encoded using microtesla-range magnetic fields. The signal-to-noise ratio (SNR) is enhanced by first pre-polarizing the sample and then measuring the resulting signal with highly sensitive superconducting quantum interference devices (SQUIDs). In comparison to high-field MRI, an ULF-MRI device is safer, potentially cheaper, and provides an open, bore-free geometry. Furthermore, in the ULF range, the relaxation properties and dependencies of MRI-related tissue parameters are expected to significantly differ from those measured in the traditional tesla range. Thus, in the future, ULF MRI may provide new kinds of tissue contrast to be used for, e.g., medical diagnosis.

In this study, we investigate the temperature dependence of T1 relaxation times in the ULF range. A sequence suitable for such measurements is presented. In addition, we show experimental results of T1 relaxation time in water as a function of temperature measured at 27 °C. The results are compared with those measured in the tesla range. Finally, taking into account the realistic SNR of a ULF-MRI measurement, an estimate regarding the method’s spatial and temporal sensitivity for in vivo measurements is presented. Non-invasive volumetric measurements of tissue temperature are useful in, e.g., the monitoring of high-intensity focused ultrasound (HIFU) surgery. Conventionally, such monitoring is accomplished using expensive high-field MRI. However, with temperature-dependent contrast emerging also in the ULF range, it might be possible that the monitoring could be performed at a lower cost and with a more flexible instrument.
We-99 - Toward high resolution images with SQUID-based ultra-low field magnetic resonance imaging

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Magnetic resonance imaging (MRI) is the state-of-the-art clinical method for imaging soft-tissue anatomy. Because signal scales with the applied magnetic field, the overwhelming trend in MRI has been to high magnetic fields, typically 1.5 or 3 T. However, there has been recent interest in ultra-low field (ULF) MRI using 10-100 microT magnetic fields. This is because at ULF there are opportunities for novel imaging applications such as MRI combined with magnetoencephalography (MEG) in a single device, imaging through or in the presence of metal, and enhanced spin-lattice tissue contrast. Loss in signal is mitigated by sensitive detectors such as superconducting quantum interference devices (SQUIDs) and sample pre-polarization, typically from 10-100 mT. There have been several proof-of-concept demonstrations based on this approach. However, ULF MRI image quality still suffers from one or more of the following disadvantages compared to HF MRI: lower signal-to-noise ratio, poor spatial resolution, and longer imaging time. Here we present recent progress toward ‘clinically relevant’ ULF MRI parameters: voxel SNR ≥ 10, voxel size < 2x2x4 mm, and reduced imaging time using arrays and sparse sampling. Data from a single channel system and a system with 16 MRI and 64 MEG channels combined are presented and discussed, as well as the potential for new applications in brain imaging enabled by ULF MRI.
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