Rhythmic entrainment source separation: Optimizing spectral and temporal analyses of narrow-band neural responses to rhythmic sensory stimulation

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The so-called steady-state evoked potential is a rhythmic brain response to rhythmic sensory stimulation, and is often used to study attentional processes. We present a data analysis method for maximizing the signal-to-noise ratio of the narrow-band steady-state response in the frequency and time-frequency domains. The method, termed rhythmic entrainment source separation (RESS), is based on denoising source separation approaches that take advantage of the simultaneous but differential projection of neural activity to many non-invasively placed electrodes or sensors. Our approach is an extension of existing multivariate source separation methods that are combined to optimize usability for narrow-band activity. We demonstrate that RESS performs well on both simulated and empirical data, and outperforms conventional analyses based on selecting electrodes with the strongest SSEP response.

MEG and EEG data processing using MNE-Python

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MNE-Python, as part of the MNE software suite, is a software package for processing electrophysiological signals primarily from magneto- and electro-encephalographic (M-EEG) recordings. It provides a comprehensive solution for data preprocessing, forward modeling, source imaging, time–frequency analysis, non-parametric multivariate statistics, multivariate pattern analysis, and connectivity estimation. Importantly, this package allows all of these analyses to be applied in both sensor or source space.
MNE-Python is developed by an international team with an open development model, with particular care for computational efficiency, code quality, readability, and facilitating reproducibility in neuroscience. The use of the Python language combined with a well-documented and concise interface allows users to quickly learn to build powerful M/EEG analysis scripts. MNE-Python is provided under the BSD license allowing code reuse, even in commercial products. MNE does not depend on any commercial product.
New features include:
- Signal space separation (SSS) for suppressing interference in MEG data, including head movement compensation and tSSS. Beyond the original implementation by Elekta, we are developing support for other MEG systems.- Interactive visualization tools for examining epochs from continuous recordings.- A new simulation module for generating artificial MEG and EEG data with various types of artifacts.- State-of-the-art decoding algorithms, such as common spatial patterns (CSPs), the xDAWN algorithm for BCI applications, and temporal generalization analysis for quantifying the temporal structure of cognitive processes.- Improved documentation on the website: http://martinos.org/mne
These additions further improve MNE-Python as a comprehensive solution for the analysis of MEG and EEG data. See http://martinos.org/mne for information about MNE-Python, and also check out the related project http://www.mne-cpp.org.

Welcome to NeuroPype: A Python-based pipeline for advanced MEG and EEG connectivity analyses

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With the exponential increase in data dimension and methodological complexities, conducting brain network analyses using MEG and EEG is becoming an increasingly challenging and time-consuming endeavor. To date, most of the MEG/EEG processing is done by combining software packages and custom tools which often hinders reproducibility of the experimental findings.

Here we describe NeuroPype, which is a free open-source Python package we developed for efficient multi-thread processing of MEG and EEG studies. The proposed package is largely based on the NiPype framework and the MNE-Python software and benefits from standard Python packages such as NumPy and SciPy. It also incorporates several existing wrappers, such as a Freesurfer Python-wrapper for multi-subject MRI segmentation.

The NeuroPype project includes three different packages:
I Neuropype-ephy includes pipelines for electrophysiology analysis; current implementations allow for MEG/EEG data import, data pre-processing and cleaning by an automatic removal of eyes and heart related artefacts, sensor or source-level connectivity analyses
II Neuropype-graph: functional connectivity exploiting graph-theoretical metrics including modular partitions
III Neuropype-gui: a graphical interface wrapping the definition of parameters.

NeuroPype provides a common and fast framework to develop workflows for advanced MEG/EEG analyses (but also fMRI and iEEG). Several pipelines have already been developed with NeuroPype to analyze different MEG and EEG datasets: e.g. EEG sleep data, MEG resting state measurements and MEG recordings in Autism. NeuroPype will be be made available via Github. Current developments will increase its compatibility with existing Python packages of interest such as machine learning tools.

References:
1. Bullmore E, Sporns O (2009), Nat Rev Neurosci 10:186-198
3. Gorgolewski et al. (2011) Front. Neuroinform. 5:13
4. Gramfort et al. (2013), Front. Neurosci. 7:267
5. Poldrack et al. (2013) Front. Neuroinform. 7:12

The HMM-MAR toolbox for the detection of quasi-stationary states of brain activity

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HMM-MAR (Hidden Markov Model - Multivariate Autoregressive) is a Matlab toolbox for estimating a probabilistic segmentation of multichannel data into states that are driven and characterised by their time and spectral signatures [1,2]. For example, this can be used to describe brain activity as a set of sequential brain states, with each state distinguished by its own unique multi-region spectral (i.e. power and functional connectivity network) properties. The inference procedure, based on Bayesian variational inference, simultaneously estimates when the states happen and what are the parameters describing their probability distribution.
In the context of neuroscience applications it can be used on both resting and task data, e.g. to identify task-dependent fast transient brain states in a simple buttonpressing motor task [1], or to find whole-brain networks in resting and task MEG [3,4] and resting fMRI data [5], and can also be switched into a HMM-Gaussian mode to detect fast transient whole-brain states in resting MEG power timecourse data [6,7].
It contains several additional features as e.g.
- Estimation of the spectral properties for each state, using either a parametric (MAR) or a non-parametric approach (statewise multitaper).
- Semi-supervised prediction of events.
- Extension to the classical inference to work with very big data sets [3].
- Routines for cross-validation and model selection.
- Simulation of data from an HMM-MAR model.
- Sign disambiguation for source reconstructed M/EEG data.

[1] D. Vidaurre. NeuroImage 2015, Biomag 2016
[2] D. Vidaurre. https://github.com/OHBA-analysis/HMM-MAR/wiki
[3] D. Vidaurre. Biomag 2016
[4] A. Quinn. Biomag 2016
[5] D. Vidaurre. OHBM 2016.
[6] A. Baker. eLife 2014.
[7] A. Baker. https://github.com/OHBA-analysis/GLEAN/wiki

COMETS2:A MATLAB Toolbox for Numerical Simulation of Electric Fields Generated byTranscranial Direct Current Stimulation

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Since there is no way to directly measure the electric current flow inside the head and no imaging modality can visualize the electric field generated by transcranial direct current stimulation (tDCS), numerical analysis based on finite element method (FEM) has been widely studied. However, because there has been no open software to simulate electric fields by tDCS, only a few groups could use this technology. In 2013, our group released a GUI MATLAB toolbox named COMETS (COMputation of Electric field due to Transcranial current Stimulation), which could simulate various electrode montages in a standard head model. Now, we are releasing a next version of COMETS, named COMETS2, which not only fixed several problems of the previous one but also adopted a realistic but computationally efficient electrode modeling method.

FEM is used for the electric field analysis, and a 4-layer head model is adopted. In COMETS2, we implemented functions for generating realistic saline-soaked sponge electrode models on user selected spots, and applied a new method to reduce the overall computational cost. We used NODE and ELE files supported by TETGEN, and superimposed the analyzed electric potential distribution, electric field intensity, and electric current density on the cortical surface. Any other head models can be applied for individualized tDCS study.

COMETS2 can help researchers who are not familiar with numerical methods. In particular, our new algorithm accelerating the computational speed might be useful for studies needing repetitive computations, for example, finding optimal electrode positions to stimulate a specific target area. COMETS2 will be available from Sep. 2016 at http://www.cometstool.com.

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NeuroCUDE: an easy-to-use python software for neuronal current dipoles estimation from MEG/EEG data

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We present NeuroCUDE(Neuronal Current Dipoles Estimator), a python software with an easy-to-use graphical user interface, for the automatic estimation of static multi-dipolar neural sources from MEG/EEG data. NeuroCUDE performs source modelling by means of two Bayesian algorithms called Sequential Monte Carlo (SMC) sampler [1] and Semi-Analytic SMCsampler (SASMC) [2]. The former analyses a single topography, looking therefore particularly suited for the estimation of the neural currents at a single point in the frequency domain, while the latter can take in input a time-series, with the obvious advantages brought by a greater amount of information. With respect to classical dipole fitting approaches, both SMC and SASMC provide an automatic estimate of the number of sources without requiring careful initialization. As for the inputs, NeuroCUDE needs the data, the lead-field and the source space, i.e. the brain grid from which the lead-field is computed. To improve usability, all inputs can be loaded in different file formats, such as the MATLAB *.mat* and the Neuromag *.fif* . Additional parameters of the algorithms are the values of the noise standard deviation and of the *a priori* variance of dipole strengths: these last can be either automatically estimated from data or manually tuned by the user. In the pure Bayesian spirit, NeuroCUDE returns in output the full posterior distribution of the unknowns. From the latter, a set of functions allows the user to compute a point estimate of the number of active sources, of their location and of the dipole moment. The results can then be either visualized withinthe NeuroCUDE\'s own visualization tool or exported to widespread neuroscientific toolboxes.Together with the program, a MEG synthetic data is available, that has been designed to show the main differences between the implemented algorithms.

[1]Sorrentino, A. et al. (2014) Inverse Probl. 30:045010.

[2]Sommariva, S., Sorrentino A. (2014) Inverse Probl. 30:114020.

Advances in online MEG/EEG data processing with MNE-CPP

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Magnetoencephalography (MEG) and Electroencephalography (EEG) enable researchers to investigate fast spatial and temporal changes of electrophysiological activity in the human brain. In parallel with advances in offline MEG/EEG analysis there is a growing interest in online data processing. Online processing paves the way for a faster and intuitive insight on instantaneous brain functions and at the same time creates the foundation for a wide range of neuro feedback scenarios. We present the recent advances in the open source MNE-CPP project, which offers a framework to develop offline as well as online data analysis and processing software. MNE-CPP provides tools to build highly efficient and user friendly MEG/EEG software applications. It is structured into libraries, which guarantee a modular and easily extendable architecture. MNE-CPP hosts libraries to support the Fiff and Free Surfer data format as well as source estimation and 2D/3D displaying routines. We have kept the external dependencies to a minimum, namely Qt5 and Eigen. Our new 3D library (Disp3D) is based on the recently released Qt3D module. Disp3D provides online visualization of neuronal activity, reconstructed MRI surfaces and sensor configurations, to name a few. Regarding the online acquisition, we included the support for two new EEG amplifiers (gUSBAmp, eegosports) and one new MEG system (Baby MEG). Furthermore, we have made our noise reduction tools (SSP, synthetic gradiometers, temporal filtering) to work directly on the incoming online MEG/EEG data streams, providing a processed data stream for subsequent online steps. Our recent efforts have shown that MNE-CPP applications can function as a strong backbone in a clinical environment equipped with MEG/EEG instrumentation (Baby MEG). In conjunction with the development of a source level BCI, we successfully demonstrated the acquisition and online processing of EEG data, recorded with newly supported amplifiers and a dry electrode cap setup.

MNE-HCP software for processing the Human Connectome Project MEG Data in Python

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The Human Connectome Project (HCP) currently provides the largest open source multi-modal neuroimaging dataset, comprising hundreds of fMRI and MEG recordings. Accompanied by sensitive bio-behavioral information, the HCP database could yield to the exploration of a wide range of promising scientific questions. In parallel to this, the Python language has gained reputation in the scientific community as a top pick among tools for data science; with its abundant resources for computational statistics and its vibrant community, Python has started to transform the data science culture in the field of neuroscience (see http://nipy.org/ for a summary). MNE-HCP (https://github.com/mne-tools/mne-hcp) is the first community contributed extension of the HCP pipelines opening its MEG data to the Python scientific ecosystem. The purpose of MNE-HCP is providing consistent programmatic access to various MEG data from experimental, task-free, and noise recordings at different processing stages. These include raw data, annotations for bad data segments, independent component analysis, cleaned segmented data,evoked magnetic fields, Freesurfer cortical segmentation outputs, and co-registration for source localization. The HCP outputs are mapped to configured MNE-Python (http://martinos.org/mne/stable/index.html) data structures, supporting all MNE processing pipelines off the shelf. Additional functionality facilitates processing the HCP data using Amazon Web Services.Three examples are presented to illustrate data analysis scenarios enabled by MNE-HCP. 1) source localization using recent inverse solvers only accessible in Python 2) validation of machine learning techniques on evoked magnetic fields 3) analysis low frequency fluctuations below the pass band of the preprocessed HCP data. In this sense, MNE-HCP contributes to the HCP community efforts by proposing complementary ways to exploit HCP data, thereby diversifying its scientific exploration.

Comparison between Hosaka-Cohen transformation and 2D source imaging in MCG study

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The Hosaka-Cohen transformation (HCT) has been used to display the pseudo current distribution from MCG data [1]. In this study, we compare the pseudo current distribution from HCT and results of source reconstruction and evaluate clinical relevance of these two methods.We used a biomagnetometer, containing 40 vector sensors and 4 normal sensors, arranged on 44 recording points [2]. MCG data were continuously recorded for 2 minutes with 5000Hz sampling frequency. The acquired MCG data were signal-averaged,and the HCT and 2D source images were computed using the averaged data. To compute the HCT, the derivatives of the normal recordings in the x- and y-directions were computed. The 2D source images were obtained by using vector recording, and reconstructed using RENS beamformer [3]. Here, a 2D plane 7cm below the sensor plane was reconstructed. Results of the HCT and 2D images were both overlaid on a patient's X-ray image.Near the middle of the P wave, a 2D source image shows significantly localized sourcedistribution, which is consistent with our clinical knowledge, this localized source may show the pathway from the right to left atrium. On the other hand, at the same time window, the HCT results show blurred distribution from which cardiac physiological activity can hardly be estimated. Thus, we conclude that 2D source imaging was more relevant than the Hosaka-Cohen transformation. Reference:[1]. Hosaka H, CohenD (1976) J Electrocardiol 9(4): 426-432.[2]. Adachi,Yoshiaki, et al. (2015) IEEE EMBC:7071-7074.[3]. Kumihashi I,Sekihara K (2010) IEEE Trans Biomed Eng 57: 1358-1365.

DSP TOOLBOX FOR REAL TIME MEG DATA ANALYSIS IN SOURCE SPACE

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There is a growing interest in analysing MEG data in real time known as real-time MEG (rtMEG). rtMEG has potential applications in training/rehabilitation of patients using neurofeedback, brain-machine interfaces, communicating with patients with locked in syndrome, brain injury diagnostics to name a few.

Recent advances in MEG instrumentation allow delivery of the MEG signal to digital signal processing (DSP) systems with sub-millisecond delay from the brain event. Earlier MEG studies showed that the brain can process sensory information in discrete time quanta as small as 12-15 ms (Joliot et al 1994). Thus to be successful, it may be crucial for rtMEG DSP system to submit its output to a feedback loop with milliseconds latency. With this performance objective in mind, we implemented a DSP toolbox to be used with the latest generation of CTF MEG electronics. In addition to basic data buffering and flow control functions, it provides on-the-fly source reconstruction using a SAM beamformer (Robinson & Vrba, 1999).

The software is written in C++ and runs on a general-purpose computer under a Linux OS. As an example, for an Intel i7-4820K CPU@3.7 GHz desktop it takes less than 1 ms to reconstruct amplitudes of 100 brain sources using 275 MEG channels input. The toolbox communicates with both the CTF MEG electronics and a client application using TCP-based messaging. The client may run in parallel with the toolbox on the same machine, or on a remote host.

As a proof of concept, we used a retinotopic mapping experiment. We presented a subject with 9Hz flickering stimuli to map the differing portions of the visual cortex. The acquired data was replayed at 300 samples per second. We were able to localize both the fundamental and the first-harmonics with less than 50 ms latency across multiple virtual sensors. We will present results of actual rtMEG collections with several subjects based on this paradigm.

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An MEG extension to BIDS: Brain Imaging Data Structure - a solution to organize, describe and share neuroimaging data

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The trend in neuroimaging studies is to aggregate large, heterogeneous datasets. These datasets range from simple text files to more complex hierarchical, multidimensional, and multimodal data formats. A single study may include multiple imaging protocols and multiple subject categories. All these factors pose a challenge for data harmonization and sharing efforts. The lack of consensus surrounding neuroimaging data formats and their organisation leads to resources being wasted on rearranging data, reproducing datasets and reimplementation of processing pipelines. For all these reasons, the adoption of a common standard to describe the organization of multimodal neuroimaging data would be extremely beneficial to the research community (minimizing curation, reducing errors and optimizing usage of data analysis software), especially in a context that promotes and experiments with data-sharing at growing scales.

The Brain Imaging Data Structure (BIDS) standard was first established for MRI and fMRI in 2015 (Gorgolewski et al. 2016). BIDS is based on simple file formats (often text-based) and folder structures that can readily expand to additional data modalities. Our consortium proposes an extension of BIDS for Magnetoencephalography (MEG) datasets. One objective is to frame the specifications of MEG-BIDS so that analysis pipelines designed with major analysis tools (such as Brainstorm, FieldTrip, MNE, SPM and others) can be readily applied without requiring software or pipeline redevelopments. Wide support across neuroimaging tools and database engines, as well as its straightforward design make BIDS particularly suited to act as an interoperable common exchange format for moving data across databases (e.g. OMEGA), and for facilitating data sharing.

For a more detailed description of the MEG-BIDS specification, example datasets, resources and feedback, please visit http://bids.neuroimaging.io.

MEG pipelines for the analysis of resting state data in the Human Connectome Project (HCP)

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The Human Connectome Project (HCP) aimed at mapping the human brain connectivity through the acquisition of multimodal data from a large number of subjects together with genotyping and behavioral data. MEG studied brain dynamics of more than 100 subjects, scanned with a 248-channel MEG system (4d Neuroimaging Inc) during Resting State- fixation and Task (Motor, Working memory and Language protocols). The project provided the scientific community with data at various processing levels together with the pipelines producing these data.

The MEG pipelines were developed in MATLAB using the Fieldtrip toolbox. They represent an improvement of existing techniques in terms of efficient implementation, new strategies for defining analysis parameters and wide testing on large subject samples.

Here, we will describe the pipelines analyzing Resting State data, some of which are also used for preprocessing Task data. First, quality check scores are estimated to remove bad runs (too noisy or affected by subject's movement). Then, bad channels and bad segments are automatically identified based on abnormal correlation with surrounding channels, ICA and large signal variance. An ICA-based pipeline decomposes and identifies artifact and non-artifact (brain) ICs. Source activities are evaluated over the individual cortex using either MNLSE (applied on the single brain ICs) or Beamforming (applied on the raw data after artifacts removal). Source level connectomes are estimated at two different time scales. Specifically, Pearson correlation-based connectomes are estimated from the slow-varying Band Limited Power. Interactions of the fast source level signal are evaluated through the Multivariate Interaction Measure. At both time scales, connectomes are estimated at the delta, theta, alpha, low and high beta, low, mid and high gamma bands. Group-level connectomes can be described using parcellation schemes. Preliminary results obtained from 80 HCP subjects will be presented.

Automated rejection and repair of bad trials in MEG/EEG

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We present an automated solution for detecting bad trials in magneto-/electroencephalography (M/EEG). Bad trials are commonly identified using peak-to-peak rejection thresholds that are set manually. This work proposes a solution to determine them automatically using cross-validation with a robust loss function. We show that automatically selected rejection thresholds perform at par with manual thresholds, which can save hours of visual data inspection, particularly in the case of large-scale studies such as the Human Connectome Project [1]. Applying this algorithm on 105 subjects of the BCI motor imagery dataset demonstrates that the learned thresholds are indeed different across subjects. Further, this method can now be used to automatically learn a sensor-specific rejection threshold. This results in detecting bad sensors with a finer precision on a trial-by-trial basis. In our proposed method, we automatically decide if the sensor in a trial should be interpolated or the trial should be rejected. Trials which have more than a certain number of bad sensors (rho) are rejected. Otherwise, the worst kappa sensors are interpolated using the rest of the sensors. The parameters rho and kappa are learnt using grid search. Finally, we illustrate the performance on a 19-subject Faces dataset [2]. The method clearly performs better than a competitive benchmark (RANSAC algorithm from the PREP preprocessing pipeline [3]) on this dataset.

References

[1] D. Van Essen, K. Ugurbil, E. Auerbach, D. Barch, T. Behrens, R. Bucholz, A. Chang, L. Chen, M. Corbetta, S. Curtiss et al., \"The Human Connectome Project: a data acquisition perspective,\" NeuroImage, vol. 62, no. 4, pp. 2222-2231, 2012.
[2] D. Wakeman and R. Henson, \"A multi-subject, multi-modal human neuroimaging dataset,\" Sci. Data, vol. 2, 2015.
[3] N. Bigdely-Shamlo, T. Mullen, C. Kothe, K-M. Su, and K. Robbins, \"The PREP pipeline: standardized preprocessing for large-scale EEG analysis,\" Front. Neuroinform., vol. 9, 2015.

Is it really the hippocampus?

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During complex cognitive processes such as spatial navigation or mnemonic processing, intricately coordinated computations are supported by the hippocampus. Magnetoencephalography (MEG) allows us to address the missing link between direct electrophysiological recordings of these signals in rodents, and spatially fine-grained, but temporally constrained, characterizations of human hippocampal functions from fMRI. Here we present an empirical demonstration of a new framework for testing, and probabilistically quantifying, whether the hippocampus is contributing to the measured MEG signal. Specifically, we use a Bayesian framework to compare two generative models of the same data; one which includes an anatomical model of the hippocampus, and one which does not.

The protocol for testing whether we can detect the hippocampus consists of four parts. Firstly, we use flexible and subject-specific head-casts to reduce head movement to <1.5 mm during scanning and thereby increase the signal-to-noise ratio (SNR). Secondly, the head-casts are constructed such that the fiducial coil locations are known in MRI space, effectively eliminating co-registration error. Thirdly, we ask subjects to perform a spatial memory task in the scanner which is known to give rise to hippocampal activation in humans (Doeller et al., 2008). Finally, we directly compare generative models based on subject-specific MRI-derived cortical and hippocampal surfaces. Preliminary findings suggest that we can make single subject inference on hippocampal involvement during a task.

Doeller, C.F., King, J. a, Burgess, N., 2008. Parallel striatal and hippocampal systems for landmarks and boundaries in spatial memory. Proc. Natl. Acad. Sci. U. S. A. 105, 5915–20. doi:10.1073/pnas.0801489105

Extended signal space separation for improved interference suppression

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Signal space separation (SSS) is an efficient method for suppressing external interference in MEG data. It is based on physics of magnetic fields and only requires accurate information about the sensor geometry of the MEG instrument, which makes SSS a general approach. The capability of SSS to suppress external interference is, however, limited by the inaccuracies in sensor calibration and geometry. After our fine-calibration procedure yielding an accuracy of 0.1%, SSS can typically suppress external interference by a factor of about 150. Still, larger suppression may be needed, e.g., in a light-weight magnetically shielded room (MSR) in a noisy hospital environment.

A different approach for interference suppression in MEG is provided by the signal space projection (SSP). It is based on statistics of the measured signals, and is thus insensitive to calibration and geometry inaccuracies. However, SSP is effective only against predefined interference field patterns, which are typically estimated from data recorded in the absence of a subject.

Here, we present an extension of SSS that increases the suppression of external interference without losing the generality of the method. We add the most dominant principal components (PCAout) estimated from an "empty room" recording to the SSS basis S = [Sin Sout, ext], where the extended external space Sout, ext = [Sout PCAout]. After orthogonalizating Sout, ext, we use it as in conventional SSS processing to model the data.

Due to the embedded statistical information, the extended SSS method is more robust towards the calibration and geometry inaccuracies than the conventional SSS. In a typical setting, we have measured that the suppression of external interference exceeds the factor of 1000, outperforming the SSS or SSP alone. The performance of the new method is demonstrated using simulations and phantom data with abundant external interference.

Time-domain signal subspace

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The notion of noise/signal subspaces has been introduced and used in biomagnetic signal processing. The representative method, signal space projection (SSP), uses it for artifact reduction [1]. So far, the signal subspace is defined in the spatial domain as the span of the source lead field vectors. This paper proposes to define the signal subspace in the time domain, i.e., the signal subspace is defined as the span of row vectors that contain the source time courses. By defining the time-domain signal subspace in this manner, we can derive key relationships for the time domain signal subspace, and clarify the correspondence between the spatial and time domain signal subspaces. For example, while the sensor array outputs at particular time is expressed as the linear combination of the source lead field vectors, the outputs of a particular sensor is expressed as the linear combination of the source time course vectors. Also, while the maximum likelihood estimate of the spatial domain signal subspace is the span of the spatial singular vectors of the data matrix, the time domain signal subspace is estimated as the span of its temporal singular vectors. Using the time-domain signal subspace, it is possible to interpret various noise/interference removal methods considered very different as the time domain SSP. Such methods include the adaptive noise canceling, sensor noise suppression [2], and recently proposed dual signal subspace projection [3]. The notion of time domain signal subspace can provide a broader perspective over existing and new noise/interference removal methods. Reference: [1] Uusitalo M et al., Biol. Eng. Comput.35, (1997):135–40.[2] De Cheveigné, et al., Journal of neuroscience methods,168(2008):195-202. [3] Sekihara K, et al. J. Neural. Eng.13(2016):036007.

Determining the importance of compensating for head movements during MEG acquisition across different age groups

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Unlike EEG sensors which are attached to the head, MEG sensors are located outside the head surface on a fixed external device. Subject head movements during acquisition thus distort the magnetic field distributions measured by the sensors. Previous studies have looked at the effect of head movements, but no study has comprehensively looked at the effect of head movements across age groups, particularly in infants. Using MEG recordings from subjects ranging in age from 3 months through adults, here we first quantify the variability in head position as a function of age group. We then combine these measured head movements with brain activity simulations to determine how head movements bias source localization from sensor magnetic fields measured during movement. We find that large amounts of head movement, especially common in infant age groups, can result in large localization errors. We then show that proper application of head movement compensation techniques can restore localization accuracy to pre-movement levels. We also find that proper noise covariance estimation (e.g., during the baseline period) is important to minimize localization bias following head movement compensation. Our findings suggest that head position measurement during acquisition and compensation during analysis is recommended for researchers working with subject populations or age groups that could have substantial head movements.

Reducing Noise in Electromagnetic Sensor Arrays Using Oversampled Temporal Projection

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Here we introduce a novel method to suppress sensor noise in electromagnetic sensor arrays. Similar to the effective method termed "sensor noise suppression" (SNS; de Cheveigné and Simon, 2008), our method requires that valid neurophysiological signals are spatially oversampled by the sensor array, which is a reasonable assumption for neural signals recorded using electro- or magneto-encephalography (EEG or MEG) sensor arrays. However, unlike previous denoising algorithms, our method suppresses artifacts by using projection in the temporal domain rather than smoothing or projection in the spatial domain. Specifically, for each channel, we form two orthonormal temporal basis sets: The first set is based on the signals of the other N-1 channels and the second set is based on the signal of all N channels. Then, we find the temporal difference of these two sets, conclude it as intrinsic sensor noise and project it out from the channel's data by orthogonal projection in the time domain. This method, which we call "oversampled temporal projection", effectively projects out any channel-specific noise that does not align with the direction of the temporal basis vectors of the other channels. For sufficiently long windows it achieves noise suppression factors on par with spatial methods. However, it has at least two important advantages over spatial methods. First, assuming that the channel-specific noise is statistically independent with other signals, our method does not impose any risk of distorting the spatial configuration of the data, and thus does not require any compensation for the spatial operation during source localization. Second, sparse channel-specific temporal artifacts, such as jumpy channels in MEG data, are suppressed by temporal projection without mixing with other channels, whereas spatial methods can inadvertently spread such artifacts to neighboring channels with a spatial profile resembling that of an electrophysiological source.

A fingerprint method for the automatic removal of physiological artefacts from EEG recordings

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Removal of physiological artefacts from electroencephalographic (EEG) and magnetoencephalographic (MEG) recordings is a challenging procedure for the extraction of genuine brain signals. Several methods have been proposed in the last decade. However, they are often (i) limited to a given electrode montage, (ii) tailored for the removal of well defined artefacts, (iii) requiring additional information on the artefactual source, (iv) developed for highly specific applications, and (v) validated on simulated artefacts.

We propose a novel ICA-based method for the automatic and unsupervised detection and removal of the most common physiological artefacts affecting EEG recordings (i.e. eye blinks, eye movements, muscle activity and cardiac interference). By means of ICA, EEG signals are separated in independent components whose features in the time, frequency, space and statistics domains are used to define the IC-fingerprints. Manually labelled IC-fingerprints are separated in artefactual and non-artefactual groups used to train a non-linear Support Vector Machine (SVM). The trained SVM is then tested for the automatic classification of ICs obtained in a large number of EEG datasets with triggered artefacts, and validated through unsupervised application in EEG datasets acquired during cycling. The outcome of automatic classifications is compared to expert-labelling.

Preliminary results show that sensitivity, specificity and accuracy of the IC classification are comparable to those of existing methods, with the advantage of being independent on the user, electrode montage and type of electrode (wet or dry), expandable with further IC features, free of additional artefact recordings. Future developments will include the detection of other artefacts of biological and instrumental origin, the method\'s optimization by selecting the most discriminant IC features, and its validation in multiple sport neuroscience applications, in neurological patients and neuro-rehabilitation.

Detection and reduction of mechanical vibration-induced interference in MEG

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Mechanical vibrations may cause unwanted interference on magnetoencephalographic(MEG) signals. Vibrations of the walls of a magnetically shielded room generate magnetic fields which are straightforward to suppress with spatial filtering methods like the Signal Space Projection (SSP) and the Signal Space Separation(SSS). However, the problems arise if the mechanical vibrations cause movementof MEG sensors. Such a vibration causes nearby interference which is difficult to reduce with spatial SSP or SSS methods.

We have used an accelerometer to detect the mechanical vibrations synchronously with MEG recordings. The aim was to identify the mechanical vibrations and the corresponding interference in MEG signals which was not reduced by SSP or SSS methods. Based on the accelerometer signals, we were able to detect the mechanical vibrations, and use these as reference signals to reduce the corresponding interference in MEG recordings. We applied the SSP method, on a narrow frequency band guided by the accelerometer signals, to reduce vibration-related disturbances in MEG data. The SSP approach showed a significant reduction of the vibration-related interference both in the emptyroom and resting state MEG data.

We show the potential of the accelerometer to detect and identify the troublesome mechanical vibrations. In addition, we demonstrate the effectiveness of the SSP method to reduce mechanically-induced interference on a narrow frequency band in MEG data.

Characterizing brain vital sign responses with magneto- and electro- encephalography

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Background: Event related neural responses provide objective, physiology-based indicators of brain function. However, the lack of translation into clinically accessible frameworks and long testing times have largely confined them to the laboratory. Recently, we demonstrated foundational work utilizing auditory sensation (N100), basic attention (P300), cognitive processing (N400) and contextual orientation (CO) neuronal responses as clinically accessible brain vital signs (BVS). This study aims to assess the feasibility of short testing times and characterize the resultant brain responses.

Methods: A short (5minutes) auditory stimulus sequence of words and tones was created to elicit N100, P300, N400 and CO-related brain responses. 151-channel MEG and concurrent EEG data were collected on 16 healthy individuals (18-40years of age). At the sensor level, MEG and EEG data were filtered (1-10Hz), segmented and conditionally trial averaged. Global field power (GFP) was measured along with non-parametric statistics. Polhemus data was co-registered with structural MRI, and utilized for dipole fitting and source localization in SPM8 software.

Results: Preliminary results confirm successful elicitation of all four neuronal responses in every individual. GFP results indicate the presence of N100-P300 complex ($p<0.001$), CO-related indicator at 380ms in EEG ($p<0.05$) and at 330ms post-stimulus in MEG ($p<0.05$) as well as N400 responses ($p<0.05$). Initial source projections indicate results consistent with previous literature (e.g. bilateral auditory cortex for N100).

Conclusions: The ability to elicit brain responses utilized as BVS within a short period of time enables the clinical translation of lab-based technologies. Confirmatory EEG results allow translating these advances into point-of-care devices, potentially enabling the utilization of this technique in bedside assessments of BVS. Continuing source and time-frequency analyses are further characterizing these responses.

Blink-related oscillations as indicators of awareness: Initial characterization using MEG

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Traumatic brain injury (TBI) often results in altered levels of consciousness, such as unresponsive wakefulness syndrome (UWS, i.e. awake but not aware) and minimally conscious state (MCS, i.e. awake with some awareness). Accurate assessment of key functional indicators like awareness is crucial to effective clinical management of TBI patients, yet no neural signatures of awareness have been identified to date. Recent low-density EEG studies point to a potential cognitive component associated with spontaneous blinks at rest, which may originate from important hubs within the brain's default mode network known to be impacted in TBI. These blink-related oscillations (BROs) may also correlate in strength with the differential awareness in UWS and MCS patients. Nonetheless, the neurocognitive mechanisms of BROs are not well understood, and we aimed to characterize BRO activity using MEG given its superior spatial resolution compared to EEG. We collected 10-minute resting state data on 40 healthy participants (age 18-40) using 151-channel MEG with simultaneous electrooculogram (EOG). Blinks were identified by convolution of EOG with a blink template, plus amplitude and temporal thresholding. Ocular artifact was rejected through independent component analysis. BROs were derived by wavelet analysis followed by inverse wavelet transform in delta range. Preliminary sensor-level results show that global wavelet spectral power was increased in the delta band (0.5-4Hz) during the first 500ms post-blink interval compared to pre-blink, consistent with prior EEG studies. The global field power of delta BROs exhibits peak activity in 300-500ms post-blink, a significant increase compared to pre-blink baseline ($p<0.05$). Ongoing work focuses on source localization of BROs and analysis of activity in other frequency bands. To our knowledge, this is the first study of BRO activity using MEG, and may provide crucial insight to a new avenue for evaluating awareness in TBI patients.

Novel sounds modulate oscillatory activity in visual cortex - the neural basis of behavioral distraction?

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Unexpected novel sounds capture one's attention, even when not relevant to the task at hand (e.g., playing video game). This often comes at costs to the task (e.g., slower responding). The neural underpinnings of behavioral distraction are not well understood and focused here. Our study was motivated by findings showing that oscillatory activity is sensitive to explicit modulations of attention. The current study tested whether modulations of oscillatory activity are also seen by a task-irrelevant auditory distractor, reflecting neural signatures of an involuntary shift of attention and accounting for the impaired task performance. Magnetoencephalographic data had been recorded to stimuli presented in an auditory-visual distraction paradigm. On each trial the task-relevant visual stimulus was preceded by a task-irrelevant sound. In 87.5% this was a regular sound (Standard), in 12.5% this was a novel sound (Distractor). We compared non-phase locked oscillatory activity in a pre-target time window as a function of the experimental condition (Distractor, Standard). We found low power in the pre-target time window for Distractors compared to Standards in the alpha frequency band. Importantly, individual alpha power correlated with response speed on a trial-by-trial basis for the Distractor but not for Standards. Sources were localized to the occipital cortex as well as to the parietal and supratemporal cortex. These data support our assumption that the modulated oscillatory activity accounts for behavioral distraction.

Using M-EEG to investigate pupillometry as a biomarker

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Pupillometry provides an inexpensive, non-invasive, involuntary measure of effort due to task difficulty. In multiple auditory behavioral studies in particular, pupillometry has been shown to correlate with the level of listening effort required to carry out selective listening tasks. Although pupillometry serves as an effective biomarker for effort, it remains unclear the extent to which different brain signals actually affect task-related pupil dilation. Previous fMRI studies have shown that the modulation of pupil dilation by task difficulty in particular is primarily related to BOLD activity in the human locus coeruleus-norepinephrine (LC-NE) system. However, behavioral and fMRI studies primarily give us insight into the long-term relationship between brain activity and pupil dilation. Although the time constant of the pupil response is on the order of a second, deconvolution of pupil signals can be used to improve timing precision to closer to 1/10th of a second. This allows us to resolve changes in pupil dilation within the time scale of single trials at a behaviorally relevant scale in auditory experiments. In the current study, we recorded simultaneous pupillometry and magneto- and electro-encephalography (M-EEG) in subjects performing a selective listening task. We use source localization combined with correlation measures to examine how cortical activity relates to pupil dilation during auditory tasks.

Switching between temporal and spatial attention in older adults: an investigation into age-related changes in underlying neural mechanisms

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One is often required to switch from attending to events changing in time, to distribute attention spatially (e.g. when driving). Although there is extensive research into both spatial attention and temporal attention and how these change with age, the literature on switching between these modalities of attention is limited regarding any age group. In a pilot study, we have found age-related changes in the ability to switch between temporal and spatial attention. To investigate the neural mechanisms that underpin these changes in attention switching, magnetoencephalography was recorded while participants performed a switching task. Age groups (21-29, 40-49, and 60+ years) were compared on their ability to switch between detecting a target in a rapid serial visual presentation (RSVP) stream and detecting a target in a visual search display. To manipulate the cost of switching, the target in the RSVP stream was either the first item in the stream (T-1st), towards the end of the stream (T-mid), or absent from the stream (Absent). Visual search response times and accuracy were recorded. Preliminary analyses of behavioural data revealed greater switch-costs in the 60+ years group (n=6) in comparison to the 21-29 years group (n=8). There were also differences in alpha, theta and gamma modulation between switch and no-switch conditions, and this modulation will be compared across age groups. Findings will help to define the neural mechanisms within the attentional network that are involved in switching between these two modalities of attention. Furthermore, we hope to explain the change in switching between spatial and temporal attention that occurs with age by revealing age-related changes in these neural mechanisms.

Spatiotemporal expectations in complex sequences

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Studies on temporal orienting of attention often investigate simple, regular rhythms and probabilities, or use explicit cues to induce expectations about when a target can be expected or when a response has to be made. However, a lot of our behaviour entails more complex, implicitly acquired patterns of temporal information embedded in sequences of events, i.e. non-isochronous rhythms. This study investigates the implicit acquisition and learned performance of combined ordinal (spatial/effector) and temporal sequences using magnetoencephalography and functional magnetic resonance imaging (fMRI). A modified version of a serial reaction time task was used, in which not only the order of targets, but also the order of intervals between subsequent targets was repeated. Occasionally probe blocks were presented, where a new (unlearned) ordinal-temporal sequence was introduced. Our behavioural results show that participants not only get faster over time, but that they are slower and less accurate during probe blocks, indicating that they (implicitly) learned the sequence information. The oscillatory signature of these combined ordinal (spatial/effector) and temporal preparatory effects is shown for a range of frequency bands, over motor and sensory areas. The fMRI localiser task shows that hippocampal and visual areas are more active for new, compared to repeated sequences.

Selectivity of tactile attention: an MEG study

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To reveal the selectivity of tactile spatial attention, we investigated the distribution of modulation of somatosensory evoked magnetic fields in a tactile spatial attention task using magnetoencephalography(MEG). Electrocutaneous stimulation was delivered to any one of five fingers of the right hand in a random order through the ring electrodes. Interstimulus interval varied randomly between 750-1250 ms. Subjects were instructed to attend to the index or ring finger or both, and to silently count the double-pulse stimulus infrequently presented there as a target stimulus. Neural responses to the electrocutaneous stimulation were recorded using a 306-ch whole-head MEG system. A response around the primary somatosensory cortex (SI) was not significantly changed by tactile attention whereas the response around the secondarysomatosensory cortex (SII) peaking at 80-120 ms~ was increased in magnitude especially when the stimulated finger was congruent with the finger attended. Thus, the present study demonstrated the selectivity of modulation of the SI and SII responses by directing tactile spatial attention to the finger.

Delayed middle latency auditory evoked response during propofol-induced loss of consciousness

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This study aims to evaluate propofol's dynamical effects on human middle latency auditory evoked response (MLAER). We received written consent of 20 patients, 18-65 years of age and both male and female, undergoing cervical spine surgery. All surgical procedures were continued under intravenous anesthesia. As baseline, we collected spontaneous electroencephalogram potentials for 4 minutes, eyes closed. Auditory evoked potentials (AEP) were measured using roving oddball paradigm. We controlled propofol concentration at target effect-site concentrations of 5, 4, 3 g/ml at steady-state for at least 10 minutes each. For each subject, the latency and amplitude of components Pa, Nb, and P1 at each target propofol condition were identified within a 0 ms to 100 ms time window. In order to compare means from each condition, we performed paired t-tests. We found that propofol's main LOC effect is accompanied by a delay in latency and decrease in amplitude at components Pa, Nb, and P1 ($p < .05$). Pa is generated in the auditory cortex, and there is good evidence of subcortical contribution to the response. P1's generator appears to be in the thalamic cholinergic neurons of the ascending reticular activating system. It is well known that the ascending reticular activating system is responsible for the neural management of wakefulness. We suggest that the delay of latency and attenuation of amplitude seen in MLAER reflects the failure of the ascending reticular activating system to be activated. Essentially, the ascending information that needs to be communicated is being withheld or suppressed at the subcortical level. This may be due to the inhibitory effects caused by GABAergic propofol, thereby leading to decreased thalamo-cortical connectivity. Acknowledgements: This study was supported by the National Research Foundation of Korea funded by the Ministry of Education, Science and Technology (2012R1A1A3007555), and the Ministry of Education (2015R1D1A1A02061486).

See the touch of the sound: Common signatures of conscious access across sensory modalities

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Everyday, we need to integrate environmental information gathered across our senses. How does our brain integrate and select incoming percepts from different sensory modalities? What are the determinants and mechanisms of conscious perception? These questions remain one of the main goals in cognitive neuroscience. Previous research showed that oscillatory activity (i.e. alpha band 8-14Hz) prior to upcoming stimuli – considered to reflect local cortical excitability – influences conscious perception. However, distinct global network states can determine whether near-threshold stimuli will be consciously perceived. In this study we aimed to investigate whether similar neural correlates can account for conscious perception independent from the sensory modality targeted during the experiment.

We presented participants (N=19) with successive blocks of near-threshold experiments involving tactile, visual or auditory stimuli during the same magnetoencephalography (MEG) acquisition. Sensory stimulation intensities were determined prior to the experiment with a staircase procedure in order to get a 50% detection rate. Group analysis confirmed previously reported pre-stimulus effects within each sensory modality. Oscillatory activity influences whether near-threshold stimuli will be consciously perceived or not. Concerning neural activity in the post-stimulus period, several frameworks emphasize the importance of global integration and recurrent activity between sensory and higher-order regions for conscious perception. We examined which brain activity predicts perception using multivariate pattern analysis of MEG data. Using decoding analysis in the post-stimulus period between sensory modalities we were able to show that the same neural activity seems to underlie conscious perception in all modalities. Interestingly, our findings reveal a common signature of consciousness across modalities and provide important new insights for the understanding of conscious perception.

Temporal and spatial differences in the theory of mind network in children with and without autism spectrum disorder

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Theory of mind (ToM), or the ability to recognize that other people have thoughts or feelings separate from one's own, is a complex social skill that is often impaired in individuals with autism spectrum disorder (ASD). While the brain regions underlying normal and impaired ToM have been explored using fMRI, few have established the timing of activity in these areas in the healthy population, and none have used MEG to investigate how this aspect of neural processing may differ in ASD during childhood, a time in which social skills are still developing. We examined whether children (8-12yrs of age) with ASD (n=19) and typically-developing (TD) children (n=22) exhibit temporospatial differences in brain activity when engaging ToM functions. To assess this ability, children performed a task that required them to understand that another person may have a mistaken or false belief about the location of an object, in the MEG scanner (CTF; MISL). Whole-brain analyses (all $p<0.005$) using SPM12 revealed that compared to TD children, children with ASD showed reduced activity in the left temporoparietal junction, a region often associated with ToM, from 325-375ms and 425-475ms, and they more strongly recruited the contralateral right temporoparietal junction at a delayed period from 475-600ms, in addition to other brain areas related to executive function, such as the right dorsolateral prefrontal cortex between 325-400ms, the left inferior frontal gyrus between 500-550ms, and the left superior temporal gyrus between 500-600ms. These results suggest that children with ASD may employ alternative cognitive strategies, such as working memory-related compensatory mechanisms, during social inference. Our following analyses will focus on brain connectivity to examine whether the ToM and other executive function networks interact or are structured differently in children with and without ASD, as we predict that in children with ASD, these networks may not be as distinct.

Inhibitory Alpha activity mediates rhythmic sampling of visual objects

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To deal with a crowded visual scene, it is important that attention is allocated over time and space efficiently. Previous studies suggest that attention acts as a moving spot light dwelling on each location serially, whereas other studies reveal that attention can stay on multiple locations simultaneously. Interestingly, recent behavioral findings demonstrate rapid temporal fluctuations in attentional behavior, suggesting that attention shifts between two spatial locations rhythmically. However, the underlying neuronal mechanisms remain completely unexplored. In the present study, we combined covert attentional paradigm and temporal response function techniques (TRF) to address the issue. EEG was recorded from fifteen human subjects as they were presented with 5-sec dynamic sequences at two spatial locations and were asked to attend to one of them. Notably, the visual sequences at the two locations were randomly modulated in luminance and were independently controlled, so that we can estimate the TRFs for attended and unattended visual sequences separately (Att vs. Unatt). First, compared to Unatt condition, TRFs for Att condition showed an alpha-band (~10 Hz) power inhibition around 100ms, commensurate with previous findings that alpha activities represent inhibitory processes during attention. Second, the alpha inhibition did not display spatial specificity as found before (e.g., decrease on contralateral side and increase on ipsilateral side), suggesting that it may represent an object-level attention independent of spatial information. Third, the alpha inhibition was followed by an alpha enhancement, indicating an attentional switching from attended to unattended location. Finally, this alpha switching pattern was modulated by attentional cuing validity. Specifically, as the cuing validity decreased (from 100% to 75% and 50%), the Att-Unatt alpha switching pattern became stronger. Our findings demonstrate that attention efficiently and flexibly distributes over space and time to accommodate changing task demands, and samples multiple visual objects rhythmically, by modulating and coordinating inhibitory alpha-band neuronal activities.

Modulation of visual gamma oscillations by selective spatial attention

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Neuronal synchronization in the gamma range (30-90 Hz) is a prominent feature of the cortical response to visual stimulation. According to theoretical proposals and empirical evidence, the modulation of gamma oscillations in visual cortex could represent a mechanism by which selective attention enhances stimulus processing [1]. A recent study reported an increase in the peak frequency of the gamma response in monkey V1 when stimuli were selected by attention, compared to when the same stimuli were unattended [2]. In human visual cortex, however, the modulation of gamma amplitude and frequency by attention remains unclear [3]. Here, we present an MEG study in which twenty healthy participants performed a visuospatial attention cueing paradigm, in which the task consisted of an orientation change discrimination. The experimental paradigm was designed to produce clearly measurable, sustained visual gamma responses in two conditions that differed only by the allocation of spatial attention, i.e. either towards or away from the stimulus. Across participants, we found a statistically significant increase in gamma amplitude for attended stimuli, compared to unattended ones. In contrast, despite peak frequency was measured unambiguously using a bootstrap method [4], we found no evidence for an effect of attention on gamma frequency. Our findings are discussed in light of the inter-individual differences in behavioural performance to the orientation change discrimination task. [1] Fries (2015). *Neuron*, 88(1), 220-235. [2] Bosman, Schoffelen, Brunet, Oostenveld, Bastos, Womelsdorf, ... & Fries (2012). *Neuron*, 75(5), 875-888. [3] Koelewijn, Rich, Muthukumaraswamy & Singh (2013). *NeuroImage*, 79, 295-303. [4] Magazzini, Muthukumaraswamy, Hamandi, Lingford-Hughes, Myers, Nutt, Wilson & Singh (2016). *Under review*.

MODULATIONS OF ALPHA POWER DURING ENCODING MEDIATE POSTERIOR ALPHA ACTIVITY DURING WORKING MEMORY RETENTION

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Oscillatory brain activity in the alpha frequency range (8-14Hz) has been associated with facilitated information encoding, retention, and working memory maintenance. Lateralized stimulus presentation typically induces hemisphere-specific modulation of alpha activity, which is indicative of the allocation of processing resources, whereas the magnitude of parieto-occipital alpha power is related to the number of items held in working memory. The present study sought to specify the relationship between alpha amplitude during encoding and during retention as a function of working memory load. The magnetoencephalogram was monitored while 15 participants performed a modified Sternberg task. Participants fixed their gaze on a centrally presented cross during each of the 320 trials, which involved 500 ms cued anticipation of lateralized memory set presentation, attending the cued hemifield of a 2000 ms bilateral stimulus array containing memory sets of varying size (1, 3 or 5 items), a 2000 ms retention interval, and central probe letter to which participants were to respond by button press indicating whether the probe was in the target memory set. During stimulus encoding, parieto-occipital alpha (11 Hz) activity decrease contralateral to the hemifield of memory set presentation varied with set size. Subsequently, parieto-occipital alpha power increased as a function of set size during retention of the stimuli. Stimulus encoding was accompanied by occipital gamma (40-60Hz) power increase, thus, inversely to alpha power modulation. Lateralized alpha power decrease during stimulus encoding correlated significantly with alpha power increase during retention, indicating the functional significance of cued attention deployment for item encoding in subsequent retention. Results suggest a mechanism of efficient stimulus encoding indexed by modulations of alpha power that mediates subsequent retention processes reflected inposterior-occipital alpha power modulations.

Alpha band functional connectivity supports successful active inhibition associated with Selective Attention

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Directing covert attention to a portion of visual space is a process that modulates inhibitory alpha oscillations in the human occipital cortex [1]. We aimed at characterizing the functional connections in the extended visual system and their relationship with anatomical connections to better understand the mechanisms modulating the inhibitory alpha band activity in relation to performance.

To this end, we relied on MEG data from a cued visuospatial attention task [2] in which visual cues directed attention to the left or the right visual field after which a pair of target Gabor patches were presented bilaterally. In this task, occipital alpha oscillations (8–12 Hz in the 1s cue-target interval prior to stimulus presentation) are robustly modulated by direction of attention.

We assessed the modulations in the alpha band based on functional connectivity (FC) with respect to bilateral occipital cortex ('reference region') in the 1s interval before the cue presentation and in the cue-target interval by the Multivariate Interaction Measure (MIM) [3], a frequency domain FC metric based on the maximization of the imaginary part of coherence between two regions. Our results show that there is directed FC from parietal to occipital cortex in the cue-target interval. This FC response is larger in the hemisphere ipsi-lateral to the cued direction. Moreover, subjects with a larger attentional modulation in FC in a given hemisphere also show a larger volume of the second branch of the superior longitudinal fasciculus in the same hemisphere, as well as a better performance for targets presented ipsilaterally to that hemisphere.

Taken together, our results support a potential role for alpha band occipito-parietal functional connectivity in active inhibition as mediated by the superior longitudinal fasciculus.

[1] Jensen & Mazaheri, Front Hum Neurosci 2010

[2] Marshall et al., Plos Biol 2015

[3] Marzetti et al., Neuroimage 2013

Integration across different spatial reference frames

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On a daily basis we are confronted with a rich environment that contains a large number of stimuli that need to be processed and integrated by our senses. It is well known that different senses involve different spatial reference frames (eye- centered, hand-centered, head-centered etc.). Yet it is not clear how these different spatial reference frames are aligned across senses and by what means such alignment is modulated by attention. In order to investigate this we manipulated attention to sensory modality in a multisensory spatial congruency task. On every trial we presented three discrete, temporally synchronous stimuli (100 ms) in different modalities (audition, vision and touch) while recording MEG. Top-down control (task) was manipulated across separate blocks. Participants were cued to pay attention to various stimuli pairs (audio-tactile, audio-visual, tactile-visual) and report whether they were spatially congruent or not. In 80% of the trials all of the stimuli were spatially aligned (right or left), while in the rest of the trials one modality acted as a distractor. We found that pre-stimulus and evoked activity differed across attention conditions, even though the stimulus was identical. This suggests that an alignment of different sensory reference frames happens"online", which we currently further investigate through pre- stimulus connectivity analyses as well as minimum-norm estimation of evoked responses in source space. A comparison of evoked response for congruent and incongruent trials will further highlight the benefits of such a spatial alignment.

The Theory of Mind network: brain connectivity patterns underlying ToM processing in adults

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Theory of mind (ToM) is the ability to understand that others can have mental states, beliefs, and knowledge different from one\'s own. ToM is crucial for positive social interactions and interpreting social cues. Although studies have investigated brain areas activated during ToM processing, the relation between activated regions and the timing of activations within this complex network are unknown. We used 151-channel CTF MEG to image 23 adults (12F, 20-35yrs) as they performed a ToM task involving understanding whether a character on screen had a true or false belief. MEG data were coregistered to a T1-weighted structural MRI (Siemens Trio 3T). Time series from 90 cortical brain regions of the AAL atlas were estimated using the FieldTrip LCMV beamformer, filtered at theta (4-7Hz), alpha (8-14Hz), beta (15-30Hz), low (30-55Hz) and high gamma (65-80Hz) bands, and phase extracted using the Hilbert transform. Connectivity between regions was estimated with the Phase Lag Index. Partial Least Squares were used to identify connections with significant activity changes during ToM processing. We found significant increases in connectivity in the false belief condition over the true belief condition. Occipital and parietal areas were highly central in early time windows (100-250ms); frontal and temporal areas were highly central later (250-400ms). Overall, central nodes in the ToM network were right lateralized. In alpha, the right angular gyrus (rAG) was a hub connecting bilateral parietal and left temporal nodes with the right inferior frontal gyrus (rIFG). In beta, the rIFG connected left mid frontal nodes with the rAG and other right parietal nodes. ToM processing in an adult control population recruits long-range synchrony in the brain with early visual occipital connections, shifting to the rAG and rIFG in both alpha and beta frequency bands. These results are coherent with MEG source localisation, showing highly right-lateralised activity, anchored in the AG.

Electromagnetic functional connectivity underlying anaesthetic-induced reductions in consciousness.

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A breakdown in parietal level electroencephalographic (EEG) brain networkfunctional connectivity is a common network change observed with different anaesthetics at doses leading toreductions in consciousness. This is particularly true for the general anaesthetic propofol (gamma-aminobutyric acid - GABA - receptor agonist) and the weak anaestheticnitrous oxide (N-methyl-D-aspartic acid - NMDA - receptor antagonist). Here we show that reductions in consciousnessinduced by the general anaesthetic Xenon (NMDA receptor antagonist) are alsolinked to a breakdown in parietal level brain network functional connectivity,as well as other network changes. Three subjects underwent increasing levels ofXenon inhalation (8%, 16%, 24% and 42% Xenon/O) until loss ofresponsiveness was obtained and while high density 64 channel EEG was recordedalong with magnetoencephalographic (MEG) data (Elekta NeuroMag). Electromagnetic (EEG/MEG) functionalconnectivity for full-brain, frontal and parietal level networks was defined asthe topological global efficiency in the network (derived fromsurrogate-corrected zero-lag correlations). Responsiveness was tracked using anauditory task. Loss of responsiveness was obtained in 1 subject and 2 subjectsat peak gas levels of 24 and 42%, respectively. For each individual, loss ofconsciousness coincided with statistically significant ($p<0.05$) reductions on the order of 25% in parietal level functionalconnectivity compared to rest. Together with prior studies, this suggests that abreakdown in parietal brain network functional connectivity is the common brainnetwork change underlying agent-invariant anaesthetic-induced reductions inconsciousness. These results aid in understanding how anaesthesia causesreductions in consciousness and suggest a potential parietal backbone forgenerating global states of consciousness.

P1 and traveling alpha waves in the MEG

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A variety of studies have shown that ongoing alpha oscillations are characterized by topographical phase relationships that can be interpreted as traveling waves. Most interestingly, the P1 component of the visual ERP in the EEG has been shown to exhibit topographical latency differences that also can be considered a manifestation of an evoked traveling alpha wave. In the current study, we aim to investigate how an ongoing alpha oscillation develops into an evoked, traveling alpha wave. We present MEG data from a visual target detection task in which we analysed the topographical phase relation of pre- and post-stimulus alpha waves on a single trial basis. Our findings indicate that prestimulus alpha waves develop almost seamlessly into the P1. In addition, the results suggest that an evoked traveling wave during a poststimulus period is initiated by a partial phase alignment in the pre- and peristimulus period.

When the brain changes its mind: oscillatory dynamics of conflict processing and response switching in a flanker task

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Stimulus evaluation and response preparation streams are activated in parallel and are seamlessly integrated with executive functions. This study examined engagement of cognitive control and the two processing streams during conflict conditions and their relative susceptibility to alcohol. Healthy social drinkers were given either a moderate alcoholic beverage or a placebo on two separate visits. Whole-head MEG was acquired while subjects performed a color version of Eriksen flanker task that manipulates S-R compatibility between central targets and irrelevant flankers. Incongruency occurred on the stimulus (SI) or response level (RI), the latter requiring a switch from the inappropriate response primed by the flanker to the correctly responding hand. Morlet wavelets were used to calculate event-related source power in theta (4-7Hz) and beta (15-25Hz) frequency bands in an anatomically-constrained MEG model. Flanker interference caused lower accuracy and longer RTs on RI trials, which were affected by alcohol. Beta desynchronization in bilateral motor areas (MOT) tracked motor preparation and response with temporal precision: an early priming effect of the flanker color induced greater beta decrease, which in RI trials was seen in MOT opposite the responding hand. Response-locked beta analysis revealed 'switching' from the incorrectly-primed to the correctly-responding hemisphere in RI trials. Theta power in prefrontal and motor regions was sensitive to the levels of incongruity, especially to RI in the right inferior frontal (IFC) and anterior cingulate cortices (ACC), which was also indicated by phase-locking measures. Theta was strongly reduced under alcohol, while beta was only subtly affected. Our results support other extensive evidence of beta as an index of motor preparation. They confirm that the preparation happens automatically but that it is monitored and regulated by cognitive control processes subserved by the ACC and IFC.
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Transient modulation of neural responses to heartbeats reflects bodily self-consciousness

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Prominent theories hold that neural representations of internal bodily signals underlie self-consciousness, which to date has primarily been based on conceptual formulations (Craig, 2009; Critchley et al., 2013; Damasio et al., 2013; Park et al., 2014a; Blanke et al., 2015) and behavioral studies (Aspell et al., 2013; Suzuki et al., 2013). Thus far, however, direct experimental evidence linking the neural representations of interoceptive signals and self-consciousness is missing. We tested this hypothesis by measuring neural responses to heartbeats (Park et al., 2014b) in the visuo-tactile full-body illusion task (Lenggenhager et al., 2007). We recorded EEG and ECG signals from 16 human participants while they were exposed to multisensory visuo-tactile stimulation. In each block, participants' backs were stroked either synchronously or asynchronously with their own back image virtually presented through a head-mounted display. Increased self-identification (Q1) and illusory touch (Q2) for the virtually viewed body were obtained in the synchronous condition compared to the asynchronous condition (both $P<0.01$). The HEP amplitude significantly differed between synchronous and asynchronous conditions (cluster-level $P=0.01$) over frontocentral regions in the 250-305 ms post R-peak period. Across blocks, we found a significant correlation between HEP amplitudes and illusory rating. Cortical sources of the differential HEP were identified in the bilateral posterior cingulate cortex (PCC) (both cluster-level $P<0.05$). Finally, control analyses excluded that cardiorespiratory parameters (e.g., ECG amplitude, heart rate, heart rate variability, respiration) or interoceptive sensitivity traits (e.g., heartbeat perception scores) could account for this finding. The present findings provide robust neurophysiological evidence supporting the proposed relationship between the brain's mapping of the internal body and self-consciousness.

The spatio-temporal dynamics of 'Theory of Mind' in school age childrenborn very preterm

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Very preterm birth (<32 weeks gestation age) has been implicated in social-cognitive deficits that persist to adulthood. However, the neural bases for these deficits have not been examined. In the current study, we used MEG to assess Theory of Mind (ToM); the socio-cognitive ability to understand the mental states of others. We used a Jack and Jill false belief task, a classic measure of ToM that assesses the ability to understand that others' beliefs can be incongruent with reality and one's own, in school age (7-13 years) children born very preterm (VPT) compared to full-term born (FT) peers. We found that VPT children employ a very different pattern of activation in false belief understanding compared to FT children,despite similar behavioural task performance. Whereas FT children recruited regions from the ToM network reported in fMRI studies, such as the temporo-parietal junction as early as 200ms, in addition to frontal, temporal and parietal regions to process the false beliefs of others, VPT children recruited only temporal regions such as the inferior temporal gyrus, the right temporal pole and the middle temporal gyrus from 100 - 500ms. These findings demonstrate marked differences in neural processing of socially relevant information in children born very preterm, suggesting quite distinct strategies. Future analyses will determine the connectivity of these regions during the Theory of Mind task to understand which regions form the 'hubs' in VPT children's ToM network.

MEG correlates of internalization of social influence

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Socialpsychology has robustly demonstrated the strong social influence of groupopinions on those of individuals. Previously, it was difficult to distinguish atrue change of opinion evoked by social influence from mere public compliance. A recent fMRI study (Zaki et al., 2011) suggested that social conformity indeedchanges subjective values as indicated by long-lasting changes of the activity inthe orbitofrontal cortex and striatum (Zaki et al., 2011). Inthe present study, weused a paradigm in which participants' initial judgments about thetrustworthiness of faces were open to the social influence of group opinion (Campbell-Meiklejohn et al., 2012). Participantsrated the trustworthiness of faces, and, after each rating, they were informedof the "average group rating" assigned to the face by a large group of people.The MEG signal was recorded with a 306-channelElekta Neuromag system (n = 15) 30 min after the exposure to the group (normative)opinion.Wecompared evoked responses to faces that were previously rated similarly both bya subject and by a group (no-conflict trials) with evoked responses to facesthat were rated differently (conflict trails). In the sensor space, we found asignificant difference at the centroparietal sites: a cluster-correctedpermutation test both for magnetometers ($p = 0.028$) and gradiometers ($p = 0.002$).Source analysis demonstrated the significant difference between conflict andno-conflict trials bilaterally in the posterior medial cortex: left precuneus:$p = 0.03$; right precuneus: $p = 0.01$. Our MEG results suggest that activity of theprecuneus encodes long-lasting effects of social influence.

Neural and pupil diameter effects of mental fatigue

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Involvement in long lasting cognitive activities associated with considerable mental fatigue leads to deficits in attention and hence difficulties in performing tasks that require concentration and sustained effort. The psychophysiological and behavioral aspects, and neural signatures of this phenomenon are still a subject of ongoing research.

To study the mechanisms of mental fatigue, we collected MEG data while subjects performed an attention demanding task known as multiple object tracking (MOT). The MOT task involved tracking several objects (target dots) moving in random directions on a screen together with other distractor dots. The number of target dots varied randomly in trials, enabling us to investigate the relationship between task difficulty, attention, and mental fatigue. We further collected data from an eye tracker and a high speed camera, aiming to develop a computational model predictive of neuro-motor representations of fatigue. The subjects performed the MOT task for 3 hours without any rest periods. Every 30 minutes they were prompted to assess their resistance against continuing the task, which is a self-report measure previously shown to highly correlate with mental fatigue.

Analysis of MEG data showed a gradual increment in alpha band power over the duration of the task, which illustrates an adverse impact of fatigue on attention throughout the experiment. Moreover, alpha power was inversely related to task difficulty and thus mental effort. The eye-tracker data revealed the pupil diameter increased with task difficulty, corroborating previous studies on pupil size as a measure of individual's attentional efforts (Alnaes et al.,2014). Furthermore, our data demonstrated that pupil diameter consistently increased over time, indicating the task necessitated increased mental efforts to maintain performance towards the end of the experiment.

Spectro-temporal and Functional Connectivity Dynamics of Visuospatial Attention

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Visuospatial attention is characterized as the preferential allocation of neural resources towards processing in a specific part of the visual space, and is paramount to normative cognitive function. This process is well studied, and involves a bilateral network of frontal, parietal, and visual cortices. Herein, we utilize a data-driven approach and the precise temporal resolution of magnetoencephalography(MEG) to map the evolution of visuospatial attention processing in a group of healthy adults. During MEG, participants completed a novel task that required attention to specific aspects of the visual space in order to make spatial judgements. Time-frequency windows that showed a significant change from baseline were imaged using a beamformer approach, and the resulting images were statistically analyzed. Time series and measures of dynamic functional connectivity were extracted from the peak voxels of the statistical parametric maps (SPM). We found significant oscillatory dynamics in bilateral regions of the inferior frontal, parietal, and visual cortices. Functional connectivity (i.e.,phase-locking value) between these regions increased significantly during specific phases of attentional allocation. We conclude that visual attention involves a widespread network of functional brain regions, and that these regions contribute to differential components of visuospatial attention processing.

Temporal expectation biases duration judgment

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Timing processes in humans are typically classified into implicit and explicit timing: explicit timing requires explicit usage of the temporal dimension to estimate duration of a given time interval. On contraire, implicit timing entails the use of the temporal dimension to create temporal expectation with respect to the upcoming stimulus. The simplest form of temporal expectation is linked to the buildup of anticipation informed by the hazard rate function. As temporal expectation is known to affect sensory processing, we set out to test how temporal expectation affects duration perception in order to address the interplay between implicit and explicit timing processes which are rarely considered. We asked participants to discriminate time intervals. On each and every trial the standard duration (860ms) was presented, followed by the presentation of the comparison interval (770, 860, 950ms; 10%, 80%, 10% of all trials respectively). Crucially, the inter-stimulus intervals (ISI), that is interval between the SI offset and the CI onset, were uniformly distributed which allowed participants to build up an anticipation function with regard to the occurrence of the CI, as evidenced by the proportion of ‘short’ and ‘long’ responses. To investigate how the expectation of the comparison interval affects duration perception, we split trials according to their short and long ISI (‘early’, ‘late’). Within these two groups we investigated differences in the oscillatory power and inter-trial coherence (ITC) between trials subjectively perceived as ‘short’ and ‘long’. For the ‘late’ trials the processing of the comparison interval has been associated with the modulation of alpha power, and the modulation of the ITC, predominantly in the theta band. Together, these results demonstrate that temporal expectation modulated duration judgments by desynchronization of oscillatory power and enhancement of ITC.

Stimulus Driven and Mechanistic Neurodynamics of Inhibitory Control

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Inhibitory control is a key facet of the mechanisms which allow for goal-directed behavior. Within this context the stimulus that drives the inhibitory process has been implicated at one's ability. We investigated the processes that are driven from the stimulus (i.e. house or face) and those processes that are more mechanistics-independent. The investigation used magnetoencphalpography whilst human participants performed a Go/No-Go task. Results indicate that a general top-down mechanism of inhibitory control was modulated by specifics of the stimulus.

Alpha-band phase synchrony connects frontal, parietal and visual cortices during anticipatory visuospatial attention

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Covert orientation of visuospatial attention facilitates neuronal processing of attended and suppresses processing of unattended stimuli. This effect, possibly mediated by prefrontal and posterior parietal cortices, is associated with stronger suppression of alpha frequency-band (8-15 Hz) neuronal oscillations in visual cortex contralateral to attention. While in primates long-range neuronal synchronization between brain areas mediates attentional effects, it is still unknown whether similar mechanisms underlie attentional control in humans. We hypothesized that long-range neuronal synchronization underlies the integration and coordination of cortical activity across frontoparietal and sensory cortices and thus supports endogenous visuospatial attention. We recorded magnetoencephalography data during a Posner-like visual discrimination task where participants attended preferentially to either visual hemifield. Using data-driven analyses,we estimated large-scale phase synchronization from source-localized MEG data to identify the cortical networks of inter-areal synchronization associated with visuospatial attention. The coordination and maintenance of visuospatial attention was associated with sustained high-alpha band (10-14 Hz) inter-areal phase synchronization in a network comprising bilateral task-relevant visual, parietal, and frontal cortices.The strength of alpha-band synchronization was correlated with attentional modulations of both local low-alpha oscillation amplitudes and RTs across participants. High-alpha-band long-range phase synchrony seems to not only regulate local neuronal activity and inter-areal cooperation in frontoparietal and visual areas during visuospatial attention but also to play a functionally significant role in both enhancing attended and suppressing unattended information. High-alpha-band large-scale synchrony may thus be the key mechanism supporting endogenous modulations of local neuronal activity in sensory cortices.

Attentional modulation of response inhibition in a Go/No-Go task: spatio-temporal oscillatory dynamics in an anatomically constrained MEG model

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Response inhibition is an integral aspect of cognitive control whose neural mechanisms have been studied extensively. However, the attentional aspects of response inhibition have not been fully elucidated. To investigate these effects on response inhibition, 22healthy right-handed participants (10 female) performed a modified Go/No-Go task. Equal numbers of Go and No-Go stimuli were altered in both size and color to be more visually salient (SAL), yet participants responded in the same manner to SAL stimuli as the regular, non-modified stimuli (REG). The MEG signal (Neuromag Vectorview, Elekta) was spectrally decomposed for each trial using Morlet wavelets in the theta (4-7 Hz) frequency band. Each participant\'s cortical surface was reconstructed from high-resolution anatomical MRIs serving to constrain the distributed minimum norm inverse estimates. Task accuracy was differentially affected by stimulus type where SAL stimuli improved accuracy on No-Go trials but hindered accuracy on Go trials. Similarly, SAL Go response times were slower than REG Go, reflecting attentional capture. Successful response inhibition elicited an event-related theta power increase,peaking at ~300 ms, in a bilateral network including the inferior frontal, anterior cingulate, and insular regions, and right lateral temporal cortex. Overall there was a greater theta band increase in response to SAL stimuli compared to their REG counterparts as well as increased theta power to No-Go compared to Go trials. However, the anterior cingulate (ACC), inferior frontal (IF), and lateral temporal regions (LT) showed particular sensitivity such that the theta power was the greatest to SAL No-Go trials. Though the activation in the ACC and IF was bilateral, the theta power increase estimated to the LT was strongly right-lateralized. Taken together, these data suggest that attentional capture plays a crucial role in informing and invoking the response inhibition system in an interactive manner.

Oscillatory Dynamics in the Dorsal and Ventral Attention Systems during the Reorienting of Attention

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The ability to orient attention to relevant sensory information and reorient attention to new incoming information is central to daily functioning. Previous research has established that activation within two networks underlie attentional reorientation: the dorsal and ventral attention networks (DAN, VAN). However, no studies to date have characterized the oscillatory dynamics serving the reorienting of attention. In the present study, we utilized magnetoencephalography (MEG) and a Posner task to investigate attentional reorientation in healthy adults. MEG data were evaluated in the time-frequency domain and significant oscillatory responses were imaged via a beamformer. Oscillatory responses underlying the presentation of invalidly cued targets were then compared to those of validly cued targets. Our results indicated strong decreases in beta oscillatory activity in bilateral superior parietal lobules (SPL) and occipital cortices during the 600 ms following the presentation of the target, regardless of whether a valid or invalid cue preceded it. Early in the time course (0-300 ms) these decreased occipital beta responses were of greater magnitude during the presentation of validly compared with invalidly cued targets. Additionally, decreased beta oscillatory activity was observed in the right inferior frontal gyrus during the initial 300 ms of validly cued targets, while this response was not present during invalid target presentation. Slightly later in the time course (300-600 ms), our results indicated stronger decreases in beta oscillatory activity in the right SPL, right intraparietal sulcus, and left frontal eye fields during the presentation of invalidly relative to validly cued targets. Thus, our results are consistent with previous research demonstrating activation within the nodes of the DAN and VAN during the reorienting of attention, and extend upon the literature to characterize the oscillatory dynamics at play.

Cortical Oscillations Accompanying Cognitive Control in a Response Switching Task Using Incidental Learning

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Ongoing brain oscillations, particularly in theta frequency band, play an important role in top-down control, ranging from internal thought to externally-observable behaviours. However, which of these signals are involved directly in cognitive control and which are consequential to sensory and motor processing remains unclear. First, we used MEG to demonstrate equivalent theta in both global and selective response inhibition, despite different response outcomes. In order to test theta levels with identical cues and responses but varied task difficulty, we used incidental learning to affect performance on a cognitive control task. 16 subjects performed 7 blocks of a go/switch task, where all stimuli required a right index finger button press (Go), except cue \'3\' required a left index finger press instead (Switch). Unbeknownst to the subjects, the cues were presented in a repeating 8-trial pattern (3-1-4-3-2-4-1-2). 90% of trials presented the cue with the pattern intact (P), whereas 10% of trials presented the cue not according to pattern (nP). There was a main effect of response hand, block, and pattern (all <0.01) on reaction times (RT). Longer RT following nP-cues over P-cues when switches are involved demonstrate subjects learned to anticipate Switch trials and subsequently improved their performance on the cognitive control task. Task-evoked pupil dilation (known to increase with cognitive demand) supported the RT results (all <0.01), demonstrating that the pattern was learned quickly while changes to required response hand or cue pattern were accompanied by increasing cognitive load for successful responding. Similarly, frontal theta power is reduced preceding faster and more automatic responding during inhibitory control (<0.031). Taken together these results implicate frontal theta in cognitive processing associated with increasing task demands, and not sensory or motor processing.

Comparison study of Attention Network Test between healthy control and schizophrenia using Magnetoencephalography

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Introduction:
Attention Network Test (ANT) is a useful tool for identifying three networks involving altering, orienting, inhibition in the brain. The ANT have been studied by electroencephalography (EEG) so far. ANT have been studied to identify neurocognitive makers of schizophrenia showing P3 amplitude modulation deficit mainly in the parietal region. In this study, by using magnetoencephalography (MEG), we conducted the ANT in healthy controls (HC) and schizophrenic patients (SP) respectively.

Method:
We evaluated the difference in event-related fields between two targets (congruent and incongruent) within and between groups. The ANT were conducted on six HC and six SP subjects with 152-channel MEG (axial gradiometer system, KRISS, Daejeon, KOREA). For analysis, cluster-based permutation test was performed to evaluate the statistical significance.

Result:
Significant difference between two targets was observed in HC at P3 component in left parietal region ($p < 0.001$). But, no significant difference was observed in SP ($p > 0.05$). Significant difference was observed between HC and SP at P1 component in frontal and parietal regions ($p < 0.05$).

Conclusion:
We identified modulation deficit between the targets in SP. Additionally our result showed that the significant amplitude increase in frontal and parietal region in the SP group.

Modulation of Induced Positive Mood on Inhibitory Control: an MEG Study

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Emotion plays a crucial role in cognitive processes. Numerous studies reported the impact of negative emotion on executive control as well as behavioral outcome. However, little is known about the role of positive emotion in inhibitory control and the underlying neural mechanism in the brain. The present study aims at investigating modulation of inhibitory control by positive emotion and elucidating the interaction between the associated brain regions. Thirteen healthy subjects were recruited. A one-minute video (neutral or comic) was displayed and then subjects reported pleasantness scales (a 10-point scale), followed by performing a stop-signal task. Event-related neuromagnetic fields (ERMF) were recorded using a whole-head 306-channel MEG system (Elekta, Neuromag). The averaged ERMF at the sensors relevant to visual perception, emotional state, and motor planning/inhibition were compared. The stop-signal reaction time (SSRT) was estimated as a measure of inhibitory control.Our results showed the reduced occipital activity responding to successful stop-trials after positive mood induction, comparing to neutral condition (p=.006). The amplitude in preSMA was positively correlated with those in the occipital sensor (p=.038). Furthermore, only in neutral condition the amplitude at the preSMA sensor was correlated with SSRT (p=.006); whereas such correlation was not found in positive condition. No difference of SSRTs between conditions was found.Positive affect, which is reported to facilitate approach-related behavior, may attenuate inhibitory control function. These results presumably reflect associative relationship between visual attention and motor control for successfully inhibiting stop signals. We speculate that primed positive emotion could selectively modulate visual perceptual processing and cognitive control as well as interactions between them. Further imaging analysis will be a need to confirm the present sensor-level findings in cortical space.

Changes in multifractal brain dynamics between consciousness and anesthetic-induced unconsciousness.

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A wide range of neurophysiological processes exhibit 1/f-like spectra (Bak et al., 1987). This power-law scaling reflects arrhythmic brain activity with no predominant temporal scale (i.e. 'scale-free'). Scale-invariance has been reported in MEG, EEG and fMRI data (Linkenkaer-Hansen et al. 2001; He et al. 2014; Ciuciu et al. 2012). Multi-scale formalisms, such as fractal analysis, allow us to describe the self-similarity and temporal auto correlation of the signal with very few parameters. These scaling parameters have been shown to vary between active tasks and rest but also between wakefulness and sleep. Much less is known, however, about how scale invariance properties vary across states of consciousness.

64-channel EEG recordings were obtained in 7 healthy human participants during normal waking consciousness, sevoflurane-induced unconsciousness, and recovery (Blain-Moraes et al. 2015). Multifractal scaling parameters were estimated using a Wavelet Leader-Based Multifractal formalism (WLBMF; Wendt et al., 2007; Jaffard et al. 2006) where the multifractal spectrum was limited to its truncated 2nd order polynomial expansion with only two scaling parameters (log cumulants) denoted c1 (self-similarity, regularity, equivalent to Hurst exponent) and c2 which corresponds to local fluctuations of scaling behaviors ($c2 < 0$ indicates multifractality, while $c2 = 0$ indicate monofractality).

In addition to observing power law behavior (scale-invariance) in both states, we found unconsciousness to be associated with an increase in c1 (i.e. self-similarity) which implies a decrease in neural excitability compared to consciousness. Furthermore, c2 was closer to zero in unconsciousness, suggesting a tendency towards mono-fractality in unconsciousness and towards multi-fractality in consciousness.

WLBMF is a promising approach to examine the neurophysiological changes associated with consciousness and unconsciousness from the perspective of self-organized criticality.

Neural Correlates of Mental Flexibility in Typically Developing Children

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Mental flexibility is a core property of cognitive executive functions and represents the ability to adapt to changing situations and can be assessed using a set-shifting task. Prior work with MEG has characterized the spatiotemporal dynamics of mental flexibility in adults, yet this has not been explored in typically developing children. To address this gap, we recruited 25 children (14F:11M) aged 6–15y to perform a set-shifting task in a 151-channel MEG CTF System. While accuracy was high (>94%), inspection of the behavioural data revealed that children <8y showed long (>1sec) and highly variable reaction times. Therefore, we only included data from children >8y in subsequent steps (N=15; mean RT=.75s±.16ms). Source activations were reconstructed using SPM beamforming with sliding, overlapping 100ms time windows from 50-500ms where shift trials were contrasted with non-shift trials. Our results revealed significant (p<0.009) activity, related to shifting, in the right frontal regions (BA 9/10) from 100-300ms post-stimulus onset, and in the left frontal regions (BA 46) from 300-450ms. Right posterior parietal association areas (BA 7) showed early sustained activity, with the left parietal regions (BA 39) coming online from 300-450ms. Additionally, regions in the temporal and motor areas were found. Our findings are consistent with the adult literature; the dlPFC (BA 9/10/46), crucial for working memory, and the posterior parietal areas (BA 7/39), crucial for perception and visuomotor integration, are key components in mental flexibility. Our findings suggest that children >8y recruit the same brain areas as adults when completing a set shifting task, while also relying on other regions to support their performance. Establishing the neural correlates of mental flexibility in healthy children is important to set a norm for future investigations into this executive function in clinical groups.

Greaterdesynchronization of upper alpha during improvisational music performanceplanning

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Improvisational music performance has been used in electroencephalography and functional magnetic resonance imagingmodels of creativity. However, no such magnetoencephlaography (MEG) studieshave been reported. Yet, MEG's high temporal resolution and its quiet operationmake it ideal for music studies. And indeed there are numerous MEG studies onmusic perception. So long as movement is controlled, MEG should likewise offeran excellent platform for studying the neurological activity associated withmusic performance. To realize this goal, we first endeavoured to build an MEGcompatible MIDI instrument, and programmed it to produce the sound of a tomdrum through a novel combination of existing hardware/software. We thendesigned an improvisational music performance paradigm for use in MEGexperimentation, in which participants first plan, and then physically respondto various sets of rhythm stimuli. Preliminary analysis of spectral resultsfound greater desychronization of alpha band (8-13 Hz) activity associated withimprovisation during the planning period prior to physical performance. Here wepresent further analyses of these results which indicate the alphadesynchronization to be concentrated in the upper band (10-12 Hz), and that itis independent of stimulus complexity. The nature of this desynchronizationcorroborates other reports of alpha desynchronization attributed to increased attentionand cortical activation, and suggest that it is the task of improvisationitself, rather than the stimulus, which increases cognitive load. Spatialanalyses of these results is underway, and further investigation is plannedwhich will compare these data to that from subjects with improvisational musicexperience.

An MEG investigation of the brain dynamics mediating Focused-Attention andOpen-Monitoring Meditation

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The phenomenologyand reported effects of meditation vary according to the technique practiced.While numerous studies have explored the cerebral mechanisms involved inmeditation, little research provides direct comparisons between the neuronalnetwork dynamics involved in different meditation techniques. Here, we exploreand compare brain signals recorded with magnetoencephalography (MEG) during (a)resting state, (b) focused-attention meditation (FAM) and (c) open-monitoringmeditation (OMM) in a group of expert meditators (12 monks).To this end, weestimated MEG source time courses using a minimum-norm solution and computed (1)spectral power in multiple frequency bands (delta, theta, alpha, beta andgamma), (2) graph theoretical measures, (3) long-range coupling using imaginarycoherence and weighed phase-lag index and (4) multifractal scaling parameters using Wavelet Leader-based Multifractal formalism. We compared all the measures in the three conditions(OMM, FAM and resting state) and tested for statistical significance using permutationtest (paired t-test) corrected by maximum statistics. We also used a machinelearning framework in order to see which features provide the highestclassification across conditions. Our findings reveal several differencesbetween FAM, OMM and the resting-state condition. Compared to OMM, FAM isassociated with an increase in power in regions involved in attention andperformance monitoring. In OMM, increases in activity were observed in regionsinvolved in memory and emotion processing. Moreover, OMM seems to have strongestand more connections, while resting state have connections that are weaker andfewer in number compared to OMM and FAM. We discuss these results in thecontext of previous cognitive neuroimaging studies of meditation and paths forfuture research are proposed.

Auditory evoked fields elicited by frequency-modulated sweeps

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Frequency-modulated (FM) sounds play an important role in human speech and species-specific communications. However, the neural activity elicited by FM sounds remains elusive in the human auditory cortex. In the present study, we measured the auditory evoked N1m and sustained field responses elicited by FM sweeps using magnetoencephalography. We adopted as sound stimuli temporally-repeated and superimposed FM sweeps that consisted of six FM tones that traversed the frequency range (500–2000 Hz) with different modulation rates. These test stimuli were balanced with respect to the spectral components at a certain time-point. Therefore, this experimental setup allowed us to investigate effects of frequency modulation rates on the auditory evoked fields. The results showed that the slower rate FM sounds caused the larger N1m source strengths and the smaller sustained field source strengths than the faster rate FM sounds. The auditory neural activity elicited by FM sweeps appears to be sensitive to the FM rate in the human auditory cortex, thereby providing a key to identify natural sounds that usually contain FM components.

Proof that Syllables are the Basic Unit of Aural Comprehension

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In clarifying the upper limit of the speech rate for Japanese reading systems, we find that syllables are the basic unit of aural comprehension. Data is collected from the neuromagnetic signals emitted from various areas of the brain while changing the speech rate of synthetic speech.

Basic Idea: Text to speech systems are becoming more widely adopted. Various benefits can be achieved by listening to text information from a wide variety of sources. If the optimum speech processing speed limits of the brain can be found, readers can be created to provide a possible faster information transfer rate. To investigate this, we captured the neuromagnetic signals emitted by the brains of subjects while we changed the synthetic speech rate.

Experiment: The corpus-based speech synthesis engine was used to synthesize the statement, and the time stretch method was used to generate eight different speech rates as stimuli. Subjects were instructed to press one of two keys (Yes / No) depending on whether they could or could not understand the speech stimuli. MEG recording: We used the PQ1400RM 400 ch made by Yokogawa Electric Corporation.

Results: It was found that when the speech rate was faster than 25 percent, the subjects could not understand the speech stimulus, and thus no auditory evoked magnetic fields (AEF) responses were observed for the syllables. However, it was discovered that when the speech rate was slower than 37.5 percent, the subject can understand the speech stimuli, and a clear AEF M100 response from the left superior temporal gyrus was observed for each syllable. The upper limit of the speech rate is about 80 ms syllable duration. It is suggested that each syllable should not have an average duration of less than 80 ms for clear speech understanding.

Conclusion: We find a clear correlation between the AEF M100 and the syllables when the subjects could understand the speech. Overly fast speech showed no such correlation.

PRESTIMULUS PATHWAYS OF FRONTAL CONTROL DURING SENSORY GATING

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Background: Sensory gating reflects an attenuation of brain responses to the second of two identical stimuli (S1, S2) presented in rapid succession. Prior research has identified some involvement of frontal regions, yet the interplay with sensory areas mediating gating of information is not well understood.

Methods: The magnetoencephalogram (MEG) was monitored in 77 healthy participants during a standard paired-click design. Sensory gating was defined as the ratio of S2 responses (M50) divided by S1 responses. Source reconstruction using spatial filters identified frontal (middle cingulum) and auditory areas (heschl's gyri) on the basis of the maximum difference between brain activity after S1 and S2. Connectivity between frontal and auditory areas was estimated by computing nonparametric Granger causality spectra in the frequency domain 2 seconds prior to stimulus presentation.

Results: Granger analysis revealed significant top-down communication from frontal to auditory areas at 15 Hz. Moreover, high prestimulus prefrontal control was significantly correlated with better sensory gating ($r_s = -0.23$).

Conclusion: Present results strengthen the proposal of prefrontal control actively mediating auditory perception and sensory gating and clarify that the mechanism involves connections active prior to stimulation.

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Bistable perception in auditory streaming is paralleled by altered evoked brain rhythms and connectivity patterns along the ventral stream

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Identifying coherent \"objects\" in sequences of presented sounds is an important feature of Auditory Scene Analysis. In the auditory streaming paradigm typically two sounds of different frequency (A and B) are presented in ABA-ABA-etc. patterns, which can either lead to an integrated percept of one continuous stream of triplets (\'galloping\' rhythm) or the percept of two separate streams. Here, we were interested in whether the percepts of triplets vs. two streams are characterized by specific oscillatory signatures. Participants listened to ABA sequences, indicating their percept by button press whether, while magnetencephaloghic (MEG) activity was recorded. We analyzed stimulus-evoked activity for integrated and segregated percepts after transforming sensor data to source level using beamforming. For both percepts the presentation frequency (1.66Hz – stimulus onset asynchrony of the ABA triplets was 600 ms) similarly dominated the evoked spectrum. Differences emerged at the second harmonic (3.33Hz) with increased power for the integrated as compared to the segregated percept. The opposite pattern (integrated < segregated percept) was observed at the 4th harmonic (6.66Hz). Effects dissociating the two percepts were mainly originating from auditory regions in the middle temporal gyrus and, inferior frontal regions. Auditory and frontal regions showed differential connectivity patterns dissociating between integrated (stronger connectivity to frontal regions from MTG) and segregated percepts (stronger connectivity to parietal regions).Our findings illustrate for the first time using a bistable auditory paradigm, that key ventral stream regions exhibit altered evoked rhythmic activity as well as network integration patterns depending on the dominant percept. This significantly extends previous works using near threshold or visual bistable paradigms, lending strong support to key assumptions of our \"windows to consciousness\" framework.

Audio-visual processing of Chinese characters and speech sounds

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Associating Chinese characters to speech sounds are crucial for Chinese in their literacy acquisition. Here we investigate the underlying neural mechanisms of orthographic–phonological associations with magnetoencephalography. Fourteen native Chinese and thirteen Finnish participants performed in a dual one-back audio-visual integration task in which auditory only (A), visual only (V), audio-visual congruent (AVC) and audio-visual incongruent (AVI) stimuli were presented randomly. To make sure the participants pay equal attention to both auditory and visual modality, there were testing trials occurring with 7.5% possibility in which the memory of character and/or sound one trial back were tested. Cluster-based permutation test of the event-related fields (ERFs) revealed that in the latency range from 525 to 725 ms post-stimulus there was a significant congruency effect ($p<0.01$) in Chinese group but not in Finnish group, the difference was most pronounced over frontal regions. Furthermore, there was a significant ($p<0.01$) suppressive interaction (A+V>AV) in Finnish group in the time window from 200 to 560ms over right temporal-occipital regions, but no suppressive interaction was found in Chinese group. Group comparison for each type of stimulus revealed that only the audio-visual congruent ERFs showed a significant difference (Chinese>Finnish) in the latency range from 210 to 430ms post-stimulus over right frontal-temporal regions. In conclusion, learned associations of characters and sounds lead to stronger cortical response for congruent pairs and diminished suppressive effects.

Fronto-temporal connectivity shows whether 'Twinkle Twinkle Little Star' song is in the music or not

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When memorizing, recalling, and singing some music, a melody seems to represent the music, which would consolidate more strongly if the melody is very familiar. It is no wonder, then, that the brain probably processes the melody in music separately, though the melody is intertwined with other elements such as harmony, rhythm, key, and timbre, etc. in music. However, it is a real challenge to investigate the neural response for only a specific element in the music.

The present magnetoencephalography study for 25 musically untrained people (15 females, mean age, 26.8 ± 3.4 years) investigated how effective connectivity among the inferior frontal gyri (IFGs) and Heschl's gyri (HGs) differs according to the theme melody conditions with 'Twinkle Twinkle Little star' song or the non-theme melody conditions (variation of the theme melody) among the five conditions (*Theme*, *Variation I*, *II*, *III*, and *IV*) in Mozart 12 variations KV 265 using linearized time delayed mutual information (LTDMI). We firstly made musical formulae dissecting the elements in music using the vertical/horizontal combination of pitch and rhythm. Using the musical formulae, we proved that two condition pairs (1st pair, *Variation I* & *II*; 2nd pair, *Variation III* & *IV*) with the different rhythmic pattern could show difference between the theme and non-theme melody conditions.

Connectivity difference between the theme/non-theme melody conditions was observed only in a connection from the left IFG to the right HG, which was common in the two condition pairs. The LTDMI values was significantly higher in the non-theme melody conditions than in the theme melody conditions (1st pair, $p = .000$; 2nd pair, $p = .003$). Our present study shows the brain selectively processes the property for the partial element in music in the specific connectivity. Our findings suggest the fronto-temporal connectivity is associated with the processing of the melody difference within music.

Connectivity from the left to the right hemisphere in frontotemporal areas processes independently syntactic violation and task complexity in harmonies

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Melodic contour in harmonic sequence is perceptually dominant, which affects the processing of syntactic violation. However, the function of harmony also affects harmonic perception because the familiar harmony is more easily detected. In harmonic perception, then, the differential melodic contour and syntactic regularity among the harmonies involves syntactic violation and task complexity. The neural responses for the two characteristics may show the relation of melodic contour and harmony.

Our present magnetoencephalography study investigated how the brain processes syntactic violation and task complexity inherent in the regular, intermediate, and irregular conditions of harmonic sequences with the final chords of the different syntactic regularity (including the irregular condition with the only different melodic contour) in terms of effective connectivity. We tested the behavioral performance and effective connectivity in 12 connections among the bilateral inferior frontal gyri (IFGs) and superior temporal gyri (STGs) using linearized time delayed mutual information (LTDMI), for 3 conditions and for 19 females (9 musicians and 10 non-musicians, mean age of 24.3 ± 3.0 years).

The LTDMI was significantly prominent in two connections from the left to the right hemisphere in the IFG and STG ($p < .05$, 2 way repeated measure ANOVA). Among three conditions, the irregular condition with the salient melodic contour showed the highest LTDMI between the bilateral IFGs related with musical syntax. The LTDMI in the bilateral STGs was higher for the intermediate condition of the most complex condition with the unfamiliar harmony and the non-salient melodic contour, which was correlated with the behavioral responses. Our present study shows that the brain processes syntactic violation and task complexity in a task, in separate connections. Our findings suggest that harmonic perception is based on the interaction of melodic contour and harmony.

Inter-subject correlation during music listening reflects musical expertise

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Musical expertise is known to shape brain anatomy, activity and processing. However, brain responses to musical stimuli have been mostly investigated using artificial or isolated sounds, such as repetitive tone beeps or chords. Brain activity during listening to natural music as heard in real life have been investigated only scarcely, and even then, mainly using functional magnetic resonance imaging (fMRI). In this study, we investigated with magnetoencephalography (MEG) how expert musicians' brains synchronize in response to complex realistic music compared to non-musicians' brains. Musically trained (n=22) and untrained (n=19) healthy adults listened to Astor Piazzolla's Tango Nuevo 'Adios Nonino' for ca. 8 min. First, we determined the frequency bands of interest by analyzing MEG power spectra during listening to music and during rest. We found that the power spectral density differed between music listening and rest condition in right temporal sensors at around 5 Hz. Then, we computed a cortically-constrained minimum-norm source estimate for each participant and correlated the envelopes of the theta (4-8 Hz) frequency band across the musicians and across non-musicians in order to assess the inter-subject correlation (ISC) in these two groups. Musicians exhibited higher ISC in the right superior temporal lobe compared to non-musicians in the theta frequency band. This auditory-cortex coupling obtained with a data-driven approach is consistent with the hypothesis that expert musicians process the structural details of the acoustic features in the music more accurately, dynamically locking their neural activity to the same time points across subjects. Non-musicians, on the other hand, seem to process music in a more variable and, hence, subject-dependent manner, without any temporal locking to specific features. The results provide an insight into the processing of real-world stimuli like music and introduce a new method for the analysis of such stimuli for MEG.

Appearance of the 8-10 Hz temporal-lobe tau rhythm during drowsiness

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It has been reported that the spontaneous 8–10 Hz “taurhythm” originates around the N100m source in the auditory cortex and that it is suppressed by sounds. Tau is rarely detected, probably due to masking by the parieto-occipital alpha-rhythm, which is larger in amplitude and overlapping infrequency. We previously recorded magnetoencephalograms (MEGs) from 26right-handed participants who listened to 6-s-long emotional sounds that were pleasant, unpleasant, or neutral. Clear sound-related suppression of 8–10 Hz rhythm was observed bilaterally in temporal areas of eight subjects. Of these, the right temporal area showed a statistically significant main effect of emotional category for the suppression. Multiple comparison tests revealed that the rhythm was suppressed more by unpleasant and neutral sounds than by pleasant sounds. These results suggested that tau rhythm, which was detected in one-third of the subjects, was modulated according to the emotional valence of the sound. We further investigated why taurhythm was detected only in those subjects. MEGs of those subjects were Fourier-transformed across the entire experimental period, and temporal-lobe theta-band (4–8 Hz) power was extracted. Theta-band power was significantly larger in “tau subjects” than in “non-tau subjects.” It is known that theta is increased and that parieto-occipital alpha rhythm is suppressed during drowsiness. The results are therefore in line with the previous suggestion that tau rhythm emerges during drowsiness.

Subject-specific dynamics of auditory cortex determined through MEG measurements and computational modelling

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We present a computational modelling framework to account for magnetoencephalography signals generated in the auditory cortex (AC). Modelling is based on the anatomical core-belt-parabelt structure of AC and describes the interactions of cortical microcolumns, each comprising excitatory and inhibitory cell populations characterized by a mean firing rate and with short-term synaptic plasticity (adaptation). The full, non-linear version of the model has been shown to account for a large variety of AC phenomena. However, due to its nonlinearity, the model is analytically intractable and computationally slow, precluding the possibility of efficient data-fitting. Therefore, we sought analytical solutions to the model by linearizing the firing rate and the adaptation term and by decoupling the state equations. The result is a description of the dynamics of AC in terms of normal modes. The framework allows one to find subject-specific model parameters by fitting simulated responses to event-related field (ERF) data in a computationally fast and efficient procedure. We applied our approach to single-subject ERFs measured in two experiments. In the first experiment, 1.5 kHz tones were presented in five separate blocks with all tones in a given block delivered at the same stimulus-onset interval (SOI; 0.5 – 10 s). In the second experiment, the tones were presented randomly at ten different SOIs (0.25 – 7 s). Model parameters were fitted according to the ERFs from the first experiment. The resulting subject-specific models were tested on their ability to predict the ERF waveforms not used in the fitting procedure. The models explain very well the ERFs, and they are validated by the good out-of-sample predictions. Our approach yields descriptions of subject-specific AC dynamics, and it therefore links non-invasive data to mechanistic models of auditory information processing in a subject-specific way. – The study was supported by DFG projects He1721/10-1,2 and SFB/TRR 31.

The cerebellum is involved in learning delayed action effects: a TMS-MEG study

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Being able to predict self-generated sensory consequences is an important feature of normal brain functioning. In the auditory domain, self-generated sounds lead to smaller brain responses compared to externally generated sounds (sensory attenuation). Here we investigated the role of brain oscillations underlying this effect. With magnetoencephalography, we show that self-generated sounds are associated with increased pre-stimulus alpha power and decreased post-stimulus gamma power and alpha/beta phase locking in auditory cortex. All these oscillatory changes are correlated with changes in evoked responses. Furthermore, they correlate with each other across participants supporting the idea that they constitute a neural information processing sequence of processing self-generated sounds, with pre-stimulus alpha power representing prediction and post-stimulus gamma power representing prediction error, which is further processed with post-stimulus alpha/beta phase resetting. Additional cross-trial analysis provides further support for the proposed sequence that might reflect a general mechanism for the prediction of self-generated sensory input. We also investigated the role of cerebellum in this process using an "inhibitory" offline repetitive transcranial magnetic stimulation protocol (1Hz-rTMS). Preliminary results showed a specific TMS effect on sensory attenuation effect. Overall, our results demonstrate that predicting the sensory consequences of actions engages a sequence of spectrally specific brain signals in auditory areas that are likely mediated by motor cortex and possibly the cerebellum.

Auditory delta-entrainment interacts with multiple fronto-parietal networks

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The timing of slow auditory cortical activity aligns to the rhythmic fluctuations in speech. This entrainment is considered as a marker of the prosodic and syllabic encoding of speech, and has been shown to correlate with intelligibility. Yet, whether and how auditory entrainment is influenced by the activity in other speech–relevant areas remains unknown. We analysed MEG data of 23 participants who listened to a 7-min long story, and computed auditory delta- and theta-entrainment, using mutual information. We then quantified the dependency of auditory entrainment on the oscillatory activity in seven frequency bands (delta to gamma) in fronto-parietal regions, parcellated using the AAL atlas. We found that auditory delta-speech tracking (i.e., prosodic entrainment) interacted with three distinct networks. First, entrainment in the left anterior superior temporal gyrus (STG) was modulated by beta power in orbitofrontal areas, likely reflecting top-down predictive modulations of auditory encoding. Second, entrainment in the left Heschl's Gyrus and anterior STG was dependent on alpha power in central areas, in line with the importance of motor structures for phonological analysis. And third, entrainment in the right posterior STG modulated theta power in parietal areas, consistent with the engagement of memory processes during challenging listening moments. These results illustrate the topographical network-interactions of prosodic entrainment and reveal distinct cross-frequency mechanisms by which auditory delta-entrainment interacts with cognitive functions related to predictions, rhythm, and memory.

Prediction of optimal auditory signals for visually-challenged people using auditory evoked magnetic responses

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Birdsong is often used as an auditory signal for visually-challenged people in public spaces in Japan. However, more than 40% of visually-challenged people reported that such auditory signals were difficult to identify. We used auditory evoked magnetic field (AEF) responses in the human auditory cortex to uncover an auditory signal that was easy to identify. As an auditory signal, we focused on birdsong, which is currently used to inform passengers about the location of stairs in train stations in Japan. We presented birdsongs to participants in silent, noisy, reverberated,and interaural time-delay conditions. We analyzed the most prominent AEF response, N1m, and the correlation between the birdsong envelopes and the AEF. We found that the N1m amplitudes were maximal when the participants listened to the song of the Cuckoo and the above-mentioned correlation was maximal when the participants listened to the song of the Oriental Scops Owl. Thus, we believe the songs of the Cuckoo and Oriental Scops Owl to be candidates for optimal auditory signals.

Inter-regional phase-amplitude coupling between inferior frontal gyrus and auditory cortex predicts near threshold pitch discrimination performance

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There is a threshold in pitch difference between auditory stimuli beyond which stimulus discrimination becomes strikingly difficult. The perception of near-threshold stimulus changes is suggested to depend on the ongoing neural activity. However, the mechanisms involved remain poorly understood. One simple example requiring auditory stimulus discrimination is the detection of changes between tones of different frequencies. Performances in terms of smallest detectable change vary between individuals [Albouy et al, 2013], with severe forms of congenital amusia (tone deafness). Anatomical evidence from diffusion-weighted MRI indicates that the connectivity of the arcuate fasciculus, which connects the inferior frontal gyrus with the auditory cortex, is essential for the ability to detect small pitch changes [Loui et al. 2009].Here, we hypothesized that effective connectivity between these brain regions is related to individual pitch-discrimination performances. Using MEG imaging, we found supporting evidence to this hypothesis: we report on higher theta to gamma inter-regional phase-amplitude coupling (IRPAC) between the right auditory cortex and inferior frontal gyrus in healthy subjects with poorer near-threshold pitch discrimination performances (18 subjects). This higher coupling may be recruited to compensate for lower anatomical connectivity. We introduce IRPAC as a new measure of effective connectivity, which is sensitive to the modulation of the amplitude of high frequency oscillations in one region by the phase of as lower rhythm from another region. In our data, coherence and other common measures of functional connectivity did not show significant differences between high and low performance participants. We further confirmed these findings by comparing data from amusics and age-matched controls (16 subjects).We conclude that IRPAC expands the range of possible mechanisms enabling effective connectivity in inter-regional brain communication.

Investigation of perception of ambiguous melodies using ASSR\'s in MEG

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We devised an ambiguous melody consistingof sustained A4 and E5 and intermittentlypresented C5, which sounded as if there were a continuous melody that sounded as if there were a continuousmelody C5-A4-C5-A4 (Dn) or C5-E5-C5-E5(Up). There was ambiguity between the two melodies. To reduce the ambiguity, either of the twomelodies was presented without the sustained notes before the test ambiguousstimulus. The purpose of this study is to present preliminary results ofneurophysiological correlates of the ambiguity and its reduction. For thepurpose, the sustained A4 was amplitude modulated at 37.5 and E5 at 42.5 Hz andthe MEG ASSRs were measured. The preceding phrase lasted for 1 s and theambiguous test simulus for 2 s. A fragmentphrase C5-A4 (dn) or C5-E5 (up) was added to see the evoked response to thelast note; the response would be larger if the last tone was incompatible withwhat the subject was hearing during the ambiguous period.

A Simultaneous MEG/EEG Study for Affective Words with Affective Voice Tone

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Sound may be most important sense to cause human being's emotion because it includes significant information like emotion or intention from only one words. Each person takes different meaning according to speaker's voice tone even if the same words were read. In this study, we investigated brain activations from MEG/EEG data when accordance or discordance affective words with affective voice tone were given. Twenty-three native Korean subjects (12 males, 11 females) participated, and 152 MEG channels (KRISS, axial gradiometer system), 21 EEG channels (Biosemi), EOG, and EKG were collected simultaneously during stimuli are given. The stimuli consisted of five positive and five negative affective Korean words, each words were vocalized with accordance and discordance voice tones; accordance means positive (negative) words with positive (negative) tone, and discordance means positive (negative) words with negative (positive) tone. MEG and EEG data were band-pass filtered with 1 – 55 Hz, baseline corrected using 200 ms before stimulation, and EEG data were re-referenced with two earlobe channels. Power spectrum was estimated every 100 ms with time window of 100 ms. MEG showed different activations in the temporal area between accordance and discordance stimuli. When negative words were given, accordance tone were more activated at 300 – 500 ms than discordance tone regardless of gender. When the positive words were given, male subjects showed more activation at 100 – 300 ms for negative tone, 400 – 500 ms for positive tone, whereas only negative tone yielded more activation at 300 – 600 ms in the female. EEG showed the similar patterns to MEG, but significant different activation area was the frontal area at slightly different time intervals. From these results, voice tone may be more influential on emotion than words, especially, negative tone may be critical and the male was more affected by words than the female.

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Using the Auditory Steady State Response to Examine Atypical Oscillatory Synchrony in Individuals with Down Syndrome

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Down Syndrome (DS) is a neurodevelopmental disorder present at birth, which has long-term consequences for cognitive development. Active cortical processing is associated with gamma oscillations, and alterations of gamma oscillations are reported in conditions affecting neurodevelopment. Auditory stimuli with a ~40Hz component show consistent entrainment of 'steady state' brain responses at this frequency. Known as the Auditory Steady State Response (ASSR), it is utilized as a biomarker of atypical auditory processing. Individuals with DS show aberrations in phase coherence, so here we use the ASSR to examine specifically the alteration in entrainment of neuromagnetic networks for individuals with DS. Data was recorded using a 151-channel CTF MEG system on individuals with DS and controls during presentation of an auditory stimulus amplitude modulated at a 40Hz frequency. Vector beamforming was used to reconstruct source activity from 90 seed points representing all cortical and subcortical regions in the Automated Anatomic Labeling Atlas. Inter-regional neurophysiological interactions were characterized for each region pair. Preliminary results revealed topographic patterns of connectivity at the ASSR stimulation frequency. Both groups showed evidence of connectivity patterns involving temporal regions, consistent with established sensor and source space results. Preliminary contrasts between groups indicate atypical neurophysiological interactions among brain regions during ASSR stimulation in individuals with DS. This suggests that entrainment of neurophysiological interactions among brain areas may be reduced in DS, which may indicate reduced capacity to recruit coordinated network function. Given the purported role of gamma oscillations in active cortical processing supporting cognition and perception, and its relevance for the development of cortical networks, these atypicalities in oscillatory brain network connectivity suggest reduced ability for entrainment of coherent large-scale networks which may reflect atypical neurophysiological communication relevant for difficulties with neurocognitive development in this group.

Being first matters: representational similarity analysis on ERP scalp maps reveals separate networks for audiovisual temporal integration depending on the leading sense

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Multisensory integration is a powerful feature of our brain whereby information processing in one sensory modality is enhanced by complementary information from other modalities. Timing is crucial as only inputs reaching the brain within a restricted temporal window are perceptually bound. Previous research in the audiovisual field has investigated various features of this temporal binding window (TBW), revealing asymmetries in size and plasticity depending on the leading input (auditory-visual, AV; visual-auditory, VA). However, little is known about the mechanisms underpinning the TBW.We here test the hypothesis that different mechanisms may underlie audiovisual integration based on the temporal order of inputs using high-density EEG. Healthy participants performed an audiovisual simultaneity judgment task including AV and VA stimulus pairs presented with different stimulus onset asynchronies (SOAs) and unisensory visual and auditory control conditions. Multisensory event-related potentials (ERPs) were extracted by subtracting the sum of unisensory trials from the AV or VA EEG signals. To examine the degree of topographical overlap of ERP scalp maps across all conditions (AV & VA x SOA), we computed representational dissimilarity matrices between the cross-correlated scalp topographies and two alternative models (maps topographically identical vs. different). Results were twofold. Within either AV or VA conditions, maps were highly correlated for SOAs up to 250ms (i.e. when synchrony is still likely to be perceived), whereas the 500ms SOAs (i.e. when synchrony is no longer perceived) generate their own distinct map. This demonstrates that temporal integration vs. separation elicits different brain activity patterns. More importantly, simultaneity judgments of AV and VA pairs generated distinct, uncorrelated activity patterns. This finding demonstrates that audiovisual temporal binding in the brain engages separate networks depending on the leading sense.

Effects of phonetic context on categorical perception of stop-consonants investigated with magnetoencephalography.

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The perception of phonemes is influenced by their phonetic context. In this experiment, we aimed at elucidating how this phonetic context effect is reflected by neural activity measured with human magnetoencephalography (MEG). To this end, we designed stimuli along a phonological continuum from /ba/ to /da/ and operationalized phonetic context by preceding vowels, i.e., /i/ or /u/.

In a psychophysical experiment, we first determined the shift of perception between category boundaries for individual listeners. Then, in an MEG experiment, we presented participants with sequences of sounds consisting of 1) a vowel: /i/ or /u/, 2) an ambiguous morph between /ba/ and/da/, and 3) an unambiguous phoneme: /ba/ or /da/. The final unambiguous phonemes served to test for repetition suppression effects that should occur when two similar stimuli are presented in sequence. Our psychophysical experiment showed that the perception of an ambiguous consonant-vowel syllable is shifted depending on the preceding phonetic context: listeners were more likely to classify an ambiguous morph between /ba/ and /da/ as /da/ when it was preceded by a /u/. Conversely, when the ambiguous morph was preceded by an /i/, listeners more often reported to hear a /ba/.

For the MEG experiment, we expected that a sequence of an ambiguous morph shifted towards /ba/ followed by an unambiguous /ba/ would lead to reduced MEG evoked fields due to a repetition suppression effect. No such repetition suppression effect was statistically significant. Instead, we observed that the magnetic field evoked by the ambiguous /ba/-/da/ was different depending on the preceding vowel, i.e., /i/ or /u/. This difference occurred at around 250-300 ms after onset of the ambiguous /ba/-/da/ stimulus at left temporal sensor positions.

Thus, our study suggests that the perception of phonemes depends on their phonetic context. Brain responses measured with MEG are possibly sensitive to shifts in perception induced by phonetic context.

Low frequency oscillations mediate de-multiplexing and encoding mechanisms during speech pre-processing.

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Speech comprises of hierarchically organized rhythmic components that represent prosody (delta band), syllables (theta band) and phonemes (gamma band). During speech pre-processing steps, neural oscillations within a fronto-temporo-parietal network track these quasi-rhythmic modulations through different neural mechanisms (de-multiplexing and encoding). Nevertheless, the full characterization of the neural basis of speech perception has yet to become complete. Indeed, it is still a challenge to understand how neural mechanisms involved in speech pre-processing are functionally connected. In the present study, we analyzed MEG data from 20 participants while hearing continuous speech. First, we determined how different brain areas within the fronto-temporo-parietal network deal with the de-multiplexing (Coherence analysis) and the encoding (Phase-Amplitude-Coupling analysis) neural mechanisms. Then, we showed how temporal and fronto-parietal regions are bidirectionaly connected during speech pre-processing (Transfer Entropy analysis). Our results indicate that, low-frequency oscillations (delta and theta band) mediate the transfer of information between de-multiplexing and encoding neural mechanisms.

Neural entrainment to speech edges in dyslexia: an MEG study

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Delta, theta and gamma neural oscillations in several brain regions are specifically entrained by the quasi-rhythmic component of the speech envelope. During speech processing, sharp large-amplitude transients (edges) in the speech envelope reset the phase of low-frequency (<8Hz) oscillations in auditory cortices. These resets improve the neural entrainment and enable efficient speech sampling. Numerous studies propose that phonological difficulties in dyslexia arise in part from impaired neural entrainment to low-frequency amplitude modulation during continuous speech. However, there are no previous studies showing how dyslexic readers deal with the low-frequency phase resetting mechanism observed in normal readers around the speech edges. Here, we analyzed MEG data from 20 dyslexic and 20 normal readers while hearing continuous speech. After low-pass filtering MEG data (<8Hz), we extracted trials time-locked to the onsets of the speech edges (from -0.4 to 1 s). Then, Phase-Locking-Value (PLV) across trials was calculated for each participant and sensor. The presence of speech edges induces a synchronization enhancement in bilateral fronto-temporal sensors in normal and dyslexic readers. Interestingly, dyslexic readers present weaker PLVs compared to normal readers after the onset (0.25 – 0.35 s) in left fronto-temporal sensors. Atypical low-frequency phase resetting affects neural entrainment to rhythmic components of the speech envelope and might contribute to the phonological deficit observed in dyslexia.

Mechanisms of Bone-conducted Ultrasonic Perceptionin the Profoundly Hearing-impaired Assessed by MEG and EEG

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Bone-conducted ultrasound (BCU) is perceived even by the profoundly sensorineural hearing-impaired, and a novel hearing-aid using BCU perception, which transmits amplitude-modulated ultrasound by bone-conduction, has been developed. We previously reported that BCU activates the auditory nerve, the brainstem pathway, and the auditory cortex in both normal-hearing and hearing-impaired subjects and hypothesized that the cochlea inner hair cells respond to ultrasound itself with peculiar vibration modes of the basilar membrane.

On the other hand, persistent refutation exists that BCU perception depends on generation of audible-frequency components in the transmission path by non-linearity of biological tissue. Various unique characteristics of BCU perception and results of our previous physioacoustical measurements on/around the living human head denied this idea, however, more straightforward neurophysiological evidence is needed.

Auditory brainstem responses (ABRs) and auditory evoked fields (AEFs) were measured in the \"complete\" hearing-impaired who show no measurable hearing sensitivity by the ordinary audiometry. 6 complete hearing-impaired and 10 normal-hearing subjects participated. As BCU stimuli, a 30-kHz tone pip and a 30-kHz tone burst were used in ABR and AEF measurements, respectively.

ABRs and AEFs were clearly elicited even in the complete hearing-impaired. In the ABR measurements, waves-I, which indicates compound action potential of the auditory nerve, were clearly elicited even in some complete hearing-impaired subjects. In the AEF measurements, the contralateral stimuli elicited larger and faster responses than the ipsilateral in both complete hearing-impaired and normal-hearing subjects.

The results strongly indicate that BCU perception does not depend on the generation of audible-frequency components. Also, the results push our hypothesis that BCU goes through the normal auditory pathway even though unique processes may exist in the cochlea. Additionally, same effects of stimulation side as air-conducted sound indicate that BCU entered the ipsilateral auditory pathway before branching to the contralateral at the superior olivary nucleus.

Auditory steady-state response modulated by stimuli inducing octave illusion

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Many type of auditory illusion has been discoveredbut it is unexplained how to occur in the auditory cortex of the brain. It isrequired measurement method with high time resolution because auditory illusionis time characteristic. We focus on “octave illusion” proposed by Deutch, andused as stimulus sound. The octave illusion occurs when each ear receives asequence of tones alternating by 1 octave but with the high and low tones indifferent ears through stereo headphones. Most listeners perceive these stimulias a high tone in one ear and low tone in other ear. But some music experiencedperson didn’t perceive illusion. Transmission path of the sound that has beeninput from the ear is the superior cross-reactivity but non-intersectingpathways that come from the same side of the ear present in the brainstem,thalamus and cerebral cortex, and therefore there are mixed reactions to thestimulus sound from both ears in the left and right of the auditory cortex. Tostudy the mechanism of “octave illusion”, we measured auditory steady-stateresponses (ASSR) with magnetoencephalography. ASSR is induced by stimuli thatare repeated such as clicking sound to be repeated at a constant interval and, amplitudemodulated sound by constant frequency. And the stationary response (ASSR) ofthe frequency component corresponding to the modulation frequency can bemeasured, and therefore it is possibility to quantitatively measure theauditory response. The responses with different modulation frequencies intoboth ears were discriminated by wavelet transform. And we compare the amplitudeof ASSR of each ear.

Evaluation of auditory impressions of HVAC sound based on time-frequency representation of magnetic cortical activity

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Evaluations of subjective impressions induced by environmental sounds using neurophysiological indices have been proposed in recent years. We have focused on developing high-value added HVAC (heating, ventilating, and air conditioning) sounds and objective evaluation of them using brain activities. In this study, relationships between subjective coolness/preference of HVAC sounds and the time-frequency representation of magnetic cortical activities were investigated. Six amplitude-modulated HVAC sounds (modulation frequency: 0.2, 0.4, 0.6, 0.8, 1.6, 3.2 Hz) and a time-invariant HVAC sound were made as stimulus. First, scale values of coolness/preference of the seven stimuli were obtained by a paired comparison method. Second, magnetoencephalographic (MEG) measurement was carried out. And third, the continuous wavelet transform was performed to obtain the time-frequency representation of MEG data. Two kinds of indices were calculated from the time-frequency representation. One was measured as decrease/increase of each frequency component from the prestimulus baseline for each frequency component, which is known as event-related desynchronization (ERD) or synchronization (ERS). The other was calculated as relative value to the average of over all stimulation, i. e., normalized time-frequency representation (NTFR). The correlation test shows that scale values of preference and the 8-13-Hz NTFR value during 3900-5000 ms in the occipital region linearly correlated. This result indicates the possibility of developing of a neurophysiological index to evaluate comfortableness induced by HVAC sounds.

Spatiotemporal characteristics of auditory activation in children with typical and atypical (SLI) language development

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Corticaldevelopment of auditory perception is reflected in the evoked responsesmeasured with electro- and magnetoencephalography (EEG/MEG). Specifically,activation at ~250ms (N250) has been reported predominantly in children and itreflects level of language skills. Specific language impairment (SLI) is linkedwith deficient processing of auditory information and with atypical brainresponses to sounds. There are however conflicting findings regardingmorphology of auditory evoked responses in children with SLI compared totypically developing children. Children often miss the clear peaks visible inthe adult waveform, emphasizing the need to include spatial information in theanalysis. This study aims to test the hypothesis that children with SLI haveatypical brain responses to sounds and to map typical and atypical variation inauditory evoked fields (AEFs) that extend beyond the generally reportedamplitude or latency differences. To better understand this variation forlanguage, it is important to analyze underlying source information of the AEF,possibly varying in time and between hemispheres. Using MEG, we compared theAEFs of children (9-10 years) with SLI (n=10) and with typical languagedevelopment (n=10) in response to passively listening to sine-wave tones (1kHz, 50ms) presented alternately to the right and left ear. In the early time-window(50-150ms), both groups showed notable variation in source configuration. Inthe later time-window (150-350ms) the activation pattern was more consistent.Controls showed a clear preference for contralateral sounds in bothhemispheres, but the SLI group showed increased ipsilateral responses in theleft hemisphere. The results indicate increased symmetry in SLIchildren compared to controls, possibly due to a maturational lag in the lefthemisphere. We focus on the N250m; a considerably underreported component that isargued to be absent in the adult waveform and likely a signature of brainmaturation.

Cross-sensory recalibration of audiovisual spatial information during long-term adaptation to left-right reversed audition

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Cross-sensory recalibration of spatial information is essential for adaptation to a spatially unusual environment. Though little has been examined about adaptation to left-right reversed audition, we have developed left-right reversed stereophonic space only using wearable devices, as reported in BIOMAG 2014, and here, additionally analysed a recalibration process of audiovisual spatial information during three participants wearing the devices for about a month. First, sensitivity of sound source localization to visual information was behaviourally tested using the ventriloquism effect every week. A video of lip movements tended to capture auditory spatial perception from the first week to the third week and peaked at the second week, though the sound source was localized normally without a visual cue. Second, MEG responses were measured every week under the audiovisual matching task, in which the participants were asked to discriminate spatially congruent (normal-image) and incongruent (mirror-image) combinations of a tone delivered to either ear and a square cue displayed in either visual hemifield. Before the second week, the mean reaction times for both congruent and incongruent stimuli became slower as the wearing time passed, but after that, they got faster and returned to the initial level at the fourth week. Similarly, continuous low gamma activity in the extrastriate cortex, cuneus, and dorsolateral prefrontal cortex was commonly appeared for congruent and incongruent stimuli, whose strength was peaked at the second week. Because of the correlation of these findings, we conclude that there exists a cross-sensory recalibration process of audiovisual spatial information around second week, in which relatively reliable visual information is presumably propagated to temporal and frontal regions more actively, and thereby causes stronger visual capture of sound source location and longer delay of behavioural decision for audiovisual combinational information, respectively.

"Lateralization and attentional modulation for auditory processing of language in children with Specific Language Impairment."

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Intact auditory processing is essential for comprehension and production of spoken language. Indeed, deficient language processing in Specific Language Impairment (SLI) have been suggested to arise from abnormal processing of sounds (McArthur & Bishop, 2004, 2005), although some authors suggest the problems are specific to speech (Mody, Studdert-Kennedy & Brady, 1997). The role of attention in impaired cortical auditory processing has not been settled. The aims of this study were 1) to determine whether the neural responses, and specifically the hemispheric balance, to speech and non-speech sounds differ between SLI children and controls and 2) to test the effect of attention in auditory neural processing in the two groups. Magnetoencephalography (Elekta Neuromag) was used to record auditory evoked fields (AEF) to speech (synthetic vowels) and non-speech (complex sounds and sine-wave tones) sounds in attended and non-attended conditions in a group of 9 SLI children and 9 controls. The activated brain areas were modeled using equivalent current dipoles. Strong transient activation was evident between 100 and 600 ms, and more sustained activation from 185 ms onwards. Activation was stronger for attended than non-attended sounds in both time-windows, and the effect was more pronounced in the left hemisphere. In the later time-window (185 - 600 ms) left hemisphere showed generally stronger activation than right hemisphere for all sounds alike. The hemispheric balance was atypical in children with SLI. Attention shifted the balance towards the left hemisphere more clearly in control children than in children with SLI: controls showed stronger left than right activation for speech but children with SLI showed more symmetric activation between the hemisphere. Our results support the theory of impaired auditory processing in SLI and suggest altered hemispheric balance that is especially pronounced for speech sounds.

Differentiating mispredicted-predicted and unpredicted-predicted transitions in human auditory cortex using magnetoencephalography (MEG)

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The predictive coding model proposes that the brain actively supports perception by constantly attempting to match predictions and sensory inputs as much as possible, that is, to minimise prediction error in the system (Rao and Ballard, 1999; Friston, 2005, 2009). Recent studies further suggest that there is a dissociation between the processing of mispredicted and unpredicted stimuli, which are associated with different prediction error (Arnal and Giraud, 2012; Hsu et al., 2015). However, the detailed nature of these different levels of predictive processes is not fully understood. The current research used magnetoencephalography (MEG) to examine the dynamics of the mispredicted-predicted and unpredicted-predicted transitions in the brain. We presented participants with cycles of four-tone-sets, where the fourth tones can reveal either the mispredicted-predicted or the unpredicted-predicted transition depending on their position within the cycle. We found that the two transitions differ in terms of the direction, the learning curve, and the cortical source of the N1m modulation. The findings expand our knowledge of how the brain functions as a prediction machine for perceptual activities.

Neural encoding of vocal emotion in multivariate spatiotemporal MEG patterns

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A key feature of social communication is the ability to rapidly identify and interpret the emotional states of the speaker. Converging neuroimaging evidence has revealed a network of regions involved in processing vocal emotion, including sensory auditory areas, inferior prefrontal cortex, and amygdala. However, the representational content at different nodes of this network and the evolution of affect encoding across time is less understood. In this MEG study, we used source-level Representational Similarity Analysis (RSA) to investigate the neural processing of affect information in voices. Stimuli consisted of 39 non-verbal vocalisations covering 5 emotions (anger, fear,disgust, pleasure, neutral). Morphs were generated at 25% intervals between each emotion (e.g. 25% anger, 75% disgust), and hyper-emotions were generated by extrapolating to 125% along the neutral-affect dimension. The acoustical structure of each vocalisation was extracted (e.g., shimmer, f0), and was used to derive acoustic-based measures of stimulus dissimilarity. After completing the scanning sessions, participants evaluated the emotional content of the stimuli in a set of behavioural tasks (speeded categorisation; valence and arousal ratings). Model-free analyses revealed early multivariate discrimination of the sound stimuli in bilateral temporal cortex which was sustained throughout the stimulus duration. Spatiotemporal searchlight RSA analyses based on the behavioural measures revealed early encoding of affective content in a fronto-temporal network at ~100 ms, and at later time-points in frontal regions. A direct contrast of acoustic- and behaviour-based models using RSA makes it possible to evaluate where and when the emotion-encoding network is driven by the low-level structure as opposed to the affective content of the vocal stimuli.

Neuro-computational modelling of lexico-syntactic representation and integration during speech comprehension

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Speech comprehension engages complex cognitive processes, including rapid analysis of lexical properties of words and their on-line integration which requires accurate lexical representations and evaluation of the prior expectation. Here, we examine the relationship between the detailed lexico-syntactic information about words and processes of integration by investigating how strongly the lexical constraints of verbs influence the expectation of an upcoming complement structure. We investigate how this relationship is reflected in the spatio-temporal dynamics of neural activity recorded by EEG and MEG. We modelled the multivariate neural activity patterns at the onset of the main verb using the relative frequency distribution of possible complement structures (subcategorisation frame (SCF)), predictability of an upcoming structure (entropy) and consistency between the expected and the actual structure (surprisal/prediction error).Our results revealed a significant SCF effect in a left-lateralised fronto-temporal language network, starting from 200ms after the verb onset in LpMTG and gradually moving into LIFG (centred on BA44). Moreover, subsequent activity in LIFG (centred on BA45) reflected the process of evaluating the prior expectancy for accurate integration after the actual syntactic structure is heard. Our study corroborates the role of left fronto-temporal network in syntactic processing and distinguishes between activation of lexical knowledge and evaluation of the prior expectancy, demonstrating a specific role for LIFG in early processes of integration.

Differential Profile of Individualized Cortical-Subcortical Grey Matter Connectome in Schizophrenia

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Objective: This study explored the network-wise neural underpinning of psychopathology and cognitive impairment in patients with schizophrenia (SCZ) as reflected in the individualized brain grey matter (GM) structural covariance network comprised of both cortical and subcortical structures. Methods: Thirty patients diagnosed with SCZ and 39 healthy volunteers (HC) participated in this study. All of the participants were aged 18-37, were scored for IQ above 80, and did not have previous history of clinically significant head injury. Using a five-echo multi echo MPRAGE sequence, high-resolution T1-weighted images (T1WI) were acquired for every participants and were subsequently processed. Specifically, cortical and subcortical brain structures were reconstructed from individual T1WI and were subsequently parcellated into 64 cortical regions and 14 subcortical regions bilateral. Graph theory approach explored the differential global and regional characteristics of binarized, individualized brain GM connectome in HC as well as in SCZ. Results: All of the individualized brain GM connectome satisfied small-worldness (sigma>1) and modular structure (Q>0.5). Compared to HC, the SCZ group demonstrated de erased eigenvector centrality values for cortical surface area in the left superior temporal cortex; for cortical thickness in the right lateral orbitofrontal, posterior cingulate cortices as well as in the left superior frontal, entorhinal cortices and in the the left temporal pole. Moreover, changed values of edge betweenness centrality illustrating importance of specific structural covariance between cortical-subcortical GM characteristics such as between cortical thickness of left post central cortex versus left amygdalae volume were also revealed. Conclusions: This study showed distinctive profile of individualized brain GM connectome encompassing cortical-subcortical regions in SCZ compared to those of HC. Acknowledgement: Data was downloaded from the Collaborative Informatics and Neuroimaging Suite Data Exchange tool and data collection was performed at the Mind Research Network, and funded by a Center of Biomedical Research Excellence (COBRE) grant 5O20RR021938/P20GM103472 from the NIH to Dr. Vince Calhoun.

Metastability and transient dynamics in a large-scale biophysical network

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Resting state activity in the brain is characterized by fast transient activation of a set of recurring (micro)states [1]. The transitions between these states are thought to be the result of metastability, such that the states are unstable but have dynamics that are strongly affected by proximity to a stability boundary, which causes the brain to dwell for a short time in each state before switching to another. However, it is not fully understood how the properties of neuronal populations and the network of connections between them give rise to these metastable dynamics.

There has been much work over the last several years examining the dynamics of synchronization in coupled Kuramoto oscillators, which exhibit metastability for appropriate network structures and delays [2]. In particular, the structure of realistic brain networks is suitable for producing metastable dynamics [3]. However, neurons and neural populations exhibit significantly more complex dynamics than simple oscillators, and more realistic biophysical models are required to investigate the effect that processes such as synaptic plasticity have on the dynamics of transient brain states.

We simulated a network of coupled Wilson-Cowan units, each consisting of an excitatory and an inhibitory neural population. We observed metastable dynamics similar to those found in the Kuramoto model, and transient increases in power similar to resting state MEG. Unlike the Kuramoto model, the metastable dynamics are also contingent on the parameters within the neural populations. In particular, transient synchronization of the network occurs when the uncoupled units lie on the edge of stability, so that they do not oscillate individually, but oscillate when weakly coupled. This mechanism of metastability likely translates to other biophysical models, e.g. conductance-based systems.

[1] Baker et al. 2014. eLife. 3:e01867 [2] Shanahan. 2010. Chaos. 20:013108 [3] Cabral et al. 2014. NeuroImage. 90:423-435

Feature analyses of brain magnetic fields associated with discrimination of imagined speech using complex wavelet transformation.

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Brain computer interface (BCI) technologies have been developed as supplementary devices to restore damaged motor functions. However, most of developed BCI systems are based on P300 or motor imagery. To develop a verbal-imagery-based BCI, which seems to be more versatile one, properties of the brain activity associated with speech imagery need to be clarified. In this study, evoked fields associated with auditory sound imagery of native language words were recorded using a whole-head neuromagnetometer. 8 subjects with normal hearing were requested to recall three Japanese words with duration of about 800 ms, /amagumo/ (rainy cloud), /ibento/ (event), and /uranai/ (fortune telling). Time-frequency characteristics of the evoked fields between 1 and 50Hz were analyzed by complex Morlet wavelet transformation and classified using a support vector machine (SVM). Features of all channels and every latency were used for training, and features of all channels or every latency was used for testing. Then significant channels and latency ranges to discriminate imagined sounds were estimated in each subject. In all subjects, the higher testing classification accuracy was observed by using both frequency and dynamic features (temporal changes of the frequency), compared with that by using only frequency. The accuracy of each channel and latency was 96.0±4.60% and 86.0±3.12%, respectively. Particularly, 5 subjects showed accuracy more than 98% at the latencies of 105-300 ms and 592.5-930 ms. Although brain activities in the both temporal channel sets indicated relatively high accuracy, more significance were observed for the latency. These results indicated that differences among imagined sounds were reflected in evoked fields. Additionally, it was also indicated that the classification considering temporal changes of frequency over latency ranges were effective to obtain higher accuracy, and more meaningful information was included in the latency ranges than channels.

Subthreshold fluctuations under parametrically varying levels of uncertainty - an MEG study

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Neural activity preceding spontaneous-self-initiated-movements continuously drifts closer to or farther from the decision threshold before an action is initiated. For the stochastic decision model[1] these ongoing sub-threshold fluctuations vary randomly and are thought to contribute to the decision-to-act under increasing levels of uncertainty. The model predicts that a very *strong imperative to act* (in the form of sensory input) will push the system over the threshold regardless of the state of ongoing fluctuations. When stimuli become more and more difficult to detect, the uncertainty increases. Thus, with a very *weak imperative to act* the system would be pushed over the threshold only if at the same time random fluctuations happened to be near a peak. Otherwise, when they slope to a trough, this is less likely to happen.

Our prediction is that as movement cues become increasingly difficult to detect, the readiness potential will become 'prominent' in the time-locked average. In order to test this prediction, we will carry out an MEG study involving a signal detection task. Participants must detect auditory stimuli (faint bursts of 'white\' noise), *in continuous time*, against a background of steady 'pink' noise and respond by pressing a button. Subjects, will have been trained in a supra-threshold practice session, and thus will know *how often* to expect target sounds but *not when*. This implies a decision about 'when' to move while being 'biased' by *perceptual priors* regarding the frequency of occurrence of events. We expect that the amplitude of the RP in the time-locked average over pre-motor areas will be inversely proportional to the \'strength\' of the imperative to act (given by the contrast between the target bursts of sound and the background noise).

[1] Schurger, A., J. Sitt, and S. Dehaene, *An accumulator model for spontaneous neural activity prior to self-initiated movement* PNAS, 2012. 109(42): p. E2904-E2913.

A Computational Model ofTranscranial Magnetic Stimulation – Activation of Layer 5 Pyramidal Neurons

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1. Introduction

Transcranial magnetic stimulation(TMS) is one of noninvasive methods that modulates neural activity in thebrain. Recently, researchers have attempted to estimate the precisestimulus-induced electric field distribution using an anatomically realistichead model based on MRI; however, which neural tissues do affect during TMS andwhat the underlying mechanisms of TMS are, still remain unclear. This workanalyzed the activation of layer 5 pyramidal neurons (L5 PNs) during TMS andpredicted the spatial extent of activated neural tissues in a quantitativemanner.

2. Methods

The three-dimensional volumeconduction model of human head was constructed based on human magneticresonance imaging (MRI). The Magstim 70 mm figure-8 coil was positioned totarget the hand knob, and the electric fields were then calculated through FEM.The L5 PNs were virtually combined with the head model and distributed over theprecentral to postcentral gyri. For a given direction specified by a vector , the electric field gradient tensor ∇ was estimated at each center point of each compartment of L5 PNs. The magnitudeof the electric field gradient was given by ∇En and was applied to L5 PNs according to the distributed mechanisms. It wasperformed in the NEURON environment [1].

3. Results& Discussion

We found that the wall of precentral gyrusclose to the central sulcus was excited, however the top of gyrus was not. Whenwe changed the direction of the current in the coil to represent the 180° coil orientation,the direction of the activated area reverses according to coil orientation fromprecentral gyrus to postcentral gyrus. By incorporating L5 PNs coupled withhead model, we found that the precise neural tissues were influenced by TMS,while the magnitude of electric fields yielded the focal and highest magnitudeon the top of gyrus. From this study, we believe that incorporation of neuronalmodel into brain model might be critical for accurate estimation of brain areatargeted by TMS.

References

[1]Hines, M. L. & Carnevale, N. T. The NEURON Simulation Environment. *NeuralComput.* 9, 1179–1209 (1997).

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Study on the Brain Functional Network Core Following Magnetic Stimulation of WaiGuan(SJ5) Acupoint Based on Electroencephalogram

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Acupuncture has existed for thousands of years in China, which is attributed to its distinctive regulation mechanism in handling diseases. However, the mechanism behind this is far from understood. Magnetic stimulation of acupoint can be equivalent to a stimulation mode to cerebral nerve in external system. The combination magnetic stimulation and acupuncture not only extends the application of magnetic stimulation, but also contributes to demystify traditional Chinese medicine. The rapid development of complex network provides new ideas for the study of magnetic stimulation of acupoint in brain science. In our research, we combined TMS, EEG,acupuncture and the theory of complex network to explore the mechanisms of acupoint specificity, to investigate the effects of magnetic stimulation of acupoint and also hope to provide reference value for the clinical application of magnetic stimulation therapy to some extent. In the study, the experiment of repeated-pulse magnetic stimulation was administered. EEG signals in resting state and following stimulation of WaiGuan (SJ5) of healthy subjects were recorded. Correlation coefficient was calculated to measure the correlation degree between channels and functional networks under different conditions were constructed respectively. The indices of network core we analyzed included degree, strengths, efficiency and between centrality.The changes in brain connection and topology attributes of network were studied. Results showed that functional network and topology attributes following stimulation of SJ5 were significantly different from that in resting state. We discovered new functional core areas following stimulation of SJ5. The stimulation enhanced the connection of the core areas and made the information exchange of these new core areas become more frequent. This probably related to the regulation mechanisms of SJ5 and our results were helpful for understanding the underlying regulation mechanisms of SJ5.

EEG Classification for Motor Imagery BCI using Hierarchical Features Extraction

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Decoding of motor imagery tasks from the EEG data is one of the main research goals of BCI community. We have used publically available BCI Competition-IV 2008 dataset IIa in this study. This is a cue-based four class motor imagery dataset. The experimental paradigm consists of four motor imagery tasks, the imagination of left hand (class 1), right hand (class 2), both feet (class 3), and tongue (class 4) respectively. We have used the first two classes in this study to perform a binary classification experiment. Nine subjects were recruited for the acquisition of this dataset. It includes separate testing and training sets recorded on different days. Each subject went through six runs of continues session. One run consists of 48 trials (12 for each class), sum up as total 288 trials. A twenty-two channel EEG recorder was used. The sampling frequency was 250Hz. A classification experiment was performed by using linear SVM classifier. We have used the mean accuracy of ten-fold cross-validation, sensitivity, and specificity as the classifier performance measures for our experimental results. The preprocessing of the data was done with Fieldtrip toolbox on Matlab platform. Preprocessing steps include NaN removal, bandpass filtering (0.5 - 100Hz), demeaning, EOG artifact removal, detrending at 125Hz and finally apply ICA to the data. Features were extracted by using a hierarchical pipeline. The features extraction pipeline includes covariance matrix calculation of the data followed by lasso-based sparse representation and finally RFE-SVM algorithm based feature ranking. After extraction, the final features were fed to the SVM classifier for binary classification.

Neural mechanism of the motor system during reaching movements

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Understanding the properties of the motor system is one of the great challenges in neuroscience. It is important not only academically, but it can be used for various application. For example, paralyzed person can drink, eat and control their environment using their motor command signals. To understand the motor system, it is required to analyze the neural activities during movements. Reaching movement is a fundamental and essential movement because the most of our daily movements consist of sequences of reaching. There has been a lot of studies on reaching and its model of the motor system. However, there is no electrophysiological study on the interaction of whole brain during reaching movements.

Here we investigate whole brain MEG signals and its relation among regions during reaching movements. Signals at source level were computed and mutual information was calculated among ROIs with 100 ms intervals in low frequency, alpha, beta and gamma bands.

We found that different frequency bands play different roles in reaching. In the low band, bilateral PF, PMd, SMA, M1, S1, putamen (PUT), pallidum (PAL), TH, PPC, CB and ipsilateral ACC have high centrality before movements. Moreover, bilateral PUT, PAL and CB have high centrality during movements. In the alpha band, bilateral CB and contralateral SMA and TH have high centrality before movements. Similarly, bilateral CB, ipsilateral PUT and PAL have high centrality before movements in the beta band. In gamma band, bilateral M1, S1, contralateral PF, PMd, ACC and TH have high centrality before movements.

We demonstrated that neural activities in low frequency play an important role in interaction during the movement preparation and execution. In contrast, alpha, beta and gamma bands are involved in interaction during the movement preparation. Moreover, most of motor related areas are related to the movement preparation, whereas PUT, PAL and CB are involved in the movement execution. Our results contribute to the understanding of the motor system and it provides the insight about neural characteristics for the brain-machine interface.

Tracking emotional face perception in space and time using MEG-based classification

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The visual cortex and associated areas are involved in emotional face processing[1], an important feature in human interaction. Here we present an automated method to resolve the spatiotemporal dynamics of face perception in MEG sensor and source space.

MEG data was collected while participants passively viewed emotional, neutral and scrambled faces. We then performed classification per sampled time point using 40 occipital channels (in sensor space) or 20 occipital, temporal and parietal virtual sensors reconstructed through beamforming in a gamma-band window (in source space). Using nested cross-validation we implemented a linear support vector machine to classify a) neutral and emotional faces; b) happy and angry faces. To assess significance we applied permutation testing[2] and corrected for multiple comparisons by thresholding using the maximum test statistic, as relying on a theoretical chance level has been shown to fail in limited datasets[3].

Both problems were successfully solved in sensor space (neutral vs. emotional faces: mean accuracy 79%±2%, <0.001; happy vs. angry faces: 79%±3%, <0.001) and source space (76%±2%, <0.001; 74%±2%, <0.01). Subject-wise accuracy varied in significance despite rising above the 50% threshold. Decoding performance peaked at ~150 ms post-onset in all conditions. In source space, classifier weights allowed us to assess the contribution of each virtual sensor, with the occipital cortex playing a key role after ~150 ms.

Our method succeeded in resolving differences in processing not only between emotional and neutral stimuli, but also between different emotional valences. We conclude that MEG offers a wealth of information for data-driven applications and recommend using empirical chance levels to assess classifier performance.

[1] Pourtois et al. (2013). *Biol. Psychol.*, 92(3)
[2] Jamalabadi et al. (2016). *Hum. Brain Mapp.*, 37(5)
[3] Combrisson & Jerbi (2015). *J. Neurosci. Methods*, 250

Decoding MEG using Classification on RiemannianManifolds

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Magnetoencephalography (MEG) is an efficient non-invasive tool in Brain-computer interface research andapplications. The goal of this work is to predict visual stimuli from MEGrecordings of human brain activity, and the extreme difficulty of this task isthe structural and functional variability across the subjects.In this paper we address the problem throughclassifications on Riemannian Manifolds and provide the following solutions:first, MEG signals are represented by Covariance matrix feature, and Riemanniangeometry on the symmetric positive definite matrices provide a convenient wayto manipulate the Covariance matrix features. We use Tangent space mapping toproject Covariance matrix features from manifold in a vector space namedTangent space. Then, these vector space features can combination withclassifiers, such as SVM, lasso.etc. Second, we use the Grassmann-based Domainadaptation algorithm to models data variability across the subjects. Finally,the domain invariant features are combination with support vector machines,which give a supervised classification result. Then, for each test subjects, anunsupervised algorithm is applied, which use the labels from SVM as an initialization for the k-means clustering algorithm, in the Riemannian manifold.On the DecMeg2014 competition dataset, we demonstrate that this new approach outperform significantly than the 1stplace\'s result of the DecMeg2014 competition.

Intra- and inter-subject classification of motor imagery MEG signals

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Motor imagery (MI) with real-time neurofeedback could be a viable approach e.g. in stroke rehabilitation. Magnetoencephalography (MEG) is well-suited for recording oscillatory brain signals. MI is known to modulate 10- and 20-Hz oscillations in the somatomotor system. In order to provide accurate feedback to the subject, relevant features should be extracted in real time from MEG data. In this study, we evaluated the capability of several MEG signal features to discriminate between left- and right-hand MI and between MI and rest.

MEG was measured from 9 healthy subjects while they were imagining either left- or right-hand finger tapping according to a visual cue. Data analysis was done offline. The evaluated features were power spectral density (PSD), Morlet wavelets, short-time Fourier transform (STFT), common spatial patterns (CSP), filter-bank CSP (FBCSP), spatio-spectral decomposition (SSD) and SSD+CSP. We estimated the within-session left-vs-right and MI-vs-rest accuracy and inter-session left-vs-right accuracy for each subject. In addition, we performed inter-subject classification using a leave-one-subject-out paradigm and spatially filtered MI signals as input features.

SSD+CSP combination yielded the best accuracy in within-session left-vs-right (mean 73.7%), MI-vs-rest (mean 81.3%) and inter-session left-vs-right classification (mean 69.0%). There were large inter-subject differences in classification accuracy. However, we achieved a mean accuracy of 61.8% in inter-subject classification with SSD+CSP.

Decoding of spatially filtered MEG data yielded good single-trial accuracy, if the classifier was trained using the subject's own data. Feature extraction methods utilizing both the spatial and spectral profile of MI-related signals provided the best classification results. However, the poor results of inter-subject classification indicate that the current methods should be improved in order to deal with subjective variations in MI-related signals.

Emotional states decoding during watching movies frommultimodal neurophysiological signals

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Emotional status is reflected in the physiological signals on central and autonomic nervous systems (CNS and ANS). The purpose of this study is to investigate whether different emotional responses to affective movies can be decoded from multimodal neurophysiological signals reflecting CNS and ANS. From 15 healthy university students, multichannel electroencephalograms (EEGs), skin temperature, Galvanic skin response (GSR), and photoplethysmogram (PPG) were recorded during watching 32 movie clips reflecting 4 types of different emotional states, which were selected from based on the valence-arousal model (high/low valence and high/low arousal). The spectral, temporal, and spatial characteristics of EEGs showing significant differences among different emotional states were determined to construct feature vectors for pattern classification. The time and frequency domain features of the physiological signals were selected so that they reflect the characteristics of the ANS, and the measures showing significant differences among the emotional states were selected as additional feature vectors. A support vector machine(SVM) with Gaussian radial basis function (RBF) kernel was adopted as a pattern classifier along with principal component analysis (PCA) for dimensionality reduction. The classification accuracy was calculated by ten-fold cross-validation. When only the EEGs were used, the classification accuracies were as high as 68.73 and 71.34%, for the decoding of valence and arousal levels, respectively. It was still as accurate as 58.75 and 62.06% for the case of using only the ANS physiological signals. By using multimodal decoding strategy, i.e., using both the CNS and ANS signals, the classification accuracies were 72.76 and 71.86% for valence and arousal, respectively. Our results demonstrate that the different emotional states to the affective movies can be decoded with high accuracy from multimodal neurophysiological signals.

A Gaussian Mixture Model -based method for extracting feedback-related MEG responses for brain–computer interfaces

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Feedback-Related Negativity (FRN) is an evoked response to an outcome of an action, indexing a theoretical prediction error. Single-trial FRN amplitudes have been shown to link to learning dynamics. FRN may thus serve as a natural feedback signal in Brain–Computer Interfaces. In this study, we estimated the FRN amplitudes in unaveraged MEG responses in a manner suitable for real-time analysis and correlated these amplitudes with the modelled "prediction error" signal derived from an ideal-observer model.

We recorded whole-scalp MEG of 14 subjects performing a task where they had to learn the values of four abstract stimuli by receiving probabilistic feedback (360 trials per subject). We extracted epochs time-locked to the feedback presentation, filtered them to 1–40 Hz, and down-sampled to 125 Hz. We then constructed a feature set by identifying the sensors and time points displaying significant differences between the responses following positive and negative feedback and by clustering them according to their spatial location, latency and the sign of the difference. Initial spatio–temporal distribution of the informative features was estimated from a training set of 30 trials (~8% of the data). We then fitted a Gaussian Mixture Model to approximate the locations and latencies of the relevant activity with a small number of Gaussian components (< 10), and obtained amplitude estimates by integrating the preprocessed MEG signal over the 50% highest-density interval of each of the mixture components. Our results demonstrate that in all 14 subjects the algorithm identified and extracted the single-trial amplitudes of the evoked-response components that displayed statistically significant correlation (average Spearman $r = 0.17 +/- 0.05$, $p < 0.05$) with the model predictions.

Optimization of non-linear permutation entropy features for EEG-based biometrics

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With the increased interests in using electroencephalogram (EEG) activity for biometrics systems, there has been growing evidence that using non-linear EEG features enhances the performance of EEG-based personal authentication. However, as complex non-linear features need to be optimized for system implementation, it is important to optimize parameters of computational models of non-linear features to realize reliable EEG-based biometrics. The study addresses this issue by exploring the optimal parameters for the computation of permutation entropy, one of the widely used non-linear EEG features. Permutation entropy quantifies the complexity of a time-series signal by two parameters, including a time embedding dimension and a time delay. In our previous work, we have developed a criteria index (CI) to assess the effectiveness of EEG features by the ratio of intra-subject variability to inter-subject variability. 30 subjects participated in our EEG recording experiments 10 times over different days. Subjects rested on a chair with their eyes closed for 2 minutes, while their EEG was recorded using a 14-channel wearable EEG device. After preprocessing with bad trial elimination, band-pass filtering (2~50 Hz), and signal trimming, we randomly divided a single EEG trial into 20 EEG epochs, each spanning 2 sec. We calculated the permutation entropy of each epoch in 40 different conditions of time embedding (3~10) and time delay (1~5). Finally, we calculated the CI of the permutation entropy for each condition of time embedding dimensions and time delay. The result showed that the best personal authentication performance was obtained when the time embedding was 3 and time delay was 3, respectively. Our analysis result suggests that a relatively short time embedding with an appropriate time delay may be sufficient to extract permutation entropy features, indicating a plausibility of using non-linear permutation entropy features for real-time EEG-based biometrics.

Evaluating the Performance of ElectrocorticographicMicroelectrodes for Syllable Decoding

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Electrocorticographic (ECoG) based brain machineinterface (BMI) have recently attracted increasing attention because it combinerelatively high spatial with high temporal resolution. Decoding words and theirconstitutive elements during overt speech has been achieved reasonable decodingaccuracy using macro-ECoG with 2.3 mm diameter and 10 mm spacing. In thisstudy, we attempt to discriminate syllables during overt speech usingmicroelectrode arrays (75micro diameter and 0.9 mm spacing). ECoG data wereacquired from the subject undergoing neurosurgical treatment of intractableepilepsy. Two micro electrode grids, one over left medial-temporal gyrus (MTG)and another over primary motor cortex, were implanted with positioning dictatedby clinical criteria. In order to learn more about the dynamic of the task anddetect the on-set of the articulation, we segment one trial of the task tothree phases, including baseline, planning and response. The planning stage isdefined as the time range between the on-set of cue time to the response time.Three frequency bands include alpha band, beta band and high gamma band wereextracted as features, which were used to train the linear classifier. The highgamma activity (70-110 Hz) was observed during the response phase for bothsubjects. And the beta band (16-31 Hz) was decreased, which is also observed inprevious study. The classification accuracy also showed that it can besignificant distinguish these three states. The syllable categories weredecoding based on the different places of articulation. Both vowels andconsonants in binary-class can achieve higher accuracy using the ECoG data fromthe channel located in primary motor cortex. The results showed that beta bandand high gamma band play a big role for the classification accuracy. The mostinteresting finding is that we can decode syllables not only during theresponse stage but also during the planning stage, which will be helpful forthe speech BMI.

Neural oscillations in the temporal pole for an audio-visual speech matching task reflect late neuronal maturation in adolescence

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Recent developmental and psychiatric studies focus on adolescence more than ever. During this developmental transition, most of teenagers have more opportunities of spending time with peers, and build complex social relationship with them. For such social communication, multimodal processing in speech perception is requisite and plays a significant role. Previous behavioral studies demonstrated late maturation of adolescent audio-visual processing, while their single modality processing is comparable to adults\'. Therefore, we aimed to reveal the neuronal development, using magnetoencephalography(MEG). In this study, we acquired MEG data from 15 adults (25.6 years old) and 14 healthy adolescents (16.8 years old) performing an audio-visual speech matching task. We selected regions of interest (ROIs) using whole brain time-frequency analyses, then applied phase amplitude coupling (PAC) to them. We identified prominent delta and beta band power in the temporal pole (TP), and a remarkable PAC between delta phase and beta amplitude in both groups. TP is a key multisenosry integration area, also known as the anterior temporal pole(ATL), which was recently hypothesized to be a convergent hub region capable of high-level visual and auditory integration (Perrodin et al. 2015). More importantly, we found a significantly lower accuracy in task, and lower phase amplitude coupling in the adolescence group. Furthermore, the index of PAC was well correlated with the scores of perceptual organization test of WAIS 3. Thus, these results firstly demonstrate the adolescent ability of binding audio-visual speech is still under development, and the neural oscillatory measurements in the TP such as PAC reflect late neuronal maturation in adolescence.

Impact of very preterm birth on the structural and functional neural correlates of emotion regulation at school age

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Emotion regulation difficulties are frequently seen in very preterm (VPT) born children and may lead to the development of poor socialization skills, and psychiatric disorders. Children born VPT are also high risk for brain structural atypicalities. Using MEG and MRI, we identified associations between the functional, structural and behavioural characteristics of socio-emotional processing in children born VPT compared to age-, sex- and IQ-matched term born (TB) children.

41 children (19 VPT, 22 TB, age range: 7-13yrs) were scanned in MEG (CTF;MISL) during an emotional go/no-go task with two conditions: an inhibition (25% no–go trials) and a vigilance condition (75% no–go trials). Children responded to 'Go' stimuli as fast as possible and withheld responses to 'No–Go' stimuli (randomized target: either blue or purple frame). Stimuli included Happy or Angry faces, presented within the frame as emotional distractors. Only correct No-Go trials were analyzed from the two conditions. MRIs (3T) allowed co-registration with MEG data, and structural brain analyses. MEG pre-processing and brain functional analyses were performed using SPM12. MRIs were analyzed with CIVET image-processing. Cortical thickness and volumes between TB and VPT children were analysed, and then associations between the MEG, MRI and behavioural measures of emotional processing were computed in both groups using regression analyses.

The VPT vs. the TB group, showed sustained reduction of inhibition-related MEG activity in the context of angry but not happy faces, across a right lateralized parieto-fronto-temporal network from 125-425ms ($p<0.005$), that included the right angular gyrus and the medial and ventral prefrontal cortex (PFC). Our structural brain analyses demonstrated that reduced gray matter overlapped functional atypicalities in VPT, and were also directly associated with poor socio-emotional performance in children born VPT.

Alterations in resting MEG spectral power in infants prenatally exposed to alcohol

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Early studies of the effects of prenatal alcohol exposure (PAE) on neonatal brain functioning indicated hypersynchrony defined by broad increases in EEG spectral power. In the Ethanol, Neurodevelopment, Infant and Child Health (ENRICH) birth cohort, we prospectively enrolled pregnant women who did or did not drink alcohol during pregnancy. At 6 months of age, brain function of children in the cohort was assessed using the Elektra Neuromag 306 channel biomagnetometer. During MEG measurements, infants participated in an interactive play paradigm which included periods of rest. MEG and synchronized video were used to identify periods of rest. MEG data were processed using Maxfilter to remove artifact. All data were registered to a standard head position to allow for direct comparisons across infants. Heartbeat artifacts were romved using signal space projection. Two-second intervals of rest data were analyzed to obtain averaged spectral power based on planar gradiometers, providing a regional estimate of spectral power. To date, good quality MEG data were obtained from 19 control infants and 13 infants with PAE. A significant 4-way interaction (p = 0.02) was obtained with group (PAE vs. controls), hemisphere (left, right), region (frontal, temporal, central, parietal, occipital) and frequency band (delta, theta, alpha, beta, gamma) as independent variables and MEG regional spectral power as the dependent variable. There was no significant main effect of group, which does not support the result of broad hypersynchrony found in neonates. However, the interaction, driven by differences in delta and gamma bands, reveals persistent alterations in spectral power in infants with PAE relative to controls at 6 months of age. These preliminary results obtained from an ongoing cohort study may provide an early marker of atypical brain development in PAE infants to better target treatment in young infants. Supported by grant NIAAA 1 R01 AA021771.

Increased beta-band connectivity during angry face processing in children with autism

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An understanding of emotional information from faces is critical for successful social interaction. A key deficit in autism spectrum disorder (ASD) is poor social functioning. Atypical interregional functional connectivity is reported in ASD, but few studies have examined functional connectivity during affective processing in ASD and none in children. We examined functional connectivity during emotional face processing in children with and without ASD using MEG. Fifty children (23 with ASD, 18M and 27 typically developing, 21M) 7-10yrs old participated. Faces (happy, angry, neutral) and scrambled patterns (target) were presented simultaneously for 80ms on either side of a central fixation cross. Children indicated the position of the target by pressing a button (left or right). Structural MRIs were obtained for MEG data co-registration.

The data were segregated into epochs by emotion. Sources for each face type were estimated at the first 90 nodes of the AAL atlas using the LCMV beamformer. Phase synchrony between region pairs was indexed with the phase lag index. Children with ASD showed significantly greater phase synchrony in the beta-band frequency vs. controls during angry face processing 333-666ms following stimulus onset, $p=0.002$, corrected. The network included the right fusiform, bilateral amygdalae and bilateral insulae with connections to other regions associated with affective processing. Increased beta-band connectivity strength of these regions (all $p<0.001$) in children with ASD relative to controls during angry face processing was also found. No significant group differences for other face types or frequency bands were observed.

We demonstrate that beta-band functional connectivity during angry face processing is greater in children with ASD than in typically developing children. Given our previous results in adolescents, this further supports an altered developmental trajectory of emotional face processing in ASD, particularly for negative affect.

Quantificationof Language Neural Network in the Developing Brain with Neuromagnetic Signals

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The objective of the present study was to investigate the neural network of word recognition in children at both sensor and source levels using Graph theory and magnetoencephalography (MEG). A better understanding of the maturational changes of neural network would help us to develop strategies to improve our language skills, and lays a foundation for clinical diagnosis of language impairments or developmental delay in pediatric brain disorders (e.g. epilepsy).Sixty healthy children were investigated with magnetoencephalography (MEG) and a word recognition task validated for use with children. Each participant was presented with word pairs, visually and auditorily, in “match” and “mismatch” conditions. The patterns of neural networks were analyzed at both sensor and source levels using graph theory.MEG data revealed that there was significant language processing development in children aged 6-17 years. First, the language network transitioned from a bilateral network to a more efficient unilateral network. Secondly, as age increases, the path length of the language network significantly shortened, while the clustering coefficient increased. Third, the connection strength of the language network increased with age. In addition, there was a gender difference in the language network: males had more visual connections, whereas females had more auditory connections.The results indicate an improvement in network efficiency and robustness, as well as the reduction of variation among connections. It seems that there was gender-dependent or optimal development of the language network.The there is a neuromagnetic developmental trajectory of language networks, which can be used as a novel imaging biomarker to study language function of the typical developing brain, and the impairments or developmental delay of language dysfunction in children with brain disorders in the future.

Receptive language mapping using the N400m in children with and without epilepsy

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Our aim is to develop a passive, noninvasive, child-friendly paradigm to test and lateralise receptive language in children with epilepsy. Current language neuroimaging tasks are often long and require active responses. This may yield inaccurate results due to the combined impact of young age and anti-seizure medication, which affect individual language ability, performance, cooperation, and attention. We tested fifty participants, including children (n=25) and adults (n=25) aged 5 to 35, using an Elekta-Neuromag TRIUX 306 channel whole-head MEG system (Helsinki, Finland).Participants listened to naturally spoken sentences that were semantically correct or incorrect in an auditory N400 paradigm. We also present data from 10 patients with epilepsy (5 adults, 5 children), collected prior to surgery using the same paradigm. We used minimum norm estimation and beamformer source analysis methods to localise the sources of the N400 in individuals. The sources of induced and evoked neural activity localised to frontotemporal regions and time frequency analyses revealed changes in oscillatory power in the dominant hemisphere. In addition, neural activity related to semantic violations were linked with out-of-scanner receptive language scores and sentence judgements, at the within-subjects level. We will discuss the clinical use of our child-friendly auditory N400 paradigm, in the context of lateralisation and maturation in the typically developing population tested. We believe that these promising results have significant potential to contribute to the routine assessment of surgical planning for young patients with epilepsy.

Cerebellar GABA concentration and intrinsic connectivity network synchrony in neurodevelopmental disorders

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Recent studies have highlighted the role ofthe cerebellum in cognition and emotional regulation, in addition to our traditional understanding of its role in movement control. Further, cerebellar dysfunction has been linked to neurodevelopmental disorders, with the suggestion that early cerebellar damage leads to a wide range of behavioural deficits which are controlled via cerebellar-cerebral circuits. γ-aminobutyric acid (GABA) modulates these circuits, and inhibitory influences driven by GABA modify synchronized networks in the cortex- in the human, these are explored non-invasively via magnetic resonance spectroscopy (MRS) and MEG. We postulated that the phasic synaptic excitatory-inhibitory balance of activity within these cerebellar-cerebral circuits is influenced by levels of GABA in the cerebellum, and that abnormal levels may play a role in neurodevelopmental disorders. Here, we investigated cerebellar GABA concentration and spectral connectivity in 4 groups of children (age range 4-19; n = 75); ASD, ADHD, OCD and typically-developing controls (TD). We measured *in vivo* tissue GABA concentration in the cerebellum using MRS, and sought to relate this to oscillatory synchronisation in cortical intrinsic connectivity networks (ICNs) during resting state measured using MEG. No significant differences were observed in GABA/creatine ratio by sex,group, or sex x group interactions; a significant correlation between age and GABA/Cr ratio was observed in the OCD group. Analysis of intra- and inter-ICN synchronisation revealed widespread group differences at multiple frequency scales within and between spontaneous resting networks. These results suggest that whilst cerebellar GABA concentration is not driven by sex or diagnosis, complex network interactions in intrinsic and spontaneous cortical network distinguished a number of neurodevelopmental disorders from each other.

Development of the semantic N400m activation and its link with behavioural skills

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Language comprehension develops during first years of age, but the maturational changes in the brain continue until late adolescence. It is thus likely that the neural substrates underlying semantic analysis change along with the maturation of the cortical network. We used cross-modal priming paradigm to study the developmental changes in the semantic N400m response in children aged 6-7, 9-10, 12-13, and adults. MEG responses were recorded for auditory words preceded by matching or nonmatching pictures, and the neural measures were correlated with behavioral skills (linguistic and nonlinguistic skills, memory, phonological processing, naming and reading). Equivalent current dipoles were used to model the neural activation underlying the sustained response emerging between 200 – 600 ms. All age groups showed enhanced activation to the non-matched condition (N400 effect). The activation emerged later and lasted longer in younger children than in adults, but in adolescents the timing of N400 was already adult-like. There was a clear change in the hemispheric balance of activation across age from more bilateral to stronger lateralization to the left hemisphere. Specifically, activation between age groups differed only in the right hemisphere being stronger in 6 to 10 -year-old children than in adults. Increased lateralization of activation in general, regardless of the size of priming effect, was linked with increased behavioral skills, but this association is likely to reflect the effect of age on performance level. Within individual age groups the brain-to-behavior association varied by age. The strongest correlations were evident in 6-10-year-old children. In contrast to the general age-related decrease of the N400 strength reported earlier, we suggest a developmental change driven by decrease in right hemisphere activation. Results also indicate strongest changes in brain basis for semantic analysis between 10-12 years.

Greater MEG response accompanies faster and effortless retrieval of an intended word in verb generation task

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Speech production relies on fast and flexible retrieval of an intended word from mental lexicon. The retrieval occurs either automatically (when the environment cues and the target word are strongly related) or requires top-down control mechanism. The previous fMRI studies using a verb generation paradigm demonstrated that the more difficult it is to retrieve the verb, the greater the activation of left VLPFC. The present MEG study utilized the same paradigm to examine the timing of left VLPFC activation underlying controlled retrieval.During MEG session 35 participants were presented with a visual noun cue and were asked to generate a semantically related verb in the inflected form. Stimuli were 130 Russian nouns divided into two categories with strong and weak association strength (SA-WA) between a noun and possible verb response. We compared MEG phase-locked response (PLR) to the onset of the nouns with strongly versus weakly associated verbs.Verbal responses were significantly faster for those nouns that have strongly associated verbs. Surprisingly, the nouns with strong verb associations elicited higher PLR within the 250–450 ms time window than the nouns that required the retrieval of the weaker associated verbs. SA-WA differences in the response magnitude initially appearing at the left temporal pole (245-258 ms), then spread to the left VLPFC (284-418 ms) with further propagation toward the left dorsolateral prefrontal cortex (410-460 ms).We hypothesized that the opposite direction of the effect in fMRI and MEG responses can be explained by the different mode of neural computation underlying automatic and controlled retrieval. MEG PL response reflects fast automatic retrieval that occurs solely for nouns strongly associated with their verbs. A failure of automatic process leads to effortful controlled retrieval, which is captured by an increase in fMRI signal.

Discrimination of word perception and imagination in a single-trial EEG basis using hierarchical extreme learning machine

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Neurolinguistics is a study toreveal the neural mechanisms of language processing. Paul Broca discover theconnection between motor production of speech and brain regions, the area tocontrol speech production is known as Broca's area. Subsequently, Carl Wernickediscovered the Wernicke's area, which extend across the region between temporaland parietal lobes and controls speech comprehension. At the level of speechperception and production, a lot of theories have been developed andexperiments conducted on words representation, but how words are encoded andaccessed in the brain remains controversial. In our present study, we comparethe brain responses to perceive and imagine two words /go/ and /back/ to findthe neural basis about the speech encoding using source localizationtechniques. Based on the findings of previous analysis, the brain responses to imaginetwo words are discriminated for each trial, using hierarchical extreme learningmachine and signal processing techniques. The classifier performance of ourstudy is estimated using mean accuracy of 10 fold cross validation. We expectthat our algorithm could be applied to miscellaneous applications correspondingto language rehabilitation, the brain computer interface (BCI).

Source-Level EEG Analysis for Vowel Speech Perception Using sLORETA

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Language processing is one of the mostimportant cognitive functions in human which is not explained clearly. EEG hasbeen widely used in various speech studies due to high temporal resolution.However, EEG has poor spatial resolution. Therefore, to improve the spatialresolution of EEG, various source localization algorithms have been developedand implemented for many researches. In this study, we measured EEG data duringperception of five different vowels (/a/, /e/, /i/, /o/, and /u/) from 8 younghealthy native Korean subjects using 64 channel EEG device by Electrical Geodesics,Inc. In the preprocessing procedure, we applied Butterworth band-pass filter with1-60 Hz bandwidth. In addition, independentcomponent analysis (ICA) was applied to the filtered data to reject theartifact component. By using multivariate empirical mode decomposition (MEMD),we removed some intrinsic mode functions (IMFs) which had noise component. Afterartifact rejection, we reconstructed the signal from IMFs. Then, time-lockanalysis was used to calculate event-related potentials. And time-frequencyanalysis was also performed with wavelet method. Source analysis was conductedby the standardized Low Resolution Electromagnetic Tomography (sLORETA)software. In addition, cross spectral density was calculated to estimate thesource in frequency domain. Finally, we applied statistical nonparametricmapping (SnPM) to test the statistical differences of our data.

Predictive brain processing of listened audio narrative: MEG evidence

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The predictive coding hypothesis offers a plausible theoretical framework to understand neural processing of listened speech and other kind of time-dependent serial-form sensory input. Predictive coding assumes an internal representation: a Bayesian model aims to predict forthcoming sensory inflow based on earlier accumulated information and is recurrently updated according to prediction error. Here we show that naturalistic auditory narrative entrains MEG activity in line with the predictive-coding scheme. We trained a Bayesian language model (N-gram) by a separate text corpus and inferred a context-dependent probability for each word in the listened 1-h-long narrative. These inferred (–log) probabilities, related to the predictability of words, correlated with MEG signal amplitudes in temporal and inferior frontal regions. The model was most accurate with long words in the narrative, in which case the correlation coefficient between the inferred probabilities and measured MEG amplitude exceeded 0.4. Our results provide experimental evidence to support the predictive-coding scheme in speech perception. The presented methodology opens up new means to study context-sensitive sensory processing under naturalistic experimental conditions.

Gestural enhancement of degraded speech comprehension engages the language network, motor and visual cortex as reflected by a decrease in the alpha and beta band

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Face-to-face communication integrates speech and visual input, such as iconic gestures, which can enhance speech comprehension in noise. Using MEG, we aimed at identifying the neural dynamics associated with enhancing degraded speech comprehension by gestures. Participants were presented with videos of an actor uttering action verbs. Speech was presented clear or degraded by applying 6-band noise-vocoding, and accompanied by videos of an actor performing an iconic gesture (clear speech+ gesture; CG, degraded speech+gesture; DG) or no gesture (clear speech; C, degraded speech; D). Gestural enhancement, calculated by comparing (DG vs D) to (CG vs C), revealed significant interactions between gesture occurrence and speech degradation in the alpha, beta and gamma band. We found a beta decrease in motor areas indicative of engagement of the motor system during gesture observation, especially when speech was degraded. A beta decrease was observed in the language network including left inferior frontal gyrus and left superior temporal regions, suggesting a higher semantic unification load when a gesture is presented together with degraded speech. We observed a gestural enhancement effect in the alpha band in visual areas, reflecting more engagement when a gesture is present and when speech is degraded, possibly reflecting the allocation of visual attention. Gamma band effects in left-temporal areas suggested a facilitated binding of speech and gesture into a unified representation, especially when speech is degraded. Our results support earlier claims on the recruitment of a left-lateralized network including motor areas, STS/MTG and LIFG in speech-gesture integration and gestural enhancement of speech and provide novel insight into the neuronal dynamics associated with speech-gesture integration: decreases in alpha and beta power reflect engagement of the visual and language/motor networks,whereas a gamma band increase reflects the integration in left prefrontal cortex.

Oscillatory signatures of hand and foot verb-movement congruency in a double dissociation paradigm

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The specificity and relevance of activity in modality-specific brain areas for semantic memory is under debate (Binder & Desai, 2011, Trends Cogn Sci). Action knowledge offers a unique link between cognition and behavior which can be capitalized on empirically. This study examined the interactions of action verb understanding, oscillatory activity in motor areas, and movement execution in a double dissociation priming paradigm. The critical manipulation was the congruence of the body part used to execute a response and the action described by the verbs.

During continuous MEG recordings, 20 subjects decided whether visually presented verbs had a concrete or an abstract meaning. A color change indicated whether a response should be executed using the hand or foot. Responses were only required following concrete verbs, i.e. hand and foot verbs. This resulted in a facilitation of congruent verb-response pairs: Hand responses were faster following hand verbs than foot verbs, and vice versa. From the MEG data we analyzed virtual channels in the hand and foot motor regions as well as in visual word processing areas. Interestingly, first results show a concerted recruitment of reading and motor areas, with strong beta suppression in the lingual gyrus preceding that in motor areas. Subsequently, particularly in paracentral sensors (foot region) we observe a more sustained beta suppression before foot responses compared with hand responses. Verbs describing foot or leg movements even increase this suppression compared to hand verbs. Further analyses will focus on inter-area connectivity.

The results support theories of embodied cognition and distributed models of semantic memory. It was previously shown that action verbs recruit motor areas and that this can interact with behavior (Mollo et al., 2016, Cortex; Klepp et al., 2015, Neuroimage). Our results offer further insights into these interactions and their neural oscillatory underpinnings in a double dissociation paradigm.

Phonemic properties of expected words modulate pre-stimulus alpha oscillations

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Prediction of future events has been proposed to be a fundamental neurocognitive mechanism. Neural oscillations could support proactive perception by selective control of neural excitability in time or space (e.g. delta entrainment, alpha-mediated inhibition), and by representational pre-activation of the expected sensory object (e.g. predictive coding). In this study we explored both mechanisms using magnetoencephalography and linguistic stimuli. Participants saw a picture of an object and after a delay of ~2 seconds heard either the corresponding word, or the corresponding word with a vowel replaced. They responded to whether the word was correct or not. In order to explore anticipatory pre-activation, we manipulated the initial phoneme of the words (either stop-consonants or fricatives and sibilants). To explore how temporal uncertainty may modulate representational pre-activation, two versions of the experiment were ran, with a fixed or a variable delay between picture and word. Cluster-based permutations revealed significant differences between stop-consonant- or fricative-initial words in the interval preceding the word, suggesting the pre-activation of its phonological features. The largest differences appeared within the alpha band both in the fixed and the variable delay experiments, however, the timing and topography of the effects appeared to be modulated by temporal uncertainty regarding the target.

Large-scale functional networks underlying semantic vs. perceptual processing of written words

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Time-sensitive MEG recordings together with recent advances in network analysis allow for sub-second snapshots of the brain's large-scale functional networks. In a time- and frequency-resolved analysis of inter-areal coherence, we show that conducting perceptual and semantic judgments on the same written words leads to the transient formation of spatially and spectrally distinct cortical networks in the brain.
We recorded MEG data from 14 healthy participants while they performed two judgment tasks on visual words, focusing either on their semantic (object size: “Is this object bigger or smaller than a rubber boot?”) or visual properties (color: “Is the word printed in blue or green?”). We applied a frequency-specific spatial filtering technique to identify task-specific interactions between cortical regions. Modulations in coherence following stimulus presentation (0-600 ms) were determined by contrasting the results for the two tasks ($p<0.0005$, cluster size 15) in pre-specified frequency bands.
For the semantic judgment task, increased coherence was detected mainly in the beta (21-30 Hz) and gamma (60-90 Hz) bands. In the beta band, we identified a bilateral frontal network. In the gamma band, increased coherence was detected in a network with nodes in classical reading regions in the left occipito-temporal and superior temporal cortex, and in the left sensorimotor and right parietal cortex. In the perceptual judgment task increased coherence in the gamma band (60-90 Hz) was observed in a visual network with connections between left occipital and parietal cortex and between parietal and frontal cortex. The results depict a task-relevant reorganization in network structure when moving from a semantic to a perceptual task. More generally, the findings support the role of inter-areal coherence as a general mechanism for integration of information across brain regions.

An MEG investigation of network synchronisation during expressive language processing in paediatric epilepsy

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An important step in the presurgical evaluation of patients with medically refractory temporal and frontal lobe epilepsies is to localise the neural structures involved in language processing. MEG has proven to be particularly valuable in this regard and has been used to successfully identify fronto-temporal sources of language in patients with epilepsy (Papanicolau et al., 2004). While previous MEG studies of expressive language have largely focused on identifying local brain structures, more recent models of language function have emphasised the importance of integration and synchronisation within distributed networks of regions. In this study we focused on characterising functional connectivity associated with expressive language processing in a group of paediatric epilepsy patients. Twenty-five children with drug-resistant epilepsy, who were assessed for surgical amenability at the Birmingham Children's Hospital NHS Foundation Trust participated in the study. Patients were recorded in a magnetically shielded room using an Elekta-Neuromag TRIUX 306 channel whole-head MEG system (Helsinki, Finland) and were asked to perform a verb generation task. Atlas-guided beamformer source reconstruction was performed, and phase synchronisation among regions was calculated. Differences in task-dependent synchronisation were investigated in alpha and beta frequency ranges. We demonstrate increased connectivity between fronto-temporal regions in alpha and beta frequency bands during covert verb generation. In addition, task dependent synchronisation was linked with behavioural measures of language abilities. We will discuss how task-based connectivity analysis can provide valuable information about synchronisation within the language network with high significance in single patients and how this may contribute to surgical planning in epilepsy.

Two opposing mechanisms underlying the audio-visual facilitation of speech tracking in prefrontal regions

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Auditory cortical activity entrains to the envelope of speech. In this study, we investigated the extent to which speech quality (acoustic SNR) and visual informativeness (presence/absence of lip information) interact in shaping the cortical encoding of the speech envelope. Participants listened to speech in eight different experimental conditions, varying speech SNR (4 levels) with the presence/absence of visual information in a factorial design. Information theoretic analyses of band-pass source-level MEG data revealed widespread speech envelope tracking in all conditions, predominantly in the right AC and in the delta-low band (0.25-1 Hz). An increase in speech SNR improved the accuracy of speech tracking in the delta-high band (1-4 Hz) in the right AC and inferior frontal and prefrontal cortices, and of beta-band speech tracking (12-18 Hz) in the right AC and in the bilateral occipital cortex. Visual speech information enhanced delta-low speech tracking in the right AC, and delta-high speech tracking in the bilateral occipital and left premotor cortex. Importantly, SNR and visual information interacted in modulating delta-low speech tracking in the right frontal cortex: speech tracking increased with increasing SNR during visual informative in the right IFG, while it decreased with increasing SNR in the absence of visual information in the right premotor cortex. This interaction reveals two distinct mechanisms contributing to the audio-visual processes underlying the cortical processing of speech in noise.

Early occipital dissociation betwen numbers and letters: A magnetoencephalography study.

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Numeracy and literacy represent two categories of culturally defined symbols, which have shown to shape our pereptuall system (Carreiras et al.,2015). While letters are preferentially processed in the left visual cortex, numbers are shown to be processed billaterally (Grotheer et al.,2016). However, literature is scarce and little is known about when this dissociation occurs. In the current study 28 young healthy native Spanish speakers were exposed to visually presented single numbers, letters and false fontsin a dot-detection task while their neuronal activity was recorded with magnetoencephalography (Elekta Neuromag 306). At the sensor level and on combined-gradiometers, time-locked event-related fields(ERFs) were calculated for each stimulus type on a 800ms time window(-0.3s to 0.5s from the stimulus onset). Statistical analysis between conditions was performed using a cluster-based permutation test. Resulting significant time-windows were selected for respective source localization. Results showed an early dissociation between numbers and letters (0.1s to0.3s) on central-right occipital sensors ($p<0.001$; numbers showing higher amplitude than letters). False fonts showed an early dissociation from numbers (0.1s to 0.2s) on central-right occipital sensors ($p<0.001$; false fonts showing lower amplitude than numbers), and a later dissociation from numbers and letters (0.3s to0.5s) on temporal sensors bilaterally ($p<0.001$; false fonts showing higher amplitude). Source analysis of the early visual response (0.1 to 0.3s) showed a left lateralized and a bilateral localization (BA19) for letters and numbers respectively. Furthermore, source localization of the critical comparison (numbersvs. letters) was localized in the right extrastriate cortex (BA19;$p<0.025$). The current results show evidence on an experience-based functional specialization of the visual system at early levels of processing(Carreiras et al., 2015).

Functional synchronization between two interacting brains during mother-child social interactions: a hyperscanning study with MEG

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Several studies have used simultaneous recordings of two brains to study social interactions in the context of games, gestural imitation, or finger movement tasks (Babiloni et al., 2007, Tognoli et al., 2007, Dumas et al., 2010, Schippers et al., 2010). However, inter-brain interactions during verbal communication is less known. Using verbal tasks, inter-brain synchronization in the theta and alpha band were reported during interactive letter naming with EEG (Kawasaki et al., 2013). Verbal interactions and imitations are essential for language learning and development in young children. To study inter-brain synchronization during social interactions between mother and child in a naturalistic setting, we used a verbal imitation task with simultaneous MEG recordings.

Nine mother-child (5 years old) pairs were tested with a 160-channel and a 151-channel MEG system (Yokogawa Ltd., Japan) housed in the same magnetically shielded room (Hirata et al., 2014). MEG signals from the mother-child pair were recorded simultaneously during a verbal imitation task. The verbal imitation task involved the mother's utterance of a phrase in Japanese, followed by the child's imitation. MRIs from each individual were also collected with a 1.5T scanner (Signa Excite, GE Medical Systems, USA). Epochs of four seconds were defined from the onsets of mothers' utterances. EOG and muscular artifacts were removed using ICA. Source estimation was performed using a single-shell head model and minimum norm estimates. To quantify inter-brain couplings, functional synchronization between two brains was estimated using phase lag index (Stam et al., 2007). In the mother-child pairs, we found inter-brain frontal-frontal, parietal-parietal, frontal- temporal, and temporal-frontal phase couplings in the theta band. Our results provide a step towards understanding inter-individual neural couplings between two interacting persons in naturalistic and social settings.

The role of cortical oscillations in speech processing in adult naive speakers of a second language

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Speech and language processing in humans is highly complex, and patterns of activity can change depending on whether or not the meaning of language is comprehended by the listener. In this study we used MEG to record the changes in cortical activity of native English speakers when listening to an unfamiliar language, both before and after a short period of language training. Participants listened to English and Spanish sentences on two consecutive days in a CTF MEG system. After the MEG session on Day 1, participants underwent a brief behavioural Spanish test, and were then trained in relevant vocabulary and sentences in Spanish. After the MEG session on Day 2, the participants took another Spanish test. MEG data were visually inspected for artefacts, band-pass filtered between 1-150 Hz and head movement above 5 mm removed. A beamformer was applied within the alpha band (8-13 Hz) and power changes within an interval of 0.5 to 1.5 s of sentence onset were visualised within the PAC and Broca's area. Results show that sentence listening induced an alpha ERD within the language network when compared to silence in both language conditions. In the native language condition, cortical activity within these regions did not differ across the two days. In the Spanish condition, results show a decrease in alpha power within the language network after the language training, compared to prior to training. These results indicate that sentences comprised of novel vocabulary can be comprehended more easily when presented after a short period of language training. Here, the degree of language comprehension is indexed by the strength of alpha ERD in the language network. Alpha oscillatory activity has been linked to allocation of attentional resources, supporting the premise that success in learning a novel language relies on appropriate direction of attention.

Neural entrainment to speech rhythms reflects temporal predictions and influences word comprehension

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Low-frequency neural entrainment to rhythmic stimulation (e.g. speech) has been proposed to constitute a timing mechanism: the brain would internalize the rhythms of preceding signals to parse the ongoing sensory input at optimal time points. This suggests that neural entrainment reflects temporal predictions built on the dynamics of recent sensory input. We tested this prediction using speech that suddenly increased or decreased in rate. We hypothesized that neural entrainment to the initial speech rhythms should persist when the speech rate changes, and should modulate perception. MEG recordings were performed while native Dutch speakers listened to spoken sentences. The beginning of the sentence (carrier window) was either presented at a fast or a slow rate, while the last three words (target window) were displayed at an intermediate rate. Participants reported the perception of the last word of the sentence that had an ambiguous vowel (perceived as short or long resulting in words with different meanings). MEG data was analyzed in source space using a beamformer method. Consistent with previous reports, the perception of the ambiguous target word was influenced by the speech rate in the carrier window. During the carrier window, neural oscillations efficiently tracked the dynamics of the speech envelope. Right auditory cortex showed oscillatory activity during the target window that corresponded in frequency to the preceding speech rate. The persisting entrainment correlated with the perceptual biases: participants whose perception was more influenced by the manipulation in speech rate also showed stronger remaining neural entrainment during the target window. We also observed persisting neural entrainment in medial prefrontal areas. The results show that neural entrainment lasts after rhythmic stimulation and provide empirical support for oscillatory models of speech processing, suggesting that neural oscillations have a causal influence on speech comprehension.

Pre-operative language lateralization determined by magnetoencephalography in patients with temporal lobe epilepsy

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Purpose: To investigate clinical applications of non-invasive language mapping with magnetoencephalography (MEG).
Methods: This study included 28 right-handed patients with drug-resistant temporal lobe epilepsy (TLE) who underwent MEG language mapping with the auditory word recognition task as apart of pre-surgical evaluation. Eighteen patients were diagnosed with left TLE. To determine the language dominant hemisphere, late MEG responses from 200 to 2000 ms after stimulus onset were investigated by two methods; equivalent current dipole (ECD) modeling analysis and statistical analysis of event-related desynchronization/synchronization (ERD/ERS). In ECD analysis, the laterality index (LI) was calculated from the number of ECDs localized on the posterior language area in each hemisphere. LI values greater than 0.5 and less than -0.5 were considered to indicate left and right hemispheric dominance, respectively, and values between-0.5 and 0.5 to indicate bilateral activation. In ERD/ERS analysis, language dominance was determined based on statistically significant changes in ERD or ERS. The MEG findings were compared with functional magnetic resonance imaging (fMRI) findings during verb generation tasks.
Results: ECD analysis indicated bilateral activation in 12 patients, whereas ERD/ERS analysis and fMRI showed left dominance in 4 patients with left TLE and 3 with right TLE among these 12 patients. ECD analysis showed right dominance in 5 patients, whereas ERD/ERS analysis and fMRI demonstrated left dominance in 2 patients with left TLE and one with right TLE among these 5 patients.
Conclusion: Different analytical methods apparently indicate different language lateralization, so the specific functional aspects of language detected by MEG analysis must be considered for accurate determination of language dominance.

Audio-visual perception of familiar and unfamiliar syllables: a MEG study

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During speech perception listeners rely on multi-modal input and make use of both visual and auditory information. When presented with contrasts of syllables, the differences in brain responses are not caused merely by the acoustic or visual differences however. The familiarity of the syllable, i.e. whether it appears in the viewer-listener\'s native language or not, may also cause distinct brain responses.

We investigated how the familiarity of the presented stimuli affects brain responses to audio-visual speech. In the ongoing data collection, 7 Finnish native speakers (right-handed with an average age of 24.86 years (SD: 3.72)) and 8 Chinese native speakers (right-handed with an average age of 24.25 years (SD: 3.20)) watched videos of a Chinese speaker pronouncing syllables (/pa/, /pha/, /ta/, /tha/, /fa/) during a MEG measurement. The stimuli presented were either audio-visual (moving pictures with simultaneous sound), auditory (still image of the speaker with simultaneous sound) or visual (moving pictures of the mouth alone). The cover task was to press a button when the /fa/ stimulus was presented in visual, auditory, or audio-visual form.

Comparisons were made for familiarity for auditory only and audio-visual stimuli. For Finnish participants, /pa/ and /ta/ are familiar because they are part of their native phonology. For Chinese participants all four syllables are familiar.

We found significant differences between the Finnish and Chinese speakers in responses to syllables familiar and unfamiliar to the Finnish. These results suggest that long term memory representations for speech sounds are manifested in the brain activity as early as around the 0-150 ms time window, but also at the 150-300 ms time window, calculated from the start of sound in the syllable stimuli.

Do cortical oscillations track natural speech rhythms in children? A MEG study

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Growing evidence shows that ongoing brain oscillations in the theta band synchronize with slow modulations in speech, which convey syllabic information and speech rhythm, crucial for comprehension (Peelle & Davis, 2012). Similar alignment of neuronal oscillations to speech signals seems to be observed for the fundamental frequency (F0), which carries prosody and stress information (Bourguignon et al., 2013). Whether such phase-locking also occurs in children, especially for natural speech produced at a fast rate, has not been investigated. We recorded brain activity of 15 French-native right-handed healthy children (8-13 years old) using a 275-channel whole-head MEG system (CTF-275), while they were listening to natural sentences produced at a normal rate (6.76 syllables per second, mean F0 was 78.6 Hz) or at a faster rate (9.15 syll/s, 88.1 Hz). Coherence between MEG signals and speech signal in each rate condition was computed at sensor and source levels (DICS), and non-parametric randomization statistics were performed (cluster-level permutation tests, Fieldtrip toolbox). Results provide evidence for an entrainment of neuronal oscillations to speech temporal envelope in the frequency bands corresponding to speech rates. Stronger coherence between auditory cortex activity and speech envelope is indeed observed at 5.6-7.6 Hz for normal rate sentences and at 8-10 Hz for fast rate sentences. Interestingly, a shift in coupling frequency is also observed for the pitch, with cerebro-acoustic coherence in the (right) auditory cortex following the increase of F0 from normal rate to fast rate (from 78 to 88 Hz). These findings in children reveal an involvement of oscillatory brain activity in the parsing of syllabic information during continuous speech perception. Synchronization between MEG and speech signals seems to follow syllabic rate and pitch, allowing to establish predictions on relevant acoustic events in speech and to ensure efficient information processing.

Shifts from normal to fast speech are associated with corresponding shifts in the frequency of neuronal entrainment: A MEG study

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A close correspondence between speech rhythm and cortical oscillations allows the brain to parse the acoustic signal into linguistic elements critical for language comprehension (Ghitza, 2011; Giraud & Poeppel, 2012; Peelle & Davis, 2012). Here we examine changes in the properties of acoustic-cortical coupling when speech perception shifts from normal to fast speech rate.
Brain signals were recorded in 24 normal-hearing participants using a 275-channel MEG CTF system. The participants listened to normal, fast or time-compressed sentences or to amplitude-modulated noise. We computed task-related modulations of oscillatory power and estimated coherence between the speech signal and MEG source time-series.
We found an entrainment of neuronal oscillations to the amplitude envelope of the speech signal in a widely distributed cortical network, but with peaks over right auditory cortex. Coherence measures revealed stronger coherence between auditory cortex and speech envelope in frequencies centered on the syllable rate: i.e. 5-7 Hz for normal speech and 8-10 Hz when processing naturally-produced fast speech. When using the raw speech signal, we found acoustic-cortical coupling at pitch frequency (F0), which also shifts up with increases in pitch. Such pitch effects were not observed for the amplitude-modulated noise stimuli.
Taken together, our findings provide novel insights into the oscillatory dynamics that mediate natural speech perception. They suggest that oscillatory brain activity displays task-specific coupling with the speech signal at frequencies that reflect syllable rate and pitch.

References

Ghitza, O. (2011), Frontiers in Psychology, vol. 2, p. 130.Giraud, A.L., Poeppel, D. (2012), Nature Neuroscience, vol. 15, pp. 511-517.Peelle, J.E., Davis, M.H. (2012), "Frontiers in Psychology, vol. 3, p.320.

Mismatch responses to linguistic stimuli along the place-of-articulation continuum recorded with MEG in children

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We have started an MEG study of categorical speech perception in children <4 years old using the mismatch negativity (MMN) paradigm. The mismatch responses were recorded with the 375-channel whole-head pediatric MEG system ("BabyMEG") which has been developed over the past 5 years. In one case, we recorded data from a 2.5-year-old typically developing female child whose first language was American English, while she was awake. Two different pairs of syllables along the place-of-articulation continuum between bilabial /ba/ and dental /da/ were synthesized according to the published parameters of Werker and LaLonde (Dev. Psychol, 1988). The syllable /ba/ was presented as the standard (75%) and another syllable along the continuum as the rare stimulus (25%) for a total of 200 stimuli with an interstimulus interval (ISI) between 1200 and 1500 ms. The responses were recorded at a sampling frequency of 1024 Hz with a bandpass filter of 1-40 Hz. Peak latency of M100, when localized in the left auditory cortex, was 115-120 ms. The mismatch response also produced in the auditory cortex was recorded between 130-160 ms when the standard and rare stimuli crossed the phonetic boundary for categorical perception (Werker and LaLonde, 1988). However, no clear mismatch response was seen when the pair of syllables were from within the category of /ba/. These results show that categorical perception may be studied in young children with a pediatric MEG system. We will present additional results using the same paradigm.

Exploring verbal-motor connections in Autism SpectrumDisorder using MEG

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Studies have shown that deficits in speech and language are correlated with oral motor and manual motor performance in autism spectrum disorder (ASD). Little, however, is known about the neurobiological relationship between these abilities in individuals on the spectrum who do not speak. The present study uses whole head magnetoencephalography to investigate the connectivity between anatomically-defined speech areas (IFG, STG) and sensorimotor areas identified using a simple button press task, in a group of minimally-verbal adults, 20-35 years, and age- and gender-matched neurotypical controls, with no history of neurological damage and with normal nonverbal IQ. Time frequency analysis revealed group differences in phase coupling (PLI) between these regions in beta and gamma bands, supported by reduced fractional anisotropy in corresponding structural connections in the ASD group using diffusion imaging.

Difference of processing visual-stimuli in children with dyslexia

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(Background) Dyslexia is a specific learning disabilitythat is neurobiological in origin. It is characterized by difficulties withaccurate and/or fluent word recognition and by poor spelling and decodingabilities. It is reported that dyslexia have a difficulty in readingletters, word and sentences, which originates from declined activities in lefttemporal lobe. A few studies demonstratedthat dyslexic subjects showed different respond to picture naming tasks from control subjects,(Objective) We conducted magnetoencephalography(MEG) while reading word, non- word and naming pictures in order to clarifydifference of process of visual stimuli. (Methods)Fourteen dyslexic and 10 control children participated in this study. The subjects' ages were 6 to 14 years old. Tasks consisted of real word, non-word andpicture (line drawing). Subjects wereasked to read aloud during word tasks and name the picture during picture task. Objects consisting of 2-5 morae werepresented to subjects for 4 seconds. Inall sessions, stimulus was presented in 107 patterns respectively. MEG data were recorded in spine position by306ch whole-head type MEG. We calculatedMNE (Minimum norm estimation) and dSPM (dynamic statistical parametric mapping)from averaged gradiometer data.(Result)In non-word task, dSPM of dyslexia group showed declined activity in lefttemporal lobe. On the other hand, inpicture naming task, dSPM and MNE of right inferior frontal lobe showedincreased activity in dyslexia.(Conclusion)Children with dyslexia showed declined activity in left temporal lobe whilereading non-word task and increased activity in inferior frontal lobe whilenaming picture task. Those resultsindicated difference of processing not only letters but visual-stimuli betweenchildren with dyslexia and controls.

Near-instant neural access of word representations between 30-80 ms as revealed by MEG and EEG

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Rapid processing of external information is vital to survival in a highly dynamic environment. A ubiquitous information medium used by humans is language, but the neural dynamics of its comprehension are still poorly understood; although the known neuroanatomical connectivity allows for transferring information from sensory inputs to high-level language cortices well within 1/10 sec, neurophysiological reflections of language processing at this early time remain elusive. In a series of studies, we scrutinised the earliest E/MEG activity elicited in the brain by words and meaningless word-like stimuli which were tightly controlled for physical and psycholinguistic features. The first signs of activation of lexical memory circuits for individual spoken words (reflected as an increased activation for meaningful>meaningless items) occur at ~50 ms and are underpinned by left temporo-frontal circuits. These earliest lexical reflections are, in turn, modified by other linguistic variables. By repeating word stimuli in an oddball design, memory-trace activations ignite even earlier, at ~30 ms after the recognition points, implying an expedited neural access to representations in real-life conditions when they can be pre-activated by available context. In visual modality, we find the earliest word-specific MEG activations from ~70 ms, this longer latency possibly being related to signal conduction from occipital visual to perisylvian linguistic cortices. Extrasylvian meaning-specific activations can be observed from ~80 ms, also suggesting additional synaptic transfer time, needed to activate semantically-specific parts of word circuits. Semantic context integration commences equally early (50-80 ms) and is manifest as facilitation of lexical MEG responses by semantically related prime words. This body of results suggests a cascade of ultra-rapid lexico-semantic processes, with micro-delays between different neural processing stages, occurring well within 1/10 of a second.

Modulation of covert speech on overt loudness perception implies the mechanism of speech monitoring

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We continuously monitor our own speech in real time without delay. One key computational component of speech online control has been hypothesized as an interaction between top-down induced processes and auditory feedback: auditory consequences of speech production can be predicted via a top-down process and the predicted speech results are compared with feedback to overcome the temporal delay. In this study, we test a critical assumption of this model which is that top-down induced mental representation can interact with speech perception. In a behavioral and a Magnetoencephalography (MEG) experiment, participants were asked to imagine speaking the syllable /da/ loudly (loud condition) or softly (soft condition) before they heard the playback of their own voice of the same syllable. Behavioral results showed that the loudness rating of the play back was smaller in the loud condition than that in soft condition. MEG results demonstrated that the magnitude of neural responses to the overt auditory stimuli was smaller in the loud condition compared to those elicited in the soft condition. These consistent behavioral and electrophysiological results suggest that the top-down induced neural representation converges to the same representational format as the neural representation established during speech perception, even for basic sensory features such as loudness. Such a coordinate transformation in a top-down process forms the neurocomputational foundation that enables the interaction with a bottom-up process in speech production monitoring and control.

Non-invasive evaluation of spatial repolarization dispersion abnormalities in patients presenting with coronary artery disease

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Backgrounds: Many years QT dispersion was a hot topic with a vast number of reports being published on its usefulness as a non-invasive marker of arrhythmia risk in coronary artery disease (CAD). The overall objective of the present study was to investigate the applicability of MCG for non-invasive evaluation of spatial repolarization dispersion (SRD) abnormalities in patients presenting with CAD. Methods: A total of 108 subjects were included in the study: there were 28 (26%) patients with angiographically significant CAD (>70% luminal stenosis) (CAD group); 47 (44%) patients with recent (10-15 days) myocardial infarction (MI group); 33 (30%) healthy subjects served as control. All subjects underwent 9-channel MCG (Oxford Cardiomox Ltd, UK) recordings in non-shielded MCG laboratory, yielding 3-D current density mapping during ventricular repolarization. The SRD was automatically defined as the time interval between the earliest T- wave end to the latest T-wave end in the different regions of myocardium by using the time evolution of current density variables map. Results: Analysis revealed an overall tendency for SRD to be low in the healthy control subjects, higher in CAD group (115.6±30.8 vs. 73.6±20.8 ms, p<0.001), and highest in MI group (124.4±33.1 vs. 73.6±20.8 ms, p<0.001). SRD showed non-significantly difference between MI group and CAD group (124.4±33.1 vs. 115.6±30.8 ms, p=0.218). Based on the receiver operating characteristic curve analysis the diagnostic sensitivity and specificity were 82% and 79% for SRD>90 ms. Application of discriminatory analysis allowed us to get classification functions, which could be used (with 81% accuracy) to qualify the just examined patient to the investigated categories. Conclusions: Our finding provided further evidence that MCG 3-D current density mapping can successfully detect SRD abnormality in patients with CAD and with augmented risk for ventricular arrhythmias.

Applying a MCG current density imaging modality to reconstruct measures of repolarisation dispersion in patients susceptible to ventricular arrhythmias

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Backgrounds: Experimental studies provided evidences of close temporal correlations between ischemia-induced alternans, dispersion of repolarization and susceptibility to ventricular arrhythmias. The purpose of this study was to evaluate spatial repolarisation dispersion (SRD) abnormalities noninvasively in patients susceptible to ventricular arrhythmias. Methods: A total of 101 subjects were included in the study: 40 (39%) patients had a history of ischemic heart disease and frequent (≥30/h) premature ventricular contractions (PVC group); there were 28 (28%) patients with angiographically significant CAD(> 70% luminal stenosis) and without PVCs (CAD group); 33 (33%) healthy subjects served as Control. All subjects underwent 9-channel MCG recordings in non-shielded MCG laboratory, yielding 3-D current density mapping during ventricular repolarization. The SRD was automatically defined as the time interval between the earliest terminal portion of the T-wave to the latest terminal portion of the T-wave in the different regions of myocardium by using the time evolution of current density variables map. Results: SRD was significantly higher in patients with presence of PVCs in comparison to those with significant CAD and without PVCs (132.7±27.6 vs. 115.6±30.8 ms, p<0.001) and Control (132.7±27.6 vs. 73.6±20.8 ms, p<0.001). In addition, CAD patients had higher SRD than controls (115.6±30.8 vs. 73.6±20.8 ms, p<0.001). For identification of patients prone to PVCs, selection of cut-off values SRD >110 ms gave sensitivity of 78% and specificity of 97% (p<0.0001, AUC=0.95). MCG SRD was a significant predictor of PVCs (odds ratio, 1.12; 95% confidence interval, 1.05 to 1.18, p=0.0001)Conclusions: According to the evidence generated from the existing clinical data, the spatial repolarization heterogeneity detected by new MCG current density imaging modality may be a new predictive tool for patients susceptible to ventricular arrhythmias.

Imaging of repolarization dispersion from the inverse solution of distributed current density

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Backgrounds: To overcome the methodological limitations of ECG-determined QT dispersion, novel magnetocardiography (MCG) variables have been recently developed. We propose MCG inverse approach for imaging the ventricular activation sequence based on the estimation of the equivalent current density (CD) and on our assumption that the result of the “inverse problem solution” can display a resulting CD vectors, whose quantity and direction correspond a quite particular allocation of CD at a certain level (depth) and reflect the architecture of the fiber through which this current flows.Methods: The activation time at any given location within the ventricular myocardium was determined as the time point with the occurrence of the maximum local CD estimate. The spatial repolarization dispersion (RD) was automatically defined as the time interval between the earliest T- wave end to the latest T-wave end in the different regions of myocardium by using the time evolution of CD variables map. Results: MCG RD in normal subjects vary mostly between 50 and 80 ms. Our studies have shown increased spatial RD in various cardiac diseases. Studies have shown the overlap of values between patients with different cardiac diseases and various clinical symptoms, the wide variation of values within each cardiac disease. For patients with coronary artery disease the lack of correlation between spatial RD derived from MCG and the number of stenosed coronary arteries was noted. Importantly, that RD measured in the MCG imaging modality does not depend on (and therefore should not be corrected for) the heart rate. Conclusion: It is reasonable to conclude that the dispersions of ventricular recovery times and dispersions of repolarization CD measured with MCG are direct expressions of repolarization abnormalities. Future efforts should concentrate on more focused and detailed aspects of RD of CD changes.

Measurement of magnetocardiogram using magnetoresistive sensor

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Background:Magnetcardiograms (MCGs) are noninvasivelyacquired maps that measure the cardiac magnetic fields on the body surface. Previous studies associated with MCGs have been using a superconducting quantum interference device (SQUID) system. Although SQUID system is the most sensitive of all instruments for measuring a magnetic field at low frequencies, it requires liquid helium for cooling the system and the running cost is expensive. Magnetoresistance (MR) magnetometers use a change in resistance caused by an external magnetic field, and are attractive for low cost applications. This study was aimed to acquire MCGs by using MR sensors.

Methods: We recorded MCGs of five healthy subjects by using MR sensors array which were developed for measuring picoTesla-level magnetic field and for reducing noise level (TDK, Japan). A 30-channel MR sensors array (sensor interval: 4.0 cm, sensor arrangement: 6 by 5 matrix)was placed in a magnetically shield room, and cardiac magnetic fields were recorded in the anterior chest. We performed chest X-ray before recording MCGs confirming that the sensor array covered the whole heart, and ECG was simultaneously recorded. We measured the normal components of the cardiac magnetic fields. All the five subjects underwent MCGs recording by SQUID system after measurement by MR sensor array, and the results were compared.

Results: In all the five subjects, MCGs are successfully recorded by MR sensors. Cardiac magnetic fields corresponding P, QRS and T wave on ECG were detectable by signal-averaging of 300 beats. Comparing with MCGs acquired by SQUID system, MR sensors array accomplished comparable wave form at each site of the heart which was confirmed by chest X-ray.

Conclusions: MR sensors array was applicable for measuring cardiac magnetic fields. Our results can contribute the development of low-cost device for recording MCGs, which enables the progression of non-invasive diagnostic modality in the cardiovascular field.

Visualization of the electrical current in atrioventricular node by magnetocardiograms

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Background: To visualize the electrical activity of cardiac conduction system, an invasive procedure such as electrophysiologic study (EPS) is usually required. What we can record in the EPS includes the electrical activity of the His bundle, right and left bundle branch, and Purkinje system. Recording of the electrical activity in atrioventricular (AV) node is challenging even by using invasive methods, and precision of AV node is sometime difficult for example during AV node ablation for complete heart block. Magnetcardiograms (MCGs) are noninvasively acquired maps that measure the cardiac magnetic fields on the body surface. This study was aimed to visualize the electrical current in AV node by measuring cardiac magnetic field and performing current source estimation.

Methods: We recorded MCGs of three healthy subjects by using superconducting interference device (SQUID) system. A 120-channel SQUID system was placed in a magnetically shielded room, and cardiac magnetic fields were recorded from the anterior chest for 120 seconds. To visualize the electrical activity, we performed current source estimation by spatial frequency filter processing and merged the data into chest X-ray images.

Results: In all the three subjects, unidirectional current source which start from upper right to lower left in the chest X-ray image was observed. The current source was recorded reproducibly and observed between the P wave and the QRS component.

Conclusion: MCGs recording by SQUID system and current source estimation enabled to visualize the electrical activity in AV node, which can be useful for the clinical practice such as the diagnosis of bradyarrhythmia.

DIMENSIONAL CONTRACTION AT NOISE REJECTION METHOD BASED ON INDEPENDENT COMPONENT ANALYSIS FOR MCG

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We studied a noiserejection method based on independent component analysis (ICA) forMagnetocardiograms (MCGs). ICA is a useful method to separate the noise and theMCGs signal. However ICA methods have two problems of process at automation ofnoise rejection. One is dimensional contraction process after principalcomponent analysis (PCA). Another is component selection process after ICA. Becausethese processes were dependent on judgement by qualitative or limited index, resultsof noise rejection differed from person to person. It is therefore desired topropose the method which can be performed automatically and quantitatively. We especiallyconsidered about dimensional contraction process in this research. This processaffects the accuracy of separation by ICA. In many case, index of dimensionalcontraction is contribution ratio. However contribution ratios are changed by signalnoise ratios (SNR). It is not suitable for automation. So, we proposed indexutilizing kurtosis which is not influenced by SNR. And we compared twoevaluation indexes (contribution ratio and kurtosis) of dimensional contractionby two simulations. First, we simulated about intensity of MCGs signalinformation after dimensional contraction. Second, we simulated about influenceof ICA separating accuracy by dimensional contraction. Fromthe simulation results, the index of kurtosis was found to be stable comparedwith that of contribution ratio.

A SQUID full-tensor MCG system and its possible use for cardiac source localization

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A full-tensor magnetocardiograph (MCG) system is developed at SIMIT based on low temperature superconducting quantum interference devices (SQUIDs). The system works within a magnetically shielded room, measuring the five independent first-order gradient components (Bxx, Byx, Byy, Bzx, Bzy) and the vertical component (Bz) of the magnetic field generated by the heart with high signal to noise ratio. Based on the single current dipole model, preliminary investigations are carried out for cardiac source localization, including simulation and some experimental results. The potentiality of the system for clinical research will be discussed.

POSSIBILITIES OF MAGNETOCARDIOGRAPHY IN DETECTION OF MYOCARDIAL INJURY IN PEDIATRIC CARDIOLOGY

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Introduction. According to clinical registry 51-81% from 327 children with systemic diseases of connective tissue have the heart injuries, but its initial signs cannot be detected by routine methods (ECG, EchoCG, biochemics). Aim of study is improving early diagnosis of the heart injuries in children with rheumatic diseases based on MCG.

Methods. 25 healthy and 31 sick children (10-17 year) with systemic disease of the connective tissue and without signs of carditis/cardiomyopathy were examined. Pts with highly active inflammation, endocrine pathology, and arterial hypertension were excluded. All pts underwent MCG examination, and reconstruction of current density vector (CDV) maps was done.

To evaluate the ventricular de- and repolarization they were calculated: abnormal index as percentage of the total CDV length directed in the \"proper\" direction at QRS and ST-T (AIQRS and AIST-T), ratio of 4 QRS phases/its \"proper\" duration (DR1-4) and for whole QRS (DR), correlation coefficient Corr at intervals, ST-T area (from begin to inflection point) in % to the whole ST-T interval (Adur).

Results. Significant differences of MCG indicators were not found at QRS, but individual ones differ in pts with active inflammatory process into heart AIQRS is 70,15% (56,4% healthy), DR and DR1 are reduced to 1,02 s and 1,2 s, DurQRS 0,089 s (0,1s healthy), CorrQRS 80,43% (84,14% healthy).

At the ST interval indicators differ at early repolarization, increasing Adur 19,85% (11% healthy), reducing CorrST 63,85% (82 4,1% healthy), downward trend in AIST-T 53,85% (91% healthy). Changes of repolarization are visualized up to 35% more frequently by MCG than ECG. Also, CDV maps are convenient for on-line visual assessment.

Conclusions. Non-invasiveness, safety and sensitivity of MCG allow recommend it as screening method for early detection of the heart injuries. The ability to visualize of electrophysiological active substrate allow MCG to detect local changes into myocardium.

POTENTIAL OF MAGNETOCARDIOGRAPHY IN PREDICTION OF MYOCARDIAL VIABILITY IN PATIENTS WITH CHRONIC CORONARY ARTERY DISEASES

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Background : The assessment of myocardial viability in patients with coronary artery disease is an important clinical challenge. The dobutamin stress echocardiography (DES) is used to assess myocardial viability reserve. The main limitations is that this technique is highly operator dependent with significant interobserver and intercenter variability. Thus, the development of another, fully automated approach to evaluate myocardial viability should be encouraged. Magnetocardiography (MCG) is non-invasive evaluation of the magnetic field of the heart that is produced by the electric activity of the myocardium. Previous studies have shown high sensitivity of MCG to detect myocardial ischemia. The objective of this work was the investigation of potential of MCG in evaluation of myocardial viability in patients with coronary artery disease.
Methods: The study included 9 patients with verified coronary artery disease. Coronary angiography was performed because of chest pain in all subjects and multivessel stenosis at least 70 % was revealed. . In all participants, the MCG examination was performed using a 9-channel MCG system located in an unshielded room.
The magnetocardiography recordings were taken from 36 positions at rest. From these CDV maps were generated during the QRS-complex with 2 ms steps. The abnormality index (AI) – the ratio of the total length of vectors directed in the \"proper\" direction to that have a different, abnormal direction (%) was calculated for all maps during QRS complex. The DES was done in all patients.. Depending on the results of DES, this group was divided into two subgroups: those with a positive response (increasing contractility in dysfunctional segments) – 6 patients and those without increase of contractility – 3 patients. The
Results: The averaged abnormality index in patients, demonstrating positive response to dobutamin, i.e. viable myocardium was significantly lover than in patients with no response (54, 2 %± 5,8 vs. 77, 6% ± 9,4, p < 0,001).
Conclusions : The MCG test at rest seema to be has the potential to be useful for the assessment of myocardial viability in patients with severe CAD. Futher investigations needed to confirm these findings.

VALUE OF MGNETOCARDIOGRAPHY: THE DIFFERENTIAL DIAGNOSIS BETWEEN CORONARY ARTERY DISEASE AND CORONARY MICROVASCULAR DISEASE USING MAGNETOCARDIOGRAPHY

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Background. The diagnostic management of patients with chest pain remains a clinical challenge. But existing non-invasive techniques may lack accuracy to distinguish epicardial and microvascular abnormalities. MCG is non-invasive evaluation of the magnetic field produced by the heart electric activity. Previous studies have shown that MCG reveal obvious changes in patients with CAD and normal ECG at rest.

The objective of this research was the investigation of MCG value in differential diagnosis of CAD and coronary microvascular disease using novel approach of current density vectors (CDV) maps evaluation based on binary classification metric.

Methods. The study included 136 pts without myocardial infarction. Coronary angiography was performed because of chest pain in all subjects. Depending on the results of coronary angiography, they were divided onto 2 groups: with at least 50 % stenosis in at least one of the main coronary arteries (group 1, 82 pts) and without hemodynamically significant stenosis (group 2, 54 pts). Pts from group 2 underwent exercise ECG and shown ST-segment depression during test. In all pts, the MCG was performed by 9-channel system at unshielded room.

The MCG were taken at 36 positions at rest and CDV maps were generated during the ST-T interval. Each point of CDV map was described by 2 parameters: brightness (current density) and angle of CDV. As the result, 32 features were calculated and binary k-NN classifier with various metrics (Cityblock, Mahalonobis, Chebychev, Eucledian) was used to classify the pts.

Results. The highest accuracy was demonstrated by classifier with Cityblock metric, 124 pts (91%) were classified correctly. Sensitivity and positive predictive value were 93%, specificity and negative predictive value – 89%.

Conclusions. The MCG at rest has the potential to be useful for the differential diagnosis between CAD and coronary microvascular disease.

A Simple and Effective Adaptive QRS Detection Algorithm Based on the Waveform Characteristics of the QRS Complex

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QRS detection in the magnetocardiogram (MCG) and electrocardiogram (ECG) signals is very crucial as the first step for evaluating the cardiac function[1, 2]. Unlike most of the reported methods which are aimed at increasing the accuracy of detection by using complex signal-processing techniques[3], we proposed a simple and effective adaptive QRS detection algorithm based on the waveform characteristics of the QRS complex. The algorithm only includes some simple operations, such as subtraction, differentiation and adaptive thresholding without complex transformations. The performance of the proposed algorithm was evaluated by the MIT-BIH arrhythmia database and MCG data recorded by the multi-channel MCG system. The sensitivity (SE) and precision for MIT-BIH database were 100% and 100%, respectively. Also, the precision of 97.22% is achieved for MCG data. The Lower complexity and good performance makes the proposed algorithm to be applied to real-time detection of MCG QRS complex.

Key Words: Magnetocardiogram, QRS detection, adaptive thresholding, QRS complex.

Acknowledgement:This work was supported by the “Strategic Priority Research Program (B)” of the Chinese Academy of Sciences (Grant No: XDB04020200).

References:

[1] S. Farashi, “A multiresolution time-dependent entropy method for QRS complex detection,” Biomedical Signal Processing and Control, vol. 24, pp. 63-71, Feb, 2016.

[2] P. Phukpattaranont, “QRS detection algorithm based on the quadratic filter,” Expert Systems with Applications, vol. 42, no. 11, pp. 4867-4877, Jul 1, 2015.

[3] C. J. Deepu, and Y. Lian, “A Joint QRS Detection and Data Compression Scheme for Wearable Sensors,” Ieee Transactions on Biomedical Engineering, vol. 62, no. 1, pp. 165-175, Jan, 2015.

Recent Progress of MCG System Development and Its Clinical Application in SIMIT

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Recently, SIMIT has development several MCG systems indifferent environment. According to the different environments, different SQUIDgradiometer configurations have been designed and fabricated to suppress theenvironmental disturbance. Also, we set up the first 36 channel MCG system inChina based on voltage-biased SQUID magnetometer. As for the liquid helium evaporationrate, special design of insert has been studied and the optimal insert configurationshave been developed to improve the performance of MCG system. Up to now, threefour-channel MCG systems have been installed in hospitals for clinicalresearch. Some preliminary clinical results will be reported in this paper.Also, we did several demonstrations on fetal MCG measurements using new developed voltage-biased SQUID magnetometers.

Simulation of ventricular bioelectromagnetic activity to support ischemia detection

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One of the biggest obstacles in the evaluation of ischemia detection methods is the establishment of a ground truth in clinical studies. There is no standard against which to evaluate a candidate method. In order to facilitate clinical studies, computer simulations may be used for the purpose of establishing a ground truth. Based on previous work at Kangwon National University by Prof. Shim et al. we would like to present our simulation of the bioelectric activity of the ventricles in healthy and ischemic hearts. The simulation model includes calculation of the membrane potentials, local currents and forward solution to a given sensor space. Furthermore, the local effects of oxygen deficiency is simulated by modulating the myocyte action potentials. The aim of this project is to evaluate the characteristic magnetocardiography (MCG) measurements related to hypoxia in different segments of the heart to support ischemia localization. We present our progress so far and show examples of how the MCG signal is modified by ischemia in different regions of the heart.

Contribution of phantom experiments to MEG study and development

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Magnetoencephalography (MEG) is commonly used in various clinical applications and research studies of brain function. The advantages of MEG are its greater spatial resolution compared to EEG and enhanced temporal resolution compared to fMRI and NIRS. In order to expand these benefits of MEG, the authors are trying to increase the reliability and the robustness of MEG systems. Phantoms have been utilized for the quantitative evaluation and verification of MEG measurements. Moreover, the phantom can contribute to the evaluation of newly developed techniques and their effectiveness. Recently, the authors developed an MEG phantom that is composed of fifty isosceles-triangle coils. This phantom has conducted the calibration based on three-dimensional measurement of the current paths in the phantom, as well as numerical calculations. In this presentation, we report some results of experimental evaluations of MEG systems using the phantom. First, we carried out the experimental evaluation of multiple MEG systems. Although the MEG systems have different sensor arraignment and different condition of the magnetic noise, the mean displacements of the estimated equivalent current dipoles (ECDs) were around 1 mm. Second, we investigated the dependence of the displacements of source localization on the number of the sensors using the recorded data with the phantom. The results show that it might be reasonable to reduce the number of the sensors in order to reduce the cost of the MEG system, without any reduction of the accuracy in source localization, as long as the source model is assumed to be ECD model. Third, we demonstrated the evaluation of a room-temperature magnetic sensor in anticipation of developing the MEG system utilizing our phantom. The result revealed the necessity of sensor calibration when the sensor is close to signal sources. The phantom can contribute not only the evaluation of MEG systems in operation but also MEG systems under development.

Non-invasive detection of nerve impulses with an optical magnetometer operating near quantum limited sensitivity

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Electromagnetic fields are generated by different sources inside the human body such as the heart, the brain and the nervous system. Detection of such fields is a keystone for medical diagnostics. We present a non-invasive technique for the detection of nerve impulses from a frog sciatic nerve using a room-temperature optical magnetometer. Our work [1] paves the road for implementing optical magnetometers operating at the quantum limits of sensitivity as practical devices for medical diagnostics.

The magnetic field from a nerve impulse was first detected by Wikswo et al. [2]. They used a SQUID magnetometer combined with a pick-up coil in which the nerve had to be pulled through. Our magnetometer consists of a millimeter-sized cesium vapor cell kept at room- or human body temperature and lasers used for optical pumping and probing. The vapor cell is placed next to the nerve, and the nerve impulse can be detected non-invasively as the magnetic field extends outside the nerve.

Our optical magnetometer operates in a small bias (< 1 μT) field, and can detect millisecond magnetic field pulses with high sensitivity. At 1 mm distance from the nerve, we measure a nerve impulse with 10-20 pT peak-to-peak amplitude with a signal-to-noise ratio close to 1. The field decreases with larger distances, but remains detectable more than 5 mm away. We also show that our magnetometer is sensitive to the direction of the nerve impulse propagation.

Future efforts will be put into developing a gradiometer consisting of two vapor cells. Differential measurements reduce the need for magnetic shielding and allow for enhanced sensitivity using quantum entanglement [3]. We will also develop a miniaturized and fiber-coupled device and investigate other applications such as fetal magnetocardiography.

[1] K. Jensen et al.,arXiv:1601.03273 (2016)
[2] J. P. Wikswo et al. Science, 208(4439):53 (1980)
[3] W. Wasilewski et al. Phys. Rev. Lett., 104:133601 (2010)

Post-cooling calibration of gradiometric SQUID magnetometers for biomagnetic measurement using a spherical coil array

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For the accurate estimation of electric activities in a human body using a biomagnetic measurement based on superconducting quantum interference device (SQUID), the position and direction of each SQUID sensor must be precisely figured out. However, the sensor array must be nonmagnetic to avoid interrupting weak magnetic measurement and hence is usually made of plastic. Therefore, the position and direction of the sensors are unpredictably shifted from their designed values because of strain of the plastic structure when it is refrigerated to the liquid helium temperature. The stray inductance of the pickup coil can cause the shifts from the designed values as well. To reveal the exact position and direction of each SQUID sensor, calibration after cooling is inevitable.

For the calibration for whole-head type MEG systems after cooling, the spherical coil array, which was proposed at Biomag2012 in Paris, was applied. The spherical coil array was composed of 16 copper wire coils with the diameter of 150 mm. All of them were wound concentrically and symmetrically around the surface of an acrylic plastic sphere.

Since Biomag2012, we had re-calibrated ten of our axial-type-gradiometer-based MEG systems using the spherical coil array. The calibration results were evaluated by our MEG dry phantom [1]. Consequently, the MEG systems which were calibrated using the spherical coil array provided the smaller error in current source analysis comparing to the MEG systems calibrated using the conventional coil array. We also discuss the calibration error using numerical simulation and the possibility of the calibration for planar-type gradiometer array.

Reference

[1] D. Oyama et al, J. Neurosci method, 2016, 251: 24-36.

IMPROVED SUPERCONDUCTIVE GRADIOMETER DESIGN FOR BIOMAGNETIC APPLICATION

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Introduction. SQUID-magnetometers need superconductive gradiometer having high SNR, mechanical strength, stability during numerous thermo-cycling, and low own magnetic noise. Aim of study is to improve the mechanical strength, reliability against thermo-cycling, weakening of external noises and reducing own magnetic noises.
Methods. The essence is following: instead of textolite, glass, or graphite as frame of gradiometer, it is proposed carbon-filled plastic, coefficient of thermal expansion (CTE) of which can be precisely adjusted equal to CTE of wire. Proposed frame is made from 2 layers of composite material, reinforced with carbon fibers. Equalization of CTE of composite material and wire is adjusted by number of fibers and their ratio into layers. Fibers have high elasticity module and mechanical strength, which allow thickness of frame 1.0 mm. Magnetic susceptibility of carbon-filled plastic is 5.8 times smaller compare to graphite.
Result. Composite CTE is equalized to CTE of the niobium wire by content and type of binding agent and number and orientation of carbon fibers into layers. Magnetic distortions caused by carbon-filled frame due to temperature fluctuations into liquid helium are smaller. Advanced methods for gradiometer balance and compensating of noises were developed, see WO2012173584, WO2013115749, and frame design is disclosed in PCT/UA2016/000001.
Conclusion. Carbon-filled plastic has high mechanical strength and noises caused by temperature fluctuations. Its provide the high gradiometer balance, stability against thermal cycles, and shielding of external noises. Authors thanks of Oxford Cardiomox Ltd for funded within project P624 Sci-Tech Center in Ukraine.

Optimization and Improvement of a 36-channel Magnetocardiography System Based on SQUID Magnetometers

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Magnetocardiography (MCG) is a non-invasive method to record and analyze the magnetic field generated by the electrical activity of heart. In SIMIT, we set up the first multi-channel MCG system based on the weakly damped DC SQUID magnetometers with average field noise of 5 fT/√Hz [1, 2]. The system consists of 36 sensing magnetometers and 12 reference magnetometers to realize software gradiometer configurations. The noise cancellation configuration has been optimized by analyzing the correlation between the MCG signal and the environmental interference in different channels both in thick magnetically shielded room(MSR) and moderate MSR. Also, using a simulated MCG signal generated by a small coil driven by ECG[3], we quantitatively evaluated the signal integrity through three key performance indexes, which are correlation in time domain, relative heights of different peaks and correlation in frequency domain. In addition, a new design of Dewar insert with liquid nitrogen interlayer was adopted to prolong the duration of liquid helium. And an automatic parameter control algorithm was developed and built into the MCG software to make the system easier to operate. MCG signal with SNR of 40 dB could be obtained from the above optimized system.

Key Words: Magnetocardiography, noise cancellation, automatic parameter control, system optimization.

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References:

[1] Liu C, Zhang Y, Mŭck M, et al. "Statistical characterization of voltage-biased SQUIDs with weakly-damped junctions" Supercond. Sci. Technol. Vol. 26(06) 065002, 2013.

[2] Qiu Y, et al,"Low-Tc direct current superconducting quantum interference devices magnetometer-based 36-channel magnetocardiography system in a magnetically shielded room", Chin. Phys. B Vol. 24, No. 7 (2015) 078501.

[3]Zhang S L, Wang Y L, Wang H W, Jiang S Q and Xie X M, "Quantitative evaluation of signal integrity for Magnetocardiography", Phys. Med. Biol. 54 (2009) 4793–4802.

Magnetocardiogram measurement using 25 channels MI sensor system

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Magnetocardiogram(MCG) is useful for a clinicalapplication and ahealth monitoring because it\'s possible to measure theheart activity without contact. In generally, MCG measurement was used SQUIDmagnetometer. For dailyhealth monitoring applications, MCG measurement devices need to be easy tohandle. Specifically, it is highly desirable that operations in easy handing, withoutliquid helium, and outside a magnetically shielded room. SQUID magnetometer is high cost of equipment, high running cost dueto the liquid helium and necessity of a magnetically shielded room. Then we developed 25 channels MIsensor system for MCG measurement. This MI sensor system is low cost and can be used under room temperature. MCG measurementfor 5 minutes was performed outside the magnetically shielded room using thissystem. The minimum interval between the MI sensor and the chest wall of anormal subject was 5 mm. ECG (lead I) was also measured for signal processing (average).Noise rejection wascarried out by time and spatial average using 25 position data. For timeaverage, all magnetic data were averaged using 5 minutes data at each position.The reference signal for averaging was the R wave of the ECG (lead I). Forspatial average, 25 position data was compressed into 9 position data. As aresult, MCG waveforms of 9 channels were obtained, and the QRS complex and Twave could be shown clearly. The developed MI sensor system is effective in the health monitoring application.

Towards a high-resolution magnetic-field camera based on an optically pumped magnetometer

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We present the concept of a magnetic-field camera which shall allow the magnetic-field imaging of centimeter-sized objects with magnetic-field resolutions in the range of pico Tesla, millimeter lateral resolution, and bandwidth of about 100 Hz. Image recordings with video rate shall be feasible. This concept is realized with an optically pumped magnetometer using an integrated cesium vapor cell assembly with high buffer gas pressure, pumped with a high-power DBR laser. This enables the operation of the magnetometer in a modified light-narrowing operational mode [1], combined with a simultaneous read-out of millimeter-sized pixels by a photo-diode array.

The potential of this concept for the recording of biomagnetic signals as – for example – the magneto-encephalograms of small animals is demonstrated by recordings of temporarily changing artificial magnetic field distributions originated by currents flowing in specially configured printed circuit board tracks.

[1] T. Scholtes et al., Light-narrowed optically pumped M magnetometer with a miniaturized Cs cell, Phys. Rev. A 84 (2011), 043416.

Characteristics of a bi-layer active shield based high-Tc rf SQUID magnetocardiography system

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We have developed a low cost active magnetic shielding technique for a single channel liquid Nitrogen based high-Tc rf SQUID magnetocardiography (MCG) system working without passive magnetic shield environment. This is while a light rf-shield which does not hinder the MCG recording is implemented overall the system for environments with very high rf-interefences such as that of wireless communication systems and tools such as mobile phones. The designed MCG system contains two high Tc RF SQUID magnetometers, which are placed in an axial gradiometeric arrangement with a base line of 10 cm. The developed active shield is a magnetically two layers shielding system each of which has been designed for different frequency and dynamic range characteristics. The active shield setups are driven using close loop systems incorporating the reference SQUID by controllers, which are designed using methods based on examined dynamic model approximation of first and second orders, leading to optimal PI and PID controllers. In this paper, investigation of the shielding performance of our bi-layer magnetic shield as the active compensation fed by the optimal feedback control system is reported. Using the designed shielding system, the disturbing magnetic signals of the environment could be attenuated such that the major heart signals peaks could be obtained in our unshielded laboratory environment.

Active magnetic shield for the MCG measurement: A compact shielding system built with a light-weight magnetic shell and the active compensation using the feedback at the zero magnetic field point

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A compact magnetic shield consisting of the detachable magnetic shells, where the upper cylindrical shell is 70 kg and the lower one is 230 kg, and an active compensation system has been developed. The diameter of the bore is 65 cm. The active compensation is applied along vertical axis. A novel points of the active compensation is a zero-magnetic field point is used as a position of the feedback magnetometer. The zero magnetic field point is a point at which the magnetic field becomes zero when the magnetic field inside the shield is made to zero by the active compensation. The advantage of using the zero-magnetic field point is that a moderate gain factor is enough for the loop gain to establish a good shielding performance, because the disturbing field to be monitored does not suffer attenuation by the magnetic shell. The magnetic noise spectral density was 90.7 pT/√Hz at 1 Hz and 1850 pT at 60 Hz without the active compensation. Those values were decreased to 10.2 pT/√Hz at 1 Hz and 269 pT/√Hz at 60 Hz, respectively with the active compensation. We have successfully used the shielding system to measure the MCG of a healthy volunteer using thirty-six (6 x 6) fluxgate magnetometers. The contour map obtained was quite similar to those by the SQUID magnetometer array.

Mu-metal-free magnetically shielded room for ultra-low field atomic optical magnetometry

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We report on the details of the improvement of a magnetically shielded room (MSR) with internal volume of 2.75 m x 2.75 m x 2.75 m for use in atomic optical magnetometry for MEG and MCG. Key features of the MSR reported include the absence of mu-metal to lower construction cost, a corridor and access door and feed through tubes for connections to external instrumentation. The existing MSR has walls made of 1.8 cm thick high purity aluminum welded in the corners, with a shielding factor of 1,000 at 60Hz. The environmental internal magnetic field in each of the three dimensions is cancelled by independent 4-coil setups that are very similar to the Merritt-type 4-coil setup configuration. The compensation coils are installed inside of the MSR and consist of total of approximately 396 meters of 6-way flat ribbon cable for easy of construction. Currents on the order 700 mA @30 volts are necessary to cancel the earth´s field. The residual magnetic field at the center of symmetry of the MSR with the compensation fields on, and without closed loop control, is below or of the order of 1 nT with long term drifts of less than 1 nT/hour. These figures potentially qualify the MSR for the operation of sub-nanotesla atomic optical magnetometers that require residual magnetic fields below or of the order of 10 nT. We are currently developing an active closed loop circuit that we expect to further decrease the background magnetic field in the MSR by 40 dB at low frequency.

Commercial Optically Pumped Magnetometer

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We present results with our compact and commercial ready optically pumped magnetometers (OPMs) with an integrated laser and average single-axis sensitivity of 15 ± 5 fT/√Hz in the 1 – 100 Hz band. Each OPM has the ability to simultaneously measure the magnetic field along two orthogonal axes. The sensor head measures 13 x 19 x 110 mm and has a stand-off distance of 6 mm from the outer surface of the housing to the center of the vapor cell. Integrated three axis coils allow each sensor in an array to locally null any background magnetic field up to 50 nT. A dedicated electronics module provides complete command and control of sensor startup and operation and provides digital and analog outputs proportional to the magnetic field. We present measurements of fetal magnetocardiography(fMCG) taken from normal and at risk patients using an array of eight sensors (16 channels). We also present results comparing SQUIDs with our OPMs for magnetoencephalography, demonstrating the ability for accurate source localization using OPMs. The results show that the performance of the OPMs are similar to Superconducting Quantum Interference Device (SQUID) systems.

Combination of MEG with EEG using dry multipinelectrode caps

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We combine for the first time EEG using flexible multipindry electrodes with MEG. The aim of this study is to test the compatibility ofthe new dry EEG setup with the Elekta Neuromag Vectorview MEG. The study includes three combined and separate measurementsof dry EEG and MEG in the following sequence: MEG without EEG (#1), combineddry EEG and MEG (#2), and MEG without EEG (#3). Each measurement includesresting state activity, eye blink artifacts and visual evoked activity. The five female volunteers have an average headcircumference of 54.3 ± 1 cm, and a hair length with an average of 34 ± 14 cm.No skin preparation is performed prior to the application of the dry EEG caps.The VEP/VEF test consists of a pattern reversal checkerboard paradigm with 300trials and is performed according to the ISCEV 2010 standard. The eye blinksare externally triggered at a rate of 0.3 Hz. The dry electrodes are based onpolyurethane (PU), subsequently coated with a thin layer ofSilver/Silver-Chloride (Ag/AgCl) and the EEG data acquisition is performedusing a 64 channel dry EEG cap with equidistant layout, an eego amplifier &software (ANT B.V., Enschede, The Netherlands). Here, we compare the meanglobal field power (MGFP) of the VEF traces with the help of Spearman rankcorrelation and the latencies of the main VEF peaks for the three measurements. As a main result, we find that the dry EEG electrodes andthe acquisition procedure do not compromise the MEG recordings. The MGFPcorrelation is 0.88±0.05 (mean ± stdev) for measurement #1 vs #2, 0.89±0.10 for#2 vs #3, and 0.89±0.06 for #1 vs #3. The latencies for measurements #1, #2, #3for the N75 are 85±10 ms, 84±8 ms, 85±10 ms (mean ± stdev); for the P100 106±10ms, 106±10 ms, 105±10 ms; and for the N145 138±16 ms, 139±15 ms, 138±17 ms. In conclusion, we provide evidence that dry multipinPU-Ag/AgCl electrodes are compatible with MEG measurements.

Fetal MCG with an Atomic Magnetometer Array

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We present results on the development of ^{87}Rb optically-pumped atomic magnetometers for the detection of a fetal magnetocardiogram (fMCG). Operating in the spin-exchange relaxation free (SERF) regime, the magnetometers\' sensitivities are reported at the □1 fT $Hz^{1/2}$ level. Environmental common-mode noise, including the □field from the maternal heart, can be suppressed by operating the magnetometers in a gradiometric configuration. We report on schemes from implementing such gradiometers along with recent fMCG measurements. This work is supported by the National Institutes of Health.

Non-magnetic compliant finger sensor for continuous fine motor movement detection

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In experimental paradigms involving sensorimotor functions, characterizing continuous fine motor movements of hand and fingers is limited by currently available technology. A non-magnetic MEG compatible device has been developed that provides continuous force and velocity information. Combined with MEG, this device may find utility in characterizing brain regions associated with force and velocity relative to individual digits or movement pattern. 15 healthy right-handed participants were given visual cues to perform 11 distinct finger movements on the prototype finger sensor for 20 seconds and then rest for 20 seconds (7 times). Respective finger flexion data was obtained, during 151-channel MEG brain scanning, by feeding the signal from finger sensor into four input ADC channels in the MEG hardware. The source activity was reconstructed using an LCMV beamformer in the beta band. The ADC channels were used as regressors for a continuous time general linear model (GLM) and a region of interest (ROI) was identified to examine time and frequency activity. Preliminary results comparing the ADC regressed contrasts using the force component of the finger sensor output produced more focal results compared to conventional contrasts between rest and active states. Moreover, because individual digits could be isolated in the ADC data, somatopy of the little and index fingers were observed consistent with the homunculus. The study confirms that the finger sensor is magnetically compatible with MEG measurements and may potentially provide a means to study complex sensorimotor functions. This prototype may offer a new therapeutic tool to examine neural correlates of finger flexions during recovery of motor function for patients with acquired brain injury. Further investigation will incorporate the velocity component of the finger sensor data. This may enable extraction of additional spatial and temporal effects in relation to specific movement patterns during complex finger flexions.

The Role of Sensor Count in MEG Array Resolution

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In MEG, it is generally assumed that more sensors produces better estimates. In terms of SNR this is undoubtedly true, though the rule of diminishing returns comes into play. Additionally we can also ask what role the number of sensors plays in the array's resolution, dynamic range, and localization accuracy. Recent experimental results have shown that spatial localization accuracy saturates for a smaller number of sensors than one might expect. Here we examine the role of sensor count in determining the resolution of an MEG array using both sampling theory and numerical simulations.

We begin with a one dimensional uniform linear array for which theoretical results can be derived with relative ease given certain common assumptions. Some of these assumptions are not valid in the context of MEG, so we adjust our assumptions as we develop the model into two and three dimensions, eventually reaching an MEG model that approximates reality. We then use this model as the basis for simulations that show that conclusions draw from the uniform linear array are also valid for the MEG case, despite being developed under different assumptions.

Many of the inverse solutions used in both clinical applications and research belong to a class of algorithms that achieve super-resolution, that is, they can separate signals that are closer than the array's nominal resolution. It is therefore a matter of practical importance to also consider how the number of sensors affects such algorithms\' ability to separate closely spaced signals. The Linearly Constrained Minimum Variance (LCMV) beamformer is a good candidate for examination both because of it is widely used and because its simple formulation makes it readily analyzed.

The analysis and simulations presented address only resolution and signal separability, but along with other experimental results, we believe they nonetheless provide a loose framework for quantitatively determining the number of sensors that an MEG requires.

Predicting individual differences in sequence learning from oscillatoryactivity in human MEG-data

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Many complex behaviors involve the ability to learn and reproduce sequences of events in their correct temporal order. Some of these sequences can occur embedded in continuous streams of information. Therefore, we often extract sequences from background information without any prior knowledge about the timing of sequence on- and offsets. While recent theoretical and empirical work indicate that the sequential structure of inputs may be inferred from perceived transitional probabilities, the ability to exploit such statistical information seems to be highly variable. A mechanistic account of what is causing such differences in behavior, however, is still missing. Here we address how the brain extracts the statistical regularities embedded in temporal sequences and whether inter-individual differences in sequence learning can be predicted from fluctuations of rhythmic brain activity. Building on previous electrophysiological studies, we hypothesized that the phase of rhythmic brain activity supports the representation of behaviorally relevant sequences in neuronal activity as well as their consolidation in memory. Our findings suggest that transitional probabilities embedded in temporal sequences are tracked by oscillatory activity in multiple frequency bands (1-150Hz). Finally, we observed that individual differences in sequence learning can be predicted with high accuracy from prestimulus beta (15-20Hz) oscillations.

Neuromagnetic and behavioral responses during encoding of sensorimotor sequence boundaries as revealed by alterations of auditory feedback

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Mounting neurophysiological evidence indicates that the acquisition of simple motor sequences relies on the neuronal encoding of start and end (boundary) elements. In more complex domains, such as speech or music performance, sensorimotor representations are acquired by encoding the mapping between the motor commands and the associated auditory feedback, a process which depends on feedback monitoring. The goal of our study was to explore how the encoding of sequence boundaries contributes to the formation of sensorimotor representations. To that aim, we examined how alterations of auditory feedback (AAF), introduced at different ordinal positions (boundary [Bo] or within-sequence element [In]), affect the neural and behavioral responses during sensorimotor sequence learning. We recorded the neuromagnetic activity from 20 participants, while they learned short piano sequences under the occasional effect of AAF. We analyzed the event-related fields and used a 2x2 factorial design with factors feedback (normal, altered) and ordinal position (Bo, In). A permutation-based factorial test revealed a main effect for both factors and an interaction within 200-500ms post-keystroke. Post-hoc analyses with cluster-based permutation tests demonstrated more significant clusters for the comparison AAF-Bo versus AAF-In relative to the equivalent comparison for normal feedback (NF). This outcome suggests an increased salience of neuronal responses in processing AAF as compared to NF, which is dependent on the ordinal position. At the behavioral level, we found that the temporal properties of the Bo and In events during performance were also differentially modulated by AAF. These findings are the first to support the relevance for sensorimotor skill acquisition of the proper mapping between auditory feedback and motor commands particularly during the encoding of sequence boundaries. Our study thus contributes towards a comprehensive understanding of sensorimotor sequence learning.

Alpha-band modulation in sequential short-term memory encoding: comparison in young and aged participants

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When memory items are presented sequentially, the beginning and ending items are memorized well (serial position effect). We recorded magnetoencephalograms (MEG) of 10 healthy young participants (mean ± SD age, 22.8 ± 0.6 yrs) during performance of a short-term memory task. In the task, seven arrow images were presented sequentially and a recall number was presented afterward. Each participant memorized the arrow directions in order and recalled the direction that was presented in the order indicated by the recall number. The accuracy rate showed a typical serial position effect. The amplitudes of alpha rhythm significantly increased from the beginning (during presentation of the 1st and 2nd arrows) to the midterm (3rd to 5th arrows) of memory encoding. We found that an increasing ratio is essential for memory performance, because the ratio was larger before a correct answer than before a wrong answer. Additionally, the region of alpha rhythm that increases around the midterm was estimated to be located in the visual cortex, in agreement with previous knowledge that alpha rhythm is increased by active inhibition of task-irrelevant visual inputs. We then recorded MEG of 24 healthy aged participants (mean ± SD age, 67.8±4.0 yrs) during performance of the same task. The accuracy rate for the aged participants was significantly lower than that for the young participants, while a typical serial position effect was still observed. However, the amplitudes of alpha rhythm decreased from the beginning to the midterm of memory encoding, in contrast to that shown in the young participants. These results suggest that the neural processes of short-term memory are different in aged people and young people. Estimation of the source of the alpha rhythm modulation might reveal some compensating memory process in aged people. This work was supported by Grant-in-Aid for Scientific Research (C)25350516 and 16K01345.

Gender differences in navigation performance are associated with differential theta activity in the right hippocampus

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Gender differences in spatial navigation are well-established, but the underlying brain mechanisms are unclear. Hippocampal theta oscillations play an important role in navigation and are thought to mediate spatial memory. This study examined whether gender differences in navigation performance are associated with differences in hippocampal theta rhythms. We measured brain activity in healthy adult males (N = 18) and females (N= 18) while they navigated in a virtual Morris water maze. Brain responses were measured with a 160 channel KIT whole-head magnetoencephalography (MEG) system. MEG theta band (4-8Hz) activity were analysed with synthetic aperture magnetometry. Males were significantly faster than females in the navigation task. In familiar environments, males, but not females showed significantly improved performance. MEG results showed that both groups exhibited comparable theta rhythm magnitudes in anterior left hippocampus/parahippocampus. In the novel environment, right hippocampal theta power was comparable in both groups. In the familiar environment, males exhibited a significant decrease in theta, while females showed no change. For males, right hippocampal theta power was significantly correlated with navigation performance in both new and familiar environment, while there were no significant associations with performance in females. These results suggest males can more readily encode the configural knowledge about the environment to facilitate flexible navigation.

Dynamics of brain activation during audio-visual association learning

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Observing changes in brain activity during learning is challenging. Here we measured brain activity using magnetoencephalogram (MEG) while the participants were learning to associate shown symbols with heard syllables. Learning was based on feedback provided after each trial. The gradual learning of the audio-visual associations was contrasted with a condition where the feedback was meaningless. This non-learnable condition showed the effects of repeated exposure to the stimuli and learning the task requirements. Condition (learnable, non-learnable) by Training time interaction indicated that three brain regions showed learning related changes in activity: temporo-occipital cortex, caudal middle cortex and posterior superior temporal sulcus. The effects started 350 ms after the onset of the visual stimulus presentation and appeared after 10 minutes of training. Changes in brain activity coincided with changes in reaction times and accuracy scores. The results show that changes in processing of visual form in the temporo-occipital area was accompanied with changes in selective attention processes at the frontal cortex and audio-visual integration at the posterior temporal areas.

Alpha synchronization between occipital and frontal regions distinguishes errors in a visual working memory task

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Introduction

Human memory is vulnerable to distortions. We designed a visual working memory paradigm to induce errors and investigate neural fingerprints from synchronization measures.

Methods

28 participants took part in this EEG study.

Each trial began with a fixation cross. Following a sequence of 4 images (250 ms / stimulus) another fixation cross was shown in retention period (1.25 ± 0.25 s). From 2 probe images, subjects selected the one(s) they remembered. *Correct* ( ), *false memory* (*FM*), and *errors* (*E*) conditions were defined.

Contrast between and was assessed. Similarities between *FM* and other conditions were explored adding *FM* trials to and reassessing differences with *C*. The same procedure was repeated merging *FM*s with *C*.

Time-frequency representations (TFR) were estimated using Fourier basis and Hanning window along retention time. Squared imaginary coherency was used to identify couplings.

was selected as seed channel since TFR highlighted higher power in α-β range. For each channel combination confidence level was set from an imaginary coherency distribution estimated by Monte Carlo method - 200 runs.
Individual α coherency peaks were identified in frontal regions and values below confidence level set to 0; differences were studied with t-test.

Results

Analysis showed significant α coherency difference in retention - between O and frontal regions - E > C, p = 0.0062, Bonferroni corrected. Addition of *FM* trials to either condition did not exhibit any significant difference.

Conclusions

The increased coupling in α band for in retention between O and frontal regions might reflect inhibition processes. Arguably, synchronization in erroneous trials might reflect failed top-down modulation for transitioning from an inhibition state, required within the retention interval, to an active state, to re-enable perception for the upcoming probes, of visual regions. No common patterns between *FM*, *C*, and *E* could be identified.

Consistency of MEG and fMRI findings in revealing the functional neurocompensatory response in early Alzheimer's disease

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Background:Alzheimer's disease(AD) is the most common cause of late life disability, progressing gradually to affect memory and thinking. Previous studies suggest that in the early stagesof the disease process, the brain can response tothe pathological change:The so-called neurocompensatory responsehas been shown withincreasedbrain activity and metabolism in the prefrontal cortex. The present study examinedthe characteristic Magnetoencephalography(MEG) and functional MRI(fMRI) findings to validate the neurocompensatory response in early AD.
Methods:Older patients with mild ADand older control subjects (n=12 in each testing group; age=65-90 years) performed a memory retrieval task by viewing graphical objects and indicating whether an object was previously presented or not (*i.e.* \"old\" vs.\"new\").Whole-head MEG and fMRI data were acquired respectively using anElektaNeuromag system (306 channel optimized to record both superficial and deep magnetic sources) and a 4-Tesla Varian-Oxford human imaging system (22 5.0mm axial slices with 0.5mm gap). After standard processing, imaging signals were time-averaged for the same task conditions. Differences between conditions were localized respectively using event-related beamformer spatial filter to estimate pseudo t-statistics,and usinga canonical haemodynamic response function fitting to task onset and duration on MEG and fMRI activation maps.

Results:Subjects with mild AD showed lower accuracy and prolonged latency than the controls. Activation in the right The AD group also showed increased activation in the right dorsal medial portion of the frontal pole, which was not observed in the HC group. The increase activation of the prefrontal lobe (bilaterally in BA9 and BA46) was associated with performance of the recognition task.
Conclusions:The MEG and fMRI datasuggest the consistency of the differential involvement of the prefrontal lobe during memory processing by subjects with early AD and with normal aging, confirming the neurocompensatory response.

Task Evoked Dynamics in HMM Brain States During Formation of Long Term Memories.

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Spatial and contextual associations in long-term memory recruit task-specific brain networks (Stokes et al 2012) within the context of substantial on-going neural dynamics. Task analyses often seek to remove these spontaneous dynamics, yet the interplay between task-evoked and ongoing activity may be substantial. We characterise the oscillatory dynamics within MEG (Elekta NeuroMag VectorView) data acquired from 16 Participants during association learning into a set of transient brain states using a Hidden Markov Model (HMM) (Baker et al. 2014; Vidaurre et al. 2016.). Critically, this decomposition is performed without any knowledge of the task conditions or timings within the dataset. The data were filtered from 3-40Hz and projected into source space using a LCMV beamformer. The data were temporally concatenated for each voxel, parcel time courses were computed using an anatomical parcellation, and multivariate leakage correction applied (Colclough et al 2015). Amplitude envelopes were then computed, downsampled to 40Hz and used to infer a Gaussian-HMM to identify transient brain states characterized by patterns of power and/or functional connectivity. Spatial maps of the relative amplitude for each HMM state were computed using the partial correlation between the state time-courses and the amplitude envelopes. To identify any task evoked changes in the occurrence of HMM states, the state time-courses were then epoched, and the average fractional occupancy of each state (i.e. the proportion of trials for which each state is active) was computed across participants for each point in time before and after learning. Task-related dynamics were identified in both sensory and fronto-parietal networks; moreover, differences before and after learning were apparent in a subset of the frontal and parietal networks. The HMM approach identifies dynamic brain networks which are robust across large datasets, retaining both a rich description of on-going dynamics and task-evoked responses.

Persistent neural activity in auditory cortex is related to auditory working memory in humans and non-human primates

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Working memory refers to neural processes used for temporarily storing information and is a fundamental prerequisite for our abilities to perform everyday functions. Working memory requires high accuracy and high flexibility for information storing and involves a broad network of brain areas including sensory cortices. In this study we investigated neural correlates of working memory in early auditory cortex. In a convergent approach with humans and non-human primates, we conducted eight experiments requiring subjects to perform different tasks on the same stimuli, sequences of two sounds separated by a delay. While subjects performed the tasks, magnetic fields were recorded in human auditory cortex, and single- and multiunit activity as well as local field potentials in monkey auditory and prefrontal cortices. Our studies provide convergent evidence from humans and monkeys for neuronal activity related to working-memory load in auditory cortex and, thus, support the hypothesis that early sensory cortex temporarily stores information. Furthermore, our magnetoencephalographic recordings revealed the involvement of both left and right auditory cortex in auditory working memory, with no indication for hemispheric differences. Collectively, the results of these experiments demonstrate that persistent activity in auditory cortex during the delay is partly related to auditory working memory and not only to other cognitive processes inevitably involved in such paradigms and intermingled with the memory process, such as anticipation of the second stimulus, preparation for motor response alternatives or expectation of a reward. The work was supported by DFG projects He1721/10-1 and 10-2 and SFB/TRR-31.

Electrical stimulation of the medial temporal lobe for verbal memory enhancement and theta activity in the temporal cortex

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The medial temporal lobe (MTL) stimulation was thought to be essential for modulating human memory performance. However, the parameter such as stimulation frequency related to memory performance and the neural change in aspect of cortico-hippocampal network that could mediate the memory formation are not clearly understood. Therefore in this study, we tested two hypotheses: firstly whether the hippocampal stimulation with several frequency bands may exhibit a characteristic change on memory related neocortical regions. Secondly, whether the MTL stimulation may improve verbal memory in humans, further the induced oscillatory changes in a certain neocortical area may relate to memory performance. To investigate this, we implanted depth electrodes on MTL and subdural electrodes on frontal, parietal and temporal cortex in 7 epilepsy patients. Four subjects were given gamma (50 Hz), beta (20 Hz) and theta (5 Hz) range stimulation at the hippocampus (n = 4) while the subjects were in resting states. Five subjects were able to complete a paired word verbal memory task. They were given electrical stimulation of 50 Hz at the hippocampus (n = 3) and the parahippocampal gyrus (n= 2) during encoding period. For statistical evaluation, we measured the increased theta amplitude and the correlation coefficient value of the hippocampus and the neocortical areas. We found that the stimulation induced theta amplitude increase at the hippocampus and the cortical regions were different depending on stimulation frequencies. Those increased amplitudes of theta power at the temporal cortex had a strong connectivity with the hippocampus of 50 Hz stimulation (<.05). Also, the MTL stimulation enhanced verbal memory compared to no stimulation (<.05). Interestingly, the rearranged word pairs were consistently enhanced while the intact pairs were unvaried or decreased. In addition, during a successful verbal memory encoding, the theta power was significantly increased at the middle and the inferior temporal cortex (<.001). We concluded that stimulation of the MTL region during encoding phase enhanced verbal memory in human. This effect may have on remembering each item rather than item association. Furthermore, the accompanied increase of theta power in the temporal cortex implies a cortico-hippocampal circuit of the successful memory formation.

Beta Oscillatory Dynamics are Modulated by Load during a Spatial Working Memory Task

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Spatial working memory (SWM) is integral to an individual's ability to successfully navigate the world and is typically divided into three phases: encoding, maintenance, and retrieval. Previous studies have demonstrated activation within a network of frontal, parietal, and occipital regions during SWM performance, and the manipulation of memory load has been shown to modulate alpha and theta oscillatory activity within these regions. However, less is known about the impact of memory load on beta oscillatory dynamics during SWM performance. In the present study, we manipulated memory load (low and high) in the context of a SWM task as healthy adults underwent a magnetoencephalographic (MEG) recording. MEG data were evaluated in the time-frequency domain and significant beta oscillatory responses were imaged using a beamformer. Across loads, strong decreases in beta activity were observed in bilateral occipital and parietal cortices, as well as the left premotor cortex (PMC) beginning shortly after the onset of encoding and spreading to include the right PMC during maintenance. Load-related effects emerged early during encoding in the right superior parietal cortex (SPC), while differences were found in the right inferior parietal cortex (IPC) during the later encoding period. Additionally, our data indicated load-related effects in the right ventral prefrontal cortex (vPFC) during the initial half of maintenance, while at the end of maintenance differences were observed in the left PMC and right SPC. Finally, stronger decreases in occipital beta activity were observed during the maintenance of more, relative to less spatial stimuli. Our results are consistent with prior work demonstrating differential recruitment of frontal, parietal, and occipital regions in response to more demanding, relative to less demanding SWM tasks, and extend upon the literature by characterizing the beta oscillatory dynamics underlying these processes.

Measurement of Dynamic Functional Networks using MEG during a cognitive Task

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How the human brain forms and dissolves a hierarchy of transient functional networks to support ongoing cognitive demand is one of the most important questions in neuroscience. Given its high temporal resolution and whole brain coverage, MEG represents the method of choice to image these networks. However multiple challenges remain, including how to process the vast data generated by dynamic network metrics. Here we describe an atlas-based independent component analysis (ICA), which elucidates functional networks during a cognitive task.

Two datasets were acquired. In dataset 1, 15 participants executed a self-paced buttonpress with the left index, approximately every 30 seconds. In dataset 2, 19 participants underwent a visual Sternberg working memory task. [Two abstract geometric shapes were presented, and after a maintenance period of 7 s, a third shape was displayed. Subjects were asked to indicate a match with a button press.] The brain was parcellated into 78 cortical regions derived from a modified AAL atlas. Source timecourses from each region were generated usinga Beamformer. Data were temporally windowed (3 and 6s respectively), leakage corrected, and the Pearson correlation of the amplitude envelopes was calculated within each window as an estimate of connectivity between all region pairs. The window was allowed to slide in time to generate time evolving connectivity information. To generate functional networks, the connectivitydata were decomposed using temporal ICA (tICA).

In the self-paced data, tICA returned two networks (sensorimotor & visual) which showed significant modulations in connectivity around the time of the button press. In the Sternberg data, 9 networks, including visual, sensorimotor, fronto-parietal and language, were derived which showed significant modulation during the task. Our results show clearly the unique potential of MEG to characterise transient network formation during cognition.

Spectrally resolved fast transient brain states in electrophysiological data

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The brain is capable of producing coordinated fast changing neural dynamics across multiple brain regions in order to adapt to rapidly changing environments. However, it is non-trivial to identify multi-region dynamics at very fast sub-second time-scales in electrophysiological data. We propose a method that, with no knowledge of any task timings, can identify and describe time-varying multi-region interactions in terms of their spectral and spatial properties [1]. The approach models brain activity using a set of sequential brain states, with each state distinguished by its own unique multi-region spectral (i.e. power and functional connectivity network) properties. This is able to identify potentially very short-lived visits to a brain state, at the same time as inferring the state\'s properties, by pooling over many repeated visits to that state.

The method, the HMM-MAR, combines two models: the multivariate autoregressive (MAR) [2] model and the Hidden Markov model (HMM) [3]. The MAR model characterises the behaviour of time series by their linear historical interactions. MARs are able to characterise the frequency structure of the data and capture interactions (e.g. coherence) between multiple brain regions. The HMM describes a time series as a sequence of states, where each state has its own model of the observed data. Here, the observation model we use corresponds to a MAR model, and, hence, each state is related to a different set of quasi-stationary MAR coefficients describing the neural oscillations.

We test the ability of the HMMMAR to extract group level information from MEG data for 8 subjects on a simple button-pressing motor task. With no prior knowledge of the task, we successfully detect task dependent states with a meaningful spectral signature.

[1] D. Vidaurre. NeuroImage 2015

[2] W. D. Penny. Vision, Image and Signal Processing, 2002.

[3] B.-H. Juang. IEEE Transactions on Acoustics, Speech and Signal Processing, 1985.

Effective connectivity applied to interictal MEG recordings of patients with refractory epilepsy

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Objective: A challenge in epilepsy surgery is the preoperative localization of the epileptogenic zone, preferably using non-invasive techniques such as magnetoencephalography (MEG). The epileptogenic zone generates epileptiform activity, which subsequently spreads to the entire brain. This spread might be captured by effective connectivity, which infers the direction of interactions between regions. We hypothesised that the epileptogenic zone has abnormally strong outgoing connections. Methods: Preoperative eyes-closed interictal MEG recordings (including interictal spikes) were acquired for 22 patients with refractory epilepsy, of whom 14 were seizure-free at least one year after surgery. Beamformer-based time series were reconstructed for 90 cortical and subcortical AAL regions of interest (ROIs). For each ROI, effective connectivity was estimated using the directed phase transfer entropy (dPTE), which was converted to a z-score using a normative database of 67 controls. The ROIs with the five maximal dPTE and z-score values were compared to the lobe containing the resection cavity. We evaluated seven frequency bands: broadband (0.5-48 Hz), delta (0.5-4 Hz), theta (4-8 Hz), lower alpha (8-10 Hz), upper alpha (10-13 Hz), beta (13-30 Hz), and gamma (30-48 Hz). Results: Accuracy (73%) was highest in the delta band; here, high dPTE values corresponded to the lobe containing the resection cavity in 10/14 seizure-free patients and 2/8 not seizure-free patients. The accuracy was the same when using z-scores, which corresponded to the lobe containing the resection cavity in 9/14 seizure-free patients and 1/8 not seizure-free patients. Conclusion: The epileptogenic zone had an abnormally strong effective connectivity to other brain areas in most seizure-free patients, but not in patients who were not seizure-free. These initial results show the potential of analysis of directed functional interactions in localizing the epileptogenic zone non-invasively.

Identifying information flows for visual motion perception from a network dynamics model of the human brain

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Recently, we proposed a method to construct a brain network dynamics model from magnetoencephalography (MEG) data with a combination of functional, structural, and diffusion MRI data. The constructed network dynamics model enables us to simulate brain activities. Using this model, we can virtually damage the brain and examine its effect on a specific brain activity (e.g. activity at MT). This procedure reveals the important information flow responsible for the focused brain activity. The purpose of this study is to demonstrate the feasibility of this idea. Specifically, by virtually damaging the brain, we identify the important information flows responsible for the activity at MT. We first estimated current sources from MEG data recoded during viewing a moving stimulus. Then, we constructed the network dynamics model by estimating a multivariate autoregressive (MAR) model from the estimated currents. Using the estimated dynamics model, we simulated brain activities with cutting a connection (e.g. from V1 to MT) and examined how large the activity at MT changed. This procedure was repeated while changing the connection to cut. Finally, we selected the most effective connections. As a result, not only simple (e.g. from V1 to MT) but also complex (e.g. from V1 to MT via V2) information flows were identified. Furthermore, by shifting focused time, we could identify time-varying information flows. These results suggest the feasibility of the idea for information flow identification and the usefulness of our network dynamics model in neuroscience research.

Unsupervised feature extraction by time-contrastive learning from resting-state MEG data

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Although independent components analysis (ICA) is a promising approach to analyze spontaneous (unlabeled) brain signals, linear blind source separation of such signals is of limited utility due to the complex nonlinearities in brain dynamics. Here, we propose a new intuitive principle of unsupervised deep learning from time series that uses the nonstationary structure of the data. Our learning principle, time-contrastive learning (TCL), finds a representation that allows optimal discrimination of time segments (windows). TCL assumes two properties for the data: (a) the observed signals are nonlinear mixtures of source signals whose components are mutually independent, and (b) the source signals have time-segment-wise nonstationarity in variance. We theoretically show how TCL can be related to a nonlinear ICA model, when ICA is redefined to include temporal nonstationarities. We also experimentally evaluate the validity of the proposed method with resting-state MEG data, in which nonstationarity is considerable, and show that the proposed method can extract brain networks consistent with previous studies on fMRI.

Spatiospectral alterations in resting state MEG networks in major depressive disorder

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It is unknown whether the spatial and spectral profiles of MEG resting state networks differ across patient groups. Here, we present an analysis of MEG recordings from 17 healthy subjects and 22 unmedicated patients with major depressive disorder (MDD). MEG recordings were acquired on a275-channel CTF system, using MRI images for localization. SAM beamformer weights were calculated from broadband (2-150Hz) filtered data, and the smoothed Hilbert envelope was calculated at 1Hz delta(δ,2-4Hz), theta(θ,4-8Hz),alpha(α,8-14Hz), beta(β,14-30Hz), gamma(γ,30-50Hz), and high gamma(γ\',50-100Hz)bands. Images were Talairach aligned, mean corrected, and variance normalized. Images in the γ and γ\' bands were corrected for muscular artifacts by linear regression of a very high frequency signal (200-250Hz).Data from all subjects and bands were temporally concatenated, and an ICA was performed within ICASSO,extracting 25 independent components (ICs). Each IC time course was divided into the portion corresponding to each frequency band and subject, and linear regression was used to extract spatial maps corresponding to each IC. ICs with Icasso quality factor<0.7, those with anticorrelated nodes, and those with time courses exhibiting correlation with eye movements were excluded. A multivariate model was used to determine main effects of frequency(F), group(G),and the GxF interaction. Eleven ICs met our criteria, and all exhibited a main effect of F. Two ICs (posterior cingulate and precuneus) exhibited a significant main effect of G. Four ICs (Left (L) fronto-parietal, Right (R)Insula, and L Cerebellum, R DLPFC) showed a significant GxF interaction. GxF effects were observed in R middle temporal gy and posterior cingulate for the RInsula IC, dorsal cingulate for the L Fronto-parietal IC, bilateral visual cortex for the DLPFC IC, and hippocampus and subgenual cingulate for the L CerebellumIC. These results could potentially be used to guide neurostimulation treatments for MDD.

Information theoretic assessment of methods for constructing functional connectomes from MEG

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Functional connectomics is an increasingly popular tool in human neuroscience. However,there are many parameters involved in deriving functional connectomes (FCs) and several FC measures to choose from. Determining which provide the most useful information is difficult. One aspect not thoroughly investigated is how atlas regions are sampled to form the nodes of an FC, for which many strategies exist. This study aims to quantify the information content of FCs derived using different sampling strategies and connectivity measures.

5min resting-state data was acquired on a 275-channel CTF-MEG system. Virtual sensors in a 7.5mm grid were derived using SAM beamformers. Surrogate datasets were created by shuffling sensor-level time-series. FCs were created using 3 methods: coherence; imaginary coherency and Hilbert envelope correlations, all in β1-band (12-20Hz). The AAL atlas defined the nodes of the FC using 6 strategies. the centre of mass; the voxel of peak power; mean of the spatial filters; mean of the virtual sensor; the principle component of the virtual sensor; mean of the connectivity estimators across all pairs of voxels. The last method provides the most complete estimate of connectivity between regions but also has very high computational demands. The information content of each sampling strategy and FC measure were assessed by computing the Kullback–Leibler divergence (KLD) between the FC matrix and its corresponding surrogate.

KLD was highest where the atlas was sampled by averaging FC measures between voxels. This suggests quicker sampling strategies may not sufficiently characterise the true connectivity. This strategy also showed the highest variance in KLD, suggesting possible increased sensitivity to individual differences. Hilbert envelopes correlations and imaginary coherency both showed higher KLD than coherence. Future work will explore more complex FC measures such as PLI. The approach can also be applied to assess different graph measures.

Task-related Cortical Networks in Language Production: Exploring Similarity of MEG- and fMRI-derived Small-world Human Brain Functional Networks

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Current research about network analyses of haemodynamic modulations has revealed functional brain networks with high consistency across subjects in a cognitive state. But the relationship between the slowly fluctuating haemodynamic responses and the underlying neural mechanisms is not well understood. The purpose of our study is to truly understand the nature of electrophysiology and haemodynamics and to explore if such networks are differentially modulated by cognitive processing.

MEG data were measured using a 306 channel Vector view MEG device (Elekta, Finland). MR images were acquired using a Prisma 3.0 T MRI scanner (Siemens, Germany). An object-naming task was performed on 10 healthy volunteers to evoke MEG responses and BOLD signal changes. MEG data were preprocessed using MNE software and fMRI data were analyzed by SPM software. After getting the brain BOLD signal and source signal from MRI and MEG data preprocessing, respectively, functional connectivity was implemented to construct the human brain network, and graph analysis was used to calculate the network properties.

The parameter Sigma of fMRI and MEG networks both ranged between 1.1 and 2.0, demonstrating the small-world property during the course of cognition. The correlation coefficient of fMRI is larger than MEG, indicating that small-world topology of MEG was closely conserved over a wide range of network definition. The MEG network was distinguished by higher local efficiency, shorter path length and greater clustering in the scaling correlation coefficient, indicating the excellently high efficiency of information transfer among nodes in MEG network compared with fMRI network.

In this study, the nodes representing the high degree, nodal global efficiency and betweenness were considered as the hubs. Task-related network hubs associated with language processing were found in cortical regions (i.e.: the posterior temporal cortex and the inferior frontal cortex), evidenced by both MEG and fMRI. Moreover, some network hubs were found in regions related to object recognition and visual processing, including the lateral occipital cortex.

Using a graph analysis approach in a parallel MEG/fMRI picture naming study, we investigated the similarities between haemodynamic networks and their electrophysiological counterparts. This study demonstrates similarities, but also discrepancies, in the spatial distribution of functionally relevant network hubs identified using data from MEG and fMRI.

Evaluation of Phase Amplitude Coupling during resting state: An MEG study

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Objective:
Phase-amplitude coupling (PAC) where the amplitude of a high frequency component modulated with phase of a low frequency component, has been claimed to play an important role in neuronal communication during learning and cognitive process. Interestingly, recent studies have indicated the presence of a ubiquitous PAC phenomenon even during resting states. Non-physiological PAC can happen due to any non-linearity (spikes) in the signal and one has to rely on surrogate measure to derive the statistical inference of a measured PAC index. Therefore, extent of a PAC phenomenon depends on surrogate measure that is used for evaluation. In present study, we evaluated the characteristics of the PAC phenomenon in various surrogate data and its implication on the resting state PAC in MEG signals.
Method:
We used resting state MEG data of 4-5 minutes duration from 27 subjects. For statistical inference of measured PAC, five different kind of surrogate measures were generated by either permuting just phase component, or by permuting the samples of signal, or just using Gaussian random signal with and without 1/f spectral characteristic. Modulation index (MI) method was used to capture PAC phenomenon in the signal. Significance of MI value from a node was evaluated using threshold value i.e. 99th quantile ($p < 0.01$) of MI value in 100 iterations of a surrogate data.
Result:
Result shows that the extent of PAC vastly depends on surrogate measures that were used for evaluation. On an average merely 24% and 9% nodes out of 58 nodes distributed over the cortex exhibit significant PAC in one or more frequency pairs when evaluated with least and more conservative surrogate measures respectively. Moreover, PAC also evaluated on short duration epochs of 15s long moving with 7.5s overlap, failed to exhibit ubiquitous PAC across the time, even evaluated with a less conservative surrogate measure.
Conclusion:
Resting state MEG signal failed to exhibit ubiquitous PAC phenomenon.

Processing of nursery rhymes in the newborn brain – A hdEEG study

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It is a common belief that learning begins far before birth. This conviction raises interesting questions about how and what exactly an unborn baby is able to learn. Yet many studies about perinatal learning rely on reports with few cases and often lacks neurophysiological data. In the present study 30 pregnant women were asked to replay twice a day (from 34 weeks of gestational week onwards), at 80 dB, a nursery rhyme that was previously recorded with their own voice. At around week two and five after birth, newborns were presented again with the same rhyme uttered either by the mother's voice a stranger's voice, or were presented with a completely new rhyme. Each stimulus type was presented for a total of 3 minutes always preceded by a 3 minutes baseline. During the experimental session, video as well as high density EEG (129 electrodes), EMG, and ECG were recorded. We here computed the speech envelope for the nursery rhyme, for each subject, and each stimulus condition, using nine equi-spaced frequency bands (100 Hz – 10 Hz) following the method from Gross and colleagues (2013).
Using 3sec segments we performed time-frequency analysis of the EEG (129 channels) and speech signal and calculated the coherence between them. Preliminary results indicate that the coherence between the EEG and speech signal is higher in the lower frequencies (2- 7 Hz) and is able to differentiate between familiar and unfamiliar stimuli already shortly after birth. Interestingly, also ECG data seem to confirm this differential response pattern. We will discuss these findings in the light of brain maturation as well as its potential relation to early mother-child "bonding" and later attachment.

Gross, J., Hoogenboom, N., Thut, G., Schyns, P., Panzeri, S., Belin, P., & Garrod, S. (2013). Speech rhythms and multiplexed oscillatory sensory coding in the human brain. PLoS Biol, 11(12).

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Affective Modulation of Cross-Frequency Coupling in Emotional Prosodic Processing of Primary Dysmenorrhea Patients

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Introduction

Patients with primary dysmenorrhea (PDM) are generally more anxious and depressed than healthy control (Dorn et al., 2009), but effects of long-term cyclic pain experience on interaction between emotion and sensory perception have not been examined. Emotional prosodic processing involves processing of emotional and auditory information. This study was to examine the association between cerebral regions related to processing of emotional prosody using cross-frequency coupling (CFC) computed from magnetoencephalographic (MEG) data in PDM.

Materials and Methods

Nine right-handed PDM patients participated in this study. The experiment using an oddball-like task with emotional prosody was conducted, which consisted of neutral, angry, sad, and happy prosodies. Event-related neuromagnetic responses of each individual during her menstrual phase were recorded with a Neuromag Vectorview 306 MEG system. Beck Anxiety/Depression Inventory (BAI/BDI) were used for psychological assessments.

The auditory-seeded CFC dynamics between cortical (theta band, 4-7 Hz) and auditory areas (high gamma band, 80-120 Hz) oscillations were computed using the beamformer-based phase-amplitude coupling analysis (Chan et al., 2015). A paired t-test was performed to examine the changes of CFC (ΔCFC) induced by different emotional prosody, followed by correlation analysis between the BAI/BDI and ΔCFC.

Results and Discussion

Significant ΔCFC in negative emotion condition wasfound in the right posterior middle temporal gyrus (pMTG), inferior frontalgyrus (IFG) /anterior insula (aIn), and lateral occipital lobe. Only the pMTGexhibited significant correlation between ΔCFC and BAI/BDI scores. Thesefindings suggest that the right MTG and IFG/aIn in PDM play important roles in functionalinteraction of affective experience and perceptual processing of emotionalprosody.

How sensitive are MEG connectivity metrics to detect non-stationary connectivity?

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Introduction: Current Functional connectivity (FC) metrics have been mostly tested in a static framework where FC is averaged over a recording lasting several minutes. Since the field is rapidly shifting towards temporally dynamic aspects of FC it is now relevant to elucidate how sensitive popular source level FC measures are to non-stationary connectivity. *Methods*: Analyses were undertaken on simulated MEG data obtained from a multivariate autoregressive model, informed by a Hidden-Markov model (HMM-MAR) as well as on empirical data (60 subjects from the human connectome project). We assessed the sensitivity of phase based metrics, phase locking value (PLV), phase lag index (PLI) and the phase lag time (PLT), and envelope correlations (AEC), all applied to source reconstructed timecourses after leakage correction, to dynamic connectivity. Using HMM-MAR, we tested how sensitive the different metrics were to detect a range of a-priori defined temporal states given different window lengths and signal to noise ratios. In real data, using different window lengths, we tested whether the metrics were sensitive to FC variability that could not be attributed to noise fluctuations around stationary FC values. *Results and Discussion:* Our simulations showed that FC variability could be detected with all metrics, but that AEC was most sensitive. The best sensitivity to variability of FC was found for window lengths approximately equal to parametrised state lifetimes and most measures were robust to detect the underlying states with decreasing SNR. In empirical data all measures were able to detect non-stationary FC, although AEC again outperformed the other metrics by SNR and number of significant connections. For all metrics, for short windows (<1s) poor SNR meant decreased detection of FC variability. Overall our results show that dynamic FC can be measured using a variety of metrics in MEG, although sensitivity depends strongly on window size and SNR.

Time Series Graphical Models as Exploratory Tools to Uncover Functional Connectivity in MEG Recordings

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Learning Gaussian graphical models from data is a powerful statistical technique to discern conditional independencies between random variables. The key result is that zeros in the inverse covariance matrix between the random variables correspond to conditional independencies. Equivalently, two Gaussian random variables are conditionally independent when they are independent after removing the linear effects of all other variables. Learning Gaussian graphical models has been widely applied to neuroimaging data to uncover functional connectivity between brain regions as conditional independence is a natural definition of functional connectivity. We consider an extension of conditional independence to Gaussian time series and develop convex objective functions and scalable algorithms to learn sparse Gaussian graphical models that take the temporal dynamics of the signal into account rather than treating the data as i.i.d. We develop convex objective functions and scalable algorithms to learn such graphs. Our formulation also allows us to account for spurious connections due to unmeasured latent processes as well as to incorporate heterogeneity between groups of recordings, such as subjects or tasks. In order to evaluate the methods on determining functional connections underlying MEG recordings we develop a comprehensive suite of synthetic MEG signals with known underlying connectivity structure and \"MEG noise\" incorporated (e.g. point-spread).

Improving the estimate of the coupling direction between brain areas in MEG by using the maximized Phase Slope Index

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The development of methods to disclose functional connections between brain areas is crucial to understand the signatures of healthy and diseased cognition. In this framework, the characterization of the directionality of coupling is of fundamental importance for characterizing e.g. top-down mechanisms.

The purpose of this work is to define a new directed connectivity measure, i.e. the maximized Phase Slope Index (Ψ_{max}), that allows for a robust characterization of the true direction of functional coupling, especially for low signal-to-noise ratio (SNR) data. The definition of this new metric is based on the Phase Slope Index (PSI) [1], a frequency domain measure of directionality robust to volume conduction.

Firstly, we generalized the PSI by introducing a collection of directionality measures comprised by several possible functions of the cross-spectra phase slopes, among which the sine function leads to the original PSI definition.

Then, we tested the ability of the measures in the collection to correctly detect the direction of interaction by a score based challenge on sets of 1000 signal pairs [2]. Each pair simulated the interaction between two brain sources which were connected through direct and indirect connections, perturbed by noise. To assess the performance, for each pair, we assigned 1 point for correctly detected direction, -10 points for a wrong direction, and 0 points for no answer. This approach has identified an element of this collection, the Ψ_{max}, with the best performance. Specifically, for SNR<1, in about 78% of sets the score obtained by Ψ_{max} is higher than the one obtained by PSI with the maximum score reached by Ψ_{max} being approximately 5% higher than the PSI score.

We expect that Ψ_{max} could impact the study of directed connectivity in situations with low SNR as, e.g., resting state or in the study of cognitive functions.

[1] Nolte et al., 2008

[2] Nolte et al., 2010

A Multi-Layer approach to MEG Connectivity Analysis

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Connectivity can be calculated as statistical interdependencies between neural oscillations within and between a large range of different frequency bands. This pan-spectral network hierarchy likely helps to mediate simultaneous formation of multiple brain networks, which support ongoing task demand. However, to date it has been largely overlooked, with many studies treating individual frequency bands in isolation. Here, we use a multi-layer network framework to derive a more complete picture of connectivity within and between frequencies.

Method: 23 healthy controls and 23 patients with a current diagnosis of schizophrenia completed a visuomotor task. Participants made continuous motor responses during the presentation of a high contrast visual grating. Individual participant MRIs were parcellated into 78 regions using the AAL atlas and a representative timecourse derived from each region. Adjacency Matrices (AMs) were constructed by computing the amplitude-envelope-connectivity between each region pair in the AAL atlas. AEC was computed across 4 frequency bands as well as between bands; generating 10 separate AMs, which were tiled to form a supra-AM (SAM) containing all within and between band connections. These SAMs were then processed to show significant connections.

Results: Task analysis revealed a motor network in the beta band comprising bilateral primary motor and sensory areas as well as secondary somatosensory area. A gamma network was also seen in the visual regions. Interestingly beta-to-gamma networks revealed a bilateral premotor network as well as visual to motor cortex interaction.

Discussion: We have shown the multilayer approach to be effective in identifying task induced changes by applying our method to a visuomotor task. Future work will aim test our methodology further by investigating within and between band connectivity in a cognitive task using a greater number of participants.

[1] Brookes et al. (2016) Neuroimage, 132, pp 425-438

Stochastic learning of quasi-stationary states of brain activity in big data sets

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Hidden Markov models (HMMs) can be used to describe brain activity as comprising a sequence of discrete brain states, characterised by distinct patterns of brain activity or functional connectivity [1,2]. These have recently been used to explore very fast transient functional connectivity in the brain in both rest [1] and task [2] in MEG data. As the same time, projects like the Human Connectome Project (HCP) and Biobank are producing an unprecedented amount of high quality data, with a number of subjects in the order of thousands. Unfortunately, group HMMs (i.e. run on data temporally concatenated over all subjects) are computationally expensive to train on such massive data sets.

To overcome this limitation, we propose a stochastic alternative [3] to the standard HMM variational inference algorithm; where, at each iteration, we randomly pick a subset of the subjects, obtain the state time courses given the current group HMM states, and update the parameters of the group HMM states.

With our method, we substantially reduce computation time and avoid the need to keep in memory the whole data set. As a proof of concept, we test our algorithm on whole-brain resting-state fMRI data (~900 subjects) and resting-state MEG data (25 subjects) using an observation model that allows us to describe the states in terms of their multi-region spectral properties [2]. We show that the proposed approach not only makes it possible to infer on big data sets, but can also often outperform standard variational learning avoiding shallow local minima.

[1] A. Baker. Fast transient networks in spontaneous human brain activity. Elife 2014
[2] D. Vidaurre. Spectrally resolved fast transient brain states in electrophysiological data. NeuroImage 2015
[3] H. Robbins. A stochastic approximation method. The Annals of Mathematical Statistics 1951
[4] M. Hoffman. Stochastic variational inference. Journal of Machine Learning Research 2013

The ATG (Alpha-Theta-Gamma) switch: A unified framework for thalamo-cortical processing

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Sensory, motor and cognitive functions are associated with oscillatory changes within task-relevant cortical regions, as well as alterations in functional and effective connectivity between those regions associated with neuronal synchronization. Magnetoencephalography (MEG) has shown that brain dynamics within and between regions often differ markedly across frequencies, and that brain rhythms often interact across widely separated frequency ranges. It has further been reported that cross-frequency interactions may play an important role in local processing within thalamus and neocortex, as well as information transfer between subcortical and cortico-cortical brain regions. Strong commonalities in rhythmic network properties have been observed across recording techniques and task demands, but strong neuroscientific theories to situate such observations within a unified framework with direct relevance to explain neuropathologies remain scarce. A comprehensive review into the animal and human literature indicates a further thinking beyond synchrony and connectivity and the readiness for more hypothesis-driven research and modeling toward unified principles of thalamo-cortical processing. We further introduced such a possible framework: \"The ATG switch\" *(Doesburg et al., Curr. Trends Neurol. 2015)*. We probed this neurophysiological framework to explain how coordinated cross-frequency and interregional oscillatory cortical dynamics may underlie typical and atypical brain activation, and the formation of distributed functional ensembles supporting cortical networks underpinning sensation and cognition. We also discussed evidence that alpha-theta-gamma dynamics emerging from thalamocortical interactions may be implicated and disrupted in numerous neurological and neuropsychiatric conditions. We present a conceptual overview of this framework as a novel plausible mechanism to integrating local and large-scale thalamocortical brain networks and its alterations in clinical pathologies. *- Support: BC LEEF, CFI, NSERC, CIHR -*

Functional connectivity estimation from MEG data with a combination of a Kalman filter and an EM algorithm

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Traditional dynamic causal modeling (DCM) is a biophysically-motivated model-driven approach that allows for the estimation of effective connectivity. Recently, attempts have been made to extend this deterministic DCM framework into a fully stochastic one. Here, we present a new approach for the estimation of neural sources and their connectivity parameters using an expectation–maximization (EM) algorithm in conjunction with a Kalman filter and smoother, and apply it to simulated magnetoencephalographic (MEG) signals. The approach is based on a Bayesian state-space model that is similar to DCM but additionally involves a stochastic formulation at the level of hidden states and is based on the use of Bayesian filtering and smoothing approaches instead of variational Bayes.

We simulated MEG signals using neural mass models in a realistically-shaped head model. We tested two scenarios: 1) A bivariate model representing interaction between two neural sources and 2) a multivariate model representing three interacting sources. The interactions and the dynamics of the underlying process was modeled as a vector autoregressive (VAR) process together with an additive Gaussian noise. The observation process was modeled by deriving a lead-field matrix using a realistically-shaped three-layer BEM model and adding Gaussian noise for a signal-to-noise ratio (SNR) of 2. The Kalman filter and EM algorithm were applied in an iterative fashion to estimate the source time courses, connectivity parameters, and process noise covariance matrix.

Our results show that the EM algorithm can reliably estimate the connectivity parameters as well as the amplitudes of the time-varying source activities, even at relatively high levels of observational noise. In conclusion, we demonstrated the applicability of a Kalman filter and smoother with the EM algorithm to estimate effective brain connectivity using a stochastic formulation of DCM.

Estimating Cross Frequency Coupling in Fast Transient Brain States

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Interdependencies between different frequency bands or cross-frequency coupling (CFC) have been observed in both the human and rodent literature and is suggested to coordinate dynamics across different spatial or temporal scales (Canolty et al 2010). Traditional methods for CFC analysis depend on having long datasets to ensure sufficient signal-to-noise in the estimation; typically requiring several seconds of data to ensure a robust estimation. However, CFC may switch on and off at faster, even sub-second, time-scales. Here, we show that phase-amplitude coupling (PAC), a form of CFC, can be estimated with high temporal resolution, by first describing the fast dynamics in a continuous dataset using a Hidden Markov Model with Multivariate Autoregressive observations (HMM-MAR; Vidaurre et al 2016). The HMM-MAR automatically identifies quasi-stationary periods (i.e. brain states) characterised by distinct patterns of power spectra and/or cross-spectral interactions. PAC can then be estimated separately for each brain state to give state-wise modulation indices. Using simulations, the HMM-MAR is shown to be able to accurately reconstruct two modes of CFC within a dataset with a high temporal precision, whilst at the same time retaining precision in the frequency characteristics of the coupling. The method was then applied to 10 minutes of real LFP data recorded from mouse CA1, which is known to contain CFC between the theta and gamma bands. The HMM-MAR successfully identified rapidly transitioning states characterised by both power differences within the theta band, and different profiles of CFC. In summary, the HMM-MAR approach uses the data efficiently and does not require assumptions about window length or specific event related time-locking. By pooling data across disjoint time-windows prior to estimating CFC we retain not only sufficient statistical power to make robust estimates within a state, but also sensitivity to rapid changes in states over time.

Oscillatory modes from MVAR models of brain networks.

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Oscillatory activity within and between nodes in distributed brain networks are thought to provide a crucial link between neuronal populations and cognitive, behavioural and psychiatric states. The activity within a single brain region may exhibit multiple oscillations each with considerable dynamics; moreover each of these may be associated with a specific, but separate, brain network. The power distribution and relative phase relations of an oscillations across an n-dimensional brain network can be explored through identification of the system\'s Normal Modes. A Normal Mode is an aspect of the behaviour of the brain network in which all the nodes oscillate at a given frequency and with a specific phase relation. Such modes can be readily identified from an eigendecomposition of the parameters of a MultiVariate AutoRegressive (MVAR) model and provides a powerful frequency-resolved description of a system. Each mode is associated with a given resonant frequency, dampening time and magnitude (Neumaier and Schneider, 2001). Here we further show that the oscillatory mode is associated with a relative magnitude and relative phase in each node, allowing the reconstruction of the spatial distribution of the oscillation across a network and their phase relations. The properties of the modal representation of brain networks are illustrated with simulations and validated with traditional MVAR connectivity estimators (DTF/PDC). The modal decomposition is then applied to source space resting state MEG data. Source activity estimates within anatomical parcels across the brain are described with an MVAR model which is then decomposed into its constituent modes. Each oscillatory mode is associated with a frequency-specific brain network in which the relative phases between nodes describes the directionality of the connection. In summary, the modal decomposition of MVAR models of brain networks is a powerful tool for data-driven exploration of oscillatory brain networks.

Predicting haemodynamic networks usingelectrophysiology: the role of non-linear and cross-frequency interactions

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Understanding the electrophysiological basisof resting state networks (RSNs) in the human brain is a critical step towardselucidating how inter-areal connectivity supports healthy brain function. Inrecent years, the relationship between RSNs (typically measured usinghaemodynamic signals) and electrophysiology has been explored using functionalMagnetic Resonance Imaging (fMRI) and magnetoencephalography (MEG). Significantprogress has been made, with similar spatial structure observable in bothmodalities. However, there is a pressing need to understand this relationshipbeyond simple visual similarity of RSN patterns. Here, we introduce amathematical model to predict fMRI-based RSNs using MEG. Our unique model,based upon a multivariate Taylor series, incorporates both phase and amplitudebased MEG connectivity metrics, as well as linear and non-linear interactions withinand between neural oscillations measured in multiple frequency bands. We showthat including non-linear interactions, multiple frequency bands andcross-frequency terms significantly improves fMRI network prediction. Thisshows that fMRI connectivity is not only the result of directelectrophysiological connections, but is also driven by the overlap ofconnectivity profiles between separate regions. Our results indicate that acomplete understanding of the electrophysiological basis of RSNs goes beyondsimple frequency-specific analysis, and further exploration of non-linear andcross-frequency interactions will shed new light on distributed networkconnectivity, and its perturbation in pathology.

Integrating cross-frequency andwithin band functional networks in resting-state MEG: a multi-layer networkapproach

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Neuronal oscillations exist across a broad frequency spectrum, and are thought to provide a mechanism of interaction between spatially separated brain regions. Since ongoing mental activity necessitates the simultaneous formation of multiple networks, it seems likely that the brain employs interactions within multiple frequency bands, as well as cross-frequency interactions, to support such networks.Here, we propose a multi-layer network framework that allows a pan-spectral picture of network interactions. Specifically, our multi-layer network consists of multiple layers (frequency-band specific networks) that are allowed to influence each other via inter-layer (cross-frequency) couplings. Using this model for MEG resting-state source-space data and envelope correlations as connectivity metric, we demonstrate strong dependency between layers and inter-layer coupling, indicating that networks obtained in different frequency bands do not act as independent entities, as is often assumed. More specifically, our results suggest that MEG frequency band specific networks are characterized by a common mode of connection patterns seen across all layers,superimposed by layer specific connectivity. Inter-layer coupling is stronger associated with this common mode than with layer specific connectivity.Moreover, using a biophysical model of neuronal network activity, we demonstrate that there are two regimes of multi-layer network behaviour; one in which different layers are independent and a second in which they operate as a single entity. Results suggest that the healthy human brain operates at the transition point between these regimes, allowing the brain to switch between two regimes and allowing for integration and segregation between layers.Overall, our observations show that a complete picture of global brain network connectivity requires integration of connectivity patterns across the full frequency spectrum.

Source connectivity analysis using multivariate autoregressive models of MEG signals

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Previously, a method for connectivity analysis in source space has been introduced that allows for the projection of multivariate autoregressive (MVAR) model coefficients from MEG sensor space to source space. The technique uses the lead fields and a lead field based inverse operator (weight matrix). Although this existing method is able to estimate causality relationship in source space, however the method shows deficits if the source positions are not *a priori* known. This might be due to the assumption that the product of the weight and lead field matrices is an identity matrix and the crosstalk between sources. In the present study, we improved the existing method in order to mitigate the above mentioned drawbacks and systematically examined the new proposed method using simulations and the analysis of a real MEG data set. For the estimation of the MVAR model coefficients in source space, we used an inverse of the weight matrix instead of the lead field matrix to reduce errors caused by the assumption that multiplying weight and lead field matrices results in an identify matrix, and we applied a nulling beamformer for crosstalk suppression between sources. As a case study, we applied our method to the interictal MEG recordings from one patient. Although two focal cortical dysplasias (FCDs) found in MRI are located in left fronto-central and right frontal regions, interictal spikes were mainly found close to the right frontal FCD only. By applying the proposed method, we could identify an information flow from left to right regions nearby the FCDs. These results suggest that the improved methodology of projecting MVAR model coefficients in MEG sensor space onto source space has considerable potential as a non-invasive approach for connectivity analysis in the brain without *a priori* knowledge about source locations.

Combining Intra and Inter-Frequency Dominant Coupling Modes into a single Dynamic Functional Connectivity Graph: Dynome, Dyconnectomics and Oscillopathies

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The brain must dynamically integrate, coordinate, and respond to internal andexternal stimuli across multiple time scales. The human connectome will provide a detailed mapping of the brain's connectivity, with fundamental insights for health and disease. However, further understanding of brain function and dysfunction will require an integrated framework that links brain connectivity with brain dynamics, as well as how connectivity patterns are linked to cognition, biology and genomics. Understanding the connectome presents many technical and theoretical challenges, which will deliver insights into brain function and dysfunction. It is already clear what some of the limitations of connectomics will be. Furthermore, the connectome can be studied at a very wide range of spatial scales, making any endpoint seem very far in the future. EEG/MEG imaging methods can give us a more detailed picture of how brain functions with high temporal and acceptable spatial resolution. Moreover, for a better understandingof how brain fluctuates using MEG/EEG, we should build a single dynamic graph that incorporates dominant intra and inter-frequency coupling modes. Apart from the weight/strength of the connection between two brain areas, it is informative to study the spatio-temporal distribution of dominant coupling modes by taking into account also the distinct role of amplitude and phase. The temporal changes of amplitude comprises low and persistent memory processes while phase synchronization is less temporally structured indicating a more fast and flexible coding of information.I will present the proposed approach in MEG resting-state databases using guidelines and directions of analysis through so called connectomic signal processing.

Connectivity Priors Informed by Functional Neuroanatomy in DCM for Evoked Responses in EEG and MEG: from simulations to an Auditory Mismatch Negativity (MMN) case study in MEG

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Dynamic Causal Modeling (DCM) explains differences in evoked responses between conditions by changes of effective connectivity between brain regions. It uses models with prior distributions of connectivity parameters and a Bayesian inversion scheme to estimate the parameters posterior distributions according to recorded data.
In this study, we propose to incorporate in DCM priors neuroanatomical knowledge derived from a new probabilistic atlas of cortico-cortical connectivity estimated from direct cortical stimulations performed in implanted epileptic patients (F-TRACT, David et al. 2013). Our goal is to demonstrate that DCMs with realistic atlas-based informed priors allow more accurate posterior estimates than DCMs with uninformed (default) priors.

First, MEG data were simulated using a 3-sources *true* generative model. This *true* model was compared with *false* models, created by adding a connection absent in the *true* model. This new connection was informed by varying mean and variance priors (from fully-informed to uninformed) to reflect the prior knowledge and the degree of confidence about the connection. Bayesian Model Selection (BMS) showed that the *true* model was the best and *false* models with fully-informed priors performed better than models with uninformed priors. BMS was evaluated for different network configurations, noise levels, and datasets.
Second, we processed real MEG data recorded during an oddball auditory task. Source localisation suggested a MMN network composed of A1, STG and IFG. Mapping the probability given by the atlas to the prior mean for each connection, we were able to build a fully-informed model and to compare it with an uninformed model.

Simulations and preliminary experimental results suggest that the model inversion is improved by neuroanatomically informed prior connectivity weights. The use of the F-TRACT atlas for informing the DCM for a single subject now needs to be extended to the context of group study.

A EEG Study on Anesthetic Effects

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In anesthesiology, many electroencephalogram (EEG) signal processing methods for monitoring depth of anesthesia (DOA) were proposed. Bispectral index (BIS) is the most common technology used to monitor DOA. However, BIS has been questioned because BIS algorithm does not rely on physiological phenomena of brain under anesthesia. Meanwhile, many reports exist about connectivity changes under anesthesia. In this study, we tried to find anesthetic effects on EEG connectivity which may provide an intuition for monitoring DOA. EEG data of healthy subjects (n = 15, male/female = 7/8, age 24-70 years) were acquired from 4 frontal (Fp1, Fp2, F3 and F4) and 2 parietal (P3 and P4) channels. Resting state EEG data were acquired as a baseline data (5 minutes). After baseline acquisition, an anesthetic (Propofol) was administrated during an hour (12mg/kg) and EEG data were collected during administration. EEG data acquisition continued to 60 minute after the end of administration. We used 4 connectivity methods such as correlation (COR), coherence (COH), imaginary part of coherence (iCOH), and phase-locking value (PLV). For three states of consciousness (Baseline (resting), Loss of Consciousness (LOC), and Recovery), these four connectivity measures between the frontal and parietal areas were estimated. The fronto-parietal connectivity during an unconsciousness state significantly ($p< 0.01$) decreased compare to baseline ("COR" baseline/LOC = 0.64/0.5, "COH" baseline/LOC = 0.41/0.24, "iCOH" baseline/LOC = 0.028/0.007, "PLV" baseline/LOC = 0.57/0.44). Connectivity difference between baseline and recovery state was also significant for all measures, while PLV difference between unconscious and recovery states was not significant ($p = 0.074$). Using four EEG connectivity measures, the disruption of cortical connectivity due to the anesthesia may be detectable. For further understanding about consciousness under anesthesia, directional connectivity analysis on cortical networks is under study.
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Decoding for information in oscillatory amplitude, phase and synchrony

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Investigation of many cognitive and clinical phenomena is based on the analysis of ongoing neuronal oscillations. Both external events and endogenous factors modulate the dynamics of oscillatory neuronal sources, in particular their amplitude and phase. More recently, there has been increased interest to neuronal synchronization. Inspection of oscillations relies on analysis of individual channels or sources, resulting in maps of statistically significant effects. Machine learning methods, however, can describe the magnitude of the effect with a single number. These "decoding" methods track the information in multivariate neuronal signals with respect to given parameters, like stimulus classes. Decoding in time-frequency plane results in a single time-frequency representation of the information content. Decoding of amplitude is straightforward, and phase can be decoded after compensating for circularity, for example by taking the sine. In principle, synchrony can be analysed between all possible source pairs. In practice this may lead to erroneous results. First, amplitude affects synchrony estimates in a complex manner, which prevents reliable estimation of synchrony in the presence of simultaneous amplitude effects. Second, independent but aligned phase effects cannot be separated from true synchronization. For example, a stimulus event may re-organize the phase in large cortical regions, which will erroneously appear as phase synchrony. Third, the number of pairwise correlations can be enormous, resulting in explosion of multiple comparisons. We use simulated and real MEG data to investigate if these problems can be circumvented by decoding for synchrony, and comparing the information content to that found for the amplitude and the phase. Decoding methods can be used to robustly inquire the information in neuronal oscillations and synchronization.

Changes in MEG scale free dynamics in patients with temporal lobe epilepsy

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Most biological signals can be characterized by their scale-free dynamics (SFD), meaning that they consist of arrhythmic signals with no preferred frequency, exhibiting frequency spectrum that follows power laws in $1/f^{2H-1}$. For a multifractal model, H exponent varies between 0.5 and 1, and characterizes long-range temporal dependencies. Lower values were reported during tasks, thus reducing long-range dependencies and suggesting increased efficiency for quickly adapting to changes [1]. In certain diseases such as epilepsy, increased H-values were found in effected brain regions [1]. Here, we investigated the differences in SFD between patients with temporal lobe epilepsy and age/gender matched healthy controls using the resting state (RS) data measured with MEG. We used coherent Maximum Entropy on the Mean (cMEM) method [2] to reconstruct broad range MEG RS fluctuations on the cortical surface. The Wavelet Leader formalism [3] was then applied to calculate the H-values. We selected epochs around interictal epileptiform discharges (IEDs) as well as epochs with no distinguishable IED (baseline). For patients we selected two regions of interest (ROIs) on the cortical surface: the IEDs generator and its homologous contralateral area. Using epochs of 4s, we demonstrated that applying wavelet formalism on cMEM source reconstruction was valid and provided relevant estimations of H (>0.5). We found: i) higher H-values at ipsilateral regions; ii) smaller mean global (whole brain) H for IED epochs; iii) increased mean global H in epilepsy patients compared to controls at the baseline, suggesting increased long range dependencies and lower efficiency. Our preliminary results suggest that the SFD might be a promising technique to characterize RS fluctuations of MEG data for patients with epilepsy.

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1. He BJ, Trends Cogn Sci 2014;18:480-487
2. Chowdhury R et al., PLoS One 2013;8(2):e55969
3. Wendt H et al., IEEE Signal Proc. Mag 2007; 24:38–48

Power and Shift Invariant Imaging of Coherent Sources from MEG data (PSIICoS)

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Connectivity analysis in the sensor space is complicated by the volume conduction (VC) phenomenon. To alleviate this effect and to perform the analysis in the source-space the existing methods primarily rely on the two-step procedure in which we first estimate the source space activity signals and then apply a synchrony measure to these "unmixed" signals. Due to the fundamental physical properties of the electromagnetic inverse problem such unmixing does not completely banish the volume conduction effect and the source signals are still mixtures of activations of various sources. These VC effects especially limit our ability to image the interactions with small phase lag. We propose to render the task of estimating network topology and synchrony temporal profiles as a source estimation problem but in the product space of interacting dipole topographies. Operating in this expanded space we isolate the subspace of the vectorized cross-spectrum spanned by the VC effect and suggest a simple projection procedure to significantly reduce it. We then suggest a systematic framework for a solving the problem of finding the coherent sources in a single step. Using realistic simulations we show that the proposed method significantly outperforms the techniques based solely on the use of imaginary part of coherence and yields equal sensitivity to the entire range of phase lags of interacting source activations. Application of the method to MEG dataset recorded from 10 subjects involved in passive listening the hand movement related words shows reproducible across subjects cross-lateral network in the beta band connecting the hand representation zones of the sensory-motor cortices. With PSIICoS we also observe the increased reproducibility of the detected networks across subjects.

A novel coherence-based method to robustly identify functional brain connectivity: Envelope of imaginary coherence operator

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Background: Functional connectivity (FC) at sensor level of EEG/MEG signals provides information regarding biomarkers towards understanding cognition and brain disorders. The main drawbacks of this approach are (1) the volume conduction problem (VCP) and (2) the mixing of undetermined (unknown location and number) underlying sources. FC methods based on the imaginary part of the coherence (iCOH) can solve the VCP but neglecting the real part leads to negligible FC when the phase difference of the interacting processes is near k*\\pi . We propose the envelope of the imaginary coherence (EIC) to alleviate this situation by using the frequency content to approximate the coherence estimate of supposedly active underlying sources.
Methods: We compared EIC with other measures like iCOH, phase lag index (PLI), and weighted PLI (wPLI) with two sources and two sensors with and without interaction between sources generated by autoregressive and neural mass models. Then we tested them in a semi-realistic scenario using SPM template cortical surface and Fieldtrip estimated lead-field wherein 3 and 5 interconnected region seeds were simulated, which in turn generated synthetic MEG for 102 standard Elekta-Neuromag channels. These signals were used to compute the FC maps. Phase lock statistics, similar to a surrogate procedure [1], was developed and implemented to test for significance of these indices.
Results and conclusions: FC maps obtained by EIC revealed a higher rate of true connections when compared to iCOH-based measures. EIC was outstandingly superior if fewer regions were active. Furthermore, we show that EIC FC maps can more robustly identify the dynamic FC in a publically available MEG data obtained during face perception tasks [2].
References:
[1] Lachaux J. et.al.(1999) Measuring phase synchrony in brain signals. Hum. Brain Mapp., 8, 194–208.
[2] Wakeman D. & Henson R. A multi-subject, multi-modal human neuroimaging dataset. Sci. Data. doi: 10.1038/sdata.2015.1 (2015).

The sequence of functional brain activity can be inferred by response variability

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Without specifying signatures in the waveform, using *apriori* models, or assuming stationary dynamics, here we propose that the sequence of functional brain activity can be inferred by response variability. Specifically, we tested this hypothesis using a visuomotor task, where sequential visual -->motor cortices activity was expected.

Lateralized checkerboard reversals were presented to subjects (n=8), who were instructed to press the ipsilateral button upon perceiving the stimuli. Whole-head MEG signals were recorded. Minimum-norm estimates were used to model neuronal current distributions. Regions-of-interests (ROI's) were delineated from group dynamic statistical parametric maps (dSPM's). Template dSPM waveforms were extracted from lateralized visual and sensorimotor cortices. The response variability was estimated by calculating the standard deviation of the latency that maximizing the cross-correlation between template dSPM waveforms and bootstrap dSPM waveforms. Spectral analysis was also performed by calculating the Temporal Spectral Evolution of the waveform at each ROI between 4 Hz and 80 Hz.

We found that the variability at the visual cortices were much smaller than that at the sensorimotor cortices(2.3/0.8 ms for left/right visual cortices; 53.2/40.2 ms for left/right sensorimotor cortices). Spectral analysis revealed that the response variability difference between visual and sensorimotor cortices was larger between 15 Hz and 35 Hz.

Our experimental design and results validated that the brain area activated later in a sequence should have larger regional response variability. Larger difference in the regional response variability at the beta band matched to previous studies showing frequency-specific responses during sensorimotor processing. Careful control on the signal-to-noise ratios of regional waveforms is critical to avoid bias due to fluctuations. Further validation is needed to apply this method in revealing unknown functional hierarchy.

Detecting interhemispheric transfer using MEG

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FMRI studies have utilized stimuli that elicit interhemispheric transfer in order to image activity across the corpus callosum. The results suggest that it may be possible to image white matter function. We aim to examine the feasibility in eliciting the same response using MEG. Fifteen right-handed volunteer participants were imaged using MEG while performing an interhemispheric transfer task. The participants were presented with word and face stimuli in either the left or right visual hemifield field. The participants were then asked to classify the stimulus as word, pseudo-word, face, or scrambled face by pressing buttons in the left and right hand. Motor interhemispheric transfer was further manipulated by changing the response hand. The stimuli were presented in blocks with periods of rest in between. The data were collected using a 151-channel CTF MEG system at 1200 Hz with a 300 Hz anti-aliasing filter. Continuous head monitoring was utilized in order to assess participant movement. Using SPM8, the participants' T1 weighted MR images were co-registered with the individual's digitized head shape and segmented. The data were filtered between 1 and 300 Hz. An LCMV beamformer was used to compute neuromagnetic activity over a voxelized brain volume. As an initial exploration of the data, a contrast was constructed between active and rest blocks using a general linear model approach. The resulting contrasts showed distributed cortical activity consistent with word, face and motor tasks. Additionally, potential activity across the corpus callosum was observed at the individual level, although the location along the tract varied in some cases between participants. These preliminary results suggest that it may be possible to use MEG to image function across the corpus callosum. However, further investigation is needed to eliminate signal leakage and other confounds as well as account for possible differences in source model before definitive results can be reported.

A statistical framework for neuroimaging data analysis based on mutual information estimated via a Gaussian copula

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Information theory provides a principled and unified statistical framework for neuroimaging data analysis. A major factor hindering wider adoption of this framework is the difficulty of estimating information theoretic quantities in practice. We present a novel estimation technique that combines the statistical theory of copulas with the closed form solution for the entropy of Gaussian variables. This results in a general, computationally efficient, flexible, and robust multivariate statistical framework that provides effect sizes on a common meaningful scale, allows for unified treatment of discrete, continuous, uni- and multi-dimensional variables, and enables direct comparisons of representations from behavioral and brain responses across any recording modality. We validate the use of this estimate as a statistical test within a neuroimaging context, considering both discrete stimulus classes and continuous stimulus features. We also present examples of novel analyses facilitated by these developments, including application of multivariate analyses to MEG planar magnetic field gradients, and pairwise temporal interactions in evoked EEG responses. We show the benefit of considering the instantaneous temporal derivative together with the raw values of M/EEG signals as a multivariate response, how we can separately quantify modulations of amplitude and direction for vector quantities, and how we can measure the emergence of novel information over time in evoked responses. Open-source Matlab and Python code implementing the new methods is available at: https://github.com/robince/gcmi

Auditory Driven Cross-modal Phase Reset of Visual Cortical Oscillations

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Physiological rhythms in cortical oscillations are implicated in the gating of information flow. Oscillations are linked to variety of cognitive processes such as visual sensory perception which cycles at the characteristic frequencies of brain rhythms. The inherent fluctuations in the phase of neural oscillations are thought to be linked to the periodicities observed in sensory perception. Previous research has shown that the presentation of a brief sensory event in one modality can affect activity within hierarchically organised early sensory cortical regions in another modality. This modulation by cross-modal input through resetting the phase of ongoing intrinsic oscillations has been demonstrated in animal[1] and human research[2]. Here we investigated this model and evaluate whether auditory induced phase resetting of primary sensory visual oscillations would impact perceptual performance. 20 Participants performed an apparent motion discrimination task of a dynamic dot pattern presented at one of 18 delays (SOAs) following a brief tone. If the target stimulus was presented at the optimal phase of the auditory-induced phase reset of visual cortical oscillations, then this should have specific behavioural consequences in sensory perception. Using magnetoencephalography (MEG), the underlying oscillatory dynamics were investigated. Results clearly show a significant cyclic pattern in behavioural d-prime accuracy performance and an oscillatory modulation in the ERF component in alpha frequency in the visual cortex. These findings are in-line with occipital alpha-oscillations underlying the periodicity in visual perception. This offers support that visual ERF component may serve as a proxy for cortical excitability that is modulated by tone-onset. Cross-modal phase resetting modulates intrinsic brain-rhythms and subsequently influences sensory perception.

1. Lakatos, et al., (2009). Neuron.
2. Romei, et al. (2012). Current Biology.

MEG and EEG Dipole Clusters from Extended Cortical Sources

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In a simulation study we compared the extent of Equivalent Current Dipole (ECD) clusters of MEG magnetometers, planar gradiometers, an EEG 10/20 montage, and the combined modalities for extended cortical sources at different Signal-to-Noise-Ratios (SNRs). A realistically shaped Boundary Element Method (BEM) head model with three compartments (6685 nodes overall: skin 1968, outer skull 1771, inner skull 2946 nodes) was used and sources on the folded cortical surface (mean node distance 2.8mm) with Gaussian intensity profiles were investigated.

First, relative sensitivities of the different MEG- and EEG-configurations normalized to point-like sources and averaged over all cortical positions were computed as a function of the source diameter (0 to 60mm FWHM). With increasing patch diameter, cancellation of tangentially oriented sources on opposing sulcal walls leads to a more and more radial orientation of the overall activity and decreasing sensitivity. Due to the different sensitivities of MEG for radial and tangential current components, as compared to the more homogeneous sensitivity distribution of EEG, increasing source sizes have a larger effect on MEG than on EEG. Areas with dominating radial orientations are better visible by EEG as compared to MEG, as expected.

Sources in the left temporal lobe area were used and field/potential maps for different source extensions and SNRs were computed. Then, single equivalent dipoles were fitted to the simulated extended sources and dipole-positions and -strengths, field deviations and dipole cluster extends were analyzed. Fitting single equivalent dipoles to extended cortical activity can result in misleading dipole orientations and positions due to cancellation (MEG and EEG) and invisible radial components (MEG). The extent of the dipole clusters mainly depends on the SNR and not on the size of the extended sources.

Source Reconstruction from Invasive Stereo-EEG Recordings

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There is increasing interest in analyzing data from invasive Stereo-EEG (sEEG) recordings in order to confirm findings from non-invasive MEG or surface EEG examinations before surgery. The depth electrode positions can be derived from Computed Tomography (CT) image data co-registered to Magnetic Resonance (MR) images, that are required for brain structure visualization and head modelling. We established a robust co-registration by three-dimensional (3D) mutual information from both image data modalities.

The measured potentials can be visualized as color-coded symbols in the anatomical MR images, which provide the reference co-ordinate system. The cortical surface is segmented from the T1-weighted MR images and a head model can be derived from the inside of the skull. Since the electric potentials are measured inside the head, Boundary Element Method (BEM) head models, that are the gold standard in surface EEG analyses and provide potentials on the outer surface only, cannot be used.

The skull exhibits a relatively small conductivity as compared to the brain, thus single shell models of the brain compartment seem to be sufficient. Infinite homogeneous and single shell spherical models fitted to the inside of the skull are simplifying analytical approximations. In order to better model the volume conductor properties, Finite Element Method (FEM) models can be used.

Due to the relatively sparse spatial sampling by the depth electrodes and their pronounced near field sensitivity, single equivalent dipole fits are often trapped in local minima. Thus, 3D-deviation scans or Current Density Reconstructions (CDR) appear to be more adequate source modelling approaches. We performed simulations for several depth electrode configurations and all three head model types to examine sensitivity distributions and localization differences.

Kalman Filter Based Dynamic Source Reconstruction for EEG and MEG data

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Identification neural activities using noninvasive measurements of magneto-electroencephalographic(M/EEG) signals is a powerful tool to study time-varying neuronal processes due to its ability to explore directly potential sources with better temporal resolution other than available imaging approaches. The M/EEG source localization is fundamentally an ill-posed inverse solution due to high sensitivity to noisy data and erroneous mathematical computations. Recently,researches toward solving the ill-posed inverse problem fall into two primary categories: non-parametric and parametric. Among the various proposed methods,a crucial concern toward real-time implementation is the estimate accuracy of data covariance matrix when only a short data at a time window is captured. Furthermore,existing methods yet consider time-varying characteristics of the brain which is believed to contribute to computational accuracy.

In this paper, we propose a novel Kalman filter based algorithm for M/EEG reconstructive sources that comes up with a solution to existing source reconstruction limitations; dynamic aspects and covariance matrix accurate concern. The main contribution is to develop Kalman filter based source constructive algorithm that is beneficial for real-time applications where the amount of data at a time window is not sufficient and where the dynamic measurement is noisy. Also, the simulation data with realistic forward model and realistic M/EEG data are designed to validate the proposed method. The obtained results show feasibility of Kalman filter based source reconstruction on online neuronal implementation over existing methods as signal-to-noise ratios are improved in noisy and lack-of-data environments. However, the observed resultants also indicate that the Kalman filter based source construction cannot detect the correlated sources.

Thermal magnetic noise spectra of nanoparticle ensembles

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In recent years, magnetic nanoparticles have gained a lot of interest due to their appealing properties for biomedical applications[1]. For instance, when exposed to an alternating magnetic field, they generate heat which can be used in the destruction of cancer cells. Furthermore, when equipped with a suitable coating, they can be ideal drug carriers or disease detectors. Finally, the combination of the small sizes enabling virtually full body detection and the large magnetic moment, enabling noninvasive detection, makes them excellent candidates for use in imaging applications. However, for these applications to work reliably, the dynamic behavior of the nanoparticles should be fully understood.

Typically, the dynamic behavior of magnetic nanoparticles is investigated by measuring their response to externally applied magnetic fields. For example, in magnetorelaxometry[2], the relaxation of the magnetic moment of the nanoparticle sample after the magnetic field is switched off, is investigated.

A new approach is to measure the noise signal resulting from the thermal switching of the nanoparticles in the absence of any external excitation. With the help of SQUIDs, an increased noise spectrum originating from the nanoparticles has been observed[3], but the shape of the spectrum and its relation to the properties of the nanoparticle ensemble remained unexplored.

In this contribution[4], we present the measured noise spectrum of several magnetic nanoparticle samples. We present a model to estimate the size distributions of the particles from these spectra and compare them to those obtained from magnetorelaxometry data of the same samples.

[1] Q. Pankhurst, et. al., J. Phys. D: Appl. Phys. 42, 224001 (2009).
[2] F. Wiekhorst, et. al., Pharm. Res. 29, 1189 (2012).
[3] T. Cheung, et. al., in IFMBE Proceedings of the 17th International Conference on Biomagnetism –Biomag 2010, Vol. 28, pp. 443–446.
[4] J. Leliaert, et. al., Appl. Phys. Lett., 107, 222401 (2015).

Source modelling of ECoG data: stability analysis and spatial filtering

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Background. Electrocorticography (ECoG) measures the distribution of electrical potentials by means of electrodes grids implanted close to the cortical surface.

A full interpretation of ECoG data requires solving the ill-posed inverse problem of reconstructing the spatio-temporal distribution of neural currents responsible for the recorded signals. Only in the last few years some methods have been proposed to solve this inverse problem [1].

Methods. This study [2] addresses the ECoG source modelling using a beamformer method. We computed the lead-field matrix which maps the neural currents onto the sensors space by a novel routine provided by the OpenMEEG framework [3]. The ECoG source-modeling problem requires to invert this matrix by means of a regularization method which reduces its intrinsic numerical instability: we performed an analysis of the condition number of the lead-field matrix for different configurations of the electrodes grid. Finally, we provided quantitative results for source modeling using a Linear Constraint Minimum Variance (LCMV) beamformer [4]. The validation of the effectiveness of beamforming in ECoG was performed both with synthetic data and with experimental data recorded during a rapid visual categorization task.

Results. For all considered grids the condition number indicates that the ECoG inverse problem is mildly ill-conditioned. For realistic SNR we found a good performance of the LCMV algorithm for both localization and waveforms reconstruction.
The flow of information reconstructed by analyzing real data seems consistent with both invasive monkey electrophysiology studies and non-invasive (MEG and fMRI) human studies.

References:
1. Dumpelmann et al., (2012), Human brain mapping, 33(5), 1172-1188
2. Pascarella et al. (2016), Journal of Neuroscience Methods, 263(5), 134-144
3. Kybic et al., (2005), Medical Imaging, IEEE Transactions on, 24(1), 12-28
4. Van Veen et al., (1997), Biomedical Engineering, IEEE Transactions on, 44(9), 867-880

Multi-resolution champagne beamformer

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The sparse Bayesian source imaging (Champagne) algorithm is effective for neuromagnetic imaging [1,2], because it is robust to various types of noise and interference, and to multiple correlated sources [2]. However, one serious problem of the algorithm is that it is computationally expensive because of its iterative nature. In this paper, we propose a novel algorithm, called multi-resolution champagne beamformer. In the proposed algorithm, the first step estimates the model data covariance by using the sparse Bayesian scheme, and the second step implements the adaptive beamformer source imaging using the data covariance estimated in the first step. The key point of the algorithm is to exploit our empirical findings that the quality of the estimated data covariance does not so much depend on the voxel size. Therefore, we can significantly shorten the computational time by using a low-resolution voxel grid in the first step but still obtain the high-quality source images by using a high-resolution grid in the second step. Computer simulation and application to real biomagnetic data verify the performance of the algorithm. Unlike the conventional adaptive beamformer, which uses a sample data covariance matrix, the proposed champagne beamformer is shown to be applicable to a case where correlated sources exist and to a case where only a short time window with a small number of time samples is available. References: [1] Wipf DP et al. , Neuroimage.2010; 49(1): 641-55. [2] Sekihara S. and NagarajanSS, Electromagnetic brain imaging: a Bayesian perspective, Springer, 2015.

Signal separation method for an accurate measurement of thalamic activity in Magnetoencephalography

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In magnetoencephalography (MEG), an estimation of weak thalamic source activity became possible in virtue of recent advances in MEG sensors, signal processing, forward modelling and inverse solutions. However, there is still few studies investigating thalamus using MEG because strong cortical sources interfere in estimated thalamic source and make results hard to be interpreted. In our study, we developed a method that separates weak thalamic signals from strong cortical signals at sensor level so the inverse solver (in our study, beamformer) could estimate more reliable thalamic source activities. We firstly analysed the amount of signal leakage from strong cortical sources to weak thalamic source by calculating analytical form of the beamformer filters and its outputs. We found that, in practical setting, when an amplitude of a cortical source is a thousand times larger than that of a thalamic source, the leaked signal power becomes an order of magnitude of the thalamic source power. To suppress these interferences, we developed a signal separation method coined as spatio-temporal signal space projection (tSSP). tSSP method is based on the spatial separation between cortical signal space and thalamic signal space, then removes common temporal components that is totally come from cortical signal space since there is a conduction delay between cortex and thalamus. To test the performance and reliability of tSSP method, we conducted resting state eyes opened/closed experiment that shows different amount of thalamic modulation of occipital alpha wave. We found that only with tSSP method case shows significant activations at both V1 and posterior thalamus. Moreover, by analysing power spectral density of reconstructed thalamic signal, we found that at eyes opened condition, there is no activations in alpha frequency band, which could implyies that eyes opened resting state occipital alpha wave is mainly generated from cortico-cortical interactions.

Iterative two-stage approach to estimate sources and their interactions

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Magnetoencephalography is a functional imaging modality that is used to measure brain activity. Estimating brain activations from MEG is possible by assuming some priors on the sources. In this work, we use a spatiotemporal prior. The source dynamics is represented by a Multivariate Autoregressive (MAR) model whose matrix elements are constrained by the anatomical connectivity obtained from diffusion MRI information. For simplicity, we assume a first order MAR model i.e. S(t) = AS(t-1), but it is possible to include further higher order terms. The model assumes that the MAR model, matrix A, is constant in a given time window. The MAR entries and sources activations are estimated iteratively. Previously, two-stage approaches have been used to estimate the source interactions. They first reconstruct sources and then compute the MAR model for the localized sources. They showed good results when working in high signal-to-noise ratio (SNR) settings, but fail in detecting the true interactions when working in low SNR. Our framework is based on two steps. First, we estimate sources activations for a given MAR model by optimizing the following objective function; U(S)=||M(1:T)-GAS(0:T-1)|| +∝||S(0:T-1)|| $_{12}$, where $M \in R^{Cx}$ matrix of the measurements (number of sensors, time window length), $G \in R^{CxN}$ is the lead field matrix and $S \in R^{NxT}$ is the source intensities (N number of sources). The $||.||_{12}$ regularization term promotes a sparse distribution of sources in the whole time window and preserve the smoothness of the remaining time courses. Then, we estimate the MAR model by optimizing the following functional; D(A)=||S(1:T-1)-AS(0:T-2)|| . We repeat steps 1 and 2 until a stopping criterion is achieved. We used synthetic data to test the performance of our algorithm. Our framework could detect the correct source interactions both in low and high SNR and outperform two-stage approaches. At each iteration, the source space is reduced because of the zero rows in A. This is similar to removing columns from G (equivalent to removing the corresponding sources). This leads to a better approximation at each iteration. A is initialized to identity so the first step amounts to a least squares solution with $||.||_{12}$ regularization. As long as the initial active set contains the true active sources, we are able to recover correct activations and interactions.

A hierarchical Krylov-Bayes iterative inverse solver for MEG with anatomical prior

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In the present study, we revisit the MEG inverse problem, regularization and depth weighting from a Bayesian hierarchical point of view: the primary unknown is the discretized current density and each dipole has a preferred direction extracted from the MRI of the subject and encoded in the prior distribution. The variance of each dipole is described by its hyperprior density: this hypermodel is used to build the Iterative Alternating Sequential (IAS) algorithm with the novel feature that the parameters are determined using an empirical Bayes approach.

We test the performance of the IAS algorithm against synthetic but realistic data. We simulate the neural activity generated by cortical patches located in several cerebral regions including deep regions as Insula, posterior Cingulate, Cerebellum and Hippocampus. Then, we reconstruct the activity by the IAS method with and without the physiological prior. The tests show that the physiological prior significantly improves the localization of the activity also in the case when the neural sources are located in deep regions. We compare the performance of the IAS method against the results obtained using two of the most popolar inversion methods: wMNE and dSPM. A measure based on Bayesian factors is used to quantify the reliability of the reconstructions. Finally, the three inversion methods are applied to a set of auditory real data.

The Bayesian hierarchical model provides a very natural interpretation for sensitivity weighting, and the parameters in the hyperprior provide a tool for controlling the quality of the solution in terms of focality, thus leading to a flexible algorithm that can handle both sparse and distributed sources.

References

1. Calvetti D, Pitolli F, Somersalo E and Vantaggi B(2015) ArXiv:1503.06844
2. Calvetti D, Pascarella A, Pitolli F, Somersalo E and Vantaggi B(2015) Inverse Problems 31(12)
3. Lin FH et al.(2006) Neuroimage 31 160–171
4. Tadel et al.(2011) Computational intelligence and neuroscience, 2011:8

Novel Hierarchical Bayesian Algorithms for Electromagnetic Brain Imaging: Extensions of the Champagne framework

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Synchronous brain activity measured via MEG (or EEG) arises from a large collection of sources of various sizes located throughout the cortex. Bayesian estimation algorithms have shown robustness for estimating the number, location, and time course of current dipole sources, overcoming the effects of source correlations, unknown orientations and the presence of interference from spontaneous brain activity, sensor noise, and other artifacts. One such algorithm that we have described in our prior work is called the Champagne algorithm. Champagne uses a hierarchical probabilistic generative modeling framework with latent variables and parameters for MEG/EEG data, and uses Bayesian maximum likelihood estimation and convex bounding techniques for robust probabilistic estimation. Champagne has been shown to outperform many existing benchmark algorithms for source localization with very data contaminated by large interference and noise. Here, we first demonstrate that we can integrate the Champagne algorithm with Dual signal subspace projection (DSSP) algorithm for removing strong levels interference from sources located outside the brain. The DSSP algorithms is a pre-processing algorithm for cancellation of signal contributions from sources outside the brain through temporal and spatial subspace projections. We then present two hierarchical extensions of the Champagne algorithm that allow modeling of sources of varying sizes, especially for taking into account source correlations within clusters of sources, and for more robust estimation of source clusters. Performance of these algorithms demonstrate superiority to existing benchmarks and the Champagne algorithm both on simulations and real MEG/EEG data. In conclusion, the power of these Bayesian algorithms for robust source localization will be demonstrated.

The Discontinuous Galerkin Finite Element Method for Solving the MEG Forward Problem

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The goal of this study is to introduce and evaluate the discontinuous Galerkin finite element method (DG-FEM) for solving the magnetoencephalography (MEG) forward problem. Solutions for both the forward and inverse problem are required for source analysis. Since the accuracy of the inverse problem solution not only depends on signal to noise characteristics of the data, but also on the forward solution, it is fundamental to increase the accuracy of the latter. In simplified scenarios, such as multi-layered sphere models, with piece-wise isotropic conductivity, analytical solutions are available. On the other hand, when dealing with realistically shaped head models, numerical methods have to be adopted. In these cases, among the multiple aspects that have to be taken into account, an important issue is the fulfilling of conservation laws even on a discrete level. This has already been remarked upon EEG studies, but not investigated in detail for MEG, and it allows for several investigations, in particular, the unwanted physical phenomena of skull leakages, which generate model errors. In this study we introduce the first application of DG-FEM for solving the MEG forward problem and investigate the propagation of the effects of conservation properties on the MEG results. Simulations are carried out analyzing the behavior of the solution via validations in multi-layer sphere models, where the analytical solution exists, and via comparisons with the standard Lagrange finite element method. Furthermore, different type of meshes, different source models and first and second order test functions are investigated. Initial results are promising with regard to the additional value of DG-FEM for MEG forward solutions.

M/EEG source localizatioon with multi-scale time-frequency dictionaries

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Source imaging with magneto/electroencephalography (M/EEG) delivers insight into the brain activity with high time resolution. It is based on solving the ill-posed inverse problem. To identify an appropriate solution out of an infinite set of possible candidates, the problem requires setting constraints depending on a priori knowledge of the source distribution. Several constraints have been proposed so far assuming that only a few focal brain regions are involved in a specific cognitive task. Source localization can be investigated on either standard (e.g. [1]) or time-frequency (TF) domain. Approaches in the TF domain used tight Gabor frames in both a convex (TF Mixed Norm Estimate: TF-MxNE [2]) and non-convex setting (Iterative reweighted TF-MxNE: irTF-MxNE [3]). irTF-MxNE was shown to outperform TF-MxNE in both source recovery and amplitude bias. However due to a mixture of signals: short transient (right after the stimulus onset) and slower brain waves, the choice of a single dictionary simultaneously explaining both signal types sparsely is hard. This work improves the source estimation using a multi-scale dictionary, i.e. multiple dictionaries with different scales concatenated to fit short transients and slow waves at the same time. WE compare our results with irTF-MxNE on simulation. Then we use somatosensory data to demonstrate the benefits of the approach in terms of reduced leakage, temporal smoothness and detection of both signal types [4].

[1] D. Strohmeier, et al. \"The iterative reweighted Mixed-Norm Estimate for spatio-temporal MEG/EEG source reconstruction\" IEEE TMI, 2016. [2] A. Gramfort, et al. \"Time-frequency mixed-norm estimates: Sparse M/EEG imaging with non-stationary source activations\" Neuro Image 70: 410-422, 2013 [3] D. Strohmeier, et al. \"MEG/EEG source imaging with a non-convex penalty in the time-frequency domain\" PRNI IEEE, 2015 [4] Y. Bekhti, et al. \"M/EEG source localization with multi-scale time-frequency dictionaries\" PRNI IEEE, 2016.

Understanding within subject variability of source localisation and functional connectivity

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Introduction. Recent work shows that, whilst group level MEG connectivity estimation is robust, individual subject metrics suffers from poor reliability1,2 This inconsistency results, in part, from errors in source localisation brought about by the intrinsically ill posed inverse problem, and also from subject movement and error in coregistration of sensor geometry to brain anatomy. Here, we employ 3D printed headcasts to minimise subject movement and coregistration error; we then compare directly the reliability of source reconstruction and connectivity estimation with and without the headcast. *Methods*. Two subjects were scanned 5 times whilst wearing a headcast, and 5 times without the headcast. In each recording, 10 minutes of resting state (eyes open) data were recorded. The MEG signal reflects underlying brain structure, with current flowing perpendicular to the cortical surface. This means that, in multiple recordings in the same subject, the estimated current orientation at any one brain location should be consistent. We measured variability in beamformer estimated current orientation as an index of localisation stability. We also estimated the reliability of functional connectivity across runs. These measurements were made with and without the head cast and using 560s, 280s and 120s of data.*Results*.The headcast had a significant effect on current orientation; using 560s of data, the rms angular difference between sessions dropped from 20 ± 4^0 without the head cast, to 13 ± 2^0 with the head cast. When using truncated datasets, this effect was diminished. The reliability of orientation correlated significantly with the reliability of connectivity, showing the direct impact of localisation accuracy on connectivity. Our results show that variability in connectivity estimation results in part from source localisation error, and that this can be minimised by optimised coregistration and elimination of subject movement. 1.Colclough et al., 2016. 2. Tewarie et al., 2016

You cannot \"correct\" for leakage in EEG/MEG connectivity analyses

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The signals measured or estimated at different spatial locations using electro- and magnetoencephalography (EEG, MEG) may reflect the summed activity over a distribution of brain sources, a problem often referred to as leakage or cross-talk. In the context of brain connectivity analysis, several “correction” methods have been introduced that remove zero-lag temporal correlations or zero phase-lags. Here, we argue that the term “correction” for these methods can be misleading, since information that is not in the measurement cannot be retrieved solely by mathematical means. After “correction”, connectivity results can still be affected by sources that are not included in the connectivity model, even non-zero-lag connectivity can suffer from spatial blurring and systematic mislocalization, and true functional zero-lag connectivity may be missed. We suggest the use of cross-talk functions (CTFs), which describe the sensitivity of spatial filters to all potential brain sources, for the objective evaluation of cross-talk. We will analyze CTFs for common spatial filtering methods, and show that CTFs do not differ among noise-normalized minimum norm methods. For adaptive beamformers, CTFs depend on the data, and conclusions about spatial resolution are difficult to generalize. We will present CTFs for a combined EEG/MEG measurement configuration, providing a “best-case scenario” for the spatial resolution that can be achieved with current methodology. The amplitude of CTFs generally falls off with depth, posing limits on the connectivity analysis of deep brain sources. We will show how the Design of Flexible Cross-Talk Functions (DeFleCT) can use different source constraints and a priori assumptions, and e.g. produce zero cross-talk among a limited number of sources, within the general spatial resolution limits of EEG/MEG data. The combination of EEG and MEG can considerably reduce the spatial extent of CTFs, especially in frontal brain areas.

Is more always better? The effect of sensor array density on beamformer performance

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The latest M/EEG systems can have over 240 sensors, yet it is unclear whether common source reconstruction methods profit from having so many channels. Here, we investigate the influence of sensor array density on beamformer performance.

We simulated data using a real MEG configuration with 248 magnetometers and a realistic BEM-based head model. Coregistration to MRI space was done once to yield a "true" forward model used for simulating dipole sources and a second time incorporating typical coregistration error. The MEG data were simulated by projecting a single dipole source through the "true" forward model and adding white noise. The sensor array density was varied to yield between 20 and all 248 channels. Sources were reconstructed using an LCMV beamformer, with performance quantified with the temporal SNR of the peak voxel. Either the sample covariance or an analytically derived (error-free) covariance was used to construct the beamformer. Finally, a real median nerve stimulation dataset acquired with a cast to fix head position was used to confirm the effects of sensor count and coregistration error in practice.

For input SNRs higher than -15 dB, output SNR decreases with more sensors. This effect is influenced by both the covariance estimate and the coregistration error: when using the analytical covariance and a model without coregistration error, the output SNR did indeed increase with the number of sensors. These effects could be replicated with real data: a higher sensor count with typical coregistration error leads to decreasing output SNR. However, when using a head cast that nearly eliminates coregistration error, output SNR remained stable.

The results suggest that higher channel counts may in fact degrade beamformer performance due to increasing covariance inversion error. More robust matrix regularization approaches could help mitigate this error. However, the use of a head cast counteracts this effect by effectively increasing forward model accuracy.

Comparison of dipole localization to interictal spikesin individual and standardized BEM upon three different age groups

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Epilepsy is one of the most common chronic neurological disorders in childhood. Around one third of the patients are medically intractable and potentially can benefit from surgery. Pre-surgical evaluation includes source localization based on electroencephalography and magnetoencephalography (MEG). Often boundary element method (BEM) models derived from patient's magnetic resonance image (MRI) data are used in source localization. However, in some cases, MRI data are missing and template based standardized BEMs have to be used. Here we aim to quantify the source localization difference when using age-specific standardized BEMs (sBEM) instead of individual BEMs (iBEM). We studied 30 epileptic patients in three age groups 4-6 years (AG1), 10-12 years (AG2) and 17.5-19.5 years (AG3), each with individual structural MRI and functional MEG data. Age appropriate MRI templates were added from open online databases. Three-layered BEM models were generated from individual (iBEM) and template (sBEM) MRI using a conductivity ratio of 1/20 (skull/brain). The peak latency of the average signal of five to ten interictal MEG spikes per subject was used for source reconstruction of equivalent current dipoles (ECD) in iBEM and sBEM. ECDs were projected in patient's Talairach space and the Euclidean distance between the two dipole positions (SLD) and the angle deviation (AD) between their normals were calculated for the three AGs. Mean SLD for all subjects was 5 mm, where 75% of all subjects demonstrated SLDs below 10 mm. Highest mean SLD of 15.8 mm occurred within AG2. Mean AD for all subjects was 23.5 deg, where 75% of all subjects had ADs below 30 deg. Highest AD standard deviation of 45 deg was present in AG3. In conclusion, age-specific sBEM models can provide a good trade-off solution in case the individual's MRI is not available. Nevertheless, those sBEMs must be used with caution, especially in patients with abnormal or pathological head shape.

Performance of Cortical LORETA and Cortical CLARA Applied to MEG Data

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In this study, LORETA and its iterative application CLARA with additional cortical constraint are compared with respect to their performance on MEG data.
For the comparison, 1000 simulated datasets without noise were created with an Elekta Neuromag 204 channels gradiometer layout. In each data set, only one active brain region was simulated.
The localization error, the depth bias, and the number of local maxima as a measure for false positives in the source reconstruction were used for the comparison. The localization error and the depth bias were calculated for both the center of activity (COA) and the point with the maximal amplitude (MA).
The methods were also applied to two real MEG recordings of an auditory double click paradigm and a visual flowfield experiment where fMRI results were available.
The correlation between the depths of simulated and estimated sources was highly significant for both methods. However, CLARA manifested stronger correlation for both COA and MA ($r_{COA} = 0.97$, $r_{MA}= 0.96$) than LORETA ($r_{COA} = 0.86$, $r_{MA} = 0.75$). The mean localization error for CLARA was 2.5 mm for COA and 4.4 mm for MA, whereas the corresponding values for LORETA were 8.5 mm and 10.9 mm, respectively. Methods differed significantly with regard to both measures with $p < 0.0001$. The mean number of local maxima for CLARA was 2.4 and for LORETA 7.7.
For the real MEG measurements both methods yielded reliable results. However, CLARA showed more focal results and a smaller number of local maxima. From the results it is evident that a) corticalCLARA yields more focal solutions than cortical LORETA, b) the localization accuracy of cortical CLARA is better than the localization accuracy of cortical LORETA, c) the iterations in cortical CLARA reduce the number of ghost sources in the estimation and d) cortical CLARA yields a more accurate depth estimation for the simulated sources than cortical LORETA.

tACS and MEG: the effect of highly correlated noise on beamformer performance

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Magnetoencephalograhpy enables to measure electromagnetic brain activity, and in particular oscillations, whereas transcranial alternating current stimulation (tACS) in turn enables the non-invasive modulation of the aforementioned brain oscillations. Therefore,a combination of the two techniques seemed logical already from the inception of the tACS method, a decade ago. The main hindrance has always been the huge magnetic artifact that is associated with the usage of the tACS technique, which precluded the recovery of the true brain signal. Recently many methods have been proposed to overcome this limitation, disentangling more or less successfully the MEG activity from the artifact.

One of the most promising techniques has been the usage of Linearly Constrained Minimum Variance beamformers, which has been proven effective to at least reduce the tACS artifact to a manageable level.

In the beamformer literature the effects of uncorrelated noise and amount of regularization has been routinely studied, highlighting the usefulness of regularization (a.k.a. “diagonal loading” or lambda) to stabilize the inversion of the covariance matrix, at the expenses of spatial sensitivity of the underlying neural sources.

In this work we accurately study the effects of beamformer regularization in the presence of highly correlated noise (such as the tACS artifact). In a first simulation we injected highly correlated noise into real MEG data, and then the applied the LCMV beamformer to remove the noise, varying the degree of lambda and correlated noise. Subsequently we did the same, this time on real MEG+tACS data, varying the tACS current amplitude. At last, we repeated the experiment shunting the two tACS electrode patches with a resistor network, to mimic the brain impedance, in order to fully disentangle genuine brain signal from tACS artifact.

We concluded that any form of regularization is detrimental for the goal of removing (or at least diminishing) the tACS-related artifact.

Measure for Clinical Diagnosis of Epilepsywith Continuous Spikes and Waves During Slow-Wave Sleep byMagnetoencephalography (MEG)

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ABSTRACT1. Rationale andHypothesisIn this study, we evaluated the etiology andspike sources of ECSWS by MEG. ECSWS is characterized by spike and wave complexduring non-REM sleep, cognitive or behavioral disability, age-related condition(Tassinari, 1971). On the other hand, Aicardi advocated the definition of AtypicalBenign Partial Epilepsy in Childhood (ABPE) that is characterized by centro-temporal electroencephalography spikes, CSWS, and multipleseizure types including epileptic negative myoclonus, but not tonic seizures (1982). From a comprehensive overview of bothsyndromes, it seems difficult to distinguish ABPE from ECSWS. This studyevaluated the localization of MEG spike sources to investigate the clinicalfeatures and mechanism underlying ABPE. Furthermore we conducted prospectivecohort analysis to evaluate the population of ABPE among patients with CSWS.2. Patients and MethodWe selected all patients with CSWS among 1547new patients of our hospital from 2003 to March 2013. Subjective patients wereevaluated by multiple MEG study with 204ch gradiometers. Equivalent current dipoles were calculated bysingle dipole method. ABPE was defined by clinical features and theconcentrated MEG spike sources at peri-sylvian and peri-Rolandic area. Weconducted a cohort study: subjective patients with ABPE were treated byEthosuximide (ESM) and other drugs were eliminated. All drugs were stopped whenthe seizures were ceased more than 2 years. MEG analysis were conducted everyonce year or less.3. ResultsFifteen patients (male: 8; female: 7; 3 to14 years old: mean 6.4 years old) were selected as patients with CSWS. Fourteenpatients out of 15 patients with CSWS were diagnosed as ABPE by MEG and apatient was Landau-Kleffner syndrome. All patients with ABPE were included inour cohort study. The seizures of the patients were controlled by ESM by a yearto 13 years (mean 6.5 years). Medicationwas stopped in 9 patients. MEG spike sources were consisted at peri-Rolandic orperi-sylvian area, and dismissed in 7 patients.4.ConclusionWe suspected that notall, but the most patients with CSWS were ABPE. MEG spike sources were locatedat the peri-sylvian area in the both hemisphere at the age of 8 years old, butmoved at the left peri-sylvian area at the age of 12 and 15 years old.

Millimetres not centimetres – an empirical validation of high resolution MEG.

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Data inversion has been shown to be highly sensitive to co-registration errors and previous work has demonstrated that these co-registration errors can be significantly reduced through the use of subject-specific headcasts in theoretical studies.

Here we test this approach empirically by quantifying the spatial resolution detectable in a cohort of 12 subjects with headcast recorded broadband resting data. This dataset was then inverted through a library of subject-specific brain meshes of varying degrees of distortion using a 3-d Fourier decomposition technique. Subsequently, we tested the ability of our inversion algorithm to distinguish between these different meshes using Bayesian statistical quantification.

We found that our inversion algorithm was able to reliably distinguish distorted from non-distorted meshes at around the 30th spatial harmonic. This corresponds to a spatial detection in the millimetre range thereby setting an upper bound on the spatial resolution using headcasts and MEG. This was found to be superior to that found with conventional MEG techniques. Here we discuss the technique and implications of both the headcast co-registration and statistical spatial resolution quantification techniques.

Novel methods for recursive multiple source classification in EEG/MEG

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Multiple signal classification (MUSIC) and its recursively-applied version (RAP-MUSIC) are standard methods for locating brain-signal sources on the basis of EEG and MEG data. MUSIC-type localization is based on dividing the data space into signal and noise subspaces and testing whether the topography of a source candidate in the region of interest belongs to the estimated signal subspace. Due to their simplicity, computational efficiency, insensitivity to temporal correlations between the sources, and robustness to noise, these methods are useful in various EEG/MEG applications with evoked or spontaneous activity.

The conventional RAP-MUSIC, however, seems to have a hidden feature that may hinder its performance in some cases. Successful localization becomes challenging especially when the data are due to an unknown number of multiple sources, and/or when the sources are mutually synchronous or close to each other. We show that the conventional RAP-MUSIC may yield high residuals in the scanning function at a recursion step, which may disturb the performance in subsequent recursions. These residuals decrease the spatial resolution and make the estimation of the true source count difficult, and may even produce false sources.

We introduce two MUSIC-like recursive source localization methods that do not produce residual peaks at/around the already-found sources, and hence, they improve the source localization especially in challenging cases. The simulations show that the new methods efficiently remove the unwanted residuals that hinder the performance of the traditional methods, suggesting that they could be more reliable in source localization. In addition, the novel methods give a more robust estimate of the number of the true sources.

Dissociating lateralized cortical and thalamic sources to sensory stimulation usinghigh-precision MEG

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The precise spatiotemporal dynamics of somatosensorypathways remain challenging to map in humans, especially for the earliest deepbrain responses. Here, we use individualized headcasts 3D-printed fromparticipant's MRI scans, which reduces co-registration error and head movementto about 1mm (Troebinger et al 2014a,b) and thus permits construction of highSNR datasets over several days. Specifically, we sought to identify early 'first-pass'sensory evoked responses and their consistency across recording sessions. Three subjects received left median nervestimulation (MNS) during 3-5 runs per daily session, with 3-5 sessions, yieldinga total of 2513-3978 trials. We performed inversion of equivalent currentdipoles using variational Bayesian (VB-ECD) modelling, which providesprobabilistic explanations of different generative models (sources) at differenttime points between 0-25 ms ('early' and 'late') after MNS. VB-ECD betweenfour models (left/right thalamus and S1) revealed two times, 15 and 18-20ms post-stimulusduring which there was substantial evidence for contralateral, right thalamusand right S1 response, respectively. In 2/3 subjects this was observed withinindividual runs of 210 trials, i.e. we dissociate thalamic laterality usingconsiderably fewer trials compared to previouswork. We thus demonstrate thefeasibility of noninvasive temporally-resolved identification of lateralizeddeep sources to sensory stimulation. This opens the avenue for investigating theroles of subcortical structures in normal and pathophysiological brainprocesses.

Two frameworks for smooth multi-dipole estimation from M/EEG time series

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We discuss two different approaches to multiple dipole estimation from M/EEG time-series.
In the first approach [1], we assume that the number of dipoles and the dipole locations do not change in the analyzed time window; we use a Sequential Monte Carlo algorithm to compute the posterior probability for the number of sources and for the source locations, given the whole time series.
In the second approach [2], we let the number of dipoles and the dipole locations change in time. In order to get smooth estimates, we approximate the posterior distribution conditioned on the whole time series, by using a particle smoothing algorithm.
We discuss advantages and disadvantages of both methods.

[1] Sommariva and Sorrentino (2014) Inverse Problems
[2] Vivaldi and Sorrentino (2016) Inverse Problems

A model for simulating a fetal-maternal biomonitor

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We have designed a fetal-maternal biomonitor to measure magnetic fields due to electrical activity in fetal and maternal organs of interest. With simulations we studied the feasibility of suppressing noise and separating the signals from target organs. We created a finite-element model of a pregnant female consisting of the torso, heart, stomach, intestines, uterus of the woman and the heart and brain of the fetus. The geometries were adapted from digital image database of FEMONUM and Slicer abdomen database. We implemented two magnetic sensor layouts, covering the torso fully and partially. For the full coverage layout, we placed 128 magnetometer sensors ~5mm above the body surface in 8 rings separated by ~5 cm with each ring having 16 magnetometers (~5 cm inter-sensor distance) around the torso from the chest to the pubic bone. For the partial coverage layout, 40 magnetometers were placed in 8 rings of 5 sensors covering only the anterior torso. The source waveform in each organ was generated based on published electrohysterogram, ECG, MCG and magnetic measurements of intestinal activity. We simulated the magnetic fields at the sensors due to the source. We evaluated how well the electrical activity of the uterus, fetal heart and brain can be detected using the partial and the full coverage. We ignored the magnetic field from the maternal heart and intestine since ICA or a high-pass filter can remove them. The signal space projection removed the external noise by a factor of 500-2000. Using a minimum norm estimate, the full coverage array detected activities in the anterior and posterior sides of the uterus, but the partial coverage array detected only on the anterior side. A beamformer was able to detect activity in the fetal heart and brain in the presence of activity of the uterus and an external magnetic noise. In conclusion, this study showed it is possible to selectively extract the magnetic signals from organs of interest using a full coverage biomonitor.

Online neuronal source localization of epileptic spikes in a novel whole-head pediatric MEG system (BabyMEG)

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In addition to the basic online processing steps, online neuronal source localization can be used to extract specific information from the incoming data. This is of particular interest for BCI and clinical neurofeedback applications. However, online source localization can also give clinicians better in sights into the patient's abnormal brain activity. We present the integration of our recently introduced online source localization method into the novel BabyMEG system with a 375 magnetometer channel setup. MEG and MRI data were obtained from a two-year-old patient diagnosed with predominantly right-sided epileptic spikes in the central temporal lobe. For computing the forward model, we generated a three layer BEM model with the help of theFreeSurfer and MNE software. Since the BabyMEG system runs on the MNE-X software, all necessary online processing tools were at our disposal. Next, we adapted the online source localization plugin to work with the BabyMEG device. The online source localization was performed on spontaneous interictal spike data using the MNE/dSPM method. Results based on a clustered as well as a non-clustered source space were generated. A new 3D online visualization was developed and was used to visualize the results on the cortical surface. For comparison, the spikes were also analyzed offline using the MNE software and same localization methods. The results show that the online source localization is able to produce similar results as shown in the offline analysis. The epileptic spikes were correctly localized, confirming the interictal spike pattern of the patient. The successful integration of the online source localization into the BabyMEG system emphasizes the feasibility of the previously proposed online source localization method. At the same time, the results demonstrate the online processing capabilities of the BabyMEG system, backboned by the MNE-X/MNE-CPP software.

Requirements for sensor localization accuracy in on-scalp MEG

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In current SQUID-based MEG systems, sensors are rigidly assembled in a helmet-shaped array. However, in an on-scalp MEG system that uses, e.g., optically-pumped magnetometers (OPM), sensors could be moved freely to conform to the head size and shape of the subject. To enable source analysis with such a system, the position of the sensors in relation to the head needs to be known.

To examine the required sensor localization accuracy, we performed a simulation study in which a hypothetical 184-channel magnetometer array was placed on the scalps of 10 subjects. First, we constructed reference sensor arrays according to the scalp surface of each subject. Then, we created displaced sensor arrays with sensor-wise random location errors: each sensor in a displaced array was moved a random distance within a disc oriented along the scalp surface. The radius of the disc represented the uncertainty in the location of the sensors, and radii of 1, 2, 5, 10, 20 and 40 mm were examined. For each simulated level of uncertainty, 50 different displaced sensor arrays were constructed per subject, resulting in a grand total of 500 displaced sensor arrays per level of uncertainty.

Using several metrics, we analysed the effect of the sensor position error on both forward models and source estimation results using a cortically constrained source space. We found that a 10-mm random error did not significantly affect minimum-norm estimates with respect to peak amplitude and position. However, as expected, such an error rendered beamformer estimates unusable while a 5-mm error had only a moderate effect, depending on the SNR. When using beamformers, even smaller sensor location errors can cause errors in the estimated source amplitude.

These results set the frame for the requirements that come from having freely moveable sensors close to the brain, and enable assessing different sensor localization methods that could potentially be applied in an on-scalp MEG system.

Calcified cortical tubers influence single dipole source localizationx

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Source localization based on electroencephalography (EEG) and magnetoencephalography(MEG)signals generally profits from accurate individual volume conductor head models.Here, we aim to investigate the influence of volume conduction effects on equivalent current dipole localizations.We consider cortical lesions with conductivities different from healthy tissue.

EEG and MEG data were simultaneously recorded from a four-year old epilepsy patient with tuberous sclerosis complex (TSC) having one large calcified cortical tuber among other smaller ones. We segmented head tissue compartments of white matter, gray matter, cerebrospinal fluid, skull, scalp and tubers from the patient's T1- and T2-weighted magnetic resonance imaging data and assigned tissue conductivity values of 0.14 S/m, 0.33 S/m, 1.79 S/m, 0.0042 S/m, 0.33 S/m and 0.099 S/m, respectively. We generated two finite element models comprising the head tissue compartments.One model contained the tubers as separate conductivity compartments.We averaged morphologically consistent interictal spikes separately in EEG and MEG signals. We localized equivalent current dipoles (ECD) to the peak of the averaged spikes from EEG and MEG.

ECDs localizedin the millimeter vicinity of thelarge calcified cortical tuber for EEG and MEG.The ECDs of the averaged EEG spike reached goodness of fit (GOF) values of 78.0% and 78.0% in the model with and without tuber compartments. These EEG dipoles varied 1.2 mm in location and 12.5 deg. in orientation. The ECDs of the averaged MEG spike reached GOF values of 98.5% and 97.5% in the model with and without tuber compartments. The MEG dipoles varied 12.1 mm in location and 26.7 deg in orientation.

Our resultsindicate an influence of cortical lesions on ECD localization and suggest the usage of appropriate volume conductor models takinginto account lesions.

Advanced Dynamic Statistical Parametric Mapping (AdSPM) for Focal Cortical Dysplasia at Bottom of Sulcus (FCDB)

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Objective: Many children with drug-resistant focal epilepsy are diagnosed with focal cortical dysplasia (FCD). FCD at bottom of sulcus (FCDB) is highly epileptogenic, but not recognized by MRI and conventional MEG. Accurate localization for epileptogenic FCDB is required for epilepsy surgery to control seizure. We developed AdSPM to delineate epileptogenic zone of FCDB. To investigate spatial congruence between FCD and 1)MEG dipole cluster and 2)spike volume in AdSPM.*Methods* : We analyzed 17 children who underwent presurgical evaluation for epilepsy surgery. “Hit” by MEG dipole cluster was defined when the area of cluster overlapped a part of FCD. “No hit” was defined when MEG dipole cluster was seen outside of FCD or there was no MEG dipole cluster. AdSPM was analyzed ±50msec of MEG spikes which localized MEG dipoles. AdSPM automatically makes summation of each unit dipoles on each patches and demonstrate the region of most statistically significant spike volume. “Hit” by AdSPM was defined when spike volume was seen within FCD and “No hit” was defined when spike volume was seen outside of FCD.*Results*: Fourteen of 17 children underwent epilepsy surgery and pathologically diagnosed as FCD type II. The other 3 children were diagnosed as FCD type II on MRI. Thirteen children had FCDB and 4 children had FCD at the brain surface (FCDS). In 13 FCDB, MEG dipole cluster showed “Hit” in 6 children and “No hit” in 7. AdSPM showed “Hit” in 9 children and “No hit” in 4. Among 7 children with “No hit” MEG dipole cluster, 4 children showed “Hit” in AdSPM. In 4 FCDS, all 4 children showed “Hit” in both MEG dipole cluster and AdSPM. *Conclusion:* FCDB has unique neurophysiological features of closed-field effect, low density of neuronal cells and small volume. Low signal to noise ratio in FCDB tend to drift MEG dipole remote from FCDB. In AdSPM, summation of magnetic activity of each patches on the brain is able to demonstrate small epileptogenic zone of FCDB.

Frequency-Encoded Magnetic Source Imaging

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Despite the fact that the brain generates signals in a widefrequency range (approximately 0-2884 Hz), signals that have been clinicallyutilized in the past have typically been limited to a low frequency range (3-70Hz). High-frequency brain signals (HFBS, > 70 Hz) are considered newbiomarkers. Recent success in the detection of HFBS has made huge impacts onepilepsy, as patients with medically intractable epilepsy can becomeseizure-free by removing the brain areas generating HFBS. Unfortunately,clinical studies of HFBS commonly use electrocorticography (ECoG) recording,which is a very invasive procedure. The present study has developed a new magnetoencephalography(MEG) method, frequency-encoded magnetic source imaging (FEMSI), to localizeand visualize brain signals in 0-2884 Hz. Simulated data have been used todetermine if FEMSI could detect both LFBS and HFBS. In addition, we havevalidate FESI with somatosensory evoked magnetic fields (SEFs). The FEMSI ofSEFS demonstrated that FESI could precisely localize the cortical and deepsources in the somatosensory system. Furthermore, we validated FEMSI withinvasive ECoG recordings from epilepsy patients undergoing brain surgery. Theresults of epilepsy data showed that FESI could accurately localize theepileptogenic zones. The sensitivity and specificity of FEMSI weresignificantly higher than the traditional dipole modeling and beamforming. Toour knowledge, this is the first method that can color-code the frequencysignatures of brain activity for functional brain mapping and localization ofepileptic foci.

Improving the SNR in pediatric MEG studies

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Pediatric magnetoencephalography (MEG) presents particular challenges tosignal processing and source imaging. The main difficulty is the fact that children tend to move substantiallyduring the measurement, which sometimes compromises the quality of data.Continuous head position tracking and sensor-level movement compensationalgorithms have been developed, such as data decomposition and reconstructionwith the Signal Space Separation (SSS) method. However, large head movementscause increased reconstruction noise if the varying distance-related SNR is nottaken into account in the SSS process. Additional difficulties arise ifpediatric patients have magnetized material or implanted stimulators, causingsignificant movement-modulated interference. We present novel signal processing methods for improved movementcorrection and for suppressing sensor noise and artifacts: 1) Improvedregularization method reduces reconstruction noise associated with large headmovements. 2) Cross-validation SSS model separates the spatially correlatedpart (brain-related signals + magnetic interference) and uncorrelated part(sensor noise and artifacts) of a multichannel MEG signal. 3) Utilization ofsignal and noise covariance information in SSS decomposition reduces the overallsensor noise levels through enhanced numerical stability. We demonstrate that the new SSS workflow potentiallybroadens the application of pediatric MEG both in clinical and researchstudies.

Statistical non-Parametric Mapping in Source and Sensor Space

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Establishing the significance of observed effects is a preliminary requirement for any meaningful interpretation of clinical and experimental data. We propose a method to evaluate significance on the level of sensors or source locations whilst retaining full temporal or spectral resolution. Input data are multiple realizations of sensor data, or of source images obtained by an inverse source reconstruction method. In this context, multiple realizations may be the individual epochs obtained in an evoked-response experiment, or group study data, possibly averaged within subject and event type, or spontaneous events such as spikes of different types. Statistical non-Parametric Mapping (SnPM) [1] is a non-parametric permutation or randomization test that is assumption-free regarding distributional properties of the underlying data.

We have previously demonstrated the application of Topographic Analysis of Variance (TANOVA) [2] to MEG [3] and EEG sensor maps and of SnPM to source images [4] obtained from single-subject EEG data, using a temporal multiple comparison correction for sample-by-sample evaluations. In this contribution, we apply SnPM to MEG sensor data and source images. The result is a time- or frequency-resolved breakdown of sensors and source locations that show consistent activity within and/or differ significantly between event or spike types.

The method is implemented in the Curry 8 software (Compumedics, Charlotte, NC, USA) and demonstrated using data from an auditory oddball paradigm with one rare and one frequent stimulus and acquired with a 160-channel MEG system (KRISS, Daejeon, Korea).

References:

[1] Nichols, T. E., Holmes, A. P. (2002), Hum Brain Mapp, 15(1), 1–25
[2] Koenig, T., Melie-García, L. (2010), Brain Topogr, 23(3), 233–242
[3] Wagner, M. (2014), in S. Supek & C. J. Aine (Eds): Magnetoencephalography, Springer, Berlin Heidelberg, 279-284
[4] Wagner, M. et al. (2014), Hum Cogn Neurophysiol, 7(1), 1-23

Study of bionic circuit model based on PPI

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The information transmission of the biology has theadvantage over electronic system in reliability, anti-jamming, self-adaptation,self-repairing etc. Studies have foundthat the cells rely on the protein signal transduction network to transmit theexternal information of the cell membrane to the nucleus, and the whole systemhas strong robustness. In order to explore the information processing mechanismof cellular signal transduction network, we use the Michaelis-Menten equationto describe protein-protein interaction. Based on that, we use the field-programmablegate array (FPGA) aided design software DSP Builder to build the correspondingbionic circuit model, and use the Matlab software simulation analysis andverification. The results show that the bionic circuit model can achieve higherdegree of simulation of cell protein - protein interaction process. This haslaid a foundation for simulating the information processing mechanism of thePPI network, and it is helpful to the final realization of the weak signaldetection based on the bionic electronic system.

Signal-space-projection (SSP) methods for extracting single-trial time courses from EEG/MEG data

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We describe several signal-space-projection (SSP) methods that may increase the SNR for single-trial time courses associated with topographies of interest: single-component signal-space-projection (scSSP), maximum likelihood estimation (MLE), LDA beamforming (BF), DeFleCT, and a novel multi-component SSP (mcSSP) method. We applied these methods to data from an EEG/MEG visual word recognition study (Neuromag Vectorview). We computed single-trial time courses for target topographies obtained from ERPs/ERFs in the N1 (150-200 ms) and N4 (250-500 ms) time window. Average SNR time courses were computed for different SSP methods. We computed distributions of single-trial latencies (based on peak and centre-of-gravity measures) for separate experimental conditions (lexical/semantic decision, words/pseudowords, living/non-living concepts). All methods produced different time courses for N1 and N4 components, respectively, with SNR peaks in their respective latency windows. Thus, SSP methods can provide information about time courses for separate ERP/ERF components at the single-trial level. MLE and BF produced the largest average SNRs (up to 3 for N1, 2 for N4), and clearly outperformed scSSP (values about 1.5 for N1 and N4). While mcSSP produced maximum SNRs comparable to MLE and BF, this appeared to be mainly due to a reduction of baseline amplitudes, which suggests that at the single-trial level noise is not stationary or additive. We did not find differences between experimental conditions with respect to component latencies. This is in line with previous results that suggested quasi-simultaneous lexical and semantic information retrieval, but also raises the question of how to link neural and behavioural responses in the presence of behavioural reaction time differences, such as for words and pseudowords.

Mesenteric Ischemia Evaluation by Biomagnetism

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Mesentericischemia is a disease with high rates of morbidity and mortality because thereis not an effective method for early detection, since it does not have specificsymptoms. This study was thought to implement a noninvasive method of detectingintestinal ischemia. Four young male pigs between 12 and 15 kg were employed inthis work. A SQUID magnetometer with 37 channels was used to record the changesin the baseline of the magnetic field and then, when the ischemia was induced onthe sigmoidal region, data acquisition with a sampling frequency of 300 Hz wasperformed in a couple of measurement modality. First, a baseline signal wasregistered for 30 minutes and then, the ischemia induced signal was obtainedduring 60 minutes. The dominantfrequencies were calculated with the FFT in 2-minutes segments, three segmentsfor base line and six segments for ischemia induced. The preliminary results indicate a decrease in the amplitude of ischemiasegments signal, which suggest a effect side on the sigmoidal segment. Moreoverit was observed a change in the dominant frequency in the post ischemia signal,it was started with a dominant frequency of 2 cpm in the first segment and itwas decreases so that in segment six, there is a dominant frequency of 4 cp.

Study of the magnetic activity in uterine contractions

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The uterus has smooth muscles in the myometrium that can contract spontaneously without the nervous or hormonal control (Wray 1993). The study of uterine contractions is important for understanding the mechanism of premature and term labor. Uterine contraction can be measured using electrohysterogram (EHG) with an array of surface electrodes placed on the anterior side of the abdomen. However, EHG signals are distorted by the intervening tissues between the uterus and abdominal surface. Also, we predict it is difficult to visualize the myogenic activity in the entire uterus, including the posterior side, based on EHG. We initiated a study of the magnetic field produced by the uterus because this signal is less distorted by the conductivity changes between the uterus and abdominal surface. The external magnetic field is strong enough to be detected outside the torso of the mother (Eswaran et al 2002). During pregnancy, contractions are regulated by changing the potential in the interstitial medium of the myometrium. We will report characteristics of the magnetic field produced by myometrial activity in the uterus during contractions. With changes of membrane potential during contractions, it is possible to estimate the magnetic field produced during contractions. This study could provide new information about uterus physiology contributing to better understanding of uterine contractions.

Evaluation of automatically detected interictal epileptic events

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Numerous publications have demonstrated the added value of magnetoencephalography (MEG) in the evaluation of patients with epilepsy. Much of the MEG's utility here comes from its ability to accurately localize the neural sources of interictal events. Most commonly in clinical practice, such events are identified and marked manually through visual inspection of MEG and simultaneously recorded EEG signals. However, this method of visual interpretation is tedious, time-consuming and very subjective, often resulting in erroneous judgment. To address these shortcomings, recently many algorithms have been developed to automatically detect such events. Here we use distributed source analysis to study one such signal processing algorithm,which was recently developed and published by the co-authors. The algorithm is based on common spatial patterns (CSP) and linear discriminant analysis (LDA). In the current study we used weighted minimum norm estimate (wMNE) to thoroughly examine the neural sources of the interictal spikes detected or missed by the algorithm or the human specialist. The aim was twofold: first, was to understand the limitations of the algorithm and identify the ways to improve it, and second, was to recognize the properties of the true spikes that were often missed by the human specialist. We used the spikes identified by the human specialist as the "ground truth" and classified the spikes detected by the CSP-LDA algorithm as true positives (TP), false positives (FP) and false negatives (FN). We examined the locations, extents and time courses of the brain sources of these interictal spikes and found significant differences between the TPs and FPs that can be used to improve the algorithm's performance. Furthermore, we found a number of spikes that were missed by the human specialist, but were correctly detected by the algorithm. The locations,extents and time courses of such spikes were in line with the TPs.

Below-3-Hz cortical dynamics adjusts steady muscle contraction

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Introduction: How the brain integrates proprioceptive afference during motor actions is still unknown. During steady contraction, primary sensorimotor (SM1) and muscle activity are coupled at ~20 Hz with a dominant motor contribution. During continuous limb movements, the ~20-Hz cortex–muscle coupling disappears, but the SM1 cortex is coupled with limb kinematics at frequencies < 5 Hz, due to proprioceptive feedback. Here, we tested whether small fluctuations in muscle contraction are monitored similarly during steady contraction.

Methods: We recorded MEG, surface electromyography (EMG) and contraction force from 17 healthy volunteers (7 females; 20–47 years) who were maintaining an isometric pinch of 2–4 N. Coherence and renormalized partial directed coherence (rPDC) were estimated between MEG and peripheral signals.

Results: Left SM1 MEG signals were coherent at ~20 Hz, not only with EMG signals, but also with minute force fluctuations in all subjects ($ps < 0.05$; surrogate-data-based statistics), and the corresponding rPDC was 5.6 times stronger in the efferent than in the afferent direction ($p = 0.00035$; Wilcoxon test). At lower frequencies (< 3 Hz), both ~20-Hz SM1 envelope and SM1 fluctuations were coherent with both small force fluctuations and their absolute change rate in 13–16 subjects ($p < 0.05$). The rPDC analysis revealed a stronger afferent than efferent coupling between 1) force fluctuations and the ~20-Hz SM1 envelope ($p = 0.0023$), and 2) the absolute change rate of the force and SM1 fluctuations ($p = 0.013$). Of notice, the force fluctuations were ~35 times stronger at 1 Hz than at 20 Hz.

Discussion: These findings lead us to propose that, at the population level, the cortex sends motor commands at ~20 Hz that are dynamically adapted based on the < 3-Hz content of proprioceptive feedback. Accordingly, the brain would be directly informed about the low-frequency force fluctuations that are the strongest, and need to be regulated to maintain a steady contraction.

Investigating Individual Differences Event Related Beta Modulation during a Visuomotor Task

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Introduction: Finger movement elicits robust changes in beta (13-30Hz) oscillations, with a reduction in amplitude during movement (movement related beta decrease, (MRBD)) and an increase above baseline on movement cessation (post movement beta rebound (PMBR)). Recent work has shown beta modulation to be perturbed significantly in a number of disorders, including schizophrenia [1]. However, little is known about the natural variation of these effects over subjects in healthy populations. Such effects could potentially obfuscate patient-control differences. Here, we investigate the effect of age, gender and schizotypy on MRBD and PMBR in a healthy population.

Methods: Forty-eight participants completed 100 trials of a visuomotor task; participants made a lateral right index finger abduction at the offset of a high contrast visual grating. Participants also undertook a schizotypy questionnaire. Data were source localised using beamforming and the location of peak contralateral change in beta amplitude identified in each individual. Virtual sensor time-series data were derived showing beta envelope modulation as a function of time, averaged across trials. Weibull curves were fitted to these data to assess the magnitude of MRBD and PMBR across individuals [2].

Results: Peak to peak change in beta amplitude increased significantly with age ($r2=0.35$, $p<0.05$). Correlation with schizotypy score showed PMBR reduction with increasing schizotypal personality trait ($r2= 0.25$, $p<0.05$). A trend for female participants to have a greater PMBR and reduced MRBD compared to males was also identified.

Discussion: Recent work shows that PMBR is reduced in schizophrenia [1]; our finding extends this result, showing the same effect in a sub-clinical population. More generally, our findings highlight the critical importance of characterising individual differences in neural oscillatory processes.

[1] Robson et al. (in press) Neuroimage: Clinical. [2] Liddle et al.(2016) HBM, 13, pp 1361-1374

The relationship between beta oscillations and variability in motor learning

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People vary in their capacity to learn and retain new motor skills, perhaps due to differences in capacity for cortical plasticity. A key determinant of the potential for plasticity is the inhibitory-excitatory balance in cortex. Neuronal oscillations are sensitive to this inhibitory-excitatory balance and so might represent biomarkers of potential for plasticity. Here, we investigate the relationship between motor skill learning/retention and neuronal oscillations in the β-frequency range (15-30Hz) measured in human subjects.

Twenty young (18-30 years) and twenty elderly (62-77 years) participants performed a continuous tracking task using wrist flexion and extension. Both groups were trained on a repeated sequence and random sequences. Motor performance was measured during and at two time points (15 min and 24 hours) after training. Electroencephalography (EEG) was recorded before and after training.

Our results show that although there was no age related difference in learning rates, older subjects had poorer retention of newly learned motor skills at 24 hours. Older subjects also had higher resting β-power and movement-related β-desynchronization (MRBD) but not post-movement β-rebound (PMBR). However, there was no correlation between pre-learning beta measures and learning or retention. Immediately after training, only older participants showed a significant increase in resting β-power. Training-induced changes in resting β-power (post-pre) correlated with 24-hour retention for the sequence-specific motor skill only.

Our data suggest that it is the capacity for change in β-oscillations rather than pre-task levels that is important for retention of new motor skills. These learning-related changes in β-oscillations provide insight into physiological processes that support long-term motor retention and, in the context of disease, offer novel targets for promoting long-term rehabilitative outcomes.

Evidence of cortico-cortical and cortico-muscular coherence in a bimanual precision-grip task using ICA on MEG-EMG data.

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Studying cortico-cortical coherence between sources in motor regions is difficult due to their close anatomical location. Indeed we may find strong but false cortico-cortical coherence due to source leakage effects. In the present study, we used Independent Component Analysis (ICA) to study cortico-cortical and cortico-muscular coherence.

Participants were asked to perform a bimanual visuomotor precision grip task in which the required precision was higher for the right hand (1). We computed the coherence between Independent Components (ICs) from the MEG data with dipolar topographies (corresponding to single and localized generator) and between ICs and EMG signals. We used the dipole fitting method to localize in the brain the ICs. We found higher coherence between ICs of sources located in the left motor regions (contralateral to the right hand involved in high precision force control) than in the right regions. Moreover, cortico-muscular coherence was found between ICs and EMG signals.

Using this new methodology, we were able to show evidence of intrahemispheric cortico-cortical coherence when the contralateral hand (right and dominant hand in this case) is involved in high precision force control. We were able to distinguish sources involved in the task which were not found using beamforming methods such as DICS (2). In summary, ICA gave promising results in the investigation of a bimanual precision-grip task, thanks to an increase in signal to noise ratio and robustness to source leakage effects.

(1) Chen et al. (2013) *PLoS ONE 8(3): e60291.* doi:10.1371/journal.pone. (2) Gross et al. (2001) Proc NatlAcad Sci U S A. 2001 Jan 16; 98(2): 694–699. doi: 10.1073/pnas.98.2.694

TASK-RELATED BETA ACTIVITY IN HUMAN PRE-MOTOR CORTEX (PM) DURING NON-BIOLOGICAL MOTION OBSERVATION

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Many monkey neurophysiology studies implicate premotor cortex (PM) in action-related decision-making (Cisek & Kalaska 2010). Voluntary movement planning and execution evoke changes in oscillatory activity in the sensorimotor network. The power of beta (15-30 Hz) synchrony decreases during movement and increases ("rebounds") after movement end (Kilavik et al 2013). This modulation may partly reflect motor-decision processes. The amplitude of movement-related beta desynchronization in PM correlates with the level of uncertainty during a decision-making task (Tzagarakis et al., 2010). The role of PM might extend beyond motor planning per se to higher-order cognitive processes. While subjects observe a 3rd party perform a known motor task, the amplitude of post-movement beta rebound in PM is related to the subjects' recognition of the correctness of observed actions after motor training (Koelewijn et al 2008). However, it is not known whether PM might contribute to the assessment of unfamiliar non-biological visual events prior to motor training. We recorded activity in PM using magnetoencephalography before and after motor training in a two-target pointing task guided by a color-location rule (CLR; Cisek & Kalaska 2004). One subject group learned the CLR by passive observation while the computer performed the task correctly or incorrectly. They then reported their assessment of the observed outcome of further computer-performed trials given the CLR (OBS Task). In a 2nd recording session, they performed the task actively with a joystick (ACT Task). A second group received the opposite training sequence (ACT, OBS). Our results demonstrate modulation of beta oscillation power over PM in both tasks. In particular, we found beta synchrony variations during visual observation (OBS Task) in the first group prior to motor training, which implicates PM in cognitive processing of choice-related information and the application of rules unrelated to known motor actions.

Recovery of the 20-Hz motor-cortex rebound after stroke

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Modulation of the 20-Hz rhythm to somatosensory input reflects alterations in motor-cortex excitability. In stroke patients, the strength of the rebound to tactile stimuli is associated with recovery of hand function. Passive movement modulates this rhythm stronger than tactile stimulation in healthy subjects. Here, we compared the modulation of the 20-Hz rhythm to passive movement and tactile stimulation in stroke patients to find out how these different afferent systems are associated with motor recovery.
Modulation of the 20-Hz rhythm was quantified from MEG measurements in 23 stroke patients with upper limb paresis within a week (T0), 1 month (T1) and 12 months (T2) after stroke, and in 22 healthy subjects. We used tactile stimulation to finger tips and passive movement (ISI 3 s to one hand) of the index fingers.
The 20-Hz rebound to tactile stimulation of the impaired (RTI) and healthy (RTH) hands were significantly weaker in both hemispheres at T0 vs.T1. At T0, the RTI was significantly weaker also compared to the controls, whereas no such difference was detected for RTH. At T1, also the RTI had reached the level of the control subjects. The rebound to passive movement of the impaired hand (RPI) increased significantly from T0 to T1, whereas no significant increase was detected for the healthy hand (RPH). The RPI and RPH remained significantly weaker at all time points as compared to the controls. Clinical hand motor tests correlated more strongly to the rebound to passive movement than to that to tactile stimulation.
In conclusion, the increase of the rebound towards normal levels occurred predominantly during the first month after stroke. The rebound to passive movement vs. tactile stimulation showed higher correlation with hand-motor function, and the incomplete recovery of the rebound to passive movement suggests that proprioceptive afference was not fully recovered in our patients.

Oscillatory activity during implicit motor sequence learning in patients with Parkinson\'s disease

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Implicit motor sequence learning refers to the ability to incidentally acquire knowledge of sequences of events and actions. The modulation of motor-cortical oscillatory activity in the alpha and beta band is assumed to play a crucial role in this type of learning. More specifically, the ability to suppress beta oscillations has been suggested to facilitate learning. Furthermore, beta power may be involved in the stabilization of movement patterns. In Parkinson's disease (PD), there is strong evidence that oscillatory activity within corticobasal ganglia circuits including motor cortical areas is altered. Increased beta synchronization has received particular attention as it is associated with PD motor symptoms such as bradykinesia. In the present study, we aim at investigating whether motor sequence learning is impaired in PD patients and to what extent this potential impairment is associated with oscillatory alterations.
To this end, PD patients and healthy controls are trained on a serial reaction time task. To assess motor sequence learning and susceptibility to interference (indicating motor stabilization), reaction times are determined during learning as well as after presentation of interfering randomly varying trials. Neuromagnetic activity is recorded throughout the task using a 306-channel whole-head magnetoencephalography system. Data are analyzed regarding oscillatory activity – with particular focus on beta power. We further examine whether and how oscillatory power and its dynamic modulation are related to the acquisition and stabilization of motor sequences.
The data are expected to reveal new insights into the functional significance of brain oscillations – specifically at the beta range – for motor sequence learning in particular and motor control in general.

Dynamics of the neuronal processes underlying abnormal reaching in the cerebello-cortical network in dystonia

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We aimed to study the involvement of cerebellar sensorimotor networks in motor reaching in writer's cramp (WC) patients.We recorded 16 WC patients and 19 matched controls (HV) with MEG (Elekta). The subject used a joystick with their right hand to move a cursor to reach one of five possible targets. There were 2 conditions: direct coupling between the joystick and the cursor (no-deviation), 25° or -30° clockwise rotation of the cursor position (deviation); each was repeated in 2 blocks of 50 trials. . Two movement phases were considered: preparation (400 to 200 ms before movement onset) and execution (1 s after movement onset). A 3D T1 MRI was acquired for each subject.The MEG data were preprocessed with Maxfilter tSSS to attenuate external interferences. Cardiac artifacts and eye blinks artefacts were removed using in-house PCA tool. Evoked potentials for the no-deviation and deviation conditions were analyzed in Brainstorm with a minimum-norm approach including deep brain structures. Using an ANOVA, we evaluated the Group, Conditions and movement phase effects on brain activation. We used a beamformer approach in Fieldtrip to extract connectivity information.Results showed that, WC had greater activation (1) in the bilateral cerebellum and left parietal areas during motor preparation; (2) in the left supramarginal gyrus during motor execution. During motor preparation, connectivity in the cerebello-parietal network was different between HV and patients in alpha and gamma frequency bands.

Motor learning induces changes in MEG resting-state oscillatory network dynamics

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Motor learning induces changes in resting-state (RS) network properties in fronts-parietal (Albert et al, 2009) and sensorimotor (Taubert et al, 2011) networks. This study explores the putative modulations of spontaneous resting-state oscillations following a sensori-motor learning task. The task consisted in lifting a load with the right hand, which triggered the unloading of a load suspended to the left forearm (Paulignan et al., 1989). Because learning stabilizes quickly, a temporal delay was implemented, hence placing the subject in a dynamic learning state. Sixteen adults performed a resting state sessions in which they fixated a grey crosshair on a white background before and after two motor learning conditions: The subjects were instructed to lift with their right arm a load (800 g) placed on the ipsilateral haptic space. In the LEARNED condition, voluntary lifting of the object with the right arm instantaneously triggered the unloading of the load placed on the left arm. In the DYNAMIC LEARNING condition, a time delay was implemented per block between lifting and the resulting unloading. MEG signals were recorded using a 275-channel MEG CTF system. The performance was constant in the LEARNED condition, while postural stabilization increased during the DYNAMIC LEARNING condition ($p<.001$). Minimum-norm estimation revealed that alpha power (8-12 Hz) generators were located bilaterally within the pre-central gyri, the post-central gyri, the inferior parietal gyri and the superior parietal gyri. Most importantly, comparison of RS power pre and post learning revealed a significant increase of sensori-motor alpha power contralateral to postural side, only after the DYNAMIC LEARNING condition ($p<.05$). Our RS MEG connectivity and graph theoretical analyses also showed significant changes following motor learning. The RS oscillatory network modulations we observed following dynamic motor learning could be specifically related to sustained sensori-motor learning processes, distinct from novel skill acquisition.

The neural correlates of automatic imitation

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Automatic imitation, the unconscious tendency to imitate another person's actions, is proposed to result from mirror-system networks specialised for the direct matching of observed and executed actions. The current study explored the pattern of neural oscillations associated with automatic imitation effects. Twenty-one participants were first tested on a stimulus-response compatibility paradigm (Boyer et al. 2012). Participants observed a hand performing a movement of either the middle or index finger and were instructed to respond with a movement with the middle or index finger of their right-hand according to the left-right spatial position of the stimulus finger. By presenting the stimuli as either left or right hands we manipulated whether the participants' actions were biologically compatible (index/index) or incompatible (index/middle) with the observed action. Results revealed an automatic imitation effect as response-times were 29 ms faster when the participants' actions were biologically compatible with the observed action ($p < 0.001$). In a second study, the oscillatory neural activity associated with this effect was examined using magnetoencephalography recordings. The sensor level analysis of 17 participants revealed that the responses were associated with prominent reductions in the power of the alpha-beta band (10-25Hz) in lateral posterior sensors. Notably, the power reduction recorded in the biologically-congruent condition was stronger than that of the biologically-incongruent condition from 250-400 ms of the onset of the observed movement. These findings suggest that automatic imitation is facilitated by oscillatory activity in the posterior-parietal area, yet, further investigations, particularly at source level will be required for final conclusions.

Effects of motor neuron disease progression on cortical beta and gamma rhythms: A single case study of amyotrophic lateral sclerosis

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Background and aim: Amyotrophic lateral sclerosis (ALS) is a rapidly progressive and ultimately fatal neurodegenerative disease characterised by muscle weakness and paralysis. The aim of this study was to investigate changes in primary motor cortical activity over the course of the disease progression in a single ALS patient.Methods: Brain activity was recorded using a 160 channel whole-head MEG system (KIT, Kanazawa, Japan) in a patient with definite ALS with onset of symptoms 10 months prior to first testing. The patient performed movement and imagery tasks developed by our group to reliably activate primary motor cortex (Burianova et al., 2013, *Neuroimage*, *70*: 50). We recorded surface EMG from the flexor digitorum to monitor muscle activity during both the motor execution and imagery tasks. The patient was clinically staged using the Amyotrophic Lateral Sclerosis Functional Rating Scale-revised (ALSFRS-R) and received 4 MEG scans, once every 3 months. Results: The patient performed the executed and imagined movement tasks with an accuracy of >90% in all four scanning sessions. Beta band desynchronization (13-30 Hz) was localised to the primary motor cortex for both movement and imagined conditions and was fairly consistent across the first 3 scans. In the fourth scan, beta band power was reduced and this beta change coincided with a rapid decline in function (ALSFRS-R score from 46/48 to 36/48). Discussion and conclusions: We have demonstrated that it is feasible to use MEG to assess motor cortical function longitudinally in ALS. Reduction in gamma synchronization coincided with functional deterioration and has the potential to be used as a biomarker for monitoring disease progression in ALS.

Oscillatory cortical dynamics of visually-guided and auditory-guided sequence learning

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Implicit sequence learning is controlled by a network of brain regions that integrate sensorimotor and cognitive parameters generating associations between the movement elements. Oscillatory dynamics of these networks remain unknown, particularly in disorders with cognitive deficits (such as schizophrenia). Here, we examined changes incortical activity over sequence learning using magnetoencephalography through a serial reaction time task during both visual and auditory-guided movements of the hand and mouth. We hypothesize that both separate and overlapping parts of these networks exist with network dynamics compromised in patients with schizophrenia. Data was acquired using a 275-channel whole-head biomagnetometer(MISL) during an eight-step movement sequence in response to visual or auditory stimuli. Manual responses were made on key presses to spatial locations on a button box corresponding to locations on the screen while vocal responses produced a short vowel appearing in one of the four spatial locations. Time-frequency source-space reconstructions were generated using an adaptive spatial filtering technique using Nutmeg (www.nitrc.org/projects/nutmeg). We observed significant ($p<0.05$, 5%FDR corrected) changes in beta (12-30Hz) and high-gamma (65-90Hz) power over regions in regions of the frontal lobe (SMA, pre-motor cortex) in both conditions. Patients learning the movement sequence showed abnormal increases in beta and low-gamma (30-55Hz) suppression over contra lateral sensorimotorcortex (SMC), with high-gamma SMC power reduced in patients unable to learn the sequence. Computerized cognitive training in patients increased beta/low-gamma suppression coincident with an ability to learn the movement sequence. This data indicates effector-specific oscillatory coding in SMC over the course of learning, with higher-level effector-independent encoding in the SMA. Impairments in high-frequency synchronization translate into learning deficits in schizophrenia.

The relationship between neurotransmitters and task-induced oscillatory modulations during working memory task

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Detailed studies on the association between neural oscillations and the neurotransmitters gamma-aminobutyric acid (GABA) and glutamate have been performed in vitro. In addition, recent functional magnetic resonance imaging studies have characterized these neurotransmitters in task-induced deactivation processes during a working memory (WM) task. However, few studies have investigated the relationship between these neurotransmitters and task-induced oscillatory changes in the human brain. Here, using combined magnetoencephalography (MEG) and magnetic resonance spectroscopy (MRS), we investigated the modulation of GABA and glutamate + glutamine (Glx) concentrations related to task-induced oscillations in neural activity during a WM task. We first acquired resting-state MRS and MEG data from 20 healthy male volunteers using the n-back task. Time-frequency analysis was employed to determine the power induced during the encoding and retention phases in perigenual anterior cingulate cortex (pg-ACC), mid-ACC, and occipital cortex (OC). Statistical analysis showed that increased WM load was associated with task-induced oscillatory modulations (TIOMs) of the theta-gamma band relative to the zero-back condition (TIOM0B) in each volume of interest during the encoding phase of the n-back task. The task-induced oscillatory modulations in the two-back condition relative to the zero-back condition (TIOM2B-0B) were negatively correlated with the percent rate change of the correct hit rate for 2B-0B, but positively correlated with GABA/Glx. The positive correlation between TIOM2B-0B and GABA/Glx during the WM task indicates the importance of the inhibition/excitation ratio. In particular, a low inhibition/excitation ratio is essential for the efficient inhibition of irrelevant neural activity, thus producing precise task performance.

Defining Epileptic Network Pathways - A combined MEG and fMRI approach

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Introduction: The aim was to define epilepticnetwork pathways during childhood absence seizures using a combined MEG and fMRI connectivity analysis.

Methods: Magnetoencephalography (MEG) and combined EEG-functional magnetic resonance imaging (EEG-fMRI) were recorded in 7 participants with untreated childhood absence seizures. EEG was used to identify timing of absence seizures during fMRI and an event related independent component analysis (eICA) method identified fMRI activity correlating with the seizures. These fMRI regions were parcellated to express the network in terms of functional nodes. These nodes were used as virtual sensor locations for a linearly constrained minimum variance (LCMV) beamformer analyses of absence seizures recorded using MEG in the same subjects. Group time frequency analysis (FFT) was used to identify the bandwidths with dominant power. After extracting source waveforms, the effective connectivity was estimated using a phase slope index (PSI) metric.

Results: eICA of fMRI data identified regions similar to those previously reported (thalamus, frontal, precuneus,biparietal). Thirty-four seizures were recorded during MEG and used for effective connectivity analysis. PSI at 3-4Hz and 13-30Hz showed connections within and between parietal cortex, precuneus, and thalami while at higher frequencies (30-55Hz) connectivity tended to be within and between frontal regions. Inter-subject variability was noted and there was a difference in the proportion of thalamic connections in treatment responders (49% ± 26%, N=5) versus non-responders (28% ± 8%, N=2).

Conclusion: fMRI-informed MEG analysis can be used to identify brain connectivity during generalized seizures, such as childhood absence seizures. We are hopeful that these types of connectivity patterns could be used in the future to explain the phenotypic diversity seen in epilepsy and predict treatment outcomes.

Function Predicts Structure: MEG derived functional connectivity (fc) predicts grey matter myelination.

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Introduction: Human brain structure varies between individuals in a systematic fashion. For example, people with high cortical thickness in Broca's area typi¬cally exhibit high thickness in Wernicke's area, representing a developed language network. This means that measurement of covariation of structural parameters over subjects offers a means to characterise 'networks', with highly correlated regions often being part of a distributed system that serves specific cognitive function. Here, we used ultra-high field MRI to map a structural network representing cortical myeloarchitecture. We then show that this structural network can be predicted by electrophysiological connectivity.
Methods: 5 minutes of resting state MEG data were acquired alongside 7T MRI data in 57 participants. MRI included quantitative magnetisation transfer (MT) mapping, which was processed to represent myelin density. Grey matter masked MT images were parcellated into 78 AAL regions and correlated (across subjects) to generate a (78x78) matrix representing a network of covarying myeloarchitecture. MEG data were beamformed to the same AAL regions, and amplitude envelope connectivity (AEC) was used to generate connectivity matrices for 5 frequency bands. Group averaged connectivity matrices were then combined in a multivariate Taylor series to predict the structural network.
Discussion: MEG connectivity predicted regional covariance in myelin ($r = 0.5$, $p < 0.001$). A linear and non-linear combination of all frequency bands was the most successful predictor, however, of the individual frequency bands, beta and gamma band connectivity matrices also allowed significant prediction. Our result implies that the brains myeloarchitecture supports distributed networks of electrophysiological functional connectivity. This has implications for our understanding of the relationship between structure and function, and for diseases involving dysconnectivity or demyelination.

Multi-Modality Visualization Tool

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The visualization and exploration of neuroimaging data is important for the analysis of anatomical and functional images and statistical parametric maps. While two-dimensional orthogonal views of neuroimaging data are used to display activity and statistical analysis, real three-dimensional (3d) depictions are helpful for showing the spatial distribution of a functional network, as well as its temporal evolution. For our best knowledge, currently there is no neuroimaging 3d tool which can visualize both MEG, fMRI and invasive electrodes (ECOG, depth electrodes, DBS, etc.). Here we present the multi-modality visualization tool (MMVT). The tool was built for researchers who wish to have a better understanding of their neuroimaging anatomical and functional data. The true power of the tool is by visualizing and analyzing data from multi-modalities. MMVT is built as two separated modules: The first is implemented as an add-on in \'Blender”, an open-source 3d visualization software. The add-on is an interactive graphic interface which enable to visualize functional and statistical data (MEG and/or fMRI) on the cortex and subcortical surfaces, invasive electrodes activity and so on. The tool can also be used for a better 3d visualization of the anatomical data and the invasive electrodes locations. The other module is a standalone software, for importing and preprocessing. The users can select the data they want to import to Blender and how they want to process it. The module support many types of analyzed data, like FsFast (FreeSurfer Functional Analysis Stream) and SPM (Statistical Parametric Mapping) for fMRI, MNE (a software package for processing MEG and EEG) raw data for MEG and FieldTrip (MATLAB software toolbox for neuroimaging analysis) data structures for the invasive electrodes. The users can also reprocess raw data using a wrappers for FaFast and mne-python (a python package for sensor and source-space analysis of MEG and EEG data).

Diffusion MR and MEG Assessment of Auditory and Language System Development in Children with Autism Spectrum Disorder

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This study integrated diffusion MR measures of white-matter microstructure and magnetoencephalography (MEG) measures of cortical dynamics to investigate associations between brain structure and function within auditory and language systems in autism spectrum disorder (ASD). Based on previous findings, abnormal structure-function relationships in auditory and language systems in ASD were hypothesized. Evaluable neuroimaging data was obtained from 44 typically developing (TD) children (mean age 10.4±2.4yrs) and 95 children with ASD (mean age 10.2±2.6yrs). Diffusion MR tractography was used to quantitatively assess the auditory pathways in the brainstem (cochlear nucleus to thalamus) and the cerebrum (thalamocortical auditory radiation). The arcuate fasciculus segment of the language system was also delineated with tractography. MEG was used to measure superior temporal gyrus auditory evoked M100 latency and auditory vowel-contrast mismatch field (MMF) latency. Abnormally slow maturation of left hemisphere auditory radiation FA ($p<0.01$) and a trend towards abnormally slow maturation of left hemisphere M100 were present in ASD. In TD children, M100 was significantly correlated with DTI measures from brainstem auditory tracts ($p<0.01$) and auditory radiations ($p=0.04$) while MMF latency was correlated with arcuate fasciculus FA ($p<0.01$). However, in ASD, we observed uncoupled structure-function relationships in auditory and language systems. Further multimodal studies are needed to characterize the different features (gray matter, synapses, local CFC) that additionally contribute to the latency of neural evoked responses and ultimately behavior in TD and ASD. Finally, the neural latency measures were found to be of clinical significance, with M100 associated with overall ASD severity, and with MMF latency associated with language performance.

Imaging Magnetic-Nanoparticles-Targeted Tumors Using Low-Power Ultrasound Excitation

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Because the magnetic field decays fast with the distance based on Biot-Savart law, the utility of strong AC magnetic field to sense few amount of MNPs in deep depth within animals seemly is the only one solution for the currently developed technologies of imaging magnetic nanoparticles (MNPs), such as magnetorelaxometry, magnetic particle imaging, old generation of scanning SQUID biosusceptometry (SSB), etc. Recently, we have found the superior characteristics of MNPs under the excitation of ultrasound waves. In addition, the decay of the ultrasound field in tissue with the distance is relatively slower than magnetic fields. Hence, the low-field ultrasound filed was utilized to replace the strong AC magnetic field. A Halbach array of magnets supports DC field to enhance the magnetization of MNPs. In other words, the novel methodology of MNP imaging by an ultrasound excitation was verified with this proposed type of SSB. The feasibility was proved by the phantom test and animal tests. The former was to examine a small volume of MNP reagents insides the phantom, simulating for MNP- targeted tumors. The later was to examine the tumors on tumor rats, injected with the MNP reagent. The superior performance indicates the high population potentiality in the future clinical application.

In-vivo Multifunctional Imagingby Scanning SQUID Biosusceptometry

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An endoscope is used to look theinterior of a hollow organ or cavity of the body for medical reasons, such asthe visual guideline of the surgery. However, small tumors are not easily foundin the organ surface or absolutely invisible in the organ interior. Currently,the radioactive contrast medium is always injected to label tumors, and thenobserved by some radioactive imaging instrument, such as a gamma camera, forthe surgical guideline. However, the existence of radioactive risk is seriouslyfor both weak patients and medical doctors. Hence, the relatively safer near-infrared(NIR) fluorescence imaging has been developed to replace the radioactiveimaging. Actually, the lifetime and optical intensity of fluorescence reagents areeasily and separately destroyed and absorbed by environments. Further, becausefluorescent reagents are not compatible for preoperative MRI, patients havedouble healthy and financial loading of contrast medium in different phases. In this work, the proposed endoscope type ofscanning SQUID biosusceptometry (E-SSB) was proposed by a commercial endoscopesurrounding by the thin pickup coil and an excitation mechanism. Besides,magnetic nanoparticles (MNPs) conjugated with florescent indicators wereutilized as both florescent and magnetic contrast reagent. In the phantom test,the thin film of the MNP reagent distributed on the cover glass. Theconsistence between magnetic image and fluorescent images proved thefeasibility of the E-SSB.

Technical solutions for Simultaneous MEG and SEEG recordings

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In order to bedetected on MEG sensors, neuronal activity needs to be summed over large areasof cortex that are well organized spatially. Thus, it is not clear to which extent deep sources such as amygdala and hippocampus can be extracted fromsurface signals. Besides simulations, the only way to understand the relationships between remote surface signals and actual brain activity is torecord simultaneously MEG and SEEG electrodes implanted within the brain during presurgical evaluation of epilepsy. However, such recordings are difficult to achieve because of the technical constraints inherent to the different techniques. We present here a strategy for recording simultaneously MEG and SEEG, despite mechanical and electromagnetic issues. For the mechanical aspects, we used new SEEG fixations that almost level with the skin, thus minimizing the added thickness around the head of the patient. Special attention was given to minimize influence of SEEG connectors. We used a MEG-compatible amplifier that minimizes artefacts on MEG while allowing recording a large number of SEEG contacts (256 channels). We obtained signals of excellent quality on both MEG and SEEG. In particular, both low and high frequency artefacts as observed in previous recordings were absent (Dubarry et al 2014). The possibility of high quality Multi-level MEG-SEEG recordings open new ways to understand the depth-surface relationships and to optimize signal processing methods. They will also be key measures for developing patient-specific computational models in a \'Virtual Brain\' environment. For clinical aspects, this procedure can be applied routinely. Thus, MEG can provide a global view on brain activity, complementing the limited spatial sampling of SEEG.

Reference

Dubarry et al. Simultaneous recording of MEG, EEG and intracerebral EEG during visual stimulation: From feasibility to single-trial analysis. Neuroimage. 2014

Non-invasive functional evaluation of lumbar nerveroot and cauda equina with high spatial resolution by magnetospinograph system

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Introduction: There are many cases of multi level lumbar spinal stenosis and foraminal stenosis, but there is still no electrophysiological diagnostic method with a high spatial resolution for these conditions. We have been developing a magnetospinographsystem which is a supine position-type biomagnetometer equipped with superconducting quantum interference device (SQUID) fluxmeter. We have reported that magnetospinography could non-invasively evaluate the spinal cordand spinal nerve activity by body surface recordings. Aim: The aim was to visualize the electrical activities of nerve roots and cauda equina in the lumbar spine non-invasively after peroneal nerve stimuli by magnetospinography. Materials and Methods: We used a newly developed 124-channel SQUID biomagnetospinometersystem (Kanazawa Institute of Technology, Japan) with a wide sensor area and a suitable curve for lumber lordosis. Neuromagnetic fields of 32 healthy subjects (64nerves), 22–58 years of age (mean age 41 years), were measured at the surface of the lower back after electric stimuli of the peroneal nerves at the knees.With the use of a unit gain normalized minimum-norm (UGMN) filter method, which is a spatial filtering technique, the direction and intensity of the currentsource on each reconstruction point was reconstructed, and the conductivedirection, distribution, and temporal change of the current source were visualized.Then, the propagation pathway of the estimated electrical currents was superimposed on lumbar spine X-rays. Results: For all subjects, we could record the nerve action magnetic fields in the lumbar spineafter peroneal nerve stimuli. In 44 nerves (68.8%), we could visualize the estimated electrical currents propagating through the surrounding fifth intervertebral foramina and ascending to the cranial direction in the lumbarcanal. The conduction velocity of the current source was 40.3–78.8 m/s (mean56.5 m/s), as calculated from the peak latency Conclusions: Usingthe magnetospinograph system, we successfully visualized the propagation of estimated neural electric activities in the lumbar spine after peroneal nervestimuli. This system holds enormous potential for establishing a non-invasive electrophysiological diagnostic method for the identification of the disordered site in lumbar spinal nerves.

Simultaneous SEEG-MEG-EEG recordings overcome the SEEG limited spatial sampling

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During presurgical evaluation of pharmacoresistant partial epilepsies, stereoelectroencephalography (SEEG) records interictal and ictal activities directly but is inherently limited in spatial sampling. Surface EEG and MEG provide global recordings and are characterized by distinct sensitivities. Some generators may be undetectable with EEG, with MEG or with both modalities. Recording simultaneously these three modalities should provide a better understanding ofthe underlying brain sources. Recording was performed in a 19-year-old female patient with pharmacoresistant cryptogenic posterior cortex epilepsy. SEEG (13 depth electrodes), MEG (248 4D neuroimaging) and EEG (23 scalp electrodes) were simultaneously recorded (2034 Hz). SEEG spikes, sub-continuous and very focal, were manually selected by an epileptologist. MEG and EEG signals were averaged locked on SEEG spikes. MEG sources were reconstructed based on dipole scanning (Brainstorm software). From SEEG results, the epileptogenic zone was defined around a left lateral occipital sulcus explored by several leads of one electrode, a propagation network involving the mesial and basal occipital cortex explained the semiology of seizure. Afocal left lateral occipito-temporal cortectomy was performed. Seizures re-occurred five days after surgery. Recordings were thus re-analyzed. No MEG nor EEG spikes were detected. MEG sources triggered by SEEG spikes revealed a more posterior (occipital pole) region than the SEEG leads which recorded the maximal number of spikes and corresponding to the EZ. SEEG did not explore the occipital pole.Simultaneous recordings provide a global brain recording and overcome the inherent SEEG limited spatial sampling. Source localizations of MEG data triggered by SEEG data highlighted a more posterior generator which was not investigated using SEEG. Simultaneous recordings are challenging but are indicated as they provide a more global view of interictal networks than SEEG alone.

Epileptic high frequency oscillations in simultaneous MEG and EEG

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Background: Ripple oscillations (80-250Hz) in invasive EEG are biomarkers for the epileptogenic zone. Identification of ripples in non-invasive MEG and EEG is possible, but impeded by a low signal to noise ratio. We studied ripples in simultaneous MEG and EEG to compare ripple yields in these complementary modalities with different sensitivity profiles. Methods: Fifteen minutes of resting state MEG and EEG were simultaneously recorded in three patients with drug resistant focal epilepsy. The 60 channel EEG was analyzed in a bipolar montage, and ripples were marked by hand. The 306 sensor MEG was preprocessed by using beamformer virtual sensors to improve the signal to noise ratio. About 2500 virtual sensors were positioned throughout the cortex. Ripples in the MEG virtual sensors were detected by an automatic detection algorithm, adapted from Burnos et al. Time instances with MEG or EEG identified ripples were compared for temporal and spatial correlation. Results: All three patients showed ripples in the EEG and the MEG. 96 moments with EEG ripples were identified, against 45 moments with MEG ripples, of which 21 were co-occurring in MEG and EEG. The spatial distribution of all ripples in MEG and EEG, as visualized in a 3D reconstruction, was concordant at the lobar level in all three patients, and was concordant with clinical EEG, MEG and PET findings. Significance: Both in MEG and EEG show ripples that originate from the presumed epileptic focus, but they are not necessarily co-occurring. The number of ripples in each modality is low. Combining the information of MEG and EEG might increase the yield of non-invasive ripples for identification of the epileptic zone. Using the same analysis method for both MEG and EEG would be preferred in future research.

[1] Burnos S, et al. Human Intracranial High Frequency Oscillations (HFOs) Detected by Automatic Time-Frequency Analysis. PLoS One. 2014;9(4):e94381.

Validation of Fast-VESTAL Source Estimation Method with Reference to BOLD fMRI

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MEG, as a non-invasive approach, features with higher temporal resolution but lower spatial resolution compared with fMRI. The recently developed Fast-VESTAL method is reported as a high resolution source imaging approach which can faithfully recover source time courses and generate accurate statistical maps of source images without signal leakage to other brain areas. To validate its accuracy in localization, the present study was conducted to compare the stationary activations between fMRI and MEG with similar task designs. We aim to prove the superiority of Fast-VESTAL in spatial localization, with reference to BOLD fMRI, over other source modeling methods.

Object naming task was performed by ten volunteers. For MEG experiment, picture stimuli were displayed in a random, non-repeating order. For fMRI experiment,the same dataset was presented in a block-designed paradigm. Same inter-stimulus intervals (i.e., 2s) and tasks were adopted by both modalities for quantification of results. Time-locked MEG data was analyzed using minimum L2-norm and beamformer in MNE software and the Fast-VESTAL method developed by one of the authors. The fMRI data was analyzed using the general linear model approach with random-effects. Our fMRI results are consistent with previous studies. MEG results with traditional methods suffer signal leakage without controlling low p value but the preliminary Fast-VESTAL results show good accordance with fMRI results.

In conclusion, we did comparative studies between fMRI and MEG in task-related responses and demonstrated the precise localization of Fast-VESTAL. We believe that Fast-VESTAL has its superiority in detecting neuronal activity with both high temporal and spatial resolutions. It can be promoted in cognitive research and clinical situations for functional localization.

Kinematic Analysis of Human Gait for Typical Postures of Walking, Running and Cart pulling

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The purpose of gait analysis is to determine the biomechanics of the joint, phases of gait cycle, graphical and analytical analysis of degree of rotation, analysis of the electrical activity of muscles and force exerted on the hip joint at different locomotion during walking, running and cart pulling. Cart pulling length have been divided into frames with respect to time by using video splitter software. Phases of gait cycle, degree of rotation of joints, EMG profile and force analysis during walking and running has been taken from different papers. Gait cycle and degree of rotation of joints during cart pulling has been prepared by using video camera, stop watch, video splitter software and Microsoft Excel. During the cart pulling the force exerted on hip is the resultant of various forces. The force on hip is the vector sum of the force Fg= mg, due the body of weight of the person and Fa= ma, due to the velocity. During cart pulling shows maximum degree of rotation of hip joint, knee: running, and ankle: cart pulling. During walking, it has been observed minimum degree of rotation of hip, ankle: during running. During cart pulling, dynamic force depends on the walking velocity, body weight and load weight. Proper care should take during cart pulling. If the way of cart pulling is changed i.e the design of cart pulling machine, load bearing system is changed then it would possible to reduce the risk of limb loss, flat foot syndrome and varicose vein in lower limb. Keywords- Kinematic, Gait, Gait lab, Phase, force analysis, degree of rotation of joints.

Differential age-related changes in N170 responses to upright faces, inverted faces, and eyes in Japanese children

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The main objectives of this study were to investigate the development of face perception in Japanese children, focusing on the changes in face processing strategies (holistic and/or cinfugural vs. feature-based) that occur during childhood. To achieve this, we analyzed the face-related N170 component, evoked by upright face, inverted face, and eye stimuli in 82 Japanese children aged between 8- and 13-years-old. The N170 signals observed after the presentation of the upright face stimuli were longer in duration and/or had at least two peaks in 8-11-year-old children, whereas those seen in the 12-13-year-old children were sharp and only had a single peak. N170 latency was significantly longer after the presentation of the eyes stimuli than after the presentation of the upright face stimuli in the 10- and 12-year-old children. In addition, significant differences in N170 latency were observed among all three stimulus types in the 13-year-old children. N170 amplitude was significantly greater after the presentation of the eyes stimuli than after the presentation of the upright face stimuli in the 8-10- and 12-year-old children. The results of the present study indicate that the upright face stimuli were processed using holostic and/or configural processing by the 13-year-old children.

Mu rhythm modulation as a neuromarker for socio-emotional interaction

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Background. Humans have evolved in a social environment where interactions with conspecifics constitute an important aspect of daily life. Such interaction is a keystone for successful social bonds and in forming collaborations. An important research question today in the field of social affective neuroscience is whether there is a distinct neuromarker for socio-emotional interaction. In a recent MEG experiment, we demonstrated that this seems to be the case.
Methods. The brain activity of 24 healthy adults was recorded by means of MEG across different conditions of social and emotional interaction. During \"social conditions\" the subject was either instructed to produce the same emotion as the one depicted by the displayed face (\"social emotional condition\"), or to produce the same letter as the one depicted by the face (\"social non-emotional condition\"). Bring \"non-social\" conditions, the subject responded to a letter presented on a screen, either associated with an emotion (\"G\" for happy and \"A\" for angry) and the subject had to produce the emotion (\"non-social emotion condition), or the letter was not associated with an emotion and the subject had to produce the letter (\"non-social non-emotional condition\").
Results. The results show that the Mu rhythm is uniquely modulated by the type of interaction, such that there is a suppression of Mu for social compared to non-social interactions. This suppression was furthermore stronger for emotional compared to non-emotional conditions.
Conclusions. The results thereby distinguish between social, non-social, socio-emotional and emotional interaction, and reinforce the notion of central Mu as a useful neuromarker for social and emotional interaction.

Coil Design for Deep Transcranial Magnetic Stimulation with Improved Focality

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Stimulation of deeper brain structures by transcranial magnetic stimulation (TMS) plays a role in the study of reward and motivation mechanisms, which may be beneficial in the treatment of several neurological and psychiatric disorders. In the last years, a method to stimulate deep brain regions was obtained by a specifically designed Halo-circular assembly coil (HCA coil). It consists of a large Halo coil placed around the head, and a conventional round coil placed at the top of the head. The HAC coil enables the stimulation of the brain at greater depth than is currently achievable with the conventional round coil. However, higher and wider spread electrical fields were inevitably induced under the perimeter of the Halo coil. In order to improve the stimulation focality of HCA coil, especially to reduce the potential disadvantage of stimulating the brain tissue at the back of the head (such as the visual cortex in occipital lobe), a deformed Halo-circular assembly coil (dHCA coil) and a semi-Halo-circular assembly coil (sHCA coil) were developed in the present study. The dHCA coil was composed of a semicircle base portion and a return portion. The base portion was obtained by bending the Halo-coil at a specific position, and the return portion was set 25 cm away from the vertex of the head model. The semi-Halo coil was composed of 5 turns of semi-circular coil which has inner and outer radii of 110 mm and 120 mm, respectively. A circular coil with mean diameter 90 mm and 14 turns was located 100 mm above either the dHCA or sHCA coil. The pulse currents with amplitude of I=5.0 kA and working frequency of 2.38 kHz was fed into each of the coils. The realistic human head model employed in this work was obtained from Virtual Family Project (VFP). The electrical properties of head tissues were modeled using the 4-Cole-Cole method. The magnetic flux density and the induced electric fields in head tissues were calculated using the impedance method. It was observed the field penetration depth in brain tissues was significantly increased by both dHCA and sHCA coils. However both the dHCA and sHCA coils achieve the improved focality of the induced fields in deep brain regions compared to the normal HCA coil. The coil design may offer a new tool for both research and clinical applications for psychiatric and neurological disorders associated with dysfunctions of deep brain regions.

Computational Estimation of The Induced Electric Fields in Visual Tissues in Using Coaxial Circular Coil for Deep Transcranial Magnetic Stimulation

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Transcranial magnetic stimulation (TMS) is a technique for brain stimulation that is able to probe the brain circuitry and network in a non-invasive manner. In the past two decades, there has been a dramatic increase in the usage of TMS for studying the functional organization of the human brain as well as a therapeutic tool to improve psychiatric disease. Stimulation of deeper brain structures by TMS plays a role in the study of reward and motivation mechanisms, which may be beneficial in the treatment of several neurological and psychiatric disorders. In the past decade, there are several coil configurations such as double-cone, H-, crown and Halo coils potentially suitable for deep TMS have been developed. In our recent work, we presented the investigation on the possibility for stimulating deeper brain regions while decreasing the electrical field in superficial cortical regions by employing the coaxial circular coils (CC coil). Better ratio of deep region field relative to field at the shallow areas was obtained for the new coil design. However, since the coils were place around the head, close to both eyebrows, safety concern about the excitation of visual tissues was therefore arisen. This work focused on investigating the induced electric fields in eyeball tissues and optical nerve by using the CC coil. Three circular coils with varied coil parameters carrying different currents were placed around the head at different axial planes. Both top and bottom coils were set at fixed position with current flow in the same direction. The middle coil can be moved freely along the z-axis carrying current flowing in opposite direction. The pulse currents with same working frequency of 2381 Hz were fed into each of the coils. The realistic human head model employed in this work was obtained from Virtual Family Project (VFP). The electrical properties of head tissues were modeled using the 4-Cole-Cole method. Three-dimensional distributions of the induced electric field in head tissues were obtained by impedance method. It was observed the induced electric field in optical nerve is higher than that in eyeball tissues. The potential risk in the excitation of visual tissues in using CC coil in deep transcranial magnetic stimulation can be alleviate by optimization of stimulation parameters.

Change of mind - Decision making in different metabolic states

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We make hundreds of decisions every day with many of these requiring the assignment of values to alternative options, which is highly dependent on current internal and external states. It remains, however, largely unknown how these states are computed and integrated into the valuation system. This is of particular relevance for decisions that we make about food as these decisions are strongly influenced by levels of hunger and satiety. Although the sum of these decisions has considerable health consequences, making optimal food choices appears to be demanding as indicated by the rising obesity rates. Related to this, it is of particular interest that most individuals seem to be able to make health and weight beneficial decisions for the future, but often fail when trying to implement them when making decisions about immediate consumption. It has been proposed that this might be related to an inability to predict in advance the impact of metabolic states on decision-making. In a magnetoencephalographic study, we explored neuronal processes during food choices (binary choice task) and associated value computations (bidding task) for different time delays (future and immediate choices) and metabolic states (hungry and satiated). As expected, subjects valued food higher for anticipated and actual hungry states in comparison to satiated states. They further were more likely to mispredict the future value of food when in different metabolic states for prediction and consumption than when in the same state. Additionally, subjects made fewer health beneficial choices for immediate than for future choices. In a next step, we will explore the neuronal mechanisms of how these internal states are transferred to and change value computation and thus decision making processes. In particular, we expect that expected and current hunger modulate the value computation in the ventromedial prefrontal cortex by different processes involving cognitive and sensory areas, respectively.

Detection of Magnetic Nanoparticles with a Large Scale AC Superconducting Biosusceptometer

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Magnetic nanoparticles are being used in several applications in medicine such as hyperthermia, magnetic particle imaging, *in vitro* and *in vivo* bioassay, and still there are many other possibilities to come as research progress in this field. One crucial step of its use it is the detection of these particles when present in a certain tissue. For *in vitro* bioassay, the sample can be harvested and placed inside the detector in optimal conditions to favor sensitivity. However, for *in vivo* bioassays one has to accept the given conditions. In this study we detect nanoparticles with an AC biosusceptometer having a homogeneous magnetic field with 145μT, provided by a set of rectangular Rubens coils with (2x3) m driven at 10Hz. The magnetization induced in the sample was detected by a second-order axial gradiometer (20 mm in diameter and 40 mm of baseline) coupled to a RF SQUID model 330X (BTi). The magnetic nanoparticles (MNPs) used were manganese ferrite-based surface-coated with citric acid (MnFe -Citrate), dissolved in water at various concentrations. The colloid is stable at physiological conditions. X-ray diffraction confirmed the spinel structure and using Scherrer's relation revealed a particle size of 17.3 nm. The magnetization curve showed a typical superparamagnetic behavior with a specific saturation magnetization of 51.2emu/g, and the stock solution of nanoparticles had a concentration of 23.17mg/ml, corresponding to 1.7 10^{15} NPs/ml. The measurements were made in a volume of 30 ml with dilutions from 20 10 to 100 10 of the stock solution of nanoparticles. Measurements were performed at distances of 1.1 cm; 1.5 cm and 2.5 cm from the top of the sample vial to the closest coil of the gradiometer. The limit of detection (LOD) found were: 8.1 10 NP/ml, 9.5 10 NP/ml and 11 10^9 NP/ml for the distances above. These values suggest that the technique might have interesting applications on real-time *in vivo* detection of nanoparticles after systemic injection.

Effects of low frequencies magnetic field and gadolinium in protein expression, DNA integrity and Caspase-3 detection of embryonic kidney cells (HEK-293T line)

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The low frequency magnetic fields (LF-MF) and MRI contrast agents based on Gadolinium (Gd) had been applied to different cell types. However, the results of the stimulation with LF-MF on cellular systems are controversial. While some studies indicate that the LF-MF stimulates cell proliferation and viability, others show the opposite. On the other hand, some studies consider Gd as a nephrotoxic agent while others consider it harmless. In this study it was analyzed qualitative and quantitative changes at proteins expression and DNA integrity, as well as the measurement of active Caspase-3 contained in human renal cells in culture after stimulation with LF-MF with or without Gd. After having analyzed the exposed cells viability, it did not show a significant variance. There were not changes found in protein expression at the SDS-PAGE as neither were alterations at the DNA integrity shown at the agarose gel. The active Caspase-3 was different in gadolinium and gadolinium + LD-MF groups compared with control group and LD-MF group. Results suggest that an apoptotic process is activated by stimulation with gadolinium and gadolinium + LD-MF.

How the Human Brain Recognizes Text-based Emoticons

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Introduction: An emoticon is a graphic of a facial expression that provides a sender's intention or emotion to a receiver in the absence of non-verbal communication such as body language and prosody. However, the question of how the human brain recognizes emoticons wasn't fully understood. Materials and Methods: Forty healthy volunteers (19 female age: mean ± s.d. =24.03 ± 3.28years) participated in the experiment. *fMRI and MEG experimental design:* Event-related design tasks consisted of 6 conditions: happy emoticons, happy faces, sademoticons, sad faces, scrambled emoticons, and neutral faces. *fMRI analysis:* First- and second-level analyses were performed with FSL'sFEAT. *MEG analysis:* Three distinct components were found in grand mean global field power (GFP) data corresponding to the M100, M170 and EPN to both text-based emoticons and face expressions. Then source analyses were performed on the three MEG components. Source reconstruction was implemented in the MATLAB package Brainstorm (Tadel et al., 2011). Results: *fMRI:* Two-way ANOVA was conducted with type of stimuli (emoticons, faces) and emotional valence (happy,sad, and neutral). Significant main effects of stimuli were found in the conjoined area, lateral occipital gyrus (LOC) and superior parietal lobule(SPL), the V1, the lingual gyrus, bilaterally, the left inferior temporal gyrus, the right ventromedial prefrontal cortex (VMPFC), and the right fusiform gyrus. Significant main effects of emotional valence were found in the inferior frontal gyrus (IFG), the paracingulate gyrus, bilaterally, the left orbitofrontal gyrus, and the left AIC. *MEG:* Overall activity illustrated that the first source activity was estimated to the primary visual cortex at around 80ms (M100) after stimulus onset. This source disseminated anteriorly along the inferior occipito-temporal area, predominantly right side peaking at around 140ms (M170), and further onto the parietal regions at around 220ms (EPN). Time-courses extracted from source maps of the emoticons vs. faces differences also showed a dynamic pattern of activity. Discussion: This study provided a text-based emoticon perception model. The input stimuli were processed first at around 80ms in the primary visual cortex as indexed by M100. Then face-specific appearances were processed in the FFA at around 150ms (M170) especially on the right.

Increasing Resolution in Magnetorelaxometry Imaging using ADMM with Total Variation and Additional Constraints

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The reconstruction of a magnetic nanoparticle (MNP) distribution in a 3D domain, by measuring its decaying magnetic response to the change in an external magnetic field, is a challenging mathematical task. For Magnetorelaxometry Imaging (MRXI) the magnetic nanoparticles in the region of interest are influenced by an external field resulting in an aligned magnetic moment of these particles. Due to the tiny magnetic impact of a single MNP, only the overlay of all provided particles is strong enough to be measured by Superconduction Interference Devices (SQUID) positioned outside the domain. Based on the modeling of these processes we derive a linear system operator A that allow us to calculate the measurement values at the SQUIDs position for a given particle distribution. Due to the non-invertibility of the operator A, the determination of the measurements underlying particle distribution provides an ill-posed problem. Using the theory of inverse problems it is possible to reconstruct a suitable solution, however, especially for high spatial resolutions we receive a highly underestimated problem, so that classic approaches like Least Squares or Tikhonov Regularization are stretched over their limits. Even for low resolutions the reconstructions of the named methods suffer from the lack of information in low-sensitivity areas within the 3D domain. It hence becomes crucial to use appropriate reconstruction models with additional prior information such as total variation regularization. Here primal-dual algorithms like the Alternating Direction Method of Multipliers (ADMM) provide a strong tool using a-priori knowledge and additional constraints on the solution of the reconstruction. With this method we are able to improve the overall quality of the reconstruction and show promising results for real data measurements even for high spatial resolutions.

Magneto-Optical Characteristics of Streptavidin Coated Au/Fe Oxide Shell/Core Nanoparticles for Faraday Bioassay

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Recently, the gold coated magnetic nanoparticles(Au@MNPs) are of interest to researchers because of their unique magnetoplasmonic characteristics. It had been reported that the Faraday effect of the Au@MNPs can be effectively enhanced because of the surface plasmon resonance from the gold shell. Besides, the Au@MNPs are ideal material for biomedical applications because of their high stability and good biocompatibility. In this study, iron oxide nanoparticles were prepared by co-precipitation of Fe(II) and Fe(III) and then the synthesized magnetic nanoparticles (MNPs) were dispersed in 0.1 M Tetramethylammonium hydroxide (TMAOH) solution. Next, the MNPs were stirred with sodium citrate to replace the surface hydroxide ions with citrate ions. Afterward HAuCl solution and hydroxylamine hydrochloride (NH OH·HCl) were added to the colloid to reduce the gold shell on the surface of MNPs. Furthermore, surface modification was used to bind streptavidin (STA) onto gold surface. 11-Mercaptoundecanoicacid (11-MUA) modifies gold shell to carboxylate Au@MNPs. For activating the surface of the gold prior to covalent coupling, N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimidehydrochloride (EDC) was added to enable the reaction of carboxyl groups on the gold surface with the amino groups of STA molecules to form the bioconjugation ofSTA-Au@MNPs. The products was characterized by powder X-ray diffraction (XRD)�transmission electron microscopy (TEM), X-ray photoelectron spectroscopy (XPS), superconducting quantum interference device (SQUID) and UV-visible spectrum (UV-vis). In addition, we measured the Faraday rotation of the Au@MNPs by our home made ac magneto-optical Faraday system and compared the results with MNPs'. Finally, we expect to apply the Au@MNPs to magneto-optical Faraday bioassay.

A sensitive bioassay method based on biofunctionalized magnetic nanoparticles and ac magneto-optical Faraday effect

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In this study, we developed a novel bioassay method based on biofunctionalized magnetic nanoparticles (BMNs) and ac magneto-optical Faraday effect. The Faraday rotation angle is used to study the clustering effect of BMNs under an ac magnetic fields. The core of BMNs used in the experiment is the Fe $_4$ magnetic nanoparticle with a surfactant dextran shell. After surface modification, the antibody of C-reactive protein (anti-CRP) was coated onto the dextran. The ac magnetic fields applied perpendicularly to the sample surface vary from 10 to 100 Gauss with a frequency of 813 Hz. The light source is a diode laser with the wave length of 532 nm. The optical responses of the BMNs fluid were detected by the photo detector and analyzed by the lock-in amplifier. We found that the Faraday effect of phosphate buffered saline (PBS) diluent, CRP antibody, CRP antigen and the conjugation of CRP antibody and CRP antigen are all imperceptible. On the other hand, due to the conjugation of CRP antibody and CRP antigen via antibody-antigen interaction, BMNs aggregate to form the bigger magnetic clusters, which result in the Faraday effect enhancement. The Faraday angle increases during the clustering of BMNs, and reaches to equilibrium in three hours after the mixture of BMNs and CRP antigen at room temperature. The results showed that the clustering of BMNs causes a variation of Faraday rotation angle. We also found that the Faraday angle variance, $\Delta\theta \equiv \theta_{\mathrm{equilibrium}} - \theta_{\mathrm{initial}}$, varies as a function of the concentration of CRP antigen. The detection limit of our Faraday assay system for CRP antigen can be as low as 1 ppb. In this study, we showed that BMNs with ac Faraday effect measurement is a promising tool for highly sensitive magnetic immunoassay.

Exposition of *Saccharomyces Cerevisiae* culture in a Magnetic Field with different frequencies

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The effect on the growth of yeasts Saccharomyces cerevisae was studied. Effects on the growth was induced by a sinusoidal magnetic field at different frequencies: 20Hz, 77.5Hz, 135Hz, 192.5Hz and 250Hz, the intensity of the current was in the range of 1A to 4A, on the haploid yeast strain Saccharomyces cerevisiae BY4741. Magnetic fields were generated by a pair of Helmholtz coils (18 cm in diameter) with 105 turns of copper wire in each and separated 9 cm. *Overnight grown* culture was mixed with clean broth in a proportion of 1:20. After mixing (time T=0 h) the new culture was divided into two Erlenmeyer flasks: one control and the other (experimental) was exposed to magnetic fields during 12 hours in the homogeneous field area of the system. All samples (including the control) were kept at laboratory temperature during exposures (24–26 °C) and the air ventilator maintained the temperature at the place of the sample. Growth was monitored during the exposition by measuring the optical density at 600 nm, every 30min. The data obtained indicates that the change in the frequencies of the sinusoidal magnetic fields induce an increase in the growth velocity of S. cerevisiae.

Terahertz biosensor based on layer-by-layer magnetic–plasmonic nanocomposites

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In this study, Au and Fe nanoparticles were used to deposit Au/ Fe /Au layer-by-layer thin film for Terahertz biosensing. Au and Fe nanoparticles were separately coated on glass substrate surface via (3-Aminopropyl) trimethoxysilane (APTMS). With the amino - carbon bonding chain, gold and Fe nanoparticle layer by layer structure can be formed in this synthesis. The coated substrate can be used as terahertz signal modulator. Afterward, streptavidin was coated on the Au layer by immersion. Streptavidin has a high affinity with biotin. The biotin was dropped on the sample for reaction and the substrate was rinsed with buffer solution. On the other hand, the interaction effect of bio-reaction was Identified by terahertz spectrum measurement. After the conjugation of streptavidin and biotin on the Au surface, the spectrum of the transmitted terahertz signal changed. The stray field of the single-layer Fe broaden the bandwidth of the terahertz spectrum. Meanwhile, signal strength was enhanced by the plasmonic of Au nanoparticles. The variance of the terahertz signal strength can be used to identify the amount of biotin. In this experiment, we demonstrated that the detection sensitivity of the Au/Fe /Au layer-by-layer chip is higher than that of the plated gold layer chip. In this work we showed that the layer-by layer Au/Fe nanocomposites thin film substrate is a promising chip for terahertz bioassay.

Changes of emotional processing in women with primary dysmenorrhea after long-term menstrual pain: an MEG study

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Primary dysmenorrhea (PDM) is one of the most common gynecological disorders in reproductive females. Neuroimaging studies have found brain structural, functional and connectivity alterations in PDM patients. Although possible links between chronic pain and emotion are studied, the effect of cyclic menstrual pain on emotional processing is yet to be unveiled. This study aimed to investigate theta activation, which might be linked to neurogenic pain, to emotionally salient stimuli in women with PDM suffering from long-term menstrual pain.

Our participants were a subset of our multimodal neuroimaging PDM research. We included 86 right-handed PDM subjects (PDMs), who have been suffering from long-term menstrual pain on average for nine years reported, and 92 age-matched otherwise healthy women (CONs) during periovulatory phase (POV; Day 12-14) in this study. Psychological inventories and pain experience were collected. Emotional processing was investigated using neutral, happy, sad, and angry voices from our validated Emotional Prosody Database. The event-related MEG data were collected using whole-head 306-channel MEG (Vectorview, Elekta, Neuromag). Beamforming source analysis within theta band (4-8 Hz) was performed at around 100 ms after stimulus onset. Group differences in each emotion were examined by two-sample t-tests.

PDMs exhibited significantly higher levels of anxiety, depression and pain catastrophizing, along with significantly decreased quality of life than CONs. In general, PDMs showed significantly decreased theta activations than CONs. Decreased activations to sad prosody in PDMs were found in middle frontal gyrus, supplementary motor area, medial orbitofrontal cortex, and dorsal anterior cingulate cortex. Theta activation to angry prosody was found significantly lower in PDMs at middle and superior temporal pole, inferior frontal gyrus, dorsolateral prefrontal cortex, primary somatosensory cortex, primary motor cortex, inferior parietal lobule, and superior temporal gyrus, which are previously reported to be related to emotion and pain processing. Our findings suggest that long-term menstrual pain might serve as a chronic stressor that intertwines PDMs' physical (sensory) pain and emotional processing and hence elevates their anxiety and depression levels.

Magnetic stimulation of human blood: a study of induced electromotive force

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Previous studies about the stimulation of cell cultures with Magnetic field variations in low or high frequencies have shown that are able to evoke effects as proliferation, agglutination, growth alteration or an increase on the cell division number. In this work a comparative theoretical analysis vs. experimental study in human blood stimulated magnetically is presented. Twenty samples of leukoreduced human blood were magnetically stimulated with an alternating magnetic field, which was generated with a Helmholtz coil configuration; this magnetic field induce an electromotive force (emf) in them. Theoretical calculations for the induced emf were performed for a simple model of blood tissue that was magnetically stimulated at different frequencies: 50 Hz, 100 Hz, 800Hz, and 1500Hz, as well as the experimental measurement of them that were done in parallel. Results show a high correlation between theoretical and experimental study. This results could be as a reference for the estimation of the deposited energy in the cells when they are magnetically stimulated.

OMEGA: The Open MEG Archive

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In contrast with other imaging modalities, there is presently a scarcity of fully open resources in magnetoencephalography (MEG) available to the neuroimaging community. Here we present a collaborative effort led by the McConnell Brain Imaging Centre of the Montreal Neurological Institute and the Université de Montréal to build and share a centralised repository to curate MEG data in raw and processed form for open dissemination. The Open MEG Archive (OMEGA, mcgill.ca/bic/resources/omega) is a continuously expanding repository of multimodal data with a primary focus on MEG, in addition to storing anatomical MRI volumes, demographic participant data and questionnaires, and eventually other forms of electrophysiological data such as EEG. OMEGA repository currently houses resting-state MEG and T1-weighted anatomical MRI data (primarily for optimal source imaging) from 97 participants at one or more timepoints (total of 140 sessions), a total volume of ~400GB and has received over 180 user requests since May 2015. OMEGA offers both the technological framework for multi-site MEG data aggregation, and serves as one of the largest freely available resting-state and eventually task-related MEG datasets presently available.
Highlights First open data repository fully dedicated to MEGContains data in raw and processed forms, including source image volumesCurrent focus in on resting-state, but task data can also be contributedSoon: a resource in electrophysiology, including for EEG and cell recordingsOMEGA will continue to expand, with contributions from the scientific community

Reference: G. Niso, C. Rogers, J.T. Moreau, L-Y. Chen, C. Madjar, S. Das, E. Bock, F. Tadel, A.C. Evans, P. Jolicoeur, S. Baillet, OMEGA: The Open MEG Archive, NeuroImage, 124B(1) Jan 2016, pp 1182-1187, ISSN 1053-8119.

AC biosusceptometry to monitor magnetic nanoparticlesin the bloodstream

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Magnetic nanoparticles (MNP)are known for their wide versatility in several biomedical applications. Theyhave been employed on stem cell tracking, cell separation and also astherapeutic agents for drug delivery or hyperthermia. This broad range of possibilitiesis a unique factor that allows their uses on both diagnosis and treatment. Preclinical characterizationof nanoparticles is a crucial step towards clinical applications and hasgarnered great interest from the scientific community. The circulation time ($T_{1/2}$),of MNPs is a parameter of major relevance for *in vivo* experimentation and clinical procedures.Among the current techniques,based on direct measurements that allow *invivo* particle detection, are magnetic particle imaging (MPI) andmagnetic resonance imaging (MRI). These methods, however, presents sometechnical and economic limitations. Thus, there is still an urgent need todevelop new simple and accessible techniques that can provide real-timeinformation and MNP availability for *invivo* applications.In this study, we introduce ACBiosusceptometry (ACB), a simple, portable and accessible tool to assess MNPspharmacokinetic parameters in real time and *invivo*. We applied the ACB to acquire circulation time in bloodstream ofmagnetic nanoparticles (MNP) and the differences due to two coating materials(citrate and albumin). We found a $T_{1/2}$ of 11±3.5 min for the citratecoating and a $T_{1/2}$ of 62±6.6 min for albumin. We found that thisvalue significantly increases after the albumin coating protocol. Our resultsindicate that the ACB system is an effective tool for *in vivo*, real-time MNP monitoring and indicate its use to study thenanoparticles behavior in living animals. Partial financial support from theBrazilian Agencies: FAPESP, CNPq andCAPES

Estimating the electrical conductivity values in the low-frequency domain using induced current MR electrical impedance tomography – a feasibility study on phantoms

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The accurate knowledge of electrical conductivity values of human tissue is essential for correct electromagnetic field calculations such as in EEG source imaging, neurostimulation, wave absorption in the human body and microwave ablation of tumors. At present, the electrical property database based on the 4-Cole-Cole model and created by Gabriel is used worldwide as a reference despite its inaccuracy due to *ex vivo* measurement, inhomogeneity of tissues, etc.

Recently, the induced current magnetic resonance electrical impedance tomography (ICMREIT) has been developed for the non-invasive *in vivo* assessment of conductivity at low frequencies (<10 kHz). Additional currents are induced in the subject by switching the gradient coils of the MR scanner (ECI gradient). The resulting internal magnetic flux densities cause variations of the phase image which is measured by the scanner and used to reconstruct the conductivity distribution. A priori information on the geometry based on anatomical scans is used, together with multiple ECI gradients with different time periods, so that a single parameter per tissue needs to be estimated with conservation of the frequency dependence.

In the past, a numerical study on a 4-layered spherical head model showed the successful reconstruction of the conductivity values. For a given ECI gradient and known tissue properties, an artificial phase difference was generated and acted as \'measurement\'. The feasibility of the ICMREIT technique is now demonstrated with real phantom experiments. Homogeneous cylindrical saline phantoms were constructed and by varying the salt concentration the electrical conductivity ranged from 0.01 to 1 S/m, mimicking human tissues. These values were estimated with ICMREIT and determined as well by measuring the voltage drop across the cylinder and the sourced current flow through the cylinder with electrical probes. Using this approach, this phantom study leads to the experimental validation of the novel technique.

Magnetic nanoparticle imaging by AC Biosusceptometry

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The AC Biosusceptometry (ACB) is a research tool,extensively explored to monitor physiological properties of the gastrointestinal tract and its response to a known drug and/or *in vivo* performance. Here, we describe the application ofan ACB sensor to acquire planar (2D) images of magnetic nanoparticles (MNPs), aiming for *in vivo* monitoring of MNP distribution in animal models and whole body imaging. Our first objective was to evaluate the ACB system spatial resolution, distance sensitivity and stability in discriminating different MNP concentrations and volumes. Using the ACB system, we scanned specific areas containing MNP that will be employed on further *in vivo* studies. We scanned a region containing MNPsamples with volumes ranging from 1 to 10 μL and concentration from 1 x 10 to 1 x10^{12} particles/ml, respectively. For this study, we employed a citrate coated, manganese ferrite (MnFe   ) nanoparticles, with an average diameter of 13 ±4 nm, and saturation magnetization of 264 emu / cm with concentration of 23 mg / ml. The ACB system was associated with a 2D table,which allowed the sensor to perform a 100 cm^2 scan area over the samples‘ surface (over a 1 mm step on both axes). All the signal and image processing were performed on Matlab® (Mathworks Inc). We determined the system spatial resolution by the full width at half-maximum (FWHM) measurement, showing a value of 6.43mm. The sensitivity test showed a detection limit around 5 x 10^9 nanoparticles/ml at a sample/sensor distance of 3mm. Also, as a complementary test, with the objective of performing future *in vivo* imaging studies, based on MNP distribution within organs and regions of interest, we injected three different MNP doses in a pork sausage and employed the same imaging protocol, at a 5 mm distance from the sample. The ACB sensor was able to detect all three spots, containing MNP in the sample,indicating the good sensitivity and promising results of the system for further *in vivo* evaluation.

Altered event-related brain dynamics associated with Posner paradigm in idiopathic REM sleep behavior disorder patients

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Objective: Prior studies have demonstrated decline in visuo-spatial performance in idopathicREM sleep behavior disorder (iRBD) patients. However, electrophysiologic evidence of visuospatial attention in iRBD patients with normal cognition is scarce. In this study, we recorded event-related potential (ERP) data during spatial cuing paradigm by a sample of iRBD patients and compared them to those of age and sex-matched control subjects.

Methods: Fifteen consecutive unmedicatediRBD patients and sixteen age- and sex- matched controls underwent Posner task. Stimulus onset asynchrony(SOA) between the cue and the target was 200ms and 1000ms for each \"valid\" and \"invalid\" conditions. The mean P300 amplitude (400-600 ms), event-related desynchronization(ERD) of alpha (350-550ms) and beta (360-500ms) compared between groups.

Results: Patients with iRBD showed decreased P300 amplitude at parietal electrodes in both \"valid\" and \"invalid\" trials with SOA 200ms(p=0.045, 0.002 respectively) but not with SOA 1000ms. There was significant effect of condition (valid vs. invalid, F(1,21)=25.254, p<0.0001) and condition x group interaction (F(1,21)=5.417, p=0.03)on the P300 amplitude with SOA 1000ms but not with 200ms.Beta ERD showed significantly decreased in SOA 200 ms(F (1,21)=7.984, p=0.01).

Conclusion: Idiopathic RBD patients demonstrated decreased P300 amplitude and beta ERD during spatial cuing task. This study confirms that iRBD also has cerebral cortical dysfunction even with normal cognitive function.

Key Words: REM sleep behavior disorder, event-related potentials, P300, brain dynamics

Refill-free low-noise MEGsystem based on reliquefaction

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PresentMEG system needs weekly refill of liquid helium to cool the low-temperatureSQUIDs. To reduce the maintenance cost for expensive liquid helium, continuous reliquefactionof evaporating helium gas is proposed as a promising solution for an economicMEG system. However, the magnetic and vibration noises from the reliquefactionsystem make the low-noise measurement of MEG signals difficult. The noisesources are compressor, valve motor, and displacer and regenerative material inthe pulse tube. We investigated vibration and magnetic noises at severallocations inside and outside of the magnetically shielded room, and reducedboth noises by shielding and damping. The final noise performance of the MEGsystem shows nearly the same noise level as the direct cooled MEG system, inboth low-frequency and white region. The MEG system is fabricated of compactfirst-order axial gradiometers installed in the vacuum. The reliquefier is madeof 1.5 W pulse tube cryocooler, and the transfer tube from the reliquefierchamber is flexible and inclined down only 3 degree fromhorizontal. Thetemperature of the pulse tube is cooled more than enough to 4.05 K,with zeroboil off of liquid helium.

LifeSpan MEG: Detecting brain activity from babyto elderly with two helmets in single dewar

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We introduce an MEG system capable of measuring MEGfrom baby to elderly population using one dewar and one magnetically shieldedroom. The dewar is horizontal shape with two helmets of differentsizes at both ends for adult and baby, respectively. Each helmet is optimizedfor adult and baby of 3-year old. The axis of helmet is 30 degree fromhorizontal plane that the subject can be measured in comfortableposition for both epilepsy localization and functional mapping.The SQUID gradiometers are in the vacuum space so that the coil is closerto the head surface than the conventional direct cooling. For refill-lessand continuous operation, the dewar is cooled by a reliquefier.

Functional connectivity biomarker for differentiating neocortical epilepsy and mesial temporal lobe epilepsy

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The main aim of the present study is to evaluate whether resting-state functional connectivity using magnetoencephalography (MEG)can distinguish neocortical epilepsy patients with focal cortical dysplasia (FCD) and mesial temporal lobe epilepsy (MTLE) patients with hippocampalsclerosis (HS). We compared resting-state functional connectivity between 43 neocortical epilepsy patients and 46 MTLE (right MTLE = 23; left MTLE = 23) patients, who had histologically proven FCD or HS, respectively. Mutual information values between the 72-predefined sources were calculated. The most informative connectivity with statistical significance across leave-one-out group comparisons were sorted in a descending manner and became candidate feature sets for support vector machine (SVM) learning to identify the optimal group classifier. As results, the optimal SVM group classifier with the top 11 ranked features in the theta and gamma frequency bands distinguished neocortical epilepsy patients with FCD and MTLE patients with HS with a mean accuracy of 86.0%(sensitivity = 84.3%; specificity = 87.9%). Neocortical epilepsy patients with FCD had enhanced connectivity in the theta and gamma frequency bands, which were key features separating patients into neocortical epilepsy and MTLE. We showed the potential of electrophysiological resting-state functional connectivity, which reflect differences of functional brain networks mainly in the theta and gamma frequency bands, as a possible diagnostic biomarker that differentiates neocortical epilepsy patients with FCD and MTLE patients with HS.

MEG cross-frequency analysis in patients with Alzheimer\'s disease

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Neurophysiological changes in oscillatory brain activity in Alzheimer's disease (AD) are well described. Brain oscillations are traditionally subdivided into different frequency bands. Previous studies found slowing of oscillatory activity in AD. However, when only studying the frequency bands independently, one does not take into account correlations between the bands. The relationship between frequency bands can be captured by cross-frequency coupling (CFC). We hypothesize to find CFC disruptions in disease-related brain areas in AD. We recorded resting-state Magnetoencephalography (MEG) data in 27 AD patients and 26 matched controls. We used beamforming to reconstruct time series of neuronalactivation for 90 regions of interest in the automated anatomical labeling (AAL) atlas. Across five conventional frequency bands, functional connectivity between all pairs of MEG channels was assessed using the amplitude envelope correlation (AEC). We constructed an amplitude-based global CFC matrix that also included the single-frequency coupling values. We transformed this global connectivity matrix into a row vector by averaging over columns in the global matrix, which characterizes the average connectivity per brain region. The CFC on regional level were compared between AD and control groups using permutation testing with correction for multiple comparisons using the false discovery rate (FDR). We found significantly (< .05, FDR corrected) lower all-to-beta CFC in AD in multiple brains regions including the left hippocampus and several regions of the default mode network (i.e. the left precuneus and the left and right inferior parietal cortex). In this pilot study, we found that amplitude-based CFC was lower in AD between beta band and all other bands in regions known to be affected by AD-pathology, compared to controls. With regard to previous work, this finding suggests that CFC amplitude analyses contain additional information to single-frequency analyses.

Comparison of Incidental Memory between Alzheimer\'s Patients and Age Matched Controls

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Alzheimer's Disease (AD) is the most common form of dementia. Around 4.6 million new cases are diagnosed each year. Some of the first signs of AD are problems with memory, which is a core feature of Mild Cognitive Impairment (MCI), a hypothetical prodromal state for AD. MCI is difficult to detect; current methods of identification rely upon a combination of family reports, Neuropsychological tests and Magnetic Resonance Imaging (MRI). Behavioural performance on memory tests can be affected by factors such as pre-morbid IQ, motivation, compensation strategies and awareness of memory problems. Furthermore, measures of brain structure are often subtle and difficult to detect using MRI. Functional neuroimaging of brain activity (using measures such as magnetoencephalography (MEG)) may prove more useful as it provides a direct measure of memory, even when participants are not explicitly trying to remember, therefore by-passing many motivation/strategic confounds and providing opportunity to detect discreet changes in cognition relating to neurodegenerative decline.
A MEG based incidental memory paradigm involving scene repetition was used. Repetition is known to activate medial temporal lobe structures using fMRI (Howard et al, 2011), the same structures affected in the early stages of AD (Braak and Braak, 1991). Participation in this task induced a Beta Desynchronisation effect upon scene repetition within a control population (N = 14). The absence of this effect in age-matched early AD patients (N = 13) revealed a potential use of this automatic Beta Desynchronisation response as a neurophysiological biomarker of AD, acting with a combined sensitivity and specificity of 86%.

Reduced Visual Gamma Oscillations in Multiple Sclerosis Patients

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Introduction: Many patients with multiple sclerosis (MS) suffer from cognitive deficits, the origins of which are poorly understood. MRI scans can detect structural abnormalities in the brain such as white and grey matter lesions [1,2], however these do not necessarily correlate with illness severity. In order to gain a better understanding of cognitive decline in MS, insights must be gained into brain function. Here we use MEG to assess brain activity elicited by a visuomotor task and assess differences in the electrophysiological response between healthy controls and MS patients. Methods: 18 patients and 18 age- and gender-matched healthy controls (both groups: 10 females, age 41±12 years (mean ± std)) took part in a visuomotor task. A black and white grating was shown on the screen for 2s and subjects were asked to respond with a button press when the grating appeared. A beamformer was used to identify changes in gamma synchrony (30-70Hz) and the peak locations in visual cortex were used to generate time-frequency spectrograms (TFS) for each subject. To compare the visual response between the two groups, the mean percentage change in the gamma band for each subject was calculated from the TFS plot during the 2s window when the stimulus was on screen. Statistical significance was determined using a paired permutation test. Results and Discussion: MS patients had a weaker gamma response following the presentation of a visual grating compared to healthy controls, with the mean percentage change dropping from 23% for healthy controls to 13% for patients. Our permutation test revealed this decrease was significant ($p = 0.039$). This finding could be related to problems with vision often experienced by MS patients, specifically in optic neuritis in which the optic nerve becomes inflamed. References: [1] Mistry, Niraj, et al. (2011): 1313-1323. [2] Tallantyre, Emma C., et al.(2010): 971-977.

Usefulness of source localization using wide time window and multiple frequency band in ictal MEG

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Purpose: We evaluated the diagnostic value of multiple frequency band MEG source localization for power spectral activity using wide time window during preictal period in relation with surgical outcome, and compared the results with manually selected time and frequency analysis at ictal onset.

Method: Thirteen patients who underwent resective surgery for intractable epilepsy and showed ictal event during MEG recording were selected for the retrospective analysis. Several seconds of preictal and ictal data (15 s, 10 s, 5 s, and 1 s before to 1 s after ictal onset) were localized in multiple frequency band of theta (4–7 Hz), alpha (8–12 Hz), beta (13–29 Hz), and gamma (30–70 Hz) bands using wavelet transformation and sLORETA algorithm. The same source localization analysis was separately performed with manually selected time and frequency. Localization concordance to the surgically resected cavity with various time windows and frequency bands analysis was compared according to surgical outcome, MRI findings, and pathology.

Results: Source localizations of gamma band in time window for 10 seconds period before ictal onset showed best concordance rate to the resection cavity among other frequencies and time windows. Eight of 13 (62%) patients showed sub-lobar concordance in 10 seconds gamma localization, whereas 3 of 13 (23%) showed sub-lobar concordance in the analysis of manually selected time and frequency. In terms of surgical outcome and pathology, 4 of 7 patients with focal cortical dysplasia pathology achieved seizure free outcome. Two of 4 showed no abnormal findings on MRI. All of 4 patients showed sub-lobar concordance, whereas none of remaining 3 showed the concordance.

Conclusion: Gamma source localization of time window of 10 seconds at preictal state may act as potential non-invasive localizing biomarkers of epileptogenic zone in candidates of surgical intervention, especially in case MRI suspected focal cortical dysplasia or even non-leisonal cases.

Differences in resting state connectivity in an injured brain under influence of Zolpidem - a case study.

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The drastic short-term improvement with Zolpidem in symptoms of aphasia and motor deficits in survivors of traumatic brain injury has been well documented. The exact mechanism underlying the temporary effectiveness of the drug is still unexplained. The analysis of the resting state brain network has been shown to provide valuable insight into the functional organization of the brain.

In this case study, we investigate the resting state network using magneto-encephalography (MEG) in a patient suffering with neurological disabilities following traumatic brain injury. The subject, having suffered brain trauma due to an accident, shows prominent difficulties in motor and speech processing. These symptoms are significantly improved upon treatment with a hypnotic drug called Zolpidem (also known as Ambien). MEG recordings of 3 minutes duration have been obtained during no-task resting condition (eyes closed, eyes open) under the influence of the drug Zolpidem and without. Generally, high source activity is seen in the alpha and gamma bands, with a marked decrease in alpha source power with Zolpidem. A connectivity analysis is performed and the differences in the resting state networks are discussed with respect to Zolpidem. This is further compared to the network activity in healthy brains.

Consistency of MEG and fMRI findings in revealing the functional neurocompensatory response in early Alzheimer\'s disease

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Background: Alzheimer’s disease (AD) is the most common cause of late life disability, progressing gradually to affect memory and cognition. Previous studies suggest that in the early stages of the disease process, the brain can respond to the pathological change - the so-called neurocompensatory response with increased brain activity and metabolism in the prefrontal cortex. The present study examined the characteristic Magnetoencephalography (MEG) and functional MRI (fMRI) findings to validate the neurocompensatory response in early AD. Methods: Subjects with mild AD and normal cognition (NC; n=12 in each testing group; age=65-90 years) performed a memory retrieval task by viewing graphical objects and indicating whether an object was previously presented or not. Whole-head MEG and fMRI data were acquired respectively using an Elekta Neuromag system (306 channel optimized to record both superficial and deep magnetic sources) and a 4-Tesla Varian-Oxford human imaging system (22 5mm axial slices with 0.5mm gap). After standard processing, imaging signals were time-averaged for the same task conditions. Differences between conditions were localized respectively using event-related beamformer spatial filter to estimate pseudo t-statistics on MEG, and using a canonical haemodynamic response function fitting to task onset and duration on fMRI, activation maps. Results: Subjects with mild AD showed lower accuracy and prolonged latency than the controls. The AD group showed increased activation in the right dorsal medial portion of the frontal lobe, which was not observed in the NC group. The increased activation of the prefrontal lobe (bilaterally in BA9 and BA46) was associated with performance of the recognition task. Conclusion: The MEG and fMRI data suggest the consistency of the differential involvement of the prefrontal lobe during memory processing by subjects with early AD and with normal aging, confirming the neurocompensatory response.

Spontaneous theta-band cortical rhythms as a sign of dysfunction in traumatic brain injury patients

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Our aim was to evaluate the changes that traumatic brain injury (TBI) causes in spontaneous oscillatory brain activity, and the applicability of these changes as biomarkers of injury in clinical evaluation.

We recorded ten minutes of resting-state magnetoencephalography (MEG) data in both eyes-open and eyes-closed conditions from 27 patients with TBI six days to six months after injury. Twelve of the patients underwent a follow-up measurement at six months. We estimated sensor-level spectra for single subjects and at the group level, and compared them with the average spectra from 139 healthy controls measured previously (Kaltiainen et al., 2016). All patients underwent brain magnetic resonance imaging (MRI) with susceptibility weighted imaging.

There were no group-level differences between patients and controls in the sensor-level spectra. In single-subject spectra, however, slow-wave activity was visible in 9/27 patients, typically at theta (4-7 Hz) band, exceeding +2 SD (standard deviation) limit of the healthy subjects. Out of nine patients with abnormal theta activity, three were without any detectable lesions in MRI.Of the 12 patients that were measured twice, 5 showed abnormal theta activity in the first recording. In three of these patients, the level of theta activity decreased to normal by the second measurement. In addition, one patient had theta activity that did not exceed the +2 SD limit of healthy subjects, but distinctly decreased in the patient's follow-up measurement.

We found aberrant theta-band activity in 9/27 patients compared with our database of 139 healthy subjects, suggesting that similar measurements could be used for objective detection of brain dysfunction in TBI. In four patients, the slow-wave activity was transient and visible only in the first recording, urging prompt timing for the measurements in clinical settings.

Altered resting state network in fibromyalgia based on persistent network homology

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Fibromyalgia (FM) is a chronic widespread pain accompanied by fatigue and tenderness. The underlying mechanism of pain processing in FM is not fully understood, brain imaging studies suggest that central processing of pain stimuli is associated with pathophysiology of pain in FM. Most of the analysis in the brain network have used thresholding, which is operator-dependent. In order to understand the network difference between fibromyalgia (FM) and healthy controls, we employed persistent brain network homology which is a multiple scale network modeling framework generating the brain network at every threshold, thereby inherently thresholding insensitive. Eighteen right-handed fibromyalgia (FM) patients (age: mean = 45, SD = 8.5 years) and Seventeen healthy controls (HC) (age: mean = 45.2, SD = 8.9 years) were recruited. Resting MEG activities were acquired for 200 seconds in an eye-closed condition. The MEG data were filtered into theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz), and gamma (31-48 Hz) bands. We constructed source activities for whole-brain ROI in each frequency band using a beamformer. The functional distance (1 – Pearson's correlation coefficient) within each frequency was calculated between ROIs to construct brain network using persistent brain network homology. Barcode represents the global topological change at every threshold. SLD represents the local network features that show what regions are connected. The slope of barcode in FM patients showed gradual decrease than that of HC in theta band, suggesting that FM patients had slower clustering than the healthy controls. SLD revealed that patients with FM had reduced connectivity within default mode network region in theta bands. FM patients also had decreased connectivity between occipital region and paracentral gyrus in alpha band (permutated p value < 0.001). These findings suggest that the altered DMN network in FM may be involved in the affective processing of pain stimuli.

Magnetoencephalography in insular epilepsy

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The semiology of insular seizures is largely variable and mimics those of frontal, temporal, and parietal lobe epilepsies. Moreover, the eileptiform activity from the insula is nearly impossible to see on the scalp EEG. Therefore, the insular epilepsy is often under-recognized and misdiagnosed, leading to many temporal lobe epilepsy surgery failures. Thus it is critic to apply a diagnostic method that can reliably detect an epilepsy focus in insula. Here we examine the utility of MEG together with the distributed source models in the evaluation of insular epilepsy. We analyzed data from a single 39 y/o female patient who had intractable seizures for 14 years. Her seizure semiology includes vague abdominal pain, followed by excessive sweating and increased heart rate, and asymmetrical hand posture. The patient's MRI was reported as normal; she was monitored for seven days using video-EEG in the adult epilepsy monitoring unit at King Fahad Medical City (KFMC), Riyadh. Ictal EEG showed non-specific slowing in the right frontal area. Simultaneous MEG (VectorView, Elekta-Neuromag) and scalp EEG (19 electrodes) were recorded from the patient in a supine position for a period of 45 minutes. Over 20 interictal events (spikes) have been identified from the MEG and EEG signals. The neural sources of these spikes have been localized using both equivalent current dipole (ECD) model and distributed source models. Most ECDs clustered around the right insular area. However we found also a number of ECDs spread across the frontal, temporal and occipital cortices. Distributed source models consistently localized the sources of the interictal spikes in the insular cortex. Our findings demonstrate that MEG, especially accompanied by an appropriate distributed source model, allows the detection and localization of insular epileptic activity that is undetectable by EEG. Thus, MEG provides important clinical information that can be used to manage patients with insular epilepsy.

MEG may reveal new population of spike in epilepsy with porencephaliccyst/encephalomalacia

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Porencephaliccyst/encephalomalacia (PC/E) is often associated with intractable epilepsy. A Limited number of studies reported Magnetoencephalography (MEG)'s potential to help construct treatment strategy for epilepsies associated with PC/E. We present here simultaneous electroencephalography (EEG) and MEG findings in three adult patients with pediatric-onset epilepsy due to PC/E. There were two types of spikes: one type was detected by MEG only, and the other detected by both EEG and MEG. Both types were seen in all three cases. The MEG unique spikes all formed tight clusters; in contrasts EEG-MEG spikes showed loose cluster in two. Our data suggest that MEG should be considered for epilepsy patients with PC/E to better identify spike populations, as it will affect the interpretation of patient's pathophysiology as well as planning of intracranial electrode placement.

Presurgical evaluation in young children with refractory epilepsy: a pediatric MEG study

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Magnetoencephalography (MEG) is a useful presurgical tool for evaluating epilepsy. MEG can be used in conjunction with clinical electroencephalography (EEG) as a noninvasive method to localize epileptiform generators and detect activity propagation to different locations in the brain. These regions may be used prior to neurological surgery to estimate the epileptogenic zone. Evaluation of epilepsy with MEG in the pediatric population can be improved by using MEG systems optimized for children. We report applications of a new 375-channel whole-head pediatric MEG system ("BabyMEG") for diagnosis of epilepsy. In one case, we characterized multi-focal activity during sleep without sedation in a 26-month old child with cortical dysplasia and infantile spasms, which was pharmacologically refractory. While no ictal activity was present, numerous interictal spikes were observed. The interictal activity was localized using the minimum norm estimate (MNE) source imaging algorithm (http://martinos.org/mne/). In the right hemisphere, multiple foci were observed in the frontal, temporal, and occipital areas; predominantly in the occipito-temporal areas. In some instances, activity in the frontal areas preceded activity in the occipito-temporal areas. In other instances, frontal activity occurred with the occipito-temporal activity. For some of the interictal spikes, activity was observed first in the right and then left hemisphere (latency difference 14-40 ms). These findings indicate multi-focal activity with clearly defined discrete zones in the frontal, temporal, and occipital regions consistent with clinical EEG. Pediatric MEG systems such as BabyMEG can provide complementary data to EEG useful for improving the diagnosis of epilepsy in children.

Mgnetoencephalogram ofdentatorubral-pallidoluysian atrophy

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Rationale: Dentatorubral-pallidoluysian atrophy (DRPLA) is neurodegenerative disordercharacterized by progressive dementia, cerebellar ataxia, involuntary movement,coordination deficit and myoclonic seizure. Some reports indicated that thehabitual seizures of DRPLA are corresponding to the partial seizures by electroencephalogram. Weanalyzed the interictal MEG activities of two patients with DRPLA in order to evaluatethe seizure types.

Methods: The patients underwent MEG using204-channel planner type gradiometers and 102ch magnetometers (Vector ViewSystem, Elekta AB, Stockholm) with a 600 Hz sampling rate. MEG spikesources were demonstrated on individual MRI using a single dipole method toproject equivalent current dipoles.

Results: Case1. A 12-year-old boy. His seizures described as generalized tonic seizure, drop attack andsursumvergence with impairment of consciousness and had been intractable forfive years. At 11year-old, the daily myoclonus began, so we diagnosed as DRPLAwith genetic test. Diffuse hypoperfusion and hypometabolism with each ^{99m}Tc-ECD-SPECTand ^{18}F-FDG-PET were shown inbilateral frontal, parietal and central lobe. MEG dipoles were accumulated at bilateral occipital lobe.

Case2. A 35-year-old male. His seizures described as atypicalabsence, generalized tonic seizure and myoclonic seizure and had been intractablefor 25 years. He was diagnosed as DRPLA by genetic test. MEG showed diffuse andmultifocal spike-waves and MEG dipoles were not accumulated.

Discussion: The MEG findings of Case 1 indicate theexistence of epileptic focus at occipital lobe during initial period of DRPLAthat is well correlated to the previous EEG reports. But the epileptogenicitywould be changed to propagate over the lobes in the latter period of thedisease that the MEG findings of Case 2 demonstrate the diffuse and multifocalspikes. MEG could show the change of epileptogenic focus in patients with DRPLAthat was potentially initiated by neuronal degeneration.

The value of \"negative\" MEG studies: Defining the functional deficit zone using spontaneous MEG in children with intractable epilepsy

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Background: The usefulness of MEG for the definition of the irritative zone through localisation of interictal epileptiform discharges (IEDs) in focal epilepsy is well established. However, IEDs occur infrequently in many patients, and it is not uncommon for MEG studies to turn out \"negative\" because an insufficient number of IEDs could be recorded within a practical amount of time. Objective: We hypothesise that MEG recordings devoid of paroxysmal epileptiform events are not without value, and may in fact serve the secondary purpose of helping define the functional deficit zone. Methods: We computed power in source space within classical frequency bands in spontaneous (task-free) MEG recordings across all healthy controls in the Open MEG Archive (OMEGA) database. Individual source maps were projected into a common space and averaged in order to define a normative map of power distribution. Source space power distributions were then computed in 10 paediatric intractable epilepsy patients, and the healthy control group source map was projected to each individual patient\'s anatomy. Statistical contrast between individual patient power spectra and healthy controls was then undertaken in source space, resulting in contrasts showing areas where individual patients\' brains differed from the norm. Results: Contrasts against controls from the OMEGA database revealed differences in regions corroborating results from interictal FDG PET and SPECT in a subset of patients. The frequency band in which differences were observed depended on the region of functional deficit. Conclusion: Preliminary results suggest that spontaneous MEG recordings can be used to define the functional deficit zone in at least a subset of patients. This could potentially be of value both for indirectly helping in identifying the epileptogenic zone, and for localising abnormally functional cortex. Further study will be needed to characterise the sensitivity and specificity of the proposed method.

Interictal High Frequency Oscillations Detected with Simultaneous Magnetoencephalography and Scalp Electroencephalography as Biomarker of PediatricEpilepsy

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Crucial to the success of epilepsy surgery is the availability of a robust biomarker to identify the epileptogenic zone (EZ). High frequency oscillations (HFOs) have emerged as a potential pre-surgical biomarker for the identification of the EZ in addition to interictal spikes and ictal activity. Although they are promising to localize the EZ, they are not yet suited for the diagnosis or monitoring of epilepsy in clinical practice. Primary barriers remain: (i) the lack of a formal and global definition for HFOs; (ii) the consequent heterogeneity of methodological approaches used for their study; and (iii) the practical difficulties to detect and localize them non-invasively. Here, we present the methodology our group follows for the non-invasive recording, detection, and localization of interictal HFOs from pediatric patients with refractory epilepsy. We report representative data of HFOs detected non-invasively from interictal scalp Electroencephalography (EEG) and Magnetoencephalography (MEG) from two children undergoing surgery. The underlying generators of HFOs were localized by solving the inverse problem and their localization was compared to the EZ as this was defined by the epileptologists. For both patients, interictal discharges and HFOs were localized with source imaging at concordant locations. Furthermore, intracranial EEG (iEEG) data were also available, thus we compared iEEG with the results from non-invasive recordings in order to validate our findings. We found that the HFO localization with MEG and scalp EEG was concordant with invasive methods. To our best knowledge, this is the first study that presents the source localization of HFOs from simultaneous scalp EEG and MEG comparing results with iEEG. Our findings suggest that interictal HFOs can be reliably detected and localized non-invasively with MEG and scalp EEG, and that their use could significantly improve the pre-surgical evaluation for pediatric patients with epilepsy.

Resting-state MEG Reveals Different Patterns of Aberrant Functional Connectivity in Combat-related Mild Traumatic Brain Injury

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Blast mild traumatic brain injury (mTBI) is a leading cause of sustained impairment in military service members and Veterans. However, the mechanism of persistent disability is not fully understood. In the present study, disturbances in brain functioning were investigated in mTBI participants using a source-imaging-based approach to analyze functional connectivity (FC) from resting-state magnetoencephalography(rs-MEG). Study participants included 26 active-duty service members or Veterans who had blast mTBI with persistent post-concussive symptoms and 22healthy control active-duty service members or Veterans. The source time-courses from gray-matter regions of interest (ROIs) were then used to compute ROI to whole-brain (ROI-global) FC for two different measures: 1) time-lagged cross-correlation and 2) phase-lock synchrony. FC analyses were conducted for different frequency bands. Compared with the controls, participants with blast mTBI showed increased gray-matter ROI-global FC in beta, gamma, and low-frequency bands, but not in the alpha band. Sources of abnormal increases in FC were from the: 1) prefrontal cortex (right ventro-medial prefrontal cortex, right rostra anterior cingulate cortex), left ventro-lateral and dorsolateral prefrontal cortex; 2) medial temporal lobe (bilateral parahippocampal gyri, hippocampi, andamygdala); and 3) right putamen and cerebellum. In contrast, the blast mTBIgroup also showed decreased FC of the right frontal pole. Group differences were highly consistent for the two different FC measures. FC of the left ventro-lateral prefrontal cortex correlated with cognitive functioning in mTBI participants. Altogether, our findings of increased and decreased regional-patterns of FC suggest that disturbances in the intrinsic organization of the brain maybe due to multiple mechanisms.

Abnormal cortical source activities in patients with rapid-eye movement sleep behavior disorder during a visuospatial attention task

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Rapid eye movement (REM) sleep behavior disorder (RBD) is a sleep disorder characterized by dream enactment behavior and the loss of muscle atonia during REM sleep. Visuospatial attention deficits in RBD patients have been recognized, however, its neural mechanism remains unknown.In this study, to investigate neurophysiological evidence about the abnormality of visuospatial attention in RBD patients, we analyzed spatiotemporal characteristics of cortical source activities from event-related electroencephalogram (EEG) of normal control and RBD patients during a visuospatial attention task.
Drug-naïve idiopathic RBD patients and healthy controls were involved in this study. Subjects performed Posner's cueing paradigm.The time intervals between cue and target (stimulus onset asynchrony, SOA) were 1000ms.Sixty channel EEGs were recorded during the task.We estimated target-elicited cortical activitiesusing weighted minimum norm estimate from event-related potentials. In addition, we applied weighted phase leg index to observe the theta-band phase synchronizationbetween cortical regions.
In the 150-250 ms period after target stimuli onset, prominent cortical sources were observed at lateral occipital cortexandposterior parietal cortexfor both groups. At the same period,source current density at N2durationwas significantly increasedin invalid condition than valid condition for normal control, but not for RBD patients.Dominant centroparietal connectionswere observed during 200-300 ms for both groups. Especially, frontoparietal connectionswereremarkablystrongerin patients than normal control for both condition.
Several studies reported that increased N2 component for invalid condition reflected the inhibitory of returns (IOR) effects during visuospatial attention tasks. No difference of N2 amplitude between valid and invalid condition and increasedfrontoparietal neural synchronies in RBD patients may reflect a deficit of attentional inhibitory system due to frontal lobe dysfunction.

Modulations of extrinsic and intrinsic connections among neuronal sources during epileptic seizures: an intracranial electroencephalographic study using dynamic causal modeling

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Modulations of synaptic weights that define connections among neuronal sources is one of important mechanisms responsible for seizure initiation. We employed dynamic causal modeling to examine whether extrinsic and intrinsic connections among neuronal sources could be modulated in different aspects depending on the phase of seizure initiation and propagation.
For ictal intracranial electroencephalographic data recorded at 256 Hz sampling rate, two sources were selected according to the features of seizure onset and propagation: (i) S1, the electrode at which seizure activity was initiated and (ii) S2, the electrode to which seizure activity was spread from S1 during seizure propagation. Time series of each source were epoched to three segments, each with 2 s duration, corresponding to three conditions: (i) C1, immediately before seizure initiation, (ii) C2, early phase of seizure propagation (before the spread of seizure activity from S1 to S2); and (iii) C3, late phase of seizure propagation (after the spread of seizure activity from S1 to S2). For C1-C2 and for C1-C3, we identified the best connectivity architecture among the two sources and estimated modulations of connection strengths as the effect of epileptic seizures.
The best connectivity architecture corresponded to the architecture with backward connections from S1 to S2 and forward connections from S2 to S1 for C1-C2, but the reverse architecture for C1-C3. For the best connectivity architectures, seizure activity was explained by changes in extrinsic connections for C1-C2, but by changes in intrinsic connections as well as extrinsic connections for C1-C3. In particular, modulations of intrinsic connections corresponded to a net inhibitory effect. These findings suggest that epileptic seizures could be mediated by modulations of connections within and between neuronal sources as well as changes in connectivity structures among the sources depending on the phase of seizure initiation and propagation.

Connectivity in Language Network after Hemispherotomy

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Hemispherotomy is a surgery isolating a diseased hemisphere, leaving an intact hemisphere connected to the rest of the brain. Now that epilepsy is more and more understood as a result of abnormal network, we could expect a large scale network change after hemispherotomy. Despite that cognitive function including language often improves following hemispherotomy, there have been few studies addressing how this improvement happens. Here we aimed to explain improved language function in a patient after the right-side hemispherotomy through comparing connectivity patterns in the language network before and after hemispherotomy using a magnetoencephalography (MEG) and diffusion tensor imaging (DTI). Overall connectivity increase in the language network measured by a partial directed coherence was obvious after the operation both in the performing and the resting brain. Post-operatively, connectivity strength was strikingly increased at the junction area of the parietal and the temporal lobes and in the inferior frontal gyrus, which have been known as powerful auditory-motor interfaces integrating language-motor information. It is particularly noteworthy that the changed language network resembled the healthy network more than before. This was also supported by the anatomical connectivity reflected in the increased fractional anisotropy in the areas aforementioned. Collectively, we propose that network integrity, both functional and anatomical, contributes to the improvement of language function in our patient. We might expect that the enhanced function was concomitant with the increased connectivity in the language network and with the sharing of more key features with the healthy language network, presumably due to the restored language network, free from the intervention of the epileptiform discharges.This finding provides a unique evidence of unilateral hemispheric reorganization enabling an effective use of the network due to a beneficial surgery, hemispherotomy.

Cortical Dis-inhibition in Chronic Tinnitus: An ERP Study

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Tinnitus, a persistent awareness of an auditory sensation in the absence of any external sound source, is often considered as an auditory equivalent of phantom limb pain. Decades of research have suggested that tinnitus is a result of cortical reorganization and transcranial magnetic stimulation (TMS) is capable of modifying tinnitus perception for a short period of time (De Ridder et al., 2005). Upon hypotheses that cortical dis-inhibition due to cortical reorganization would be stronger in intractable chronic tinnitus, we compared cortical inhibition by TMS between responder and non-responder groups. Magnetic stimulation was administered at a frequency of 1 Hz using Medtronic system (MagPro; Medtronic, Minneapolis, MN, USA). TMS site was individually determined using an international 10–20 EEG system as is proposed in Langguth et al. (2007). Tinnitus severity was quantified using Tinnitus Handicap Inventory Questionnaire(THI, Newman et al., 1969) and responsiveness was determined based on the subjective report of a patient. Data were recorded from 64-channel Neuroscan system (Compumedics, Ltd.) before and after treatment. Electrode impedance was maintained atless than 5 kΩ all the time. Cortical inhibition was quantified using a paired-pulse suppression index (Lim et al., 2015). Prior to any measurements being performed, informed consent was obtained. As shown in Figure 1, our result shows that cortical inhibition was increased in responder group while non-responder group did not show any significant suppression. Moreover, the responder group was marked by relatively stronger inhibition compared to that of the non-responders even before the treatment. From this we might expect that the inhibition index before treatment can be a useful factor for prognostic markers.

Decreased corticokinematic coherence in patients with Friedreich's Ataxia

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Friedreich'sataxia (FA) is a genetic neurodegenerative disorder characterized by aprogressive loss of spino-cortical and spino-cerebellar proprioceptive neurons leading tolimb ataxia and gait instability. This pilot studyinvestigates whether the corticokinematic coherence (CKC) could serve as apotential marker of the degeneration of spino-cortical proprioceptive pathwaysin FA. CKC reflects the coupling between cortical magnetoencephalographic (MEG)signals and movement kinematics and is mainly driven by proprioceptiveafferents to the primary sensorimotor (SM1) cortex. CKC was evaluated using whole-scalp MEG (Elekta,Helsinki, Finland) in 11 right-handed FA patients (8 females; mean age: 29 y, range 9–46y; mean SARA score 21.7, range 14–30.5) and five healthy adultsubjects (3 females; mean age 34, range 30–43 y) performing repetitiveright index-finger flexion–extension movements. Indexfinger acceleration was monitored with a 3-axis accelerometer. Coherent brain areas were identified using dynamic imaging of coherentsources. Non-parametric permutation statisticswas used to assess the statistical significance of local coherence maxima. Movementfrequency (F0) was significantly different between patients and controls (patients 1.4 ± 0.5 Hz; controls 2.4 ± 0.5Hz). Inboth groups, significant coherence was found at movement frequency (F0) and itsfirst harmonic (F1) in the left SM1 cortex but the coherence values weresignificantly lower in patients than in controls (patients 0.08 at F0 and 0.17at F1; controls 0.22 at F0 and 0.31 at F1). This pilotstudy demonstrates lower CKC levels in FA patients compared with healthysubjects. A previous study of ours demonstrated that movement speed does not influencesignificantly the coherence values at F0 and F1 [1]. CKC might thereforerepresent an interesting method to evaluate spino-corticalproprioceptive pathways degeneration in FA.

[1] Marty et al. (2015), Neurophysiol Clin.

Effective connectivity of epileptic networks using intracranial ictal EEG recordings

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Epilepsy is characterized as paroxysmal changes in spatiotemporal dynamic interaction in neural network to generate seizure discharges. Effective connectivity analysis can be applied for epilepsy to provide an essential understanding of the process that regulate seizure activities, especially causal relationship between neuronal sources involving epileptic network. In this study, we investigated the causal relationship of neuronal dynamics involving epileptic seizure events within and outside of the epileptic focus in intracranial electroencephalographic (icEEG) recordings. We analyzed the spatiotemporal dynamics before, during, and after seizures in epilepsy surgery patients who performed presurgical evaluations including icEEG seizure recordings. A directed transfer function (DTF), a multivariate autoregressive modeling (MVAR) technique, based on the concept of Granger Causality (GC) was used to analyze the effective connectivity changes during seizures in seizure onset, early and late propagation channels in 7 different frequency bands; delta (1–4Hz), theta (4–8Hz), alpha (8–13Hz), beta(13–25Hz), gamma (25–55Hz), ripple (80–249Hz), and fast ripple (250–500Hz). To illustrate the spatiotemporal epileptic network in seizure onset and propagation process, GC method was analyzed for 7 different frequency components, respectively. Patterns of effective connectivity abruptly increased even before the ictal EEG onset that was analyzed by expert neurologists using conventional visual analysis, which was more prominent in higher frequency bands such as beta, gamma, ripple and fast ripple. However, causality in slower frequency bands including delta and theta frequencies did not show this kind of increased activity at seizure onset. Also, the directional effective connectivity increased especially in the seizure onset electrodes that was evolved rapidly into the other channels involving epileptic network. In summary, the effective connectivity shows spatiotemporal dynamic patterns before, during and after ictal periods in focal epilepsy patients, especially in higher frequency bands including beta, gamma, ripple and fast ripple. This kind of analysis methods applied to ictal EEGs could provide a fundamental understanding of the spatiotemporal dynamics involving epileptic network.

Corticomuscular Coherence Correlates with Critical Flicker Frequency but not with GABA+/Cr Levels in Patients with Hepatic Encephalopathy

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Hepatic encephalopathy (HE) is a major complication in patients with liver cirrhosis encompassing motor and neuropsychological impairments. In HE patients, neuronal oscillatory activity is globally slowed across frequency bands and cortical subsystems (Butzet al., 2013). For instance, corticomuscular coherence (CMC; Timmermann et al.,2008) and critical flicker frequency (CFF; Kircheis et al., 2002) are decreased in HE patients, with the CFF being a reliable parameter for disease severity in HE. Although current studies indicate decreased occipital GABA+/Cr concentrations in HE patients (Oeltzschner et al., 2015), it remains unclear if changes in CMC are related to sensorimotor GABA+/Cr levels. Here, we investigated the links between CMC, CFF, and GABA+/Cr concentrations in patients with varying grades of HE (minimal HE/manifest HE1) and healthy controls.

43 subjects (age: 58,1 y ± 9,5) performed an upper limb holding task. Neuromagnetic activity was recorded and individual frequencies of maximal CMC and CFF were determined. In addition, GABA+/Cr concentrations were measured in contralateral sensorimotor cortices using magnetic resonance spectroscopy (MRS). To determine the link between CMC, CFF, and GABA+/Cr concentrations, CMC was linearly correlated to CFF and GABA+/CR concentrations. Correlations were corrected for age and gray matter fraction within the MRS voxel.

A significant positive correlation between CMC during stretching of the arm and the CFF was observed (= 0.33, = 0.027). No significant correlation was observed between CMC and GABA+/Cr levels in the contralateral sensorimotor cortex (= 0.035, $p = 0.85$).

The observed linear relation between CMC and CFF tallies earlier findings (Timmermann et al., 2008).The missing link between CMC and sensorimotor GABA+/Cr concentrations may suggest that sensorimotor GABA+/Cr levels do not have a direct impact on CMC or that CMC modulation is mediated by altered neurotransmitter levels in different brain regions.

Late restructuring and atypical development of resting state neural synchrony in autism

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Autism spectrum disorder (ASD) is a common, highly heritable condition associated with abnormalities in brain connectivity. Theories claiming that altered brain network connectivity is a critical factor in ASD have often argued that disconnection between brain areas contributes to ASD symptomatology, although recent findings also report hyper-connectivity. It is possible that findings of hypo- and hyper-connectivity in ASD can be reconciled using a developmental framework. We used resting-state MEG to investigate spontaneous inter-regional neural synchrony from 180 children, teens and adults (89 ASD, mean age=15.6, 70 males; 91 typically developing (TD) controls, mean age=15.6, 73 males). Beamformer analysis was used to reconstruct brain activity from 90 regions of the AAL atlas. Neural synchrony was measured using the phase lag index (PLI) in delta(1-4Hz), theta (4-7Hz), alpha (8-14Hz), beta (15-30Hz), low (30-80Hz) and high gamma (80-150Hz) ranges. We report increased synchrony in gamma frequencies with age in ASD, which was not seen in the TD group, where the greatest age effects were in the alpha band. When PLI was grouped according to the lobes of the brain and analysed by permutation testing, neural synchrony differed between ASD and TD groups in a region- and frequency-dependent manner. Analysis of group differences using the Network Based Statistic revealed over-connectivity in ASD compared to control adults in theta, alpha, beta and high gamma bands and these networks implicated subcortical and frontal-temporal regions involved in socialcognition, with the largest network in high gamma. Our results indicate distinct maturational patterns of spontaneous network synchronization in ASD that is dynamic throughout development and involves restructuring into adulthood.

Comparing phase- and amplitude-mediated intrinsic connectivity networks in mild traumatic brain injury

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Mild traumatic brain injury (mTBI) perturbs resting spectral connectivity, and can affect amplitude coupling and phase synchrony across frequency scales and regions of the brain. These measures are associated with lingering symptomology, known as post-concussive syndrome (PCS). However, the impact of injury on spontaneous 'intrinsic connectivity networks' (ICNs), such as the default mode network, and the oscillatory-mediated coordination of activity in these systems has so far received little attention. Characterising abnormal spatiotemporal organisation of ICNs could help explain PCS and guide precision therapy (such as targeted brain stimulation). Here, we used MEG in 21 participants with mTBI in the sub-acute stage of injury (<3 months post-concussion) and a group of age and sex-matched controls. We acquired 5 minutes resting data at 600 Hz using a 151-channel CTF system. A linearly-constrained minimum variance (LCMV) beamformer was used to derive time-series from coordinates that capture activity in 7 ICNs – the default mode, salience, dorsal & ventral attention, vision, motor, and language networks (48 ROIs in total). Data were filtered in canonical frequency ranges (3-7, 8-14, 15-30, 30-80, 80-150 Hz), and two measures of functional connectivity were computed for all source pairs - phase synchrony using the Phase Lag Index (PLI), and amplitude coupling calculated by the correlation of the amplitude envelope. Between-groups contrasts using non-parametric permutation tests revealed differences in both intra- and inter-network synchrony, in the default, language and attention networks, in the theta, beta and high-gamma bands; only modest differences were observed in amplitude coupling, between language and salience networks, and were confined to the theta band. These observations suggest that concussion perturbs the efficient segregation and integration of spectrally-mediated connectivity within and between intrinsic networks related to psychological sequelae.

MEG/MSI of Epilepsy Patients with VNS implantation: ECD and sLORETA analysis

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Magnetoencephalography has been developed into an effective tool for pre-surgical evaluation in drug-resistant epilepsy patients. In VNS implanted patients, it has been challenging to acquire interpretable data,because of the battery of VNS generating artifacts much stronger than brain magnetic waves. Technologies such as tSSS and SAM has been applied to Neuromag and CTF equipment to improve data interpretation in VNS implantation patients. Using Curry 7, we reanalyzed 13 patients with VNS implantation from Minnesota Epilepsy Group who underwent MEG study with 4DNEUROIMAGING equipment(Magnes 2500). Patients: Five male and 8 female patients (5 to 56 yrs, median 16 yrs) withVNS implantation underwent MEG/MSI study at our institution. Patients' MEG data were recorded with a 148 channel magnetometer whole head system. Twenty-one or64 channel Scalp EEG was recorded simultaneously. The data were analyzed with Curry 7 (Compumedics Inc.). Single dipole model (ECD) and sLORETA were appliedfor data analysis. Results: With ECD model, only 7 of the 13 patients yield localizable information. With sLORETA and ECD combined analysis, we are able to achieve localizable information in 4 of the 6 patients who failed by ECD only analysis. Even among patients with localizable information from ECD model, ECD plus sLORETA analysis provides more reliable information than ECD model only analysis. More details will be presented at the meeting. Conclusion: MEG/MSI is susceptible to metal artifacts. Multi model analysis, such as Combining sLORETA and ECD analysis may improve analysis among patients with VNS implantation .

Dual-modeNoninvasive Brain Stimulation for Post-Stroke Cognitive Impairment

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Objective: We investigated whether dual-mode noninvasive brainstimulation (NBS) using the transcranial direct current stimulation (tDCS) andrepetitive transcranial magnetic stimulation (rTMS) over bilateral dorsolateralprefrontal cortices (DLPFC) is more effective than single rTMS for patientswith post-stroke cognitive impairment.Methods:Twenty-five left-hemisphericischemic stroke patients (mean age 56.7) were recruited within 1 month afteronset. In dual-mode stimulation group, 10 Hz rTMS overthe left DLPFC and anodal tDCS over the right DLPFC were appliedsimultaneously. Single stimulation group underwent 10Hz rTMS only over the left DLPFC. Ten daily sessions were conducted for twoconsecutive weeks. Cognitive function was measuredbefore, after, and two months after the intervention. Results: The accuracy of verbal workingmemory (VWM) was significantly improved over time in both dual-mode and singlestimulation group. The changes in accuracy of VWM were significantly better indual-mode group than single stimulation group after ten sessions ofstimulation. Executive function (trail making test A, B), non-verbal working memory,and attention tests scores were also significantly higher in dual-mode group thansingle stimulation group. However, cognitive function tests at 2 months afterstimulation showed no significant group difference.Conclusions: Dual-mode NBSfor 2 weeks during subacute period of stroke was safe and superior to rTMSalone for improving cognitive function in patients with stroke. However, thiseffect was not maintained until 2 months after stimulation. The method forimproving the effect duration of dual-mode NBS need to be investigated in the future.Acknowledgments This study wassupported by the NRF grant funded by the Korea government (MSIP)(NRF-2014R1A2A1A01005128).

A Study on Interictal MEG Source Imaging in Epilepsy

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Although many antiepileptic drugs have been developed, about 30% of patients with epilepsy are still resistant to drug therapy and a complete remission is rare even in well controlled patients. The most effective treatment for drug resistant epilepsy patients is an epilepsy surgery which resects epileptogenic zone. The outcome of surgery is dependent upon the accuracy of localization of epileptic focus. Magnetoencephalography(MEG) is neurophysiologic technique to detect magnetic field generated by electric current of the brain in noninvasive manner. We performed source localization using MEG on epilepsy patients, and compared its result with presurgical evaluation. MEG recordings were performed on 152 epilepsy patients in a shielded room to detect spontaneous epileptic discharges. KRISS MEG system covering the whole head was used for recordings with a sampling rate of 1024Hz during 60 to 120 minutes. Patients' recordings were performed in sleep deprivation state in order to induce more interictal spikes. Head positions of patients were digitized in a three dimensional coordinate system for co-registration with patients' MRI. After creating each patient's head model with MRI data, we analyzed dipole sources of epileptiform discharges from MEG signals. The results of source locations were compared with presurgical evaluations including electrocorticography(ECoG). In 132 (87%) patients out of 152, MEG spikes were detected. 106 (80%) patients of their source dipoles were well concordant to the final result of presurgical evaluation and partially concordant in 16 (11%). Five (3%) patient's dipole locations were not concordant or uncomparable. Temporal and frontotemporal brain area showed higher concordance rate than other areas. Twenty (13%) patients' dipoles were not visible. In conclusion, MEG source localization is useful method in finding accurate epileptic focus. It is a noninvasive electrophysiological method which ensures high time resolution. This is useful to improve the efficacy of epilepsy surgery and can be used for the research and clinical purpose of other brain diseases and neuroscience research.

Assessing Recovery of mTBI Patients using Functional Connectivity: A Resting State Magnetoencephalographic Study

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In the present study we investigated whether functional connectivity can be used to assess recovery in patients with mild traumatic brain injury (mTBI). We estimated functional connectivity networks from Magnetoencephalographic (MEG) activity obtained at the resting state with eyes closed from 13 mTBI patients and 9 normal controls, on three different visits, scheduled two weeks and four weeks, respectively, after the first recording. We analyzed 3 minutes of artifact free data, filtered between 0.1 and 40 Hz, from 65 channels. Connectivity strength and directionality of connections were measured using Granger causality. Statistical, topological, and spatial filtering was used to identify significant connections, keeping only the strongest links starting with a p-value of 0.01, which was then Bonferroni corrected to account for multiple comparisons. The local and global topological properties of the resulting brain networks were captured by six simple graph features, namely Global Efficiency, Transitivity, Assortativity, Core/periphery partition, and Louvain and Newman\'s spectral community structures. The statistical models tested included group, visit, and interaction of group and visit as fixed effects. Our results showed that only the effect of group was statistically significant, whereas visit was not. Furthermore, four measures were enough to separate the two groups. In general, the control group showed significantly stronger connections between the two hemispheres, whereas the mTBI group had significantly stronger connectivity within the right hemisphere. The same analysis was repeated separately in the delta, theta, and alpha bands with similar results. The lack of significant differences across the three visits for the mTBI group indicates that mTBI subjects are not improving at the rate that we might have expected, confirming our previous findings with EEG recordings on the same study participants and reports that mTBI deficits may persist for years.

Neural correlates of emotional face processing in young adults with Autism Spectrum Disorder

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Impaired social functioning is hallmark of Autism Spectrum Disorder (ASD). The ability to perceive and interpret affect is integral to successful social functioning and has an extended developmental course, thought to reflect protracted maturationin neural areas implicated in emotional face processing. Few studies have focused on investigating the temporal and spatial neural correlates of affect processing and the links between the neural activity and social deficits observed in ASD. This study explored the temporal and spatial properties of MEG activation during implicit emotional face processing in young adults with and without ASD.

Twenty-six young adults with ASD (8F, 26.3+4.2 years) and 26 healthy controls (8F, 26.3+4.1 years) participated. A scrambled pattern (target) was presented rapidly (80ms) alongside an emotional (happy or angry) face on either side of a central fixation cross. Participants indicated the location (right or left) of the target by pressing a response button. 3T structural MRIs were obtained in all participants for co-registration with MEG data.

MEG data were pre-processed and analyzed using SPM12. Emotion-related activation sources for each emotion were estimated using the Empirical Bayes Beamformer. Preliminary analyses indicated that to angry faces, controls showed early (100-150ms) greater right inferior temporal activity relative to adults with ASD. To happy faces, increased right amygdala activity (125-175ms) was seen in controls, compared to the clinical group.

While data analyses are ongoing, these initial findings show early latency differences in both temporal and spatial correlates of neural activity during affective processing exist in ASD in young adulthood. These results will be compared with existing data from our group on this same task in children and adolescents with and without ASD. Investigating atypical patterns of neural activation will aid in understanding the maturation of atypical affective processing in ASD.

Evidence for state dependent direct effects of alpha band transcranial alternating current stimulation

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Introduction: Transcranial alternating current stimulation (tACS) is used to modulate brain oscillations to measure changes in cognitive function. It is only since recently that brain activity in human subjects during tACS can be investigatedObjectives: In the current study we examine entrainment effects caused by tACS at the individual alpha frequency (IAF) in humans.Material & Methods: We analyze magnetencephalographic (MEG) data transformed to source space following a method we recently showed to diminish the tACS artifact, which makes analysis of brain activity during tACS possible. Using source level data from our previous study here we investigate the phase relationship (coherence) between the external tACS and the neural signal in two resting state condition.Results: We find proof of entrainment in visual cortex areas. Interestingly, this entrainment is only significant when subjects had their eyes open; visual areas were not significantly entrained to tACS when subjects closed their eyes. Furthermore, we find considerable variation across subjects in the delay between tACS and the entrained brain activity.Conclusion: In conclusion, tACS at individual alpha frequency entrains brain activity in visual cortices, however, in a state dependent manner as this effect can only clearly be observed with eyes open.

Online State-Dependent Effects of transcranial Alternating Current Stimulation

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Transcranial alternating current stimulation (tACS) enables the direct yet non-invasive modulation of endogenous brain oscillations. It can be used to induce long-term changes in cerebral networks and to draw causal inferences on the role of oscillatory activity in cognitive functioning. However, the mechanisms of action of tACS are not yet clear and the impact of the stimulation can depend on the ongoing brain state. Recent advances in data analysis can uncover electrophysiological human brain signal even during tACS. We registered magnetencephalographic (MEG) brain activity of 17 healthy participants as they kept their eyes open (EO) and closed (EC). They repeated this for three blocks with the application of sham, weak, or strong tACS at the individual alpha frequency. We reconstructed the activity of sources inside the brain from the recorded MEG signal in all stimulation conditions, by means of beamforming. We computed a contrast normalized on power change relative to no stimulation in order to assess the dependency of tACS on EC and EO states. The analysis of resting-state data during different tACS conditions shows that the alpha enhancement driven by external stimulation interacted with the endogenous alpha increase observed from EO to EC. By aligning the frequency space to the individual stimulation, we show how power modulations and phase-synchrony in the harmonics are driven by the tACS. State dependent effects observed at the alpha frequency cannot be explained by phase-alignment as it is generally assumed.

On the relationship between cortical excitability and visual oscillatory responses: a concurrent tDCS–MEG study

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Neuronal oscillations in the alpha band (8–12 Hz) in visual cortex are considered to instantiate ‘attentional gating’ via the inhibition of activity in regions representing task-irrelevant parts of space. In contrast, visual gamma-band activity (40–100 Hz) is thought to represent a bottom-up drive from incoming visual information, with increased synchronisation producing a stronger feedforward impulse for relevant information. However, little is known about the direct relationship between excitability of the visual cortex and these oscillatory mechanisms in humans. We used transcranial direct current stimulation (tDCS) in an Oz–Cz montage to stimulate the visual cortex of 19 healthy volunteers whilst concurrently recording oscillatory activity using magnetoencephalography (MEG). Participants performed a visual task known to produce robust modulations of alpha- and gamma-band response. We found that visual stimuli produced the expected modulations of oscillatory activity – presenting a moving annulus stimulus led to a strong gamma increase and alpha decrease. In spite of signal artefacts introduced by simultaneous tDCS, this pattern was observable both during active (anodal and cathodal) and sham tDCS. However, tDCS failed to produce systematic alterations of these oscillatory responses. The present study thus demonstrates that concurrent tDCS/MEG of the visual system is a feasible tool for investigating visual neuronal oscillations. However, based on the current study, tDCS over the visual cortex does not appear to effectively change the amplitude of stimulus-induced oscillatory responses.

Modulations on cortical oscillations by levodopa and Subthalamic deep brain stimulation in patients with Parkinson's disease, a MEG study

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Objective: To explore the modification to cortical oscillations of PD patients by levodopa and STN DBS. Methods: With Magnetoencephalogram (MEG) detection, we examined the changes in power spectrum of cortical oscillations in the PD patients at the treatment of levodopa and STN DBS respectively. Results: With the administration of levodopa, the increments of alpha and beta band activities in temporal and occipital lobes of PD patients were reversed. STN DBS on significantly raised the power of gamma band of PD patients in frontal and parietal relative to DBS off state.The improvement of motor dysfunction by levodopa treatment was associated to the suppression of alpha and beta oscillations; besides the suppression of alpha and beta oscillations in temporal, the alleviation of motor symptoms by STN DBS on also negatively correlated to the increase of gamma oscillation in frontal cortex.Comparing to the preoperative state, the PD patients at DBS off state displayed reduced beta oscillation in temporal and occipital cortex. Conclusion: The resonance of STN DBS triggered both the augmentation of gamma activities and suppression of alpha and beta activities. Significance: The modulation on the cortical symphony by STN DBS involves in the adjustment of gamma activity.

Keywords: Parkinson's disease; MEG; Deep brain stimulation; Cortical oscillations; Levodopa.

Detecting the Pathway of tACS in Human Brain

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Background: Although transcranial alternating current stimulation (tACS) has been applied in many cognitive studies by manipulating cortical oscillation, the in-vivo distribution of current density in the brain has not yet been fully known. In this study we used a novel MRI sequence named spin-locked rotary excitation(SLOE) which is sensitive to oscillatory magnetic fields of specific frequency to detect the oscillatory magnetic fields created by tACS and thus reveal its pathway in human brain.

Methods: In the present study, a sinusoidal current of 1 mA was applied at 10Hz using a battery-driven stimulator (DC-Stimulator MR, NeuroConn). Stimulation electrodes were positioned over Cz and Oz (International 10/20 EEG System). An OFF-ON block design with an 80 TR interval was used. Two sample t-test was performed to determine the activation map after the data was high pass filtered at 0.01 Hz. For better visualization, the activation map was registered and overlaid to MNI standard brain using FSL.

Results: Significant activations were detected from occipital cortex underneath the stimulation electrodes. High t-values were obtained in cerebrospinal fluid (CSF) than tissues around it, which agrees with the observation in previous tACS simulation study. However, the current in the cable, either from the left or the right side of the brain, caused an asymmetric activation map.

Discussion: Through detecting the oscillatory magnetic fields caused by tACS, MRI can give a spatial distribution map of the tACS pathway. Although the magnetic fields created by the current cable will inevitably interfere with the distributed current near the scalp to some degree, the deep activation underneath the stimulation electrode gives us the confidence of the tACS effect without rather than just previous simulation results. The current results achieved can be a good reference for tACS-MEG/EEG studies model estimation.

Effect of transcranial direct current stimulation on visually induced motion sickness

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Visually induced motion sickness (VIMS) has psychophysiological symptoms that occur when physically stationary individuals view visual stimuli of self motion (Hettinger, 1992). Previous research has demonstrated that features of visual stimuli in virtual reality (VR) can influence the magnitude of VIMS. While visually driven manipulations have widely been investigated, little is known whether direct modulations on visual areas which are associated with VIMS in the brain could manipulate the symptoms of VIMS. In this study, we induced a transient change in brain activities using transcranial direct current stimulation (tDCS) and measured its effect on symptoms of VIMS.

Subjects were divided into two groups depending on their tDCS montage (left V5 anode – Cz reference vs. left V5 cathode – Cz reference). Subjects in the two groups underwent active (2 ▯, 10 min) or sham (2 ▯, 1 min) tDCS in a counterbalanced manner. After the stimulation, they experienced a virtual roller coaster and completed a simulator sickness questionnaire (SSQ). A repeated-measures ANOVA was conducted on SSQ scores with stimulation types (active vs. sham tDCS) as a within-subject factor and groups (cathodal vs. anodal stimulation) as a between-subject factor.

Results showed that a significant interaction between the type of stimulation and the group ((1,5) = .028), indicating that the tDCS effect is greater in cathodal stimulation compared to anodal stimulation. To be specific, the active cathodal stimulation showed the highest SSQ score from the rest of conditions, demonstrating that this montage can exacerbate the VIMS. Also, there was a marginal main effect of stimulation types ($F(1,5) = .059$).

These results suggest that modulating the brain activities can influence the severity of VIMS. In the future study, we will investigate the neural correlates of perceptual changes in VR due to the electric stimulation and narrow down a specific tDCS montage for alleviating VIMS.

Therapeutic Implication of CombinedrTMS and tDCS for Post-Stroke Motor Impairment

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Introduction: Noninvasive brain stimulation (NBS) usingthe repetitive transcranial magnetic stimulation (rTMS) or the transcranialdirect current stimulation (tDCS) were recently adopted for modulating motorfunction of stroke patients. We applied dual-mode stimulation using both rTMSand tDCS over bilateral primary motor cortices (M1) for stroke patients withmotor impairment and compare the effect with that of single stimulation usingrTMS .Methods: Twenty-two subacute stroke patientswhose total Fugl-Meyer Assessment (FMA) score markedunder 84 were recruited in this open-label study. In the dual-mode stimulation group, the 10 Hz rTMS (90% of resting motorthreshold, 1,000 pulses) were applied over the ipsilesionalM1 for 20 minutes with simultaneous application of the cathodal tDCS (2mA) on the contralesional M1 for20 minutes. Single stimulation group underwent 10 Hz rTMS without tDCS. Tendaily sessions were conducted for 2 weeks. Thetotal, upper, and lower scores of FMA were measured before, after, and 2 monthsafter the intervention.Results: The scores of total andupper FMA were significantly improved over time in both dual and singlestimulation group ($p<0.05$). However, therewere significant group and time interaction effects in both total and upper FMA($p<0.05$). Post-hoc study showed that the mean changes in total ($p=0.024$) andupper FMA ($p=0.019$) scores were significantly better in the dual stimulationgroup than the single group after 10 sessions of stimulation.Conclusion: The dual-mode NBS using 10 Hz rTMS and the cathodal tDCS overthe bilateral M1s was safe and superior to 10 Hz rTMS alone for improving motorfunction in subacute stroke patients. AcknowledgmentsThis study was supported by the NRF grant funded by the Koreagovernment (MSIP) (NRF-2014R1A2A1A01005128).

Imaging phase locking dynamics during transcranial alternating current stimulation (tACS) in the MEG

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Transcranial electric stimulation (tES) can affect cognition, behavior and learning. While the underlying neurobiological mechanisms are not well understood, it was suggested that stimulation effects are mainly mediated by modulations of brain oscillations influenced by cortical excitability, or, in case of e.g. transcranial alternating current stimulation (tACS), phase locking to an externally applied stimulation signal. However, a major limitation in investigating the immediate effects of tES on brain oscillations is posed by the strong stimulation artifacts that exceed the biological activity by many magnitudes. In 2013 we have introduced a novel strategy using whole-head magnetoencephalography (MEG) that allows for in vivo assessment of brain oscillations during tES. Using this technique, we recently demonstrated feasibility of millimeter-precise mapping of phase-locked brain oscillations. Another advantage of using such combined tES/MEG approach is the possibility to image phase locking dynamics reflecting physiological processes during the application of tACS. By calculating single-trial phase locking values (SPLV), we image such phase locking dynamics for the first time and show that tACS-related stimulation effects are highly dynamic and brain state dependent. Shedding light on the physiological dynamics during tES might help to better understand the underlying neurobiological mechanisms, and may explain the variability of stimulation effects reported across different studies.

An Innovative Technology to Quantitatively Detect Liver Iron With Ultrasensitive Magnetoelectric Susceptometers

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Iron is a trace mineral that plays a vital role in a human body. Over the past two decades, remarkable progress has been made on the details of the iron absorption mechanism. It is concluded that absorbing and accumulating excessive iron in body organs (iron overload) can damage or even destroy an organ, such as the liver. The concentration and total amount of iron in different tissues are critical parameters that determine the clinical outcome in all forms of iron overload that can be caused by hereditary hemochromatosis, thalassemia intermedia, etc. According to the Centers for Disease Control and Prevention (CDC), even hereditary hemochromatosis alone affects as many as 1 in every 200 people in the U.S. Therefore, it is critical to develop effective means for early and quantitative iron overload detections. Here we report a recent advance in the development of a state-of-the-art biomagnetic liver susceptometry (BLS), utilizing novel magnetoelectric (ME) composites. Our prototype device maintains the ultrahigh sensitivity of ME sensors to detect weak AC biomagnetic signals and introduces a low equivalent magnetic noise of 0.99 nT/rt Hz at 1 Hz under the presence of a strong DC magnetic field (~ 0.05 Tesla). The results, from investigations on liver-tissue-mimicking samples of assorted iron concentrations (known as liver phantoms), indicated its output signals to be linearly responsive to iron concentrations from normal (0.05 mg Fe/g liver phantom) to 5 mg Fe/g liver phantom iron overload level (100X overdose). It was demonstrated that our device not only reached an equivalent sensitivity of the conventional BLS but also achieved dramatic reductions in both its size and costs. The results here open up many innovative possibilities towards compact-size, portable, cost-affordable, and room-temperature operated medical systems for quantitative determinations of liver iron. Considering the wide presence of biomagnetic signals in human organs, the potential impact of such biomagnetic devices on medicine and health care costs could be enormous and far-reaching.

Magneto-Trichography: Magnetic Fields Produced by Human Hair Follicles

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We had previously verified that healthy human hair follicles produce a sizable DC (direct current) in the scalp when subjected to mild pressure, first reported years ago by one of us (Cohen) using only a single gradiometer. We here report further studies of this phenomenon,using an advanced system.

Our motivation in this work is twofold: 1. This DC in the scalp significantly contaminates or even masks the important detection of DC from the brain. 2. DC in the human body generally is increasingly of interest, because it has a role in signaling and healing.

For our DC detection system, we continue to use the 204 planar gradiometer outputs of our Elekta MEG system, where DC in the scalp can be directly seen online as a map of arrows, looking down on the head. That is, we have performed an online inverse solution to approximately show the actual DC. For a measurement, the subject first rests his or her head outside the helmet, and the arrows are zeroed. Then the subject puts his head into the helmet, lightly presses a designated part of the head against the inner helmet, and the new arrows are seen recorded, all in a few seconds.Our method is rapid, using only a single out-in motion. In our present effort, after about 30 sessions with a variety of subjects, we readily reproduce that old follicle effect, but now simultaneously looking over the whole head, where the arrow pattern due to pressing is seen to be quite dipolar. Subjects with inactive hair follicles show much less DC, from a variety of non-scalp sources including the mouth. Recently, as one of various experiments to understand the detailed follicle source, we created an "ion wind" in the scalp, by passing an external DC from ear-to-ear, seeking to influence the follicle source. This was surprisingly found to have no effect.

All in all, we believe the source to be the arrector pili muscle, attached to each follicle. We call this magnetic phenomenon "magneto-trichography", where tricho is Greek for hair.

The Potential of Optically-Pumped Magnetometers for Magnetoencephalography: a Simulation Study

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Introduction

Despite its unique potential, magnetoencephalography (MEG) remains limited by both the inherently small magnetic fields generated by the brain and the relatively large scalp-to-sensor distance. The scalp-to-sensor distance is large due to the requirement for superconducting quantum interference devices (SQUIDs) that operate at low temperature. However, this limitation could be overcome by using optically-pumped magnetometers (OPMs), which have the advantage that they can be brought to within few millimetres of the scalp, thus potentially offering increased sensitivity.

Methods

Using forward and inverse (beamforming) simulations, we quantified the advantages of a hypothetical simulated OPM system (sOPM) over a simulated SQUID system (sSQ), the latter being based upon a CTF MEG device. We compared both systems in terms of sensitivity, by calculating the ratio of forward field norms; reconstruction accuracy (with and without simulated error on the forward fields), by correlating simulated and beamformer-reconstructed dipole time courses and spatial resolution, by assessing separability of dipole pairs.

Results and conclusion

The sOPM system offers a fivefold increase in sensitivity for most of the cortex for an adult brain. Clear improvements in reconstruction accuracy are shown: the average temporal correlation increases from 0.87 (sSQ) to 0.98 (sOPM). However, we also show that such improvements depend critically on forward model accuracy; indeed, the reconstruction accuracy of the sOPM system only outperformed that of the sSQ when forward field errors were below 5%. The sOPM system also shows marked improvement in spatial resolution: separability is reduced from 6.3 mm (sSQ) to 2.5 mm (sOPM). Overall, our results imply that the realisation of a viable whole-head, multi-channel OPM system could generate a step change in the utility of MEG.

Room Temperature Magnetoencephalography using Optically-Pumped Magnetometers

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Introduction

Significant advances in the field of quantum sensing mean that magnetic field sensors, operating without cryogen, are now able to achieve sensitivity (10 fT/√Hz) comparable to that of superconducting quantum interference devices (SQUIDs). This has opened up the possibility of magnetoencephalography (MEG) with a greatly increased flexibility of sensor placement and lower cost. Furthermore, these new sensors can be placed directly on the scalp surface giving a theoretical fivefold increase in the magnitude of the measured signal.

Methods

Using median nerve stimulation, we recorded MEG data with a single optically-pumped magnetometer (OPM), and repeated the experiment in a SQUID-based MEG system (CTF MEG) for comparison. The OPM was used in combination with a 3D-printed head cast designed to accurately locate and orient the sensor relative to the subject's brain anatomy. Since the OPM is configured as a magnetometer (rather than a gradiometer) it is highly sensitive to environmental interference. This problem was addressed by using simultaneous SQUID reference magnetometer recordings to facilitate synthesised gradiometry.

Results and conclusion

We recorded both evoked (phase-locked) and induced (non-phase-locked oscillatory) stimulus-related changes, with OPM signals exhibiting approximately five times the magnitude and twice the signal-to-noise ratio (SNR) of the equivalent SQUID metrics. These OPM measurements, coupled with the accurate knowledge of sensor placement (due to the head cast) allowed us to localize the N20 evoked response to primary somatosensory cortex. Our results highlight the possibility of a new generation of wearable, cryogen-free MEG systems providing unprecedented SNR.

In vivo and *in vitro* magnetic recordings of neuronal activity with GMR sensors

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Electrical activity of neuronal cells generates the magnetic fields recorded at the macroscopic scale in magneto-encephalography (MEG). This technique uses Superconducting Quantum Interference Devices (SQUIDs) cooled down to liquid helium temperature (4.2K), which imposes a distance to the cortical surface and thus limits the spatial resolution to several mm . Direct experimental access to the local sources of the magnetic signals would represent an essential tool to interpret their macroscopic counterpart. We report on the development of micron-sized non-cooled magnetic sensors based on the Giant Magneto-Resistance (GMR) effect. This technology provides highly-sensitive sensors in the sub-nanotesla range, while allowing an adaptable shaping to any type of biological preparation.

We performed the first invivo magnetic recordings of neuronal activity in the visual cortex of cats with magnetrodes, specially developed needle-shaped probes carrying 4x30 um^2 GMR sensors. We also demonstrate the ability of this technology to record locally biological magnetic fields generated by action potential (AP) in adult mouse neuromuscular preparations in vitro. Considering the size of the muscle (9 mm long), we designed three aligned sensors of 1.7x0.4 mm^2 to measure simultaneously the field generated by axial currents flowing through the fibers. The temporal pattern of the AP magnetic signature and its amplitude (2.5 nT_{pp}) are fully consistent with electro-physiological characterization and computer simulations. Those findings open the way to reference-free and contact-free investigation of neuronal currents and might represent a new fundamental tool to investigate the local sources of macroscopic MEG signals.

Innoccuous alginate-based hydrogels for rapid EEG monitoring and cleaning

Patrique Fiedler [1,2*], Paulo Pedrosa [3,4], Lorenzo Schinaia [2,5], Beatriz Vasconcelos [3], Ana C. Martins [3], Maria H. Amaral [6], Silvia Comani [2,5], Jens Haueisen [1,7], and Carlos Fonseca [3,8*]

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Analysis of the human brain function is increasingly important in clinical and non-clinical applications like neuro-rehabilitation, sports science, and brain-computer interfaces. Conventional EEG pastes are often inapplicable due to risk of allergic reactions, paste running/spreading, and extensive preparation/cleaning requirements.

We propose novel, innocuous alginate-based hydrogels, specifically developed for sensitive skin and designed to minimize cleaning efforts. We studied the optimization of the gelation time, analysed the electrochemical characteristics, and compared simultaneous in-vivo EEG recordings on three healthy subjects.

Adaption of gelation time to the application requirements is possible, as it linearly decreases with increasing calcium sulphate/alginate molar concentration ratio. At 0.5 Hz the impedance varies from ~110 Ω.cm to ~100 Ω.cm . Potential drift of both electrolytes stabilize after 5 min. Electrochemical noise ranges from ~0.24 µV /√Hz to 0.3 µV /√Hz at 0.5 Hz. Simultaneously recorded EEG signals using hydrogels and conventional paste exhibit very similar results. RMSD varies between 5.1 ± 1.1 and 5.6 ± 1.0 µV for spontaneous EEG with eyes closed and eye blink recordings, respectively, while correlation varies between 60.4 ± 7.2 and 73.3 ± 8.9. The power spectral densities overlap each other for frequencies above 10 Hz with a clear alpha activity peak during closed eyes. Visual evoked potentials do not show substantial differences in time and spatial domain or SNR. After taking off the cap, the hydrogel positions are free of remnants or can easily be cleaned, while conventional paste requires extensive hair washing.

The electrochemical characteristics of the proposed hydrogels are suitable for EEG applications and no remarkable differences in the EEG signals were observed in time, frequency and spatial domains. In conclusion, we consider the novel hydrogels to be suitable for rapid EEG with considerably reduced cleaning efforts.

Active magnetic shield for optical neuromagnetic measurements

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Optically-pumped magnetometers (OPMs) operating in the spin-exchange relaxation-free regime are emerging as a promising alternative to SQUIDs for recording magnetic fields generated by the human brain. However, these OPM sensors can only operate at very low absolute magnetic fields (typically < 2 nT) and therefore efficient shielding against the ambient DC magnetic field is required. The remanent field in a typical passive magnetically shielded room employed in biomagnetism often exceeds the limits of these new magnetometers.

Here, we set up a suitable ultra-low-field environment for using OPM sensors in a standard magnetically shielded room. First, the magnetic fields inside the two- and three-layer shielded rooms of Aalto University were surveyed and then a movable lightweight active compensation system for further reducing the fields was built.

Without compensation, the measured remanent magnetic fields were on the order of 100 nT and 5 nT in the two- and three-layer rooms while the gradients were about 40 nT/m and 5 nT/m, respectively. In both rooms, low-frequency field drifts were approximately 1 nT during a measurement period of 200 s.

The constructed compensation system consists of six computer-controlled coils, which can produce homogeneous fields and diagonal first-order gradients. In addition, the feedback loop of the system allows using same OPM sensors both for compensation and brain measurement.

With the constructed compensation coil set, the static field could be reduced by a factor of better than 12 in a head-sized volume. The feedback loop of the compensation system was also capable of locking the field to zero at the sensor site and could also remove the low-frequency fluctuations in the field.

We suggest that neuromagnetic measurements with optically-pumped magnetometers should be feasible in standard shielded rooms by utilizing the constructed compensation system.

Visualization of electrophysiological activity in cervical spinal cord and spinal nerves by magnetospinography

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Background:Conventional electrophysiological diagnostic techniquesofcervical spine such as somatosensory evoked potentials, electromyography, and motor evoked potentials cannot be used to diagnose detailed lesions of the spinal cord or spinal nerves. Although nerve potential recordings using the inching technique can be used to reveal the position of lesions, electrodes must be placed close to the spinal cord to obviate distortion of currents by bone and other tissue. Thus, this invasive technique is typically used for only intraoperative measurements.We have developed Magnetoneurography of the spine (magnetospinography, MSG) and here we visualized neural activity in the cervical spine by MSG following median nerve stimulation.

Methods:All recordings were performed in a magnetically shielded room using a newly developed 120-channel magnetospinograph system.Neuromagnetic fields in 10 healthy subjects (20 nerves)were measured at the dorsal neck surface in response to surface stimulation(3Hz) of the median nerve at the elbowand 2,000–4,000 responses were averaged.Evoked action currents were computationally reconstructed by a spatial filter, recursive null steering beamforemer and the estimated electric current map was superimposed on X-ray images of the cervical spine.

Results: Neuromagnetic fieldswere successfully recorded in all subjects. Estimated currents entered the spinal canal from intervertebral foramina between C4/5 and Th1/2. Then these currents propagated caudal to cranial at 53.3 m/s to 120 m/s (mean, 73.0 ± 15·8 m/s).

Discussion:We demonstrate for the first time that MSG with high spatial and temporal resolution can visualize electrical activities of cervical spinal cord and spinal nerves in response to non-invasive peripheral nerve stimulation. MSG has potential clinical use for the noninvasive functional assessment of the spinal cord and the spinal nerves.

Quantifying the benefit of high-T_c SQUID-based MEG: comparison of three practical layouts

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Commercial MEG systems are the state-of-the-art in functional neuroimaging spatio-temporal resolution; however, the sensors on which they are based have not changed significantly since the 1990s. New sensors for MEG, e.g., high- SQUIDs, optically-pumped magnetometers (OPMs), and giant magneto-resistance-based hybrid magnetometers, are of increasing interest because they enable reduction in head-to-sensor standoff and less extreme operating temperatures than conventional MEG sensors. High- SQUIDs and OPMs have been used for proof-of-principle MEG recordings [1,2]. However, such studies fail to demonstrate the neuroimaging advantage of these technologies in full-head systems as compared to the state-of-art.

Theoretical studies [3,4,5] pave the way for an evaluation of new sensors in realistic full-head arrays while demonstrating their advantages and guiding the practical design of next-generation MEG systems. We present such a comparison of several high- SQUID-based sensor arrays and the standard Elekta Neuromag® magnetometer array in MEG recordings on an adult and a 2-year-old child. Realistic noise levels, sensor geometries, and array designs are based on ongoing developments in our lab. Realistic head models were obtained via FreeSurfer-based [6] segmentation of MR images and MNE-based [7] forward calculations.

We verify a previous estimate [3] i.e., a high- SQUID-based MEG system can extract at least 40% more information as compared to Elekta Neuromag® in recordings on an adult. We furthermore estimate at least 70% more information is available to a high-T_c SQUID array in MEG recordings on a 2-year-old child.

[1] Öisjöen et al., *Appl. Phys. Lett.* 100, 132601 (2012)[2] Sander et al., *Biomed. Opt. Express.* 3:5, 981 (2012)[3] Schneiderman, *J Neurosci. Methods* 222, 42-46 (2014)[4] Luessi et al., *Biomag2014*, P2-027[5] Iivanainen et al., *Biomag2014*, P2-051[6] Dale et al., *Neuroimage*, 9, 179-194 (1999)[7] Gramfort et al., *Neuroimage*, 86, 446-460 (2014)

Development of a 7-channel High-T_c MEG System

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Over the last 40 years MEG has become avaluable tool in neuroscience. However the use of liquid helium for cooling ofthe low- SQUID sensors instate-of-the-art MEG systems brings several disadvantages. Apart from high costand dependence upon helium as a finite resource, it limits the minimum distancebetween the sensors and the subject's head. Previous works have shown that bycoming closer to the head, a dense array of comparatively noisy sensors cantheoretically outperform state-of-the-art low- SQUID systems [1,2]. Our aim is therefore to build an"on-scalp" MEG system with significantly reduced sensor-to-scalp distance. Our group has already performed "on-scalp" MEGmeasurements with single-channel high- SQUID cryostats [3]. We are currently developing a 7-channel high- SQUID- based MEG system ina single cryostat. The system uses SQUID magnetometers made from thin YBa Cu $_{7-x}$films on 10 mm × 10 mm bicrystal substrates. The cryostat is comprised of aliquid nitrogen dewar in a vacuum shell. For optimal thermal connection theSQUIDs are placed on a sapphire disk that is in contact with the liquidnitrogen bath. The sensors are arranged in a dense hexagonal pattern with 2 mmseparation. To match the average curvature of the head the sensors are alignedto the surface of a sphere with 80 mm radius. A thin, transparent window isbuilt into the outer shell of the cryostat above the sensor array. The heightof the window can be adjusted to achieve distances between the sensors and roomtemperature of less than 3 mm. With additional pumping, the cryostat reaches anoperating temperature of 68 K at the sapphire disk with a temperature stabilityof 0.1 K. It can hold this base temperature for more than 24 hours. We will present the progress of development andtesting of our 7-channel MEG system.

[1] Schneiderman, *J Neurosci.Methods* 222, 42-46 (2014)[2] Luessi et al., *Biomag 2014*,poster P2-027 (2014)[3] Öisjöen et al., *Appl. Phys.Lett.* 100, 132601 (2012)

High-T_c SQUID magnetometers for on-scalp MEG

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On-scalp MEG systems based on a dense array of high- magnetometers with noise levels of 50 fT/√Hz can theoretically outperform a state-of-the-art low- system [1]. This is possible due to the one order of magnitude reduced scalp to sensor distance, even though the individual sensors have higher noise levels. Our group has successfully made MEG measurements with single high- $_c$ SQUID magnetometers [2] and is currently developing a prototype 7-channel on-scalp MEG system. The magnetometers are based on YBa Cu $_{7-x}$ grain boundary Josephson junctions and are fabricated on 10 × 10 mm^2 SrTiO bicrystal substrates. They will be packed inside a single 7-channel liquid nitrogen dewar with a gap of 2 mm between the sensors and placed as close as 3 mm from the scalp. One key issue with the integration of several magnetometers into a dense array of sensors is the crosstalk between neighboring sensors arising from the feedback scheme used for the read-out [3]. We are therefore testing different feedback options to see their effect on sensitivity and crosstalk. Possible approaches are standard external feedback coils, on-chip superconducting feedback coils, and direct injection into the SQUID loop. We will present magnetometer designs with the different feedback options, the fabrication process, characteristic parameters of the individual SQUIDs including their noise figures, and an analysis of the performance of different feedback options. We are also exploring alternative approaches to improve the sensitivity of high- $_c$ magnetometers, e.g., via increasing the effective area with multilayer flux transformers [4] and reducing the magnetic flux noise with nanoSQUIDs [5].

[1] J. F. Schneiderman. *J.Neurosci. Methods* 222, 42-46(2014)

[2] F. Öisjöen et al., *Appl. Phys. Lett.* 100, 132601(2012)

[3] M. I. Faley et al., *IEEETrans. Appl. Supercond.* 25, 3(2015)

[4] M. Chukharkin et al., *Appl. Phys. Lett.* 101, 042602(2012)

[5] R. Arpaia et al., *Appl. Phys. Lett.* 104, 072603 (2014)

Measuring Long-Lived Magnetisation using a Magnetoencephalography (MEG) System

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Introduction: A long lived magnetisation has beenobserved when a magnetic field is applied to human tissue. This type of magnetisationhas previously been seen in post-mortem studies of tissue samples from various organs (Kirschvink etal. PNAS 1992; Grassi-Schultheiss et al. Biometals. 1997; Sant'Ovaia et al. Biometals2015)and has been attributed to deposits of magnetite, $Fe_{\ \ 4}$ howeverfurther studies are required since the mechanisms to explain the existence ofthis form of iron oxide in human tissue are unknown. This is of interest due tothe suggested link between irregular concentrations of magnetite and disease.

Methods: To study the long lived magnetisationof small biological samples, a system consisting of an electromagnetic coil (500turns, 20mm inner diameter, 30mm length) powered by a programmable signal generator and audio amplifier has beendesigned. This allows a precise control over the duration and amplitude of botha magnetisation pulse and a decaying-sinusoid, demagnetisation waveform. Thissystem has been tested by inducing and removing an isothermal remnantmagnetisation (IRM) in small (~4g, 3cm) a sample of blackpudding. Since the magnetic fields generated by the IRM of these samples is onthe order of pico-tesla, a superconducting quantuminterference device (SQUID) gradiometer located in a MEG device has been usedto probe the induced magnetization.

Results and Conclusion: The system is able to producepulses and linearly-decaying sinusoids with amplitudes of up to 300mT anddurations of up to 500ms. Our results show that the system was able to reliablymagnetise black pudding, yielding typical peak fields of 25pT when the samplewas placed at the surface of the MEG helmet and the measured IRM was comparableto measurements carried out on post mortem samples in previous studies. Theseresults show the effectiveness of our system and further testing will involve measuringthe long-lived magnetization of a finger.

Uninterrupted noise-free operation of a magnetometer-based MEG with a closed cycle helium recycler

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We will present continuous uninterrupted operation of zero-boil off magnetometer-based whole-head magnetoencephalography (MEG) systems using a closed cycle helium recycler. The recycler, having a 2-stage 4 K pulse-tube cryocooler, was mounted on the roof of the magnetically shielded room (MSR), housing a 375-channel, whole-head pediatric MEG system ("BabyMEG") (Okada et al submitted). A flexible liquid helium (LHe) return line attached to the bottom of the cryocooler is inserted into the fill port of the MEG system in the MSR through a slotted opening in the ceiling. The helium vapor from the MEG vent is captured through a line that returns the gas to the top of the recycler assembly. A high-purity (99.9995%) helium gas cylinder connected to the recycler assembly supplies the gas,which, after it is liquefied, increases the level of LHe in the MEG system during the start-up phase. No storage tank for evaporated helium gas nor a helium gas purifier is used. The recycler is capable of liquefying helium with a rate of ~17 L/d after precooling the MEG system. It has provided a fully maintenance-free operation under computer control for more than 1 year. Vibration and acoustic noise of the recycler are dampened to an ultra-low level to enable uninterrupted operation during MEG measurements. The synthetic gradiometers taking advantage of the 2-layer sensor array design of the BabyMEG reduce the recycler noise below the instrumentation noise level. This new capability introduced by the helium recycler greatly lowers the operating cost and increases the versatility for MEG for wider utilization.

Detection of magnetic signals from the spinal cord using a single channel MEG sensor

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Spinal cord disease and injury associated with partial and full paralysis of limbs lead to disruption in current flow along the spinal column. There are limitations in commonly available technologies for directly characterizing the functional capacity of an injured or compressed spinal cord. Until recently, the use of MEG to detect spinal cord activity has been largely overlooked. Recent work by Adachi, et al. have demonstrated the signals can be detected using a multi-channel purpose-built magnetospinography system. We utilized a tibial nerve stimulation paradigm to examine the feasibility of detection using a commercial single channel CTF MEG system. The sensor was a hardware third order gradiometer with a 25.4 mm detection coil located 9.8 mm from the outside surface of the dewar. The system was placed inside a 2-layer mu-metal shielded room. Two volunteer participants underwent tibial nerve stimulation of the right foot, which was repeated over ten separate days. The sensor was placed against the lumbar spine at various locations. Between 4,000 and 45,000 epochs were recorded in blocks of 10 seconds stimulus on and 5 seconds rest. A sample rate of 19,200 Hz and anti-aliasing filter of 9,600 Hz were used. The data were high-pass filtered in post processing at 1 Hz. The data were segmented into a pre stimulus interval from -20 to 0 ms and post stimulus interval from 5 to 25 ms. The pre and post stimulus intervals were statistically compared across epochs using paired-sample t tests at every time point. A cluster-mass permutation correction was used to account for multiple comparisons. The results indicated significant differences ($p<0.05$) for both participants between 14 to 16 ms and at 23 ms. These results are consistent with previously reported findings using EEG. Our results provide additional confirmation that magnetic spinal signals can be detected using MEG and provide evidence for the use of MEG in functional spinal cord applications.

Evaluating eyes open versus eyes closed resting-state in Schizophrenia MEG datasets through spectral analysis and functional connectivity

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Resting-state oscillatory findings have been inconsistent in schizophrenia EEG and MEG imaging studies, partially due to the heterogeneity in data collection protocols. This data heterogeneity poses a problem when sharing, reusing, and merging datasets. Here, we performed secondary data analysis of previously collected schizophrenia datasets to directly compare eyes opened versus eyes closed data from two separate resting-state studies. The goals were: 1) to examine spectral content and functional connectivity in two different arousal states to determine neurophysiological-based markers of normal activity vs abnormal activity found in schizophrenia, and 2) to evaluate reliability of group results across resting state protocols. MEG data from patients with schizophrenia (n=71) were age-gender matched with healthy controls (n=64) between and within individual studies. First, we looked at sensor space data within the parietal cortex. We found significant differences in alpha power, half-power and Shannon's spectral entropy between patient and control groups, as well as arousal states. Patients with schizophrenia showed significantly reduced alpha reactivity in parietal regions. There was significant increased entropy observed within eyes open condition relative to eyes closed condition across all groups. MEG data were mapped to cortical space using minimum-norm estimate and functional connectivity matrices were compared. Consistent with the differences in parietal alpha reactivity, there were significant reductions in left parietal connectivity with left temporal lobe and bilateral frontal lobe in patients with schizophrenia relative to healthy controls during eyes closed condition. There were no group differences in parietal connectivity in eyes open condition. Our findings suggest that variations in rest data protocols result in differences in effect sizes. Further understanding these variations may inform future resting-state study design and improve MEG data sharing.

Characterization of resting state networks using MEG in a large cohort of healthy subjects.

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Connectivity analysis of neural activity during resting state has been shown to provide valuable insight into the functional organization of the human brain. Statistical dependencies across different brain regions, observed using magneto-encephalographic (MEG) recordings provide us with the functional connectivity maps of the resting state brain. Recent studies show specific changes in resting state networks in various neurodegenerative disorders like Alzheimer's, Parkinson's disease as well as in cases of brain injury. However, a clear understanding of the network dynamics, as described MEG, in the resting state brain of healthy subjects is lacking. Here, we intend to characterize the resting state interactions in a large set of healthy subjects.

In this study we analyze the functional resting state networks in 33 healthy volunteers using continuous three minute MEG recordings obtained during no-task (eyes open and eyes closed) conditions.The data is preprocessed and special care is taken in order to avoid distortions in the phase space. In order to solve the problem of identifying regions of interest (ROIs), a novel method involving group level spatial independent component analysis (ICA) of Fourier coefficients is used. Functional connectivity analysis is performed on the time courses restricted to the ROIs identified using the above method. The differences in connectivity between conditions and to that of standard functional magnetic resonance imaging (fMRI) based networks are compared and discussed.

Automated Analysis of Resting State Cortical Oscillatory Characteristics using Magnetoencephalography (MEG)

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Neural oscillations are ubiquitous across the brain. Although they are widely implicated in both neural computation and across numerous diseases, they are typically examined in terms of pre-defined frequency bands that ignore rich individual variation in frequency and topography. These methods limit quantification and comparison between brain regions, conditions, and populations. To address this, we analyzed MEG from over 50 healthy adults using data from the Open MEG Archive (OMEGA) and the Human Connectome Project (HCP). Rest data (5-10 mins/subject) was pre-processed, artifact-corrected, and projected to a common template brain. Power spectra were calculated on source-projected data and oscillations were identified as "bumps" atop the background 1/ spectrum using automated methods. We find that, although there are oscillations whose center frequencies cluster near canonical bands, oscillations exist at all frequencies examined (3-40 Hz) and for any given subject are idiosyncratic. We find systematic relations between oscillatory parameters, including a strong negative correlation between centre-frequency of an oscillation and power, and a moderate negative correlation between the power of an oscillation and it's bandwidth. Finally, clustering oscillations into canonical bands allowed us to compute band-specific topographic maps of the probability of an oscillation of a given frequency, quantifying resting oscillatory activity. When doing so, we find that oscillatory bands are not independent; for example there is a strong negative correlation between the spatial distribution of theta (4-8) and alpha (8-13) oscillations, suggesting these are distinct processes that do not spatially co-exist. To conclude, we show how data-driven, automated methods can characterize resting state oscillations across the brain in such a way as to offer quantified norms across a large population of healthy subjects.

Synchronous intra and cross-networks interactions of the default-mode network

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Recent studies of resting-state networks (RSNs) focused on the fast fluctuations in functional connectivity (FC) and identified multiple short-lived resting-state FC (rsFC) patterns involving interactions both within and across RSNs [1–4]. However, little is known about how connections covary to generate these transient patterns. Here, we explore this question by mapping brain couplings that fluctuate in synchrony. We focus on both intra and cross-RSNs interactions of the default-mode network (DMN) in view of its dynamical centrality [3].

Time-dependent rsFC was derived using sliding-window (length: 10 s [2, 3]) alpha-band source envelope correlation (see [5] for details on FC estimation) from magnetoencephalography (MEG) recordings of 78 right-handed adults (5 min rest, eyes open). We concatenated spatially the rsFC maps from 4 DMN seeds (mesial prefrontal and posterior cingulate cortices and left and right temporo-parietal junctions) and applied a group-level temporal independent component (IC) analysis to reveal DMN-based rsFC covariations. Each IC represented a dynamical mode of synchronous coupling fluctuations.

Four types of covariation patterns were obtained: intra-DMN couplings only (2 ICs), cross-RSNs couplings only between the DMN and other RSNs (sensorimotor, visual, language, or dorsal-attentional; 8 ICs), mixed intra-DMN and cross-RSNs couplings (3 ICs), and all brain couplings (1 IC). We identified multiple dynamical modes of FC synchrony (both within and across RSNs) matching known RSNs or sub-networks [4]. These results may unify previous findings on dynamic MEG-based rsFC [3, 4] and shed new light on the formation of transient sub-networks and cross-RSNs integration.

[1] Baker et al. (2014), Elife 3, e01867
[2] de Pasquale et al. (2010), Proc Natl Acad Sci U S A 107, 6040-6045
[3] de Pasquale et al. (2012), Neuron 74, 753-764
[4] O\'Neill et al. (2015), Neuroimage 115, 85-95
[5] Wens et al. (2015), Hum Brain Mapp 36, 4604-4621

Heritability of Resting-State Functional Connectivity in MEG and fMRI

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This work demonstrates that there is significant genetic influence on the strength of functional connectivity (FC), and suggests that genetics may be a more determining factor than the development environment which is shared between twins.

Using resting-state recordings in twin pairs, collected as part of the Human Connectome Project, FC networks were constructed from source-localised MEG data and from fMRI recordings. The HCP500 dataset provided fMRI (MEG) scans from 56 (11) monozygotic twin pairs and 57 (11) dizygotic twin pairs. In each modality, networks were constructed between the same set of 39 regions of interest, derived from fMRI recordings from the 1st 200 HCP subjects.

Functional networks were constructed in fMRI by computing partial correlations between ROIs. Unlike for fMRI, a wide range of FC metrics is available for MEG. To guide our analysis, we performed a comparison of the group-level and within-subject repeatability of FC inference using 12 common network measures. We selected correlations between envelopes of oscillatory activity in three bands (theta, 4-8 Hz; alpha, 8-13 Hz; beta, 13-30 Hz), after an orthogonalisation correction for spatial leakage artefacts, as the most reliable FC method.

We fitted a linear variance-components model to each edge in the functional networks. This ascribes the covariance of FC between twin pairs (as a proportion of the total observed variability) to additive genetic factors (h) and to shared environmental factors (c). We assessed significance by permuting twin-pair statuses and investigated whether genetics outweigh the shared environment with bootstrapped confidence intervals on h^2-c^2.

The average heritability of coupling strength in MEG is 30% in alpha, and 50% in beta (with no significance in theta); for fMRI it is 17%. Only in fMRI does the 95% confidence interval on the difference of h and c exclude zero (0.14, [0.10, 0.16]); although there was 25 times as much fMRI data as MEG.

MEG resting state network connectivity dynamics from childhood to late adulthood

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Networks in the brain are constantly active, coalescing and fractioning even during resting state in the absence of a defined task. These network dynamics and patterns also change dramatically over the lifespan. Although lifespan resting state has been studied in fMRI and MEG, little is known about how dynamics and variance change with age. We used 151-channel CTF MEG to image 91 subjects (16F, 36 children, 30 adolescent, 25 adult) during eyes-open resting state. MEG data were coregistered to T1-weighted structural MRI (Siemens Trio 3T). Twelve 10s segments were epoched from each subject selected for the least head motion under 5mm. Time series from 116 brain regions of the AAL atlas and 48 regions known to be associated with intrinsic connectivity networks were estimated using the FieldTrip LCMV beamformer, filtered at theta (4-7Hz), alpha (8-14Hz), beta (15-30Hz), low (30-55Hz) and high gamma (65-80Hz) bands, and amplitude and phase extracted using the Hilbert transform. Connectivity between regions was estimated using the weighted phase lag index (wPLI) and amplitude correlation (ACor). Partial Least Squares was used to identify significant age group differences or significant correlations with demographics or neurobehavioural measures. We found the mean and variance of ACor in resting state was significantly correlated with age across all the frequency bands. In theta, ACor mean increases and variance decreases consistently across the entire brain network with age. Mean ACor in alpha, beta, low and high gamma show both increases and decreases. wPLI mean and variance are similarly mixed. Alpha and beta variance consistently decreases and low and high gamma variance consistently increases with age. Our lifespan MEG dataset reveals strong and consistent age-related changes in resting state amplitude correlation and phase synchrony that varies with frequency band. We plan to use this normative data to guide future study of our clinical resting state datasets.

Measurement of magnetomyography using an array of magnetoresistive(MR)sensor

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Background: Magneto-resistive (MR) sensor is compactand available at room temperature and has potential validity in biomagnetic measurement. This study was aimed to acquire evoked magnetomyography(MMG) which is relatively strong in biomagnetic fields by using MR sensors.Methods: All recordings were performed in a magnetically shielded room using a newly developed 30-channel high sensitive MR sensor array (sensor interval: 2.0 cm, sensor arrangement: 6 by 5 matrix)system (TDK, Japan). Magnetic fields in 4 healthy subjects were measured at palmar surface in response to surface stimulation(3Hz) of the median nerve at 4cm proximal to the wrist and 25 - 100 responses were averaged. Evoked electromyography(EMG) at the thenar muscles was simultaneously recorded.Results: Evoked MMG were successfully recorded in all subjects by MR sensors. Latencies of MMG were almost consistent with EMG. Isomagnetic field map (contour map) shows dipolar pattern, suggesting electric currents parallel to muscle fibers.Discussion: We demonstrate that our newly developed MR sensor could detect evoked MMG and the sensor array system could visualize distribution of magnetic fields. MMG using the MR sensor which is available at room temperature has potential use not only for identifying muscle disorders and neurological disorder but for rehabilitation and sports training in future.

Phase-amplitude coupling in the resting human brain

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Phase-amplitude coupling describes the association of a slow frequency's phase to the amplitude of a higher frequency. Phase-amplitude coupling may serve to orchestrate neuronal oscillations and associated brain networks across frequencies. However, the measurement of phase-amplitude coupling is complicated by physiological artifacts and the dependency on spectral estimation procedures. To investigate this, we systematically characterized phase-amplitude coupling in the resting human brain using MEG and different analytical approaches. We show that limitations in the specificity of current phase-amplitude coupling detection methods lead to spurious phase-amplitude coupling estimates. We dissociate these spurious results from true neuronal phase-amplitude coupling.

The electrophysiological connectome is maintained in healthy elders: a power envelope correlation MEG study.

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Previous fMRI studies have demonstrated age-related modulations in resting-state functional connectivity (rsFC) with ageing that correlated with age-associated cognitive decline. Considering the age-related changes in neurovascular coupling and the high prevalence of neuropsychiatric comorbidities in elders, we further studied using MEG and a connectome approach the age-related rsFC changes in a group of highly selected young and old healthy subjects.
Resting-state data were recorded with a whole-scalp MEG (Elekta) in two sex- and education-matched groups of 25 right-handed young (age=23±3 years, mean±standard deviation) and elder (68±2 years) healthy subjects. Participants were screened for depression, anxiety and dementia, and were free of psychotropic drugs. The connectome was estimated as rsFC matrices involving 40 nodes of the default mode (DMN), visual (VN), motor (MN), language (LN), dorsal (DAN) and ventral (VAN) attentional resting-state networks. Source-level rsFC maps were computed in the α (8-13Hz) and β (14-25Hz) bands using leakage-corrected envelope correlation (Wens *et al.*, 2015) and normalized power (dSPM). Group differences were statistically assessed using unpaired, two-tailed permutation tests (10 permutations, p-value<0.05, family-wise error control as in Wens *et al.*, 2015). Power was also linearly regressed out of rsFC to subtract power-induced rsFC differences.In the α-band, no age-related rsFC difference was found despite significant power decrease with age in the DMN, VAN and MN. In the β band, cross-RSNs couplings increased with age between DMN-VAN, MN-DAN and LN-DMN concomitantly with power increase in the DMN and LN. No rsFC difference subsisted after regression of power effects.
Consequently, the electrophysiological connectome appears maintained in healthy elders, suggesting that the age-related evolution of rsFC reported in previous studies may be due to age-related changes in neurovascular coupling or to neuropsychiatric confounds.

Neuromagnetic default-mode network connectivity correlates with occipital α-band power at rest

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Neuromagnetic default-mode network (DMN) resting-state functional connectivity (rsFC) has been uncovered at the group level using α-band power envelope correlation. Considering the modulations of the α rhythm by fluctuations in cognitive and vigilance states, we investigate using magnetoencephalography (MEG) the link between inter-subjects variability in DMN rsFC, α-band power and α-band peak frequency.

Resting-state activity (4.5 min, eyes open, fixation cross) was acquired in 100 right-handed healthy adults (49 females; mean age: 25.9 y, range: 18–40 y) using a whole-scalp-covering MEG (Elekta). Single-subject DMN seed-based rsFC maps were derived from α-band (8-12Hz) source envelope correlation with seed in the mesio-prefrontal cortex (Wens et al., Clin Neurophysiol 2014) and geometric leakage correction (Wens et al., HBM 2015). Spatial similarity (SS) with a canonical DMN rsFC map was used to estimate the topographical reliability of individual maps (Wens et al., Brain Topogr 2014). Power spectra (dSPM) in mesial occipital and posterior parietal cortices were computed. After removing the 1/f trend, we calculated the relative α power (RP) and the α peak frequency (PF) to investigate their relation with SS. These analyses were then repeated after excluding subjects with no occipital PF within a restricted α-band (8.5–11.5 Hz).

Individual DMN rsFC maps were found to vary substantially across subjects; only 56% of them presented significantly positive SS ($p<0.05$). The SS correlated with occipital RP ($r=0.56$, $p<10^{-8}$) and PF ($r=-0.47$, $p<10^{-6}$) and parietal RP ($r=0.34$, $p<10^{-3}$). However, after excluding 23 subjects based on their occipital PF, the SS correlated only with the occipital RP ($r=0.5$, $p<10^{-6}$) and PF ($r=-0.28$, $p<10^{-2}$).

This MEG study demonstrates a link between individual occipital α rhythm and DMN rsFC. These results highlight the importance of controlling subjects\' vigilance state and possibly spontaneous cognition content during MEG resting-state recordings.

Critical dynamics in resting state brain activity is associated with impulsivity and dopamine-related polymorphisms

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Brain critical dynamics is reflected by enhanced long-range temporal correlations (LRTC) in the neuronal time series, and it allows the system an optimal information processing capacity. The Catechol-O-methyltransferase (COMT, rs4680) is the most widely studied gene that is involved in regulating the balance of dopamine especially in prefrontal cortex. This gene contains a single nucleotide polymorphism (Val/Met) that is important for prefrontally mediated cognition, such as executive functioning. This polymorphism has also been associated with response inhibition and impulsivity, whereas problems with executive functioning are related to impulsive behaviors. Here, we investigated the influence of COMT polymorphism and impulsivity on critical dynamics in resting state brain oscillatory activity. We recorded resting state magnetoencephalography (MEG) data from 88 healthy volunteers, who were genotyped using Infinium PsychArray-24 v1.1 (Illumina). The sample consisted of 20 Val/Val, 51 Val/Met, and 17 Met/Met carriers. Impulsivity was measured with the Fun Seeking subscale (of the BIS/BAS) that implies impulsiveness. The LRTCs were quantified as the exponents of the detrended fluctuation analysis (DFA) calculated for cortically reconstructed sources at 31 frequency-bands ranging from 3 to 120 Hz. We found that Met carriers scored higher on impulsivity than Val homozygotes ($p<.05$). Moreover, the genotypes differed in brain dynamics during rest in beta (20–30 Hz) and gamma (30–50 Hz) frequencies. Compared to Val homozygotes, Met carriers exhibited greater scaling exponents ($p<.01$), particularly, in regions belonging to the default mode network (DMN). Further, for Met carriers, impulsivity was associated with greater LRTC exponents ($p<.05$) especially in the DMN areas at beta (20–30 Hz) and gamma (30–60 Hz) bands. Our results support the involvement of dopamine-related polymorphism and impulsivity in the resting state critical brain activity.

Dynamic scales of spontaneous neuromagnetic activity

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In the last decades, cognitive neurophysiology has highlighted two principal constituents of brain dynamics: oscillatory and arrhythmic processes. The neuromagnetic power spectrum is characterized by a global decay of power as a function of frequency with local peaks interpreted as transient oscillatory fluctuations and regions of linear decay on a logarithmic scale, commonly interpreted as "scale-free" or 1/f exponential power-law regime. When statistically accounting for the global decay of power by detrending the spectra, local frequency peaks surface that correspond to conventional definitions of neuronal oscillations, i.e. most prominently theta (4-7Hz), alpha (8-12Hz) and beta (14-30Hz). On the other hand, at least two local 1/f regimes can be found discerned, one below 1 Hz and one above 20 Hz, that have been termed arrhythmic. While neural oscillations have been associated with cognition and behavioral performance, it is only recently that the notion of 1/f dynamical regimes as merely reflecting systemic noise has been challenged. Statistical dependencies between oscillators across frequencies and cortical regions have received consideration recently, often conceptualized as cross-frequency coupling or functional connectivity. However, the statistical relationships between oscillatory and arrhythmic processes themselves and their potential functional significance for cognition remain elusive. Here, we analyzed MEG resting-state data from 29 subjects drawn from the Human Connectome Project, both, at the sensor and source level, and evaluated inter-individual variability as well as population trends in changes of oscillatory and arrhythmic processes across time, sensors and cortical regions. Additional 36 MEG datasets recorded at our laboratory were included. All analyses focused on a normative description of the two dynamic regimes within and across datasets backed by statistical inference through permutation procedures and comparisons against surrogate data.

An Exploration of Differences in Oscillatory Resting State Networks between Patients with Schizophrenia and Controls

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Introduction

Synchronised oscillatory activity is thought to be a marker of functional connectivity.A recent body of evidence suggests impairments in such activity in schizophrenia, particularly in the gamma range (30-90Hz). (Uhlhaas et al., 2008) Much of this research has focused upon neural synchrony during task performance. Analysis of activity at rest is useful in understanding whether changes in neural synchrony are due to inherent impairments in their generation or whether they are task-related. We performed an exploratory study of resting-state activity in patients with schizophrenia, compared with healthy controls using MEG.

Method

- 28 patients with schizophrenia and 30 healthy controls were recruited.
- Participants completed two resting-state tasks, each lasting 5 minutes; one with their eyes open and one with their eyes closed.
- We used the temporal standard deviation (SD) of the amplitude envelope as a measure of activity; as well as excess kurtosis, a measure of how non-gaussian the data is in the temporal domain.
- Temporal SD and kurtosis were calculated per voxel in sixfrequency bands; delta-gamma. We then performed a T-test comparing patients and controls in each frequency band in both the eyes-open and eyes-closed conditions separately.

Results&Conclusion

- We found differences in both temporal SD and temporal excess kurtosis between patients and controls, which varied between brain regions and among frequency bands.
- The preliminary results suggest that there is a modulation in low-frequency activity in patients with schizophrenia which is consistent with other MEG and EEG studies. (Boutros et al., 2008; Fehr et al., 2003)
- Differences between patients and controls were consistent between the eyes-open and eyes-closed conditions.

Boutros et al. (2008).Schizophr Res, 99(1-3), 225-237.
Fehr et al. (2003).Schizophr Res, 63(1-2), 63-71.
Uhlhaas et al. (2008) Schizophr Bull, 34(5), 927-943.

Consideration of the electromagnetic signal generated by the neural activity assuming pulse-frequency modulation

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Generally, the duration of the neural activity measured by EEG and MEG is in the range of several hundred ms from dozens of ms. It is said that this activity originates from the post-synaptic potential. The action potential generated along with the axon is also known as another neural activity, and has a very short pulse width (~1ms). It is very difficult to measure the action potential even if its electrical potential has higher than the post-synaptic potential. On the other hand, the human nervous system is said to use pulse-frequency modulation to transmit information. Therefor it seems to be very useful for brain function analyzing to observe the pulse train of the action potentials. In this study, we examined what kind of electromagnetic signal was observed if the source was a pulse train with pulse-frequency modulation. As an example, we show the results that the pulse train of which plus width is 0.1ms was modulated at 10Hz. In spectral analysis, there was a peak at 10Hz and other components were widely spread to 10kHz like a white noise. In this case, this 10Hz component may be detectable by MEG and EEG, but it seems to be difficult to distinguish it from a signal generated by the post-synaptic potential. Due to a spread spectrum, the higher frequency components are difficult to extract from a frequency range where white noise is dominant with general methods. As a solution to this problem, we applied a non-linear processing to this high frequency signal. Actually, we calculated absolute values of the high passed signal (>100Hz). We could find a 10Hz frequency spectrum in the processed signal. This processing is a kind of demodulation from a signal with pulse-frequency modulation. We also confirmed that this demodulation was effective even if it included a certain level of white noise and/or even if it was limited with a certain frequency range. These findings are expected to open the door to detecting action potentials in neural activity.

Laminar specificity of high and low frequency oscillations during action selection

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Recent proposals suggest that within the hierarchical organization of cortex, feedback connections originate from deep layers and feedforward connections from superficial layers. Neurophysiological evidence suggests that low (e.g. β) frequency oscillations predominantly arise from deeper layers, while higher (e.g. γ) frequency signals stem largely from superficial layers. In line with the laminar dominance of feedback and feedforward connections, deep layer β oscillations are thought to convey top-down predictions, while bottom-up γ oscillations reflect prediction errors in the superficial layers. We used high precision MEG with subject-specific 3D printing based head-casts to test this frequency- and layer- specific account in a framework of predictive action selection. A predictive stimulus (PS; random dot kinematogram with left/right motion at low, medium, or high levels of coherence) was followed by an imperative stimulus (IS; left or right arrow) that required a corresponding response as quickly as possible. On most trials, the motion direction of the PS was congruent with the IS, providing a strong prior about the required response, but on some trials this prediction was violated by an incongruent IS. Focusing on sensorimotor cortices, our key finding is that movement-related β desynchronization and rebound originated predominantly from deeper layers, while movement-related γ synchrony was biased towards superficial layers. Furthermore, prior to the IS, β power scaled with the motion coherence of the PS, consistent with β oscillations signaling predictions about forthcoming actions. After the IS, γ power increased with decreasing coherence in congruent trials and increasing coherence in incongruent trials, suggesting that γ activity reflects errors in top-down predictions about expected actions. Collectively, our results show laminar specificity for predictions conveyed by β oscillations and prediction errors in the γ range, for the first time in humans.

Non-invasive recording of laminar dynamics

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Magnetoencephalography (MEG) is a direct measure of neuronal currentflow; its resolution is therefore not constrained by physiology but rather bydata quality and the models used to explain these data. Recent simulation workhas shown that it is possible to distinguish between signals arising from the supra-granularand infra-granular cortical layers given accurate knowledge of these surfaceswith respect to the MEG sensors. We set out to test this empirically using longduration and high SNR MEG recordings. To this end, participants woreindividualized head-casts within the MEG scanner that minimized head movementto ~1mm, allowed for high-precision mapping to individual anatomy, andincreased the signal to noise ratio (SNR) by a factor of ~5. Participantsperformed sequential finger movements cued by auditory tones. In order todemonstrate the specificity of our inference, we leveraged recent empiricalevidence and theoretical predictions that the supra- and infra-granularpyramidal cell populations can be distinguished by their effective timeconstants. We found that low frequency evoked components in the beta range(15-30Hz) were much more likely to originate from deeper layers (log oddsratio=52). By contrast, high frequency evoked gamma components (60-90Hz) were muchmore likely to originate from superficial layers (log odds ratio=49). Thesefindings were robust across a range of functional and anatomical priorassumptions. Our data thus support the recent proposals for spectrallydistinguishable laminar responses in the cortex, and are the first demonstrationof non-invasive laminar specific electrophysiology in humans.

Appraisal of appropriate definition of baseline for somatosensory evoked magnetic fields

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[Introduction]Pre-stimulus interval was generally served as baseline (BL) segment to measure the amplitude of the somatosensory evoked activities. However, there are no particular criteria for the length of BL segment. [Purpose]We appraised BL segment for the amplitude measurement for somatosensory evoked magnetic fields (SEFs). [Methods]Six right-handed healthy subjects participated in this study. Right median nerve was stimulated at the wrist with three different fixed inter-stimulus intervals (ISI; 4, 2 and 0.5 s) and SEFs were collected by 306 ch whole-head magnetoencephalography (MEG). The recording passband were 0.10-300 Hz and all recorded data were sampled at 1012 Hz. In the three different ISI conditions, we compared the amplitude of N20m component in SEFs based on five different lengths of BL segment. Five kinds of pre-stimulus BL segments were defined with respect to the ISI; whole range (FULL),1/2, 1/5, 1/10 and 1/20 of the respective ISI. We measured the amplitude of N20m peak in SEFs from the sensor that indicate maximum amplitude in whole channels. The amplitudes were measured from five kinds of BL to peak and normalized at the amplitude measured from the stimulus onset (time = 0) in 4-s ISI. Locations of N20m sources were estimated from single equivalent current dipole (ECD) analysis. [Results]The means of normalized amplitudes of all subjects was the largest in 4-s ISI condition. The means of normalized amplitudes of all subjects were 93.5±14.0%, 90.0±14.1%, 90.2±13.3%, 90.2±14.2% and 91.2±13.6% in BL segment of FULL, 1/2, 1/5, 1/10 and 1/20, respectively. The mean across all the subjects for the difference between maximum and minimum normalized amplitude ranged from 7.8 to 9.6%. All estimated ECDs of N20m were localized at around the central sulcus. The inter-subject mean of the average for the max-distance between ECDs from five BL segment conditions ranged from 2.1 to 3.7mm. [Conclusion]Taking the estimation error of ECDs into account, “FULL” BL segment can be served as basis for amplitude measurement.

Laminar profile ofcross-frequency interactions

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Cross-frequency coupling interactions between e.g. alpha (~10Hz) and gamma (>30Hz)oscillations have been observed both during resting, stimulus anticipation and stimulus processing periods using magnetoencephalography (MEG) and electrocorticographic data. To determine the laminar profile of these interactions observed at the cortical level, we analysed the coupling between alpha and gamma oscillations in different layers of V1 in four macaque monkeys during both spontaneous activity and attentional tasks. We observed that granular/supragranular (feed-forward related) gamma oscillations were nested within infragranular and supragranular (feedback related) alpha oscillations both during resting and stimulus processing periods. Moreover, we observed that infragranular alpha oscillations magnitude was higher and that(supra)granular gamma oscillations magnitude was lower when attention was directed away from the stimulus. More specifically, the decrease of gamma oscillations magnitude was locked to the trough of alpha oscillations. More generally, the stronger the alpha oscillations, the lower the gamma oscillations during the trough of alpha oscillations during both resting and stimulus processing periods. These results are in line with (1) recent MEG data we obtained in a working memory task and (2) the idea that alpha oscillations are associated with pulses of inhibition approximately every 100ms.

EEG characteristics in First Psychotic Episode Patients

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In this paper, we present an advanced electroencephalography (EEG) data analysis approach applied to First Psychotic Episode (FPE) data from emergency room patients, pre and post medication intake. The aim of this study is to find discriminative objective features in the EEG data of FPE subjects. By extracting different synchronicity features (namely coherence and synchronization likelihood) from 64 channel EEG recordings, we build complex networks and extract graph features. The next step of our analysis is to use machine learning techniques combined with genetic algorithms for the classification of the different subject groups (FPE subjects, schizophrenics (SZ) after the FPE, patients that did not evolve as SZ after the FPE and healthy controls) based on such features. We reach results as good as 100% in one of our classification problems, indicating that EEG contains relevant data to discriminate between conditions among patients.

Neural oscillations during social exclusion - a MEG study

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Social stress is a common psychological strain in daily life, which can range from ostracism and social exclusion. Previous studies using fMRI and EEG have revealed a large distributed network when experiencing social exclusion induced by the 'Cyberball' paradigm – a computerized ball-tossing game. The network comprises: the insula, anterior cingulate cortex, temporal gyrus, and prefrontal cortex. The present study used 275 channel MEG to detect neural activity of social exclusion in 16 healthy volunteers. Source analysis localized the generation of neural oscillations in theta, alpha and beta bands (6, 11, 16, 21 and 26Hz) comparing 'exclusion' vs. 'inclusion' conditions. Averaged power in significantly activated clusters was correlated with self-report scores of Need Threat Scale and Mood questionnaire.Results showed increased activity in left temporal cortex in all frequency bands (bilaterally in 26Hz). Additional activations were found in left fusiform and rolandic operculum in 11Hz band; left supramarginal, rolandic operculum, postcentral cortex, right superior parietal and right posterior cingulum in 16Hz band; left Heschl, insula, rolandic operculum, and hippocampus in 26Hz band. Averaged power of activated clusters in 6 and 11Hz bands showed significantly negative correlations with mood scores, and power in 26Hz band negatively correlated with Need scores. Activities in the left temporal and hippocampus cortex suggested memory related process of social exclusion, activation in the fusiform reflected increased valuation of faces, activation in the supramarginal area was associated somatosensory process of 'social pain', and activations of the left insula and rolandic operculum suggest distress and negative emotion caused by social exclusion. Taken together, different frequency oscillations in certain brain areas may reflect various respects of neural process during social exclusion.

Multi-frequency analysis of brain connectivity under negative stimulus in depression: a magnetoencephalography study

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Major depressive disorder is characterized by deficits in emotional processing and associated with abnormal functional connectivity. However, the inter-regional connectivity within different frequency bands in depression remains to be explored. In this paper, we explored the difference of functional connectivity within a large range of different frequency bands between depressive patients and healthy controls under negative stimulation.

Magnetoencephalography (MEG) data were acquired at a sampling of 1200 Hz. Subjects were 40 depressive patients and 40 cases matched healthy controls. The preprocessing and source reconstruction of MEG signal were undertaken via Filedtrip. The MEG recordings of 0-600ms under neutral and sad stimuli were chosen for analysis. Signals under the neutral stimuli were taken as the baseline. 90 regions were selected according to the automated anatomical labelling (AAL) atlas. Regional timecourses were frequency filtered into four separate frequency bands; theta (4-8Hz), alpha(8–13Hz), beta(13–30Hz), and gamma(30–50Hz). The envelope correlation was used as a means to quantify connectivity between 90 regions within each frequency band and between each pair of frequency bands. The permutation test was used to compare differences between groups and FDR correction was performed.

Compared with healthy controls, the functional connectivity within occipital alpha , frontal gamma and fronto-parietal theta-gamma band decreased significantly and increased significantly within cortico-limbic theta band in the depression. ($p<0.00001$-FDR corrected).

The increased theta band connectivity indicated that the depressed patients paid more attention to the negative emotion, and easier to transmit and process negative emotions in alpha band. The significantly diminished gamma and theta-gamma band connectivity of emotional responses might act as an impaired integrative mechanism underlying cognitive processing or emotion processing in depression.

Differences in task performance between \'High\' and \'Low\' sub-clinical Obsessive Compulsive Disorder checkers is reflected in MEG recorded Theta activity during a working memory task.

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Deficits in executive function together with anxiety serve to degrade memory performance and confidence in obsessive-compulsive checkers. To investigate the role of these deficits in OCD checking, Magnetoencephalography (MEG) measurements of the cortical oscillatory activity of sub-clinical participants (n=28), classified as either 'high' or 'low' checkers, were recorded during a working memory experiment. To elicit performance differences between the two participant groups, the task was made more taxing, firstly by employing images of electrical kitchen appliances likely to be distracting to 'high' checkers and secondly by an intermediate task presented before the working memory probe. Within the limits of permitted responses, the intermediate task was designed not to be resolvable in half the trails. Comparing resolvable and unresolvable trials, working memory performance was worse in trials containing the unresolvable intermediate probe. In support of the hypothesis that poorer performance for high checkers in the working memory task is in part a result of increased memory process arising from an inability to resolve the unresolvable probe and increased anxiety arising from the kitchen appliance imagery, statistically significant group level differences between high and low checker participants are found in both working memory task performance and in Theta band activity in task relevant brain regions. In particular high checkers showed increased Theta activation in Amygdala and Medial Temporal Lobe, associated with finding the images of kitchen appliances threatening and with increased memory processing of the to resolve the unresolvable probe. In contrast, during the unresolvable probe, high checkers showed lower Medial Frontal Lobe activation, suggesting impaired processing of the unresolvable probe.

Oscillation power analysis of resting state brain networks in depression: a Magnetoencephalography study

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Background: Oscillation power distributions of major resting state brain networks in depression exhibit disease-related abnormality. In this study, we interested in the oscillation power of depression-related resting state brain networks in different frequencies, and differences between depression patients and healthy control to find physiological characteristics related with depression.

Methods: We collected Magnetoencephalography（MEG） data of depression patients and healthy control in resting state to compare the power of brain networks between two groups for each frequency band separately. Thirty-two depression patients and twenty-eight healthy control were included. Six frequency bands: Delta (0.1-3Hz), Theta (4-8Hz), alpha1 (8-10Hz), alpha2 (10-13Hz), beta (13-30Hz), gamma (30-48Hz) were studied and we chose default mode network (DMN), frontoparietal network (FPN), salience network (SN) as networks of interest. After source reconstruction, the time series of DMN, FPN, SN were extracted using regions of interest (ROI) templates. The powers of principal components were computed and compared between groups.

Results: In patients group, the power of anterior DMN was significantly reduced compared with healthy group in alpha1, alpha2 and delta band.

Conclusions: Alpha1, alpha2 are major frequency bands of DMN power distribution. We inferred that the power decrease of anterior DMN may be related to inhibitory dysfunction of depression patients. The ability of inhibiting irrelevant information in anterior DMN is damaged, and the downstream networks are activated unusually, result in deviation in recognition and processing of negative emotions and thoughts. Moreover, studies focus on DMN in alpha band are urgently needed for studying depression.

MEG functional connectivity features between bipolar and unipolar depression patients

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BACKGROUND: Nowadays, the recognizing of potential biomarkers could be crucial in helping to distinguish between BD and UD. We hypothesize that different affective disorder patients may present distinct patterns of functional connectivity among cortical areas in resting state.Methods: Whole-head magnetoencephalography scan was performed in an resting-state condition in 12 bipolar depression patients, 27 unipolar depression patients and 21 gender-, age-, level of education- matched healthy controls. The strength of cortico-cortical functional connections was measured with synchronization likelihood (SL) value, and the SL value within θ, $\alpha 1$, $\alpha 2$, β and γ frequency bands were compared in three groups. Group-wise two post-hoc t-test was performed according to the results of ANOVA. Results: Compared with the unipolar depression patient and the controls bipolar patients showed increased local θ(0.249±0.087, 0.181±0.029, 0.196±0.032; F=8.511,P=0.001); $\alpha 1$(0.200±0.051, 0.164±0.020, 0.175±0.028; F=5.292, P=0.008), $\alpha 1$(0.200±0.051, 0.164±0.020, 0.175±0.028; F=5.292, P=0.008) and $\alpha 2$(0.200±0.047, 0.175±0.025, 0.183±0.025; F=4.721, P=0.013) SL in the left occipital lobe and local β(0.186±0.027, 0.166±0.024, 0.159 ± 0.026; F=4.195, P=0.020) and γ (0.151 ± 0.020, 0.128 ± 0.019, 0.133 ± 0.019; F=5.521, P=0.006) SL in right frontal lobe. Compared with the controls, the bipolar patients presented increased β(0.076±0.013 vs. 0.087±0.011, P=0.009) and γ(0.062±0.010 vs 0.069±0.01� P=0.020) inter-hemispheric SL between bilateral frontal lobe, whereby the unipolar patients showed decreased γ(0.057±0.013 vs 0.050±0.005� P=0.009) band intra-hemispheric SL in the right frontal-parietal regions. Conclusions The BD patients displayed further dysfunction of cortical resting connectivity over the fronto-parieto-occipital regions than UD patients. The loss of temporal synchronization in the frontal and occipital lobe may be a biomarker to differentiate bipolar from unipolar depression.

Investigating the Regulation of Sensory Gamma-Band Activity in Autism Spectrum Disorder (ASD)

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The sensory issues reported by individuals with autism spectrum disorder (ASD) are thought to be related to atypical patterns of high-frequency gamma-band activity in response to visual and auditory stimuli. One of the mechanisms used to regulate local gamma-band activity is phase amplitude coupling, whereby the phase of a low frequency oscillation is related to the amplitude of gamma-band activity. Although reduced PAC has been observed in ASD, no study to date has investigated the phenomenon in relation to early sensory processing. To explore this in individuals with and without autism we utilised MEG combined with an engaging audio-visual paradigm. Visual stimuli elicited characteristic increases in gamma-band power and a reduction in alpha-band power, whilst auditory stimuli elicited a characteristic steady state response at 40Hz. Next various methods of phase amplitude coupling (PAC) were applied to the data, including the modulation index, the general linear model approach and event-related PAC. Results from a group of neurotypical participants indicate that ,as anticipated, gamma-band activity is related to low frequency oscillations, implying that PAC acts as a mechanism to regulate early sensory gamma-band activity. These analyses will be applied to an adolescent ASD sample to determine if there is evidence of atypical gamma-band regulation via PAC. This could possibly underlie many of the sensory issues affecting ASD individuals and also relate to theories of atypical brain connectivity and an excitation-inhibition imbalance in autism.

Effective connectivity of the fronto-striatal pathways in unipolar and bipolar depression

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Objective To detect the difference of fronto-striatal regions\' effective connectivity between unipolar and bipolardepression in the gamma frequency in the resting state. Methods 23 patients with unipolar depression, 11 with bipolar depression, and 21 healthy controls were recruited. All participants underwent 275-channel MEG recording in the resting state for four minutes. The regions of interest was selected as the orbitalfrontal cortex(OFC), the anterior cingulatedcortex(ACC), the ventral striatum(VS), and the ventromedial prefrontal cortex(VmPFC). The effective connectivity was calculated with granger causalitymodel (GCM) in the gamma frequency. Comparisons of differences between groups were tested by One-Way ANOVA analysis. Results Significant differences of effective connections were:Right VS to ACC(=3.300, =0.045),left ACC to VS(=3.453, =0.039),left ACC to OFC (=5.042, =0.010). Compared with unipolar depression, bipolar depression showed increased effective connection from the left ACC to OFC (=-2.178, =0.037) and right VS to ACC(=-2.652, =0.012). Unipolar depression exhibited increased couplings from the left ACC to OFC (=-2.652, =0.012) compared to the controls, while bipolar depression displayed enhanced effective connection from the left ACC to OFC (=2.939, =0.006). Conclusions The couplings of prefrontal-striatal circuitis was disruptive with different parterns for unipolar and bipolar depression.The unipolar depressive patients showed weakened regulation of the frontal lobe while the bipolar disorder displayed a enhanced subcortical activity. The effective connectivity of pretrontal-striatal in gamma band may be a potential electrophysiological marker to distinguish unipolar and bipolar depression.

Spatial components of magnetic mismatch negativity with the cortical thickness of its structural correlates in schizophrenia

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The automatic auditory change detection response observed through the mismatch negativity (MMN) component of event-related potentials has been methodically studied in schizophrenia. MMN amplitude attenuation is a consistent finding in this population, and its generators are said to be localized in temporal, contributing to auditory perception and discrimination, and frontal, attention-switching, cortices. Studies of brain structure in schizophrenia have reported abnormalities in several areas, including those that are thought to be involved in the MMN response. However, the potential relationship between MMN and the characteristics of related brain areas is unclear and warrant further exploration. We conducted a magnetoencephalography study of MMN in 16 schizophrenia patients and 18 healthy control subjects. Through source reconstruction, we extracted whole-brain current source density (CSD) strengths using minimum norm estimation, and focused on areas previously reported as potential generators of MMN. We also went on to examine structural MRI data for cortical thickness. In comparison to healthy control subjects, patients with schizophrenia showed significantly decreased CSD strengths in both temporal and frontal areas of interest. The CSD strengths of both temporal and frontal areas showed positive correlations with cortical thickness in the control group. On the other hand, we observed a negative relationship between CSD and thickness of frontal areas in the patient group. Our findings may provide insight on the complex relationship between functional and structural abnormalities observed in schizophrenia.

Multi-layer network connectivity in schizophrenia

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Schizophrenia is a mental disorder manifesting as a disturbance of internal reality and perception. Symptoms include hallucinations and delusions, alongside persistent features such as disorganization and avolition. Abnormal network connectivity has been suggested as a cause of these psychotic deficits. Here, we apply a multi-layer connectivity approach to visuo-motor and resting state MEG data in patient and control groups. Connectivity measurements are compared to a measure of illness severity derived from scores of psychosis and social function. MEG data were inspected visually and 1-150 Hz band pass filtered. Datasets with head movement above 7 mm were discarded. The cortex was parcellated into 78 AAL regions, each yielding a beamformer time course reconstruction. Time courses were frequency filtered, Hilbert transformed and the amplitude envelope calculated. Connectivity was estimated as a correlation between amplitude envelopes, between all AAL region pairs, within and between all frequency bands. This multi-layer approach allows visualisation of all within- and between-frequency interactions, between all brain regions. Both visuo-motor and resting state data showed significantly increased alpha connectivity in controls compared to patients in a network of occipital brain regions. Illness severity correlated significantly with alpha connectivity, with the most severe symptoms associated with low connectivity. Visuo-motor task results show no significant difference in task induced alpha power between groups. Our results support a hypothesis that dysconnectivity is a core feature of schizophrenia. Specifically, given the recent hypothesis that alpha oscillations act to gate information flow to higher order cortical regions, it follows that a lack of coordination between alpha oscillations may be reflective of an inability to direct visual attention, and thus an inability to accurately gate incoming visual information to higher order brain regions.

Altered auditory gamma oscillatory responses in oddball paradigm with schizophrenia patients and subjects at clinical high risk for psychosis: An MEG study

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Gamma-band auditory steady-state response (ASSR) impairment has been reported in schizophrenia patients and subjects at clinical high risk (CHR) for psychosis using electroencephalography (EEG). However, it is unknown whether alteration in gamma-band ASSR are present in more localized regions and in relationship with attentional switching process. The present study assessed gamma-band ASSR in 22 patients with schizophrenia, 20 subjects at CHR for psychosis, and 21 healthy controls (HCs) using magnetoencephalography (MEG). Participants were presented with 40-Hz click trains in conventional pure ASSR paradigm. In oddball ASSR task, subjects were instructed to response with button press when they hear target sound which was 40-Hz click train. We conducted time-frequency analysis and calculated event-related spectral perturbation (ERSP) and inter-trial coherence. Patients with schizophrenia showed increased gamma-band ERSP in pure and target ASSRs compared to those of CHR subjects and HCs. In addition, gamma-band ASSRs were correlated with duration of illness, duration of antipsychotics exposure, positive symptom severity, executive function, and verbal memory in patients with schizophrenia. Pure and target gamma-band ASSR alteration in schizophrenia may represent a focal hypo-functioning of NMDA receptor in temporal cortex which is related with cognitive dysfunction.

The dynamic effective connectivity of the subcorticalpathway during the early emotion processing state in the major depressivedisorder

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Objective The facial processing is one of the most developed visual perceptual skill in human. It has been reported that the major depressive disorder showed negative emotion bias, which was related to the hyperactive ofthe limbic system. While previous research demonstrated that the subcortical pathway was also involved in the nonconscious emotion processing. There hasbeen increasing evidence that the subcortical pathway was related to theautomatic emotion processing. However, whether the subcortical pathway wasrelated to the negative emotion processing was still in debate, thus we aimedto explore whether the subcortical pathway was modulated by the negative emotional in the major depressive patients and the aberrant functionalconnectivity during the early stage of emotion processing. Methods The technology of the magnetoencephalgraph (MEG) was used to recordthe brain response when 19 depressed patients and 17 healthy controls were underthe emotion recognition task. The interested facial emotion was negative facialemotion, neutral facial emotion was taken as baseline .The preprocessing and source reconstruction of MEG signal were undertaken via SPM8. Theinterested time periods in this study were 0-100ms, 0-150ms, 0-200ms. The dynamic causal model was selected to compute the constructed model and thebayesian model was used to pick out the best model. Under the best model, theparameters of effective connectivity were statistical analysis with the methodof permutation. Results Compared to the healthycontrols, the modulatory connectivity in the depression from the left primary visual cortex(V1) to the orbitofrontal cortex(OFC) was obviously decreased (=0.01) during the period of 0-100ms, as well as the endnogenous connectivity from the right thalamus(Tha) to the orbitofrontal cortex(OFC) (=0.04). During the period of the 0-150ms, the endnogenous connectivity from the right V1 to the OFC was heightened in the depressed patients (=0.01). The modulatory connectivity from the left Tha to the left OFC and the endnogenous connectivity of the right Tha-amygdala were also reduced between the period of 0ms and 200ms in the depressed patients. Conclusions During the early period of the emotion processing, the depressed patients displayed later perception ofnegative emotion than the healthy controls in a dynamic state, which wasdistinct to the healthy controls. In addition, the subcortical pathway in the early stage was aberrant in the depressed patients.

Topological properties of brain structural networks in bipolar disorder patients initially diagnosed of Major Depressive disorder: a 5-year prospective longitudinal study

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The consistent evidence of changed brain circuits in affective disorders was supported by different brain imaging techniques. The bipolar disorder (BD) and major depressive disorder (MDD) were associated with different brain structural abnormalities. Very little studies have directly compared patients with BD and patients with MDD. And only 20% of patients who are experiencing a depressive episode are diagnosed with the disorder in the first treatment, and the mean delay between illness onsets and accurately diagnose is 5-10 years. The aim of this study was to examine whether the topological properties of brain structural networks could distinguish BD before the first manic episode from MDD.To our knowledge, this was the first original study to use DTI to evaluate disruption of the topological organization in the whole-brain network, in depressive episode participants with BD or MDD, as a 5-year prospective longitudinal study. Eighty MDD patients and 53 healthy controls (HC) were examined using diffusion tensor image (DTI). After at least 5 years of bi-annual follow-up with assessments of the HRSD-17 and Young Mania Rating Scale, 78 patients completed the study. Of these, 1 changed into dementia, 1 was amended schizophrenia, 12 were identified as BD and 64 patients initially diagnosed with UD, the conversion rate to BD was 15.4%. Considering the matching problems of general population such age, education among three groups, the final sample comprised 12 patients with BD, 44 patients with UD and 37 HC subjects. ANOVA (one-way) followed by FDR comparison test showed that local efficiency was significantly different among three groups in the left inferior frontal ($F=8.729$ and $=0.003$), and there were also differences in other frontal and insula regions belonging to limbic system (uncorrected).At baseline, the BD initially diagnosed of MDD displayed reductions in the nodal local efficiency compared with HC and MDD respectively, located within the left inferior frontal gyrus. There was no significant difference in the nodal global efficiency.The findings suggested that the nodal local efficiency could serve as a potential objective neuroimaging biomarker to distinguish bipolar disorder before they experience manic episode from MDD in the early time. Potential differential diagnostic biomarker could be predicted for BD before they were diagnosed, but the biomarker may be more significant after the manic episode.

Corticalthickness, cortical and subcortical volume abnormalities in patients withanxious depression

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Introduction:Anxious depression is a common, distinct clinical subtype of major depressivedisorder (MDD). Clinically, patients with anxious depression exhibit moresevere depressive symptoms, more somatic symptoms, and a higher proportion ofsignificant suicidal ideation than patients with nonanxious depression. But wehave little known about its neurobiological basis, and a few studies attempt toexplore brain structure change in patients with anxious depression.
Methods:MDD patients in anxious depression group with high levels of anxiety symptoms(n=23), whose score of ≥7 on the anxiety/somatization factor score of theHAM-D, the others whose score of ?7 in nonanxiousdepression group (n=22), and healthy controls (n=43) which matched age, sex,and education level. All participants were subjected to T1-weighted structuralmagnetic resonance imaging (MRI). We used an automated procedure of FreeSurferto analyze differences in cortical thickness, cortical and subcortical volume.
Results: MDD patients showed thinner cortical thickness in leftinferiortemporal, right superiortemporal, and right parsorbitalis compared withcontrols, between subgroups, anxious depression shows thinner corticalthickness in left superiorfrontal, right superiortemporal, and right lingual. Cortical and subcortical volume reduction of the left hippocampus in the MDD group, and the patients with anxious depression exhibited significantlyincreased subcortical volume in the bilateral caudates compared to those withnonanxious depression. Meanwhile, in anxious depression group, the volume of bilateral caudatewere directly proportional to the anxiety/somatiztion factor score. Conclusions:These findings suggested that smaller hippocampal volume might be a commonbrain structural change in patients with depression and/or anxiety, and the changeof caudate nucleus volume may be a possible neurobiology of anxious depressionand to separate it from nonanxious depressio.

Auditory steady-state gamma responsesof MEG in children with typical development and those with autism spectrumdisorders

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Background: Clinicalfeatures suggestive of atypical auditory information processing are frequentlyobserved in children with autism spectrum disorders (ASD). Gamma band activityhas been associated with many sensory and cognitive functions, and is importantfor cortico-cortical transmission and the integration of information acrossneural networks. Since auditory steady-state responses (ASSR) task can beeasily conducted in children and even in animals, it is gaining greaterinterests in translational research of psychiatry. In this study, weinvestigated auditory evoked magnetic fields during ASSR task in children with ASD andcontrol children with typical development (TD). Methods: Magnetoencephalographic (MEG) recordings during ASSR task were obtained for10 children with ASD and 20 with TD. Subjects listened to 500 ms durationbinaural click trains with a 25 ms inter-click interval during 306-channelElekta Neuromag® MEG recordings. Structural MRI data were also obtained for thesubjects. Distributed source analysis was performed using FreeSurfer and MNEsoftware. Time-frequency analysis was conducted using Fieldtrip toolbox ofMATLAB. We also examined the quantitative autistic traits with the SocialResponsive Scale. Results: Allthe subjects showed magnetic N1 (M100) component that peaks approximately 100ms withits generator located around the auditory cortex. Increased gamma oscillationpower dominant around right auditory cortex was only found in TD children withlow autistic traits.Conclusions: Childrenwith ASD showed atypical gamma oscillation, and our results suggest thatauditory evoked gamma band activity might be a useful biomarker related to autistictraits.

Spectral hypoconnectivity underlies perception of emotional faces in adolescent-onset borderline personality disorder

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Adolescent-onset Borderline Personality Disorder (BPD) is a highly prevalent condition in adolescent psychiatry that is characterized primarily by difficulties with emotional regulation; however, little is known about the neurobiological substrates that underlie BPD. Using MEG, we investigated emotional face perception in female adolescents (age 13-17) with BPD and an age-and sex-matched control group. Participants viewed an emotional face (happy or angry) and a scrambled face that appeared on either side of a central fixation point; they were instructed to respond to the side showing the scrambled face. Event-related perturbations in oscillatory synchronisation were calculated in canonical frequency bands (theta through high-gamma) to characterise task-related functional connectivity changes. A neuroanatomical atlas defined 90 *a priori* seeds, a vector beamformer recovered time-series from these nodes, and the cross-trial phase synchrony was computed between areas using the Phase Lag Index (PLI). Both groups displayed increases in mean whole-brain spectral connectivity across low-frequency ranges during stimulus presentation; however, the greatest apparent between-group difference was observed in the beta (15-30 Hz) band, with the BPD group exhibiting hypoconnectivity compared to controls. Moreover, this difference was greater for viewing angry expressions, and the enhanced beta in controls compared to BPD was localised to edges connecting right fronto-parietal seeds. An ROI analysis of insula, amygdala, and ventromedial prefrontal cortex also revealed a consistent pattern of hyposynchrony in the BPD group. These distinguishing spatiotemporal patterns show that adolescents with BPD exhibit reduced spectral connectivity in key regions and systems involved in emotion regulation - this suggests atypical oscillatory dynamics may play a central role in one of the defining pathophysiological features underlying adolescent-onset BPD.

A multimodal investigation of inhibition in schizophrenia

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A longstanding theory of schizophrenia has been an abnormality of the cortical inhibitory/excitatory balance [Curley et al., 2011], especially in the subset of inhibitory neurons responsible for gamma oscillatory activity [Lewis et al., 2005]. Intuitively, patients have demonstrated reduced oscillatory activity across frequency bands, including gamma band frequency and amplitude during rest and when completing cognitive tasks [Chen et al., 2015].Previous studies in this patient group have tended to investigate one or two modalities with varying success. Here we have combined all 3 of these measures to create a multi-modal investigation of cortical inhibition in patients with schizophrenia and healthy controls.Using occipital MRS GABA, visually induced oscillatory measures, and an orientation discrimination task previously linked with inhibitory processes [Edden et al., 2009; Katzner et al., 2011], we investigated levels of inhibition in 28 patients with schizophrenia and 30 cohort matched controls.Patients demonstrated significantly reduced occipital GABA levels, gamma amplitude and frequency and poorer performance on the orientation discrimination task.These findings strongly suggest reduced inhibition in the patient group across all modalities tested. Interpretation of these results could also benefit from neurophysiologically-informed modeling such as dynamic causal modeling (DCM) to make inferences about associated neuronal parameters and, in this instance, how these differ between patients and controls, as well as predicting gamma oscillation parameters, GABA levels and performance on the orientation discrimination task [Kiebel et al., 2009].

Testing two neurobiological models of client speech during intervention sessions for alcohol use using MEG

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Client change talk (CT: a type of client speech that suggests behavior change) and sustain talk (ST: a type of client speech that opposes behavior change) occur during intervention sessions and have accumulated evidence as mechanisms of behavior change for problematic health behaviors such as alcohol use disorder. The brain networks that underlie this speech are not well understood. Two competing models have emerged: a data-driven neurobiological model and a model based in speech act theory. This study used magnetoencephalography (MEG) to elucidate the brain networks underlying client change and sustain talk. Intervention sessions were conducted by an expert clinician, digitally recorded, and rated using a behavior coding system that permitted extracted of utterances for use as experimental stimuli. During MEG acquisition participants heard utterances of their speech, presented in a random order. After standard preprocessing, brain networks for epochs of change talk and sustain talk were assessed in a seed-based analysis using the weighted de-biased phase lag index with seeds in insula and transverse temporal gyrus (TTG), and the results compared using cluster permutation tests. Consistent differences in connectivity with the TTG seed between client change language (i.e., the combined estimate of CT and ST) and neutral speech were seen in the left hemisphere in the insula, and in the right hemisphere in insula, temporo-parietal cortex, and middle frontal cortex. Significant connectivity differences between CT and ST with the TTG seed were seen with left temporo-parietal cortex, and with the insula seed in right middle frontal cortex and parietal-occipital cortex and left temporo-parietal-cortex. Results are more broadly consistent with recent MEG studies of speech act theory than with the competing data-driven model. Further specification of the data-driven model may be desirable to incorporate the interactions and timing of network components.

Functional connectivity during auditory verbal hallucinations in schizophrenia patients

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Auditory verbal hallucinations (AVH) are highly distressing to patients with schizophrenia and can result in clinically significant depression, impaired social and occupational functioning, and increase risk of suicide. An auditory activation model (AAM) of AVH suggests that AVH result from abnormal synchrony between parietal and auditory cortex, leading to the erroneous interpretation that the patient's internal monologues come from a third party. Specifically, theta/alpha band synchrony with temporal auditory cortex stamps that internal monologue as coming from the external environment. The goal of the present study was to test the AAM by evaluating seed-based connectivity with auditory cortex in a sample of schizophrenia patients during AVH. Twenty adult schizophrenia patients (SP) with AVH were recruited and scanned using a whole-cortex 306-channel MEG array. During the scan, SP were instructed to respond with their right index finger to indicate that an AVH had begun, and with their left index finger to indicate that the AVH had ended. After standard preprocessing and epoching, phase lag index (PLI) was computed relative to transverse temporal gyrus (TTG) and superior temporal sulcus (STS) for AVH onset and offset in the theta and alpha ranges. Subject PLI estimates were compared across conditions using permutation cluster tests in MNE-python. In the theta band, significant differences in TTG connectivity between AVH-on and AVH-off were observed in anterior temporal, medial temporal, and posterior parietal cortex. Auditory cortex connectivity estimates differed significantly between AVH vs. non-AVH. The heightened connectivity observed between TTG and parietal cortex suggests that the experience of AVH is linked to abnormal synchrony that is related to SP perception that the voices they hear derive from an external source. While this generally supports the AAM, further study is required to assess the criticality of temporal-parietal synchrony in AVH.

Machine-learning-based diagnosis of schizophrenia using combined sensor-level and source-level EEG features

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Recently, an increasing number of researchers have attempted to differentiate patients with schizophrenia from healthy controls using machine learning methods with EEG biomarkers. Some of these studies used sensor-level biomarkers, such as ERP amplitude and latency, as features for classification. However, source-level features have not been widely applied to clinical applications, and have especially never been applied to machine-learning based diagnosis of schizophrenia. In this study, we used both sensor-level features and source-level features for the differentiation of schizophrenia patients and healthy controls. EEG signals elicited by an auditory oddball paradigm were recorded from 34 patients with schizophrenia and 34 healthy controls. The P300 component used as sensor-level feature was measured by assessing positively going maximum peak and latency in time window 250–500 ms. Also, cortical source activity was localized using minimum norm estimation, and time series at multiple cortical regions were evaluated, which were used as source-level features. The 1 to 20 candidate features were selected using Fisher's score from sensor, source and combined feature sets, and the classification accuracy was evaluated using leave-one-out cross-validation. A maximum classification accuracy of 88.24% was obtained when the combined feature set was used, whereas the highest classification accuracies were 80.88% and 85.29% for sensor-level and source-level feature sets, respectively. By investigating 15 features selected from the combined feature set, we also found that eight sensor-level features were located in the frontal area and seven source-level features were distributed in the left temporal cortex. The features selected from both sensor-level and source-level feature sets reflected well-known electrophysiological dysfunction in schizophrenia, which might contribute to the high classification accuracy of our approach.
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Neuromagnetic signatures of impaired cognitive control in schizophrenia

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Cognitive impairment is a core feature of schizophrenia that presents independently of general intellectual impairment, is present prior to first psychotic episode, and is present in the first degree relatives of patients. Additionally, cognitive impairment is strongly predictive of functional outcome whereas other clinical symptoms, especially psychotic symptoms, are not. In combination, these factors suggest that cognitive dysfunction may be an endophenotype of schizophrenia. Of the impairments identified, those pertaining to cognitive control processes, which enable flexible adjustment of thought and behavior giving rise to goal-directed activities, are among those most consistently observed. The aim of the current study was to further understand the neural basis of impaired cognitive control in schizophrenia using a prototypical cognitive control paradigm, the stop-signal paradigm, which operationalizes the ability to inhibit a cued motor response (response inhibition) upon presentation of a countermanding \'stop-signal\' cue. Critically, stop-signal procedures enable estimation of the latency of the inhibitory response, the stop-signal reaction time (SSRT), which is strongly associated with both the amplitude of hemodynamic activity and low frequency oscillatory activity (alpha-theta band) in the right inferior frontal gyrus (rIFG) during successful inhibition trials. Studies consistently report that SSRT is slowed in SZ, and in previous work we linked slow SSRT in SZ to diminished hemodynamic activity in rIFG. In the current study, patients with schizophrenia (SZ) and healthy controls (HC) performed 560 trials (28% with stop-signals) of the stop-signal paradigm that titrated a 50% inhibition rate (~80 successful inhibitions) while under-going magnetoencephalography (MEG; ELEKTA Triux) recording. Preliminary analysis of one HC data set has revealed a strong broadband response at a sensor over rIFG peaking about 30 ms before estimated SSRT (238ms).

MEG analysis of connectivity changes due to DBS in a single patient with OCD

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Objective: Deep Brain Stimulation (DBS) has shown some promise in the treatment of refractory obsessive-compulsive disorder (OCD). We present a preliminary analysis of changes in neural connectivity pre- and post- surgery measured using MEG in a single patient with bilateral implantation of 4 direct-contact electrodes in the nucleus accumbens and stimulation protocol of 130Hz.

Methods: As part of a larger protocol, 5 minutes of resting state data was collected using an Elekta TRIUX 306 channel MEG both pre- and post-surgery, with the stimulator turned on during the second session. The brain was partitioned according to the automated anatomical labelling (AAL) atlas and source modelling was carried out using a SAM beamformer to produce estimates of the time course at each anatomical location for a range of temporal frequency bands. The Phase Lag Index (PLI), a measure of connectivity which is robust to zero phase artifacts, was used to calculate the connectivity between every pair of regions. The difference in the entries in the resulting weighted adjacency matrices for the pre- and post- recording sessions were then tested for significance using a non-parametric permutation procedure.

Results:
i) A bilateral increase in the strength of connections to the lingual gyri in theta band (4-8Hz), and also the right middle occipital gyrus in both theta and alpha (8-13Hz) bands was observed. These regions have been found to be involved in a previous PET study of OCD patients who had undergone a capsulotomy [1], where increased metabolism in precentral and lingual gyri post operative for OCD patients was measured, and clinical improvement in patients was found to be correlated with metabolic changes in the right middle occipital gyrus.
ii) Widespread increases in connectivity in gamma (30-80Hz) and high gamma (80-120Hz) were found across the whole brain, with particularly large increases in the strength of connections to right thalamus and right temporal regions.

Conclusion: Nucleus accumbens DBS at 130Hz modulates brain connectivity in theta, alpha and gamma networks and these changes can be measured using MEG.

1. Zuo C et al. Metabolic imaging of bilateral anterior capsulotomy in refractory obsessive compulsive disorder: an FDG PET study. J Cereb Blood Flow Metab. 2013 Jun;33(6):880-7.

Revisiting the functional neuroanatomy of post-traumatic stress disorder: insights from meta-analysis and whole-brain connectomics

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An extensive body of research has shown that exposure to extreme stress and traumatic events can have a profound impact on the structure and function of the brain (1), possibly leading to post-traumatic stress disorder (PTSD). The traditional and most established neuroanatomical model of PTSD (2) posits a limbic-prefrontal imbalance caused by hyperactivity of the amygdala and hypoactivity of the medial prefrontal cortex. However, over the last decade, this model has been contradicted by many studies showing different activation patterns (3) and involvement of additional areas not considered initially (4, 5). These inconsistencies could be partly due to the use of different control groups across studies, i.e. non-PTSD individuals with or without a history of trauma exposure.

We have conducted a large quantitative meta-analysis contrasting trauma-exposed individuals with and without PTSD. Our results show that, compared to trauma-exposed controls, regions of the basal ganglia were differentially active in PTSD, whereas the comparison with trauma-naïve controls revealed differential involvement in precuneus, cingulate and orbitofrontal cortices (6). Our current work focuses on the role of these circuits in PTSD and trauma regulation by investigating differences between war veterans with PTSD, war veterans without PTSD, and trauma-naïve civilians using 3 highly complementary imaging techniques (diffusion weighted, functional magnetic resonance imaging and MEG) with a strong focus on whole-brain, anatomy-guided computational modelling of functional connectivity.

[1] Cerqueira (2007) The Journal of Neuroscience, 27 [2] Rauch (2006) Biological Psychiatry, 60 [3] Bryant (2005) Biological Psychiatry 58 [4] Chen (2009) BMC Psychiatry 9 [5] Fonzo (2010) Biological Psychiatry 68 [6] Stark (2015). Neuroscience and biobehavioral reviews 56

Magnetoencephalographical Targets for Measuring Theory of Mind Deficits in Schizophrenia

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heory of mind(ToM) is widely known as a crucial component of social cognition. ToM deficits can be associated with other neurocognitive factors and psychotic symptoms in patients with schizophrenia. Several ToM studies with MEG have been conducted but still we need to find proper targets to be measured in MEG. Objective: This study was conducted to find MEG measurement targets which could provide differences between patients with schizophrenia and a healthy control group in ToM and to examine relationships among intelligence, ToM, and delusion in patients with schizophrenia. Method: Data was collected from 50 patients of schizophrenia and 32 healthy subjects. The PASW 21.0 program was used for t-test, ANCOVA, and, Pearson's Correlation. Measurements used for this study were Korean-Wechsler intelligence scale, Hinting task, False belief task, Emotional attribution test (EAT), and Peters delusion inventory. Results: Performances of the ToM and intelligence in patients were lower than healthy controls. After controlling the impact of intelligence, education level, and age, there was a difference between patients and healthy controls on the performance of the Hinting task. The false belief task was correlated with delusions and intelligence. The hinting task was not correlated with any clinical variables. EAT was correlated with intelligence. Through the finding of this study, ToM and emotion attribution is highly recommended as new target factors considering to develop interventions for schizophrenia. Consequently, the ToM deficits imply significant changes in cognitive functions such as memory, attention. Therefore, reasonable hypothesis is that a lack of integrity in fronto-limbic networks of the brain are associations with social cognitive impairments in schizophrenia patients and the functional connectivity and interband modulation of the relatively shallow cortex sources in the frontal area can be proper targets in the MEG measurement.

Automatic inhibition function in the somatosensory and motor cortex: An MEG-MRS study

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Background: Sensory gating (SG),an index of automatic inhibition function, can be reliably measured in theprimary somatosensory cortex (SI). The beta oscillations (13-30 Hz) induced byelectrical stimulation is considered to be located in the primary motor cortex(MI) and also associated with inhibition function. Furthermore, it has beenreported that the neurotransmitter GABA plays a vital role in the inhibitionmechanisms. However, the functional significance and the relationships amongthese neural functions remain unclear. Thus, we aimed to examine whetherautomatic somatosensory inhibition, as indexed by P35m SG ratio, and automaticmotor cortical inhibition, as indexed by beta rebound power, would be modulatedby GABA concentration in the sensorimotor cortex. Methods: We recruited 15 healthy young adults (aged 20-34 yearsold, 5 females) in this study. In one MEG session, the left median nerve wasstimulated by paired-pulse electrical stimulation to evaluate the P35m SG ratioof the SI. In another MEG session, a repetitive electrical stimulation wasdelivered to the left median nerve to assess the beta rebound power of the MI.In the MRS session, GABA levels were measured with a region of interestcentering at the left central sulcus. The associations among P35m SG ratio,beta rebound power, and GABA levels were assessed. Results: A lower P35m SG ratio of the SI was significantlycorrelated with a higher power of beta oscillations of the MI ($r = -0.737$, $p =0.001$). We also found that the power of beta rebound was positively correlated withGABA levels ($r = 0.505$, $p = 0.039$). The association between P35m SG ratio of theSI and GABA concentration did not reach statistical significance. Conclusions: There is a strongassociation of automatic inhibition function between SI and MI. However,compared to the SI, sensorimotor GABA concentration plays a more important rolein the modulation of MI rhythms regarding automatic inhibition function.

Co-operation between S1 and S2 neuronal population is crucial for the high-frequency (> 100 Hz) vibrotaction

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How our brain perceives various tactile frequencies differently is largely unknown. Many single-unit studies have investigated this issue in S1 and S2; however, population activities can also contain important information about stimulus characteristics. We aimed to investigate whether the population activities in S1 and S2 show different patterns when vibrotactile stimuli are delivered. Specifically, we investigated the possibility that these patterns can also be observed during texture scanning. Six patients with intractable epilepsy participated in this study. ECoG signals from S1 and S2 were obtained during pin-point vibrotactile (5, 20, 35 Hz for flutter; 100, 250 and 400 Hz for vibration) and texture (coarse and fine) stimuli (1 and 1.5 s, respectively). Stimuli were delivered to the index fingertip contralateral to the recording site. For time-frequency analysis, wavelet transform was applied to the data, and then the transformed data were normalized. To test significance among stimulus conditions, high-gamma (HG) powers were averaged across 50-140 Hz and stimulus period. To investigate temporal dynamics of HG power during stimulus periods, we calculated binned HG power time series of each condition. For single-trial classification of stimulus frequency based on the HG power, we performed simple and multiclass SVM analyses. We found that S1 and S2 neuronal population activities for vibration (>100 Hz) are distinct from those for flutter, and their differences can be observed in HG powers. In S1, HG powers in vibration were attenuated more quickly than that in flutter, and their patterns were frequency-specific. Specifically, we found that prominent frequency-specific S2 HG power changes during vibration stimuli, and their difference were highly consistent. More importantly, we found that these HG patterns can also be observed in coarse/fine texture stimulation. Our results indicate that co-operation mechanism between S1 and S2 is critical for neural processing about high-frequency vibrotaction.

Somatomotor Mapping in MEG

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Introduction: Somatotopic/motor mapping allows separation of the brain's representation of individual digits. This is possible using functional magnetic resonance imaging (fMRI), but is typically thought to be more challenging in MEG. However, whether this is an inherent problem of the ill-posed inverse problem, or results from errors in co-registration, forward modelling and movement, remains to be resolved. Here we use a subject-specific headcast to allow repeated MEG measurements to be made on a single subject, negating both co-registration errors and subject movement. We generate a subject specific somatomotor map using MEG data and contrast our findings to results obtained at ultra-high field (7T) fMRI. Methods: 1 subject (male, age 26) took part in a right hand finger tapping MEG experiment on 8 separate occasions using a subject-specific headcast. The subject, when prompted, tapped digit 2 for 2s, followed by 8s rest, then digit 5 for 2s followed by 8s rest, repeated for 44 trials. Beamformer pseudo-T-statistical images contrasting the beta rebound to rest were constructed for each finger on each run to find a peak location in motor cortex. The same experiment was repeated once using 7T-fMRI (8s tapping, 20s rest, repeated 6 times for each digit). Peak locations were found using FSL FEAT [1]. Results: The general pattern of the peak locations for the 2 digits in MEG agrees significantly with results from fMRI, with digit 5 shifted superior and medial compared to digit 2. Specifically in MEG we see a significant (p=0.0001) increase in the z-coordinate of the peak moving from Digit 2 to Digit 5 (4+/-1.5mm [mean+/-STD]), as well as a significant (p=0.002) movement in the medial direction (2.3+/-1.3mm [mean+/-STD]). Overall results show that the use of a headcast enables somatomotor maps to be formed in MEG which match significantly to those in fMRI. References: [1] Woolrich,Mark W., et al. Neuroimage 45.1 (2009): S173-S186.

Evidence for a proprioceptive mismatch response: Distinctive responses to actual and predicted stimulation

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Oddball paradigms have been extensively investigated in the auditory modality where a so-called electrophysiological mismatch negativity (MMN) is elicited by oddball stimuli, i.e. stimuli that differ from an expected pattern. It is theorized that predictive information is encoded in the brain, and that the MMN reflects the mismatch between predicted and actual stimulation. Here, we extend this research topic into the little explored domain of proprioception. We measure magnetoencephalographic (MEG) activity while generating passive proprioceptive stimulation to the right index finger with a custom-made stimulator (\"PAM\"), using artificial muscles to generate the finger movements. In Experiment 1, we move the finger at a 2.8 Hz rate, using pseudo-random omissions of movements as oddballs. In Experiment 2, we instead use a 1 Hz rate, with oddballs that are time-shifted, so they either come earlier or later than expected.
The results for Experiment 1 show that two different frequencies exist that reflect cortico-kinematic coherence, one at the frequency at which the finger is moved ( ) and one at its first harmonic ( ). With source reconstructions using beamformers we find that the MEG activity cohering with   and   can be clearly localized to separable and expected parts of the somatosensory cortex. The results show that *only* F is shared between unexpected and expected stimulation, thus indicating that F_0 coheres with the *actual sensory stimulation*, while F_1 coheres with the *prediction or expectancy of future sensation*.
In Experiment 2, the results show that longer and shorter oddballs give rise to amplitude differences in the event-related fields after ~ 120 ms, thus revealing a typical mismatch response. The results also show evidence of the mismatch response being bilateral. This particular pattern may be interpreted as an alertness response for the ipso-lateral hemisphere.
In conclusion, we believe that we have shown the first proprioceptive mismatch response.

Positive and Negative emotions affect the somatosensory cortex

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To examine changes in somatosensory cortical activity associated with the processing of emotional images, we measured steady-state somatosensory evoked fields (SS-SEFs) of magnetoencephalograms (MEGs) under tactile stimulation. We used the International Affective Picture System (IAPS) which is increasingly used in brain imaging studies to examine emotional processes. Those images, along with synchronous tactile stimuli, were randomly presented for 2.0 s using a video projector and a screen set at 120 cm in front of the subject. The tactile stimuli were applied to the tip of the right index finger. A stimulus epoch consisted of a 2.0 s period of vibration at 10-Hz or 20-Hz and a silent period of 1.0 s. At least 50 epochs were recorded for off-line averaging of the MEG signals for each condition of negative, positive, or neutral images, according to the prior categorization by each subject. The amplitude of the SS-SEF was larger for the negative impression images than for the neutral and positive impression images ($p < 0.05$) for the 10 Hz stimulation, suggesting that the amplitude of the SS-SEF that originated from the somatosensory cortex was modulated by the visual emotional stimuli.

MEG-compatible pneumatic movement actuator to study stretch-reflex of human plantar flexors

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Brisk angular displacements elicit distinct short- (M1) and long-latency (M2) muscular activations in the stretched muscles, i.e., a stretch-reflex. M1 response is mediated mainly through monosynaptic input from muscle mechanoreceptors to the spinal cord whereas M2 response may have transcortical contribution. We have developed a non-magnetic movement actuator for the ankle joint to study the stretch-reflex, and the associated cortical processing.

The ankle joint movements were produced by pneumatic artificial muscles that shorten with increased air pressure. We studied cortical stretch-reflex-evoked fields (SR-EFs) by stretching the plantar flexor muscles briskly (~200 deg/s) 75 times once every 6 s, while the subject's brain activity was measured with whole-scalp MEG, soleus muscle activity with surface electromyography (EMG) and foot kinematics with a 3-axis accelerometer. The measurements were carried out at the Jyväskylä Centre for Interdisciplinary Brain Research.

The movements were repeatable with only ~5% variation in the peak acceleration magnitude. In all ten subjects (25 ± 3 y) tested, a clear SR-EFs were detected above the vertex with starting 46 ± 11 ms after movement onset (main peak latency was 109 ± 31 ms). A typical stretch-reflex response was observed in soleus EMG starting 48 ± 17 ms after the movement onset with M1 peaking at 73 ± 21 ms and M2 peaking at 101 ± 21 ms.

Our novel ankle-movement actuator thus provides a robust tool to elicit stretch-reflexes for plantar flexors in MEG, and to study the movement-related cortical proprioceptive processing in relation to various types of ankle movements, and, e.g., to quantify proprioceptive afference using corticokinematic coherence. Finally, the timing of SR-EFs and M2 responses indicates that transcortical loop can influence the long-latency components of the stretch-reflex.

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Affective touch in the brain: MEG recordings to pleasant touch using a novel brush robot

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Although many magnetoencephalographic (MEG) studies have focused on cortical responses to transient electrical or mechanical stimuli, our knowledge about somatosensory evoked fields (SEFs) to ecologically meaningful touch is limited. The sensory system of unmyelinated afferents with low mechanical thresholds, C-tactile (CT) afferents, plays a key role in signaling pleasantness of touch. CT firing measured in single unit recordings is highest when a soft object strokes the hairy skin with a velocity near 3 cm/s. Previous studies using functional magnetic resonance imaging have shown that CT afferents project to the insula but not to primary or secondary somatosensory cortices. In this study, combined MEG and EEG was recorded in 19 healthy volunteers (22-45 years) with an Elekta Neuromag® TRIUX system during 200 ~3 cm/s brush strokes delivered to the left arm using a custom-made MEG-compatible brush robot. Horizontal and vertical movement of the brush was controlled with two computer-controlled pneumatic muscles that enabled precise and replicable timing, length and velocity of brush stroke stimuli. A multifilament fiber-optic sensor was attached alongside the bristles of the brush, marking the timing of brush contact with the skin, and a load cell was used to measure the pressure applied on the skin. Preliminary results show clear and consistent SEFs to the onset and offset of the brush strokes i.e., contact with the skin. The earliest SEF component peaks at 100 ms from stimulation onset and is strongest over contralateral parietal sensors. Time-frequency analyses show patterns of early onset beta and alpha de-synchronization, most prominent over parietal areas, and alpha synchronization with a very late onset of around 700 ms. The brush robot is a promising tool for future clinical and basic MEG research regarding social touch, e.g., in autism spectrum disorder and anorexia nervosa.

Inhibition in the Somatosensory System – A Neuro-pharmacological Magnetoencephalography (MEG) Study

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Background: Inhibition and thus the GABA-ergic system appears to be a powerful mechanism to orchestrate cerebral information processing. Interestingly, different GABA-receptors have specific reaction-kinetics. In the somatosensory system, we anticipate that fast GABA-A receptors play a major role in rapid information processing at the level of primary sensory cortex (SI), while GABA-B receptors are assumed to be involved at the level of secondary somatosensory cortex (SII) operating at longer time constants. To test this hypothesis, we studied neuromagnetic source activity evoked by tactile stimuli delivered to the index finger of the left hand while subjects received either GABA-A agonists alprazolam (Alp) or ethanol (Eth), the GABA-B agonists baclofen (Bac), or placebo (Pla). GABA-dependent decreases of source activities in contralateral SI and ipsi- and contralateral SII with respect to activations under placebo were assessed.
Method: 16 male subjects participated in 8 sessions receiving each of the four drugs (Alp, Bac, Eth or Pla) in two sessions. Somatosensory evoked responses were recorded using a 275-channel MEG system. For each subject, activities in SI and contra- and ipsilateral SII were modelled and source activities were estimated. Drug dependent differences of peak amplitudes were statistically evaluated using repeated measures ANOVA.
Result: When comparing the effects of GABA-agonists to the placebo condition a significant reduction in source activity was found for Bac in contralateral SII. Furthermore, a trend towards a reduction of amplitudes in SI could be found for Alc and Eth.
Discussion: Results tentatively confirm the hypothesis that fast inhibition in SI is mediated by GABA-A receptors while slow inhibitory processes in SII appear to be mediated by GABA-B receptors. A combined neuropharamcological and -physiological approach provides a valuable tool to disentangle inhibitory control in paradigms using multiple competing stimuli.

Declination of geomagnetic field acts as a positive geotactic modulator in the fruit fly

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The geomagnetic field (GMF) has been known for asensory cue in magnetoreceptive navigational animals such as birds,butterflies, and sea turtles in their long distance migrations. Those animals perceiveand exploit the information of total intensity or inclination of GMF for suchmagnetoresponsive journey. Recently, we reported that GMF modulates positivegeotactic i.e., downward movement of the fruit fly, *Drosophila melanogaster* in a defined magnetic fields space producedwith a 3-axis Helmholtz coil system. Here, we show that declination (angle between magnetic north and true north ata certain position on the earth), one of the parameters of GMF modulatespositive geotactic movements of fruit fly. In a tube positioning assay, absolutevalue of declination and downward movement of the flies showed an inversecorrelation each other. Interestingly, the antennae of flies significantly movedup and down by the change of declination compared to the ambient GMF condition,suggesting that the antennae were responsible for the magnetoreceptivebehaviors in the GMF condition. Moreover, pinching with forceps either one of orboth the second segments of the antennae, remarkably hampered the declination-dependentgeotactic movement and the declination-dependent antennal motion. These resultsshown in flies suggest for the first time that declination of GMF isdiscriminated and used as a geotactic modulator in magnetoreceptive organism.

Somatosensory evoked magnetic fields in patients with free flap reconstruction of the tongue

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Purpose

Whether reconstruction of the tongue with radial forearm free flap can lead to functional recovery remains unclear. Magnetoencephalography (MEG) was performed to obtain objective evidence for functional recovery of reconstructed tongue.

Methods

Six patients aged 52 to 71 years (5 males)who received partial glossectomy and reconstructive surgery with forearm flap for tongue carcinomagavewritten informed consent, according to the guidelines of Tohoku University Graduate School of Medicine ethical committee and the Declaration of Helsinki. MEG was performed 27 to 111 months after surgery. Electrical current dipole analysis was conducted for somatosensory evoked magnetic fields (SEFs) of both the healthy and reconstructed sides of the tongue. SEFs were recorded in a magnetically shielded room with a 200-channel whole-head type axial gradiometer system, and individual T1-weighted magnetic resonance images were obtained with a 3-T magnetic resonance imaging scanner. Presence of the cP55m response was evaluated, which is indicative of the contralateral response at the peak latency of 30-100 ms with posterior orientation (Nakahara et al., 2004).

Results

Cortical responses of the reconstructed side of the tongue were recorded in the contralateral side to stimulation in 3 of 6 hemispheres (mean +/- standard error, 60.5 +/- 12.2 ms), whereas cortical responses of the healthy side of the tongue were seen in all 6 hemispheres (50.2 +/- 2.7 ms). All equivalent current dipoles were estimated at locations on the central sulcus.

Conclusions

MEGcould demonstrate functional recovery ofthe reconstructed tongue with free flap.

Reference

Nakahara H, et al.(2004)J Dent Res. 83: 307-311.

Neuromagnetic responses to tactile stimulation of the fingers: Evidence for reduced post-synaptic GABAergic inhibition in children with Autism Spectrum Disorder and Epilepsy

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The recording of somatosensory magnetic fields (SEFs) is common place for the assessment of the functional integrity of the somatosensory system. The first cortical response following transient tactile stimulation has been termed the N30m, which peaks at about 30ms, has an anterior orientation, and is believed to reflect EPSPs within Rolandic cortex. This is followed by a P50m component which has a posterior orientation indicating intracellular current flow directed from superficial to deeper cortical layers, and is thought to be due to post-excitatory GABA mediated IPSPs. Recently, there has been considerable interest in in vivo MRS measures of GABA in clinical pediatric populations such as Autism and Epilepsy, and while clinically distinct, both disorders have been associated with reduced GABA levels. In this study, the somatosensory P50m response was compared for three groups of children: typically developing (TD), autism (ASD), and epilepsy (EPI). We anticipated that ASD and EPI groups would have reduced P50m magnitudes compared to TD.

MEG was recorded during pneumatic stimulation of the right and then left index fingers. The P50m was used as a measure of primary somatosensory cortex activity. We collected 500 trials (400ms epochs; -0.1s to 0.3s, BP 1-40Hz). P50m peak amplitude was averaged across both hands for each group (TD: 670±293fT; ASD: 488±157fT; EPI: 444±108fT). P50m peak amplitude was significantly higher for TD than both ASD ($p=0.006$) and EPI ($p=0.001$), however ASD and EPI were not significantly different ($p=0.138$). These results demonstrate that the P50m peak amplitude is significantly reduced in children with autism and epilepsy. As the P50m response may index GABA signaling, the decreased P50m amplitude may reflect low GABA signaling in EPI and ASD children. Further study of in vivo MRS measures of GABA in these clinical populations may help to further understand the role of GABA in the generation of the P50m response.

Response Gating in the Somatosensory System: A MEG study of the spectro-temporal dynamics, functional connectivity, and developmental trajectory

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Sensory gating is a phenomenon in which neuronal responses to subsequent similar stimuli are suppressed when they occur in a series. It is thought to represent a mechanism by which redundant stimuli are partially “filtered out,” preventing excessive environmental stimulation from overloading shared neural resources. Gating has been demonstrated in a number of sensory domains, including in the somatosensory system, but the underlying neuronal dynamics and developmental trajectory have been only partially identified. In the current study, we adopted a data-driven approach to map the spectro-temporal amplitude and functional connectivity (FC) dynamics that support sensory gating in the somatosensory system (somato-SG) in healthy children and adolescents. We applied paired-pulse electrical stimulation to the tibial nerve of the non-dominant leg of each participant during magnetoencephalography (MEG). These data underwent time-frequency decomposition and bands with significant signal changes were imaged using a beamformer. Virtual sensors (voxel time series) were then extracted from the peak voxels and these signals were examined in spectral- and time-domains, and subject to FC analysis using phase coherence. Our results indicated a significant decrease in the amplitude of the 10-75 Hz neural response following the second stimulation relative to the first in the primary somatosensory cortex (SI). A significant decrease in stimulation-to-response latency was also found between stimulations, and each stimulation induced a sharp decrease in phase locking between somatosensory cortical regions. Further, the relationship between somato-SG metrics and age was completely flat. We conclude that somato-SG involves oscillatory responses stretching from 10-75 Hz, with rich dynamics and alterations in inter-hemispheric dynamic connectivity, and that this phenomenon has already matured by early childhood.

Magnetoencephalographic study of neuromagnetic responses to vibrotactile stimulation

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Cutaneous receptors in skin, such as cutaneous mechanoreceptors, nociceptors and thermoreceptors, can receive sensory inputs including touch, pressure, vibration, temperature and pain. Among different cutaneous mechanoreceptors, the Pacinian corpuscle is known to detect high frequency vibrations (50-400 Hz). The cortical responses to the high frequency vibration are known to be different from the responses to the relatively low frequency flutter (5-50Hz). Since the cortical information processing occurs very fast, i.e., in the range of milliseconds, the magnetoencephalography (MEG) was used to study the temporal processing of tactile information in many studies. Most studies, however, were about tactile responses to light touch or flutter stimuli. We recorded whole-head MEG data during high frequency vibrotactile stimulation on fingertips. The vibrotactile stimuli were delivered to the tip of an index finger using an MEG-compatible polymer based tactile actuator. Sinusoidal displacements were applied to the skin at around 150 Hz for 200 ms duration repeatedly. We investigated the ipsilateral and contralateral responses to the tactile vibrations, initially using the time domain analysis to identify the cortical activation areas. Then we performed the frequency analysis to real the cortical alpha and beta band activities in response to the vibrotactile stimuli. Since the vibration at 150 Hz was within the audible range, the auditory evoked responses were also recorded and compared with the vibrotactile responses at the same frequency.

Magnetoencephalographic Study on Cortical Activity Evoked by Warm Stimulation in Human

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Warm sensation has rarely been studied although other cutaneous sensation are being investigated actively because of weak cortical responses evoked by warm stimulation and limitation of stimulator. For a research of warm sensory processing, we developed warm stimulator using diode laser with 980nm wavelength and measured magnetoencephalographic cortical activity of warm sensation without pain and tactile sensation. To generate warm sensation, 400ms pulsed laser beam was guided into the left index finger of 30 healthy subjects. Experimental paradigm consists of three blocks which warm stimuli were delivered 50 times with 10s inter-stimulus interval. 500Hz auditory beep sounds were provided as trigger signals 3 seconds after the warm stimuli. When the subjects hear the auditory sound, they press 'yes' or 'no' button by right index finger to evaluate whether they could perceive warm sensation or not. The recorded Magnetoencephalographic signals divided into epochs (-1s pre- to 3s post-warm stimulus onset) and were band-pass filtered at 0.02~40Hz. We rejected artifacts using ICA method and selected trials that subjects pressed 'yes' button. We obtained Warm-related fields (WRFs) from averaging the selected trials and applied time-frequency analysis to determine event-related desynchronization (ERD) and synchronization (ERS). WRFs were found about 1.3 seconds after the stimulus onset. The field distributions on MEG sensor space at the peak of WRFs show bi-lateralized activation in the somatosensory area. Cortical sources of WRFs were seen in the bilateral secondary somatosensory area and contralateral primary somatosensory area. The amplitude of alpha and beta oscillations in the somatosensory area decreased around 1 second after the warm stimulation. The late latencies of WRFs support the slow activation of the warm specific unmyelinated C-fiber. The cortical activation of the contralateral primary somatosensory area as well as bilateral secondary somatosensory area are associated with the warm sensation. The amplitude decreases of alpha and beta oscillations in the somatosensory area may represent activation of somatosensory area during warm sensation.

Proprioceptive stimulation in magnetoencephalographic recordings

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Our ability to detect and control the movements of own body parts is largely based on proprioceptive input from joints, tendons, and muscles. Proprioception has not been studied in detail with modern neuroimaging methods due to lacking stimulation methods. Here I summarize approaches that we have developed for stimulation and analysis of proprioception-related MEG signals.

We use accelerometers to monitor active (self-paced) or passive movements, calculate “corticokinematic coherence” (CKC) between the accelerometer and MEG signals to reveal the active brain regions, and elicit precise and reproducible passive movements with pneumatic artificial muscles, driven by a computer.

We found robust sensorimotor MEG signals at the movement frequencies and their harmonics, with sources in the sensorimotor cortex. Self-paced and passive movements elicited rather similar proprioceptive responses.

Proprioceptive stimulation provides a robust tool for sensorimotor mapping and proprioceptive assessment of both healthy and diseased brain. It may also be useful in rehabilitation as an ecological connection to the sensorimotor processing.

References: Bourguignon et al., Neuroimage 2011; 55:1475–1479. Bourguignon et al., Neuroimage 2012: 59:1648–1691. Piitulainen et a.., Neuroscience 2013; 238:361–370. Bourguignon et al., Neuroimage 2015; 106:382–390. Piitulainen et al., Neuroimage 2015; 112:310–317. Marty et al., Neurophysiol Clin. 2015; 45:469-474.

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A modular and field-tolerant ultra-low-noise multichannel SQUID system for ULF MR and high frequency MEG

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We present the prototype module of our extendible, modular and robust multichannel SQUID magnetometer system intended for high-precision measurements of biomagnetism and spin precession within the Berlin Magnetically Shielded Room 2. Further demanding applications are magnetorelaxometry and ultra-low-field magnetic resonance (ULF MR), where pulsed magnetic fields of up to 100 mT are typically applied.

As this is a multipurpose device we opted for a hybrid concept featuring the use of overlapping magnetometer pick-up coils with different dimensions enabling maximum signal-to-noise ratio for different source depths. It is equipped with 18 magnetometers consisting of niobium (Nb) wire-wound pick-up coils. A total of 16 small pick-up coils form a regular grid with channels sensitive to all three spatial directions and sufficient spatial frequency resolution necessary for MEG. Two large hexagonal pick-up coils sensitive in z-direction surround the grid at two different heights and are suitable for the detection of deep sources. Feedback into the pick-up coils is employed to minimize crosstalk between channels. For protection against large field pulses the current sensor SQUIDs are equipped with integrated input current limiters and housed inside superconducting shields of Nb. The distortion of homogeneous background fields due to the configuration of the SQUID packages was evaluated by simulations.

The measured noise of the small-size magnetometers was between 0.85 $fT/Hz^{1/2}$ and 1.5 $fT/Hz^{1/2}$, and well below 1 $fT/Hz^{1/2}$ for the large ones. Using software gradiometer we achieved a minimum noise level of 0.5 $fT/Hz^{1/2}$. We performed ULF NMR experiments verifying the system\'s robustness against pulsed fields and magnetoencephalographgy (MEG) on somatosensory evoked neuronal activity. The low-noise performance of our 18-channel prototype enabled the detection of high frequency components at around 1 kHz by MEG.

Investigation of ultra-low field relaxation times of post-mortem pig brains and rotationally cross-linked proteinsin the laboratory frame and in the rotating frame

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Nuclear magneticresonance relaxation dispersion (NMRD)—the magnetic field dependence of thelongitudinal and transverse relaxation times T and T —revealsthe internal dynamics of macromolecules in tissues. The lowest accessible fieldstrength of existing field-cycling scanning NMRD is typically above 235 μT (10kHz frequency). As a result, the longitudinal relaxation time in the rotatingframe, $T_{1\rho}$, is often used as an analog for T below 235μT. In this work, we report the direct measurement of and T from 55 to 240 μT using an ultra-low-field (ULF) magneticresonance imaging (MRI) system involving a superconducting quantum interferencedevice (SQUID). These ULF relaxation times and the $T_{1\rho}$ values measuredat 7 T are compared for post-mortem pig brains and rotationally cross-linked bovineserum albumin (BSA). For both specimens, the dispersions as well as theabsolute values of ULF T and 7-T $T_{1\rho}$ are significantly different. On theother hand, the cross-linked proteins exhibit similar values of T and similar values of $T_{1\rho}$ to those of the brain tissues. Thesesimilarities imply that the degree of protein immobilization determines thefrequency-dependence of both T and $T_{1\rho}$, and suggest thatULF MRI may be used to image stroke or traumatic brain injury without the unacceptablyhigh specific absorption rate (SAR) associatedwith $T_{1\rho}$ imaging.
This research was supported by the Henry H. Wheeler, Jr. Brain Imaging Center, the Donaldson Trust, NIH grant 1R35GM118117-01,the Chinese Academy of Sciences and the KRISS World Class Laboratory program.

Neuronal current imaging (NCI) by Ultra-Low-Field MRI

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One main goal in brain research is the determination of the sources of brain activities with high spatial and temporal resolution. Limitations of existing technologies: a) methods like EEG/MEG are limited by the non-uniqueness of the electromagnetic inverse problem; b) others like functional MRI measure neuronal activity indirect via blood oxygenation level and are limited in temporal resolution.

The goal of NCI is to detect the influence of weak neuronal magnetic fields on an MR image. Such MR images do not suffer from the lack of uniqueness since its localization via MRI is a linear problem.

We present in this work an ultra-low-field MRI setup developed for direct brain current measurements. It consists on an ultra-low-noise SQUID-system with a pickup loop diameter of 45 mm and a white noise level of 0.5 fT/sqrt(Hz). It tolerates polarization pulses up to 50 mT. The second part of the setup consists of three coil systems providing the polarization (~30 mT), the measurement field B0 (~10 μT) and the imaging gradients. The setup is operated in a magnetically shielded room with two layers of mu-metal plus one aluminum layer. A head phantom with an integrated current dipole is used in order to simulate the dipolar field distribution and the time trace of the long-lasting brain activity. The phantom is filled with an aqueous solution containing 0.079 wt% of $CuSO_4$ to adjust the relaxation times T and T to the relaxation times of grey brain tissue of about ~100 ms respectively.

These phantom studies show promising results to apply this technology in the future to long lasting neuronal activities in human brain. The resolution of our NCI setup needs to be increased by only a factor of about 2 or 3 to detect directly human brain activity.

ULF-MRI of *in vivo* human brain using inversion recovery to suppress magnetization of cerebrospinal fluid

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We present the application of an inversion recovery sequence in ultra-low field magnetic resonance imaging (ULF-MRI) of in vivo human brain to suppress the longer relaxation-time signal from cerebrospinal fluid (CSF). CSF has significantly longer magnetic relaxation times T and T compared to other brain tissue, including gray and white matter, so that its presence makes proper determination of T and T for brain matter difficult. Even with complicated analysis routines involving multi-exponential decay fitting, it is very hard to separate rapidly relaxing brain matter signals from slowly relaxing CSF signals, resulting in increased uncertainty in the computed relaxation time or, even worse, a bias towards longer T- or T-values. Inversion recovery takes advantage of the fact that different tissues have different relaxation times at significantly different magnetic fields, so that the magnetization of nuclei within a certain range of arbitrarily chosen relaxation times can be suppressed during prepolarization. By suppressing the magnetization of CSF in this manner, we can fundamentally remove the slowly-relaxing CSF signals. ULF-MRI of human brain with inversion recovery to suppress CSF magnetization reveals that brain-matter T measured with single-shot echo (SSE) sequences and T measured with Carr-Purcell-Maiboom-Gill (CPMG) sequence at B = 134 μT were both around 55 ms, whereas the apparent T for the same subject without inversion recovery was longer, around 70~75 ms, while the apparent T remained around 55 ms. We further show ULF-MRI inversion-recovery images of the same human brain at 8 different B fields, from 67 μT to 235 μT, over which T and T did not vary significantly and remained in the 50~55 ms range.

This research was supported by the Henry H. Wheeler, Jr. Brain Imaging Center, the Donaldson Trust, the Chinese Academy of Sciences and the KRISS WCL program.

Magnetization loops of type-II superconductors in SQUID-based ultra-low field nuclear magnetic resonance: A numerical study

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Recently, we have reported that a strong prepolarization field (B) can magnetize type-II superconductors, like Nb and NbTi, which are vulnerable to flux pinning when exposed to a strong magnetic field.[1,2] This finding has a significant impact in development of ultralow field nuclear magnetic resonance (ULF-NMR) since these type-II superconductors have been widely used as the materials of choice for SQUID sensor pick-up coils. Also, there have been efforts to build the B coil itself out of superconductor in order to further increase B strength. The strong B in the order of tens of millitesla or higher is a critical component of ULF-NMR as it can magnetize the sample prior to measurement and boost the magnetic resonance signal to overcome one of the major weaknesses of ULF-NMR, namely weak signal due to the extremely low measurement field (B). However, this B needs to be completely removed after prepolarization period so that the uniform B is not perturbed in order to obtain quality NMR signals. With a type-II superconductor exposed to a magnetic field exceeding its H_{c1} due to the strong B the superconductor traps magnetic flux and becomes magnetized. The magnetized superconductor then generates a superflous magnetic field, after B has been removed, to perturb B and deteriorate resulting NMR signals. In this presentation, we numerically simulate magnetization loops of type-II superconductor using critical state models, including Kim\'s model and Nested Ellipse model. The simulation results will be compared against a set of experimental magnetization data obtained from sample superconductors to insure validity of the numerical methods. Once verified, these numerical methods will then be used to replicate the experimental magnetization and demagnetization results previously published.[1] Furthermore, the numerical methods will be applied to the case of type-II superconducting B coils to obtain an optimal counter-pulse to minimize the effect of self-magnetization.

[1] S.-m. Hwang et al., Appl. Phys. Lett. 104(6), 062602 (2014)[2] S.-m. Hwang et al., IEEE Trans. Appl. Supercond. 25(3), 1601304 (2015)

Ultra-low field MRI based on high-T_c SQUID and flux coupling

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In this work, a high-T SQUID based low field MRI system integrated with flux coupling technique was set up. An electromagnetic shield room made out of aluminum was built to reduce the surrounding noise. For NMR and MRI detection, we designed and optimized the pick-up coil with inner diameter of 20 cm for enlarging sample area. The NMR signal of water phantom has been measured. Furthermore, the 2-D images and 3-D images of water specimen are obtained by using our low-field MRI system. Our high-T SQUID-based low-field MRI system promises a low-cost and feasibility for biomedical application.

A data driven approach for artifacts rejection in Very Low Field Magnetic Resonance Images

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In the recent years, Ultra-Low Field (ULF) MRI has gathered increasing attention thanks to the associated advantages, such as the possibility of integrating MRI with MEG in the same device, the increased tissue contrast and the opportunity to scan patients who cannot undergo standard high field MRI. Unfortunately, actual operating ULF-MRI systems produce images with low spatial resolution, low SNR and long acquisition times (Tacq). A strategy to reduce Tacq without depleting the SNR is to increase the field up to 10-20 mT such as in Very Low Field (VLF) MRI systems, with the additional advantage of reduced scanner weight and lower costs. However, the quality of VLF images is still far from being suitable for practical clinical applications. Here, we present a data-driven strategy to improve the SNR of VLF-MRIs through the use of spatial FastICA [1]. Image series obtained at B0 = 8.9 mT, using the VLF system installed at the University of Chieti [2], were Tukey filtered and processed through an iterative approach, running FastICA with deflation method from different initial conditions [3]. At each iteration, artifact ICs were automatically labeled according to a set of criteria, based either on the IC spatial properties (e.g. an artifact IC is located outside the object volume [4]), or on their temporal properties (e.g. the weight of an artifact IC poorly correlates with B0 fluctuations). Among all the iterations, the one providing the largest spatial SNR and the lowest artifact contamination was retained. The resulting preprocessed images show increased SNR, better contrastand emergence of details which were embedded in noise in the original images. This approach could be adapted to process images obtained by other systems, improving the quality of ULF and VLF MRI and eventually minimizing the acquisition time.[1] Hivarinen and Oja, Neural Netw, 2000[2] Galante et al., Plos One, 2015[3] Mantini et al., Brain Connectivity, 2011[4] Smith S et al., Neuroimage,2014

Optimized pipeline for 3D co-registration of low- and high-field MRI

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The ultra- and very-low-field (ULF/VLF) MRI scanners developed in different labs represent innovative, cost effective and safer systems suitable to be integrated in multi-modal (MEG-MRI) systems, improving MEG localization accuracy through virtual elimination of the MEG-MRI co-registration error. However, building the individual volume conductor model could be hampered by the poor LF-MRI spatial resolution and SNR. Also, current LF systems can acquire images of only a portion of the head in a reasonable time. Thus, for practical usage, a possible strategy could be to co-register the LF and HF MRIs. We implemented an optimized co-registration pipeline with Normalized Mutual Information (NMI) as cost function and Adaptive Simulated Annealing as the minimization strategy. The pipeline uses a 3D floating-window approach to manage sub-voxel resolution of ULF images, applying different grouping strategies in the xyz-space directions to adapt the HF to the LF-MRI grid before co-registration. The pipeline can deal with different transformation models, using 6 (rigid body), 9 (6 par + scaling) and 12 (9 par + shear) parameters. First, we analysed the NMI and a set of similarity indexes (S_IND) as a function of the SNR in VLF images of a geometrical phantom [1]. Then, by comparing the NMI and the S_IND for our pipeline and for well-known toolboxes for fMRI analysis, we evaluated the co-registration quality of ULF and HF MRIs of human brains [2,3]. Our pipeline always outperformed the fMRI toolboxes. Besides, given the poor SNR, the transformation model using 9 parameters was the best one for the majority of S_IND. Our pipeline provides a suitable co-registration between LF and HF MRIs, even if only part of the volume is imaged and at low SNR. This paves the way for the possibility of speeding up ULF recordings through minimization of the number of repetitions and volume to be imaged.

[1] Galante A et al., PLOS One 2015
[2] Zotev V et al., JMR 2008
[3] Vesanen P. et al, MRM 2013

Eliminating co-registration in MEG–MRI: automatic nonlinear calibration of ULF MRI

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When superimposing MEG source estimates and structural MRI, an accurate mapping between the coordinate systems of the two modalities is required. Co-registering a high-field MR image with MEG data involves many manual steps, even involving potential human error. Moreover, geometrical distortions in high-field MR images, related for instance to magnetic susceptibility variations, worsen the local co-registration accuracy.

With a hybrid MEG–MRI device using ULF-MRI-tailored sensors for both modalities, the co-registration problem can turned into an automatic calibration step. After this, the MEG and MRI coordinates will be the same. With accurate modeling of the non-idealities of the system, the equivalent of co-registration errors can be reduced to a negligible level.

The key component in our calibration method are the sensitivity profiles of the superconducting pickup loops, which in ULF MRI are independent of the sample and therefore well-defined. In the most basic form, the spatial information of the profiles, captured in parallel ULF MR acquisitions, is matched with profiles computed in the sensor coordinate system to find coordinate transformation between the modalities. Special attention is put towards being independent of other calibrations in a data-driven manner.

Furthermore, the transformation does not have to be affine as usual but, for example, second-order corrections can be included. Accurately modeling the sensitivity profiles and field nonidealities, a nonlinear mapping can be used to correct remaining minor image distortions. Thus, after the calibration, distortion-free MRI and a high spatial accuracy for MEG source localization can be achieved.

The spatial calibration method is assessed by simulations assuming known geometry for the magnetometer pickup array. It is analyzed how the calibration method performs in different conditions, including nonlinear image distortions and high noise levels.

Accurate mapping of magnetic fields generated by an ultra-low-field MRI device

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Spatial accuracy of structural brain images is of high importance in locating and visualizing brain sources. If not taken into account in reconstruction, the inhomogeneities and non-idealities of the applied magnetic fields in magnetic resonance imaging (MRI) cause distortions and blurring in the final image. Thus, a detailed knowledge of the MRI fields within the volume of interest (VOI) is essential. In contrast to high-field MRI, the magnetic fields in ultra-low-field (ULF) MRI are not distorted by the susceptibility variations due to the subject, and hence the fields can be accurately known. This information can be used in all measurements. In this study, we experimentally mapped the fields produced by MRI coils in our hybrid device combining magnetoencephalography (MEG) and ULF-MRI. The obtained information will be used for accurate reconstruction of ULF-MRI images for superimposing MEG and MRI.

We measured field patterns of ULF-MRI coils (main field, prepolarization field, excitation field, and three gradient fields) at the points of a regular grid inside a measurement helmet of the MEG-MRI device, using a three-axis fluxgate magnetometer. The measured magnetic field data are fitted in a least-squares sense to a linear combination of a set of basis functions consisting of spherical multipole fields up to a given order. With the obtained magnetic multipole expansions, we interpolated and extrapolated the fields in order to create accurate field maps. In addition, we calculated different parameters such as field and gradient strengths and field homogeneities.

The magnetic multipole expansions showed the most significant components of different fields and also revealed the multipole moments that correspond to the field non-idealities. Moreover, we obtained precise field maps within the VOI. The calculated field parameters were close to the simulated parameter estimates. The results are for use in accurate reconstructions of ULF MRI images.

Nuclear Magnetic Resonance detection with an atomic magnetometer toward ultra low field Magnetic Resonance Imaging with non-cryogenics

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We report on the use of an atomic magnetometer for the nuclear magnetic resonance (NMR) measurement. We demonstrate detection of a free-induction decay (FID) signal from flowing water with non-cryogenics: potassium atomic magnetometer based on the spin-exchange relaxation free (SERF) regime. A potassium atomic magnetometer was operated at 180 degree in celsius and have noise level with about 80 fT/Hz1/2 at 10 Hz. To avoid magnetization of the magnetic shield and complicated setup inside of the shield we designed a flowing water system where the water is prepolazied by permanent magnet outside of the shield. And a dimension of the flowing water system consisted of a transmission tube and water reservoir was determined by considering T2*, T1 of single proton and flow rate. NMR signal was detected at an ultra low field about 230 nT with signal-to-noise ratio of 25 with a single shot. Nuclear dynamic polarization (DNP) method was also utilized with an atomic magnetometer. We performed an experiment with a small pre-polarization field about 20 uT, in which the DNP can enhance the proton NMR signal. We obtained nearly ten fold enhanced NMR signals in 2mM TEMPOL solutions. The experiment shows promising results for implementation of future transferred DNP experiment with an atomic magnetometer toward ultra-low field MRI with non-cryogenics.

Breaking the Nonuniqueness Barrier in Electromagnetic Neuroimaging: the BREAKBEN project

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In the BREAKBEN project (funded by Future and Emerging Technologies program of the European Union), our goal is to improve the accuracy and reliability of neuronal activity localization and characterization in the brain. Two methods involving ultra-low-field MRI (ULF MRI) using SQUIDs will be developed: 1) Combined MEG and MRI measurements, and 2) neuronal current imaging.

In ULF MRI, the signals are recorded at about 100 microtesla instead of the several tesla in conventional MRI. BREAKBEN's predecessor project MEGMRI (2008–2012) indicated that the power signal-to-noise ratio in the MRI measurement should still be improved by a factor of at least 1000 for the structural MRI to be clinically useful. This can be done by lowering sensor noise and by making the prepolarization magnet more powerful.

In addition to improving the reliability of locating and characterizing brain activity, the new technology may also enhance the diagnosis of cancer patients thanks to improved MRI contrast at ultra-low fields. Cost reductions may be expected on the basis of improved workflow and more accurate diagnostics. Furthermore, there is hope that the new device can be used to measure the conductivity structure of the brain, which would improve the accuracy of locating brain activity with MEG as well as with EEG.

Aalto University and Elekta Oy will build the hybrid MEG-MRI device using a new generation of SQUID sensors developed by VTT Technical Research Centre of Finland. The resulting technology will be used by the BioMag Laboratory of the Helsinki University Hospital in patient trials and by the University of Chieti–Pescara in studies of brain connectivity. Physikalisch-Technische Bundesanstalt (PTB) Berlin will attempt the detection of neuronal activity by ULF-MRI and NMR techniques. Sophisticated "phantoms" will be developed by the Technical University of Ilmenau to mimic the properties of the human head and brain to allow testing the sensitivity and accuracy of the new devices.

Recent advances in ultra-low-field MRI and its compatibility with other modalities

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Ultra-low-field magneticresonance imaging (ULF MRI) is an emerging technology that, by contrast to the opposite, ultra-high-field (UHF) MRI, has a different set of challenges. On the one hand, while high-field MRI suffers from distortions in magnetic fields and resulting images, ULF MRI has well-defined fields and sensitivity maps, and can therefore provide undistorted, quantitatively accurate images. On the other hand, UHF MRI produces strong signals by normal metal receiver coils, while such coils are useless at ULF because of the low Larmor frequencies of proton precession. Therefore, in ULF MRI, we instead aim at the most sensitive magnetic sensors available. However, the various parts of the system –including the sensors, field coils and associated electronics – must be made to tolerate MRI pulse sequences and recover quickly after the pulses. To further avoid wasting valuable acquisition time within the sequences, technological advances are needed for fast spin manipulations, including applying flip angles.

Many of these issues are solved in software by so-called dynamical methods. However, various topics on the hardware side require in-house solutions, because electronics to properly address these issues are not commercially available. As opposed to ultra-high-field MRI, which is a direct extension to conventional MRI, ULF MRI suffers from lack of support from large industries, and is in need of more researchers and R&D personnel to push the technology to be commercially viable. The past MEGMRI project and the ongoing BREAKBEN project mitigate this issue; we are in the process of making ULF MRI ready for neuroimaging research and for clinical applications.

We will present technological advances at Aalto University, including methods, electronics, software and obtained results. We further review other developments related to the evolution of ULF MRI, its combination with other modalities such as MEG, and methods thereof, such as current-density imaging.

Prepolarization coil design using ceramic aluminium nitride cooling disks for ultra-low field magnetic resonance systems with highly effective cooling and low thermal noise

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A prepolarization, or pre-magnetization (B) coil is one of the most important parts of ultra-low field nuclear magnetic resonance (ULF-NMR) systems which requires a strong B field to align the nuclear spins of the sample. In order to generate such a strong B field, the B coils are supplied with high currents so that they generate huge amount of heat. Management of the heat generated in the B coil has always been a significant challenge in B coil designs. Among many methods used to manage the generated heat, only a few still remain in use: 1. In the case of very small solenoid-type B coil, air-cooling via natural or forced convection of the air, 2. Water-cooling by forcing water into a hollow conductor which the B coil is wound of, and 3. Immersion of the B coil in liquid nitrogen, usually by encasing the B coil inside a dedicated liquid nitrogen dewar. Unfortunately, all three methods mentioned above have outstanding drawbacks and/or limitations. We introduce here a new design of B coil that can be cooled with many kinds of liquid coolants, including water and silicone oil. Our new design incorporates several disks of ceramic aluminium nitride (AlN) embedded between thin pancake coils wound of Litz wire. The AlN disks act as thermal dissipation layers as well as the coil frame as a whole. Ceramic AlN is one of the rare electrical insulators with extremely high thermal conductivity (~170 W/m-K at 300 K), which makes it an ideal material for cooling the B coil that can develop high inductive voltage spikes in operation. In this presentation, we describe numerical method used for thermal simulation of our coil designs, simulation results for 3 different materials (AlN, AlO , and G-10) for cooling layers, optimal prototype coil design determined from the simulation, and actual measurements from the prototype coil built for final evaluation.

Spatio-temporal localization of predictive visual mechanisms using MEG

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Although traditionally associated with stimulus driven processes, we have demonstrated the N170 visual event related potential to be strongly modulated by contextually mediated expectations. Using a novel MEG beamformer metric (the Difference Stability Index: DSI) we explored the spatiotemporal bases of the \"expectancy violation M170\" signal. Participants viewed sequences of images (of heads or statuettes) which established rigid-body rotational implied motion trajectories, which were either conformed to (Predicted condition) or violated (Unpredicted condition) by the final image in the sequence. Careful experimental controls meant that the set of final image transitions were perfectly matched across the Predicted and Unpredicted conditions, ensuring that any observed effects must be due to context rather than to any differences in low-level stimulus properties. Unpredicted final images were associated with a large effect-size increase in M170 amplitudes. The DSI beamformer revealed that the increased amplitude M170 was attributable to sources in visual motion areas MT/V5+ and STS, whereas the later latency signal amplitude increases were generated in the insula and sensorimotor cortices. The localisation of the “expectation violation M170” differs from previously reported localisations of the “face M170”, but is consistent with a role for MT/V5+ in testing predictions about stimulus motion.

Oscillatory correlates of the use of world knowledge in predictive models for the perception of causal events

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Recent human and non-human electrophysiological studies - mainly in the visual domain - have linked low-frequency oscillatory activity in the alpha-/beta-bands to top-down predictive signals and gamma-band activity to bottom-up prediction-errors, consistent with predictive coding theory. In a recent MEG-paper (van Pelt et al. 2016, SCAN), we have found a similar spectral dissociation for higher-order cognitive processes involved the perception of causal events, when systematically manipulating the probabilities of ball direction-outcome relations of animated bowling actions in an action observation task. In daily life however, the brain makes use of world knowledge – i.e. day-to-day experience – in constructing predictive models. Here, we investigated the use of world knowledge in perceiving causal events using magnetoencaphalography in 30 healthy subjects. As in our previous study, subjects viewed animated videos of a bowler throwing a ball down a bowling alley. Ball direction and score were manipulated independently, with 4 possible ball directions and 9 possible scores. All 36 combinations were shown 8 times, thus having equal probability. After the MEG-part, participants rated the likeliness of the observed actions on a scale of 1-7. Our hypothesis was that for a given event, beta and gamma band activity would reflect the predictability of the causal relation between ball direction and outcome as based on world knowledge (different for each event), rather than the probability of the action occurring in the experiment (identical for each event: 1/36). We analyzed MEG data analyzed using FieldTrip, and reconstructed beta and gamma data time courses in the causal perception network. These oscillatory activities were subsequently correlated to the subjects' (behavioral) action likeliness ratings, to explore how oscillatory predictive coding mechanisms make use of world knowledge information in modeling causal relations between events during action observation.

Frequency-resolved directed neural interactions support expectation and detection of visual target stimuli

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The recognition of expected visual stimuli has been shown to affect neural activity particularly in the inferior temporal and fusiform gyri, as well as in the inferior and superior parietal cortex. Moreover, efficient detection of target stimuli has been demonstrated to be mediated by frontal and parietal regions. Here, we aimed to characterize how network interactions between the brain regions related to attentional and visual processing would be modulated in the detection of human faces in a temporal stream. In a magnetoencephalography experiment, we presented sequences of human faces to the subjects whose task was to detect a target face among this sequence. Activation (evoked and oscillatory responses) and cortico-cortical coherence analyses were conducted to identify the set of brain regions that were involved in the perception of the faces, and in which the pre-target and target faces elicited differential responses. Frequency-resolved analysis of directed neural interactions was then conducted within this network using conditional Granger Causality. Our results revealed very similar networks in the left and right hemisphere, comprising nodes, e.g., in the precuneus, the superior parietal cortex as well as the fusiform and middle frontal gyri. The perception of target faces was associated with increased bottom-up influences in the gamma-band, whereas the processes related to attention and the expectation of target stimuli manifested as wide-spread top-down as well as bottom-up interactions in both the beta- and gamma-band, especially in the right hemisphere. Our results demonstrate the role of frequency-specific directed neural interactions in the recognition of visual stimuli and in guidance of executive attention resources towards expected inputs.

The visual gamma response to faces reflects the presence of sensory evidence not awareness

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It has been suggested that gamma (30-100Hz) oscillations mediate awareness of visual stimuli, but experimental tests of this hypothesis have produced conflicting results (Aru et al., 2012; Fahrenfort et al., 2012; Fisch et al., 2009). We used phase noise to vary the perceptibility of face stimuli presented to 25 participants. MEG was used to measure the gamma response while individuals viewed three conditions in which faces were presented either above, below or at the perceptual threshold. In each of 400 trials (100 each for the sub- and supra-threshold conditions, and 200 for the threshold condition) participants indicated whether or not they perceived a face in the stimulus. Gamma-band activity during the task was localised to bilateral ventral occipito-temporal cortex. We found that gamma amplitude was significantly increased both for threshold relative to subthreshold stimuli and for suprathreshold relative to threshold stimuli. However, for the threshold condition we did not find a significant difference in gamma amplitude between trials in which the face was percieved vs those in which it was not perceived. We conclude that the gamma response to faces is modulated by the amount of sensory evidence present in the stimulus and not perceptual awareness of the face itself.

Visual system traces temporal evolution of band-limited quasi-rhythmic stimulation

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Neural processing of dynamic continuous visual input, and cognitive influences thereon, are frequently studied in paradigms employing strictly rhythmic stimulation. However, behaviourally relevant natural stimuli are hardly ever fully rhythmic but possess certain spectral bandwidths (e.g. lip movements in speech, gestures). Examining periodic brain responses elicited by strictly rhythmic stimulation might thus represent ideal, yet isolated cases. Here, we tested how the visual system responded to quasi-rhythmic stimulation with frequencies constantly varying within ranges of classical theta (4 – 7 Hz), alpha (8 – 13 Hz) and beta bands (14 – 20 Hz). EEG data collected from 17 Human participants substantiated a systematic and sustained neural phase-locking to stimulation in all three frequency ranges. Further, we found that allocation of spatial attention enhanced EEG-stimulus locking in theta- and alpha bands. Our results bridge recent findings regarding phase locking ("entrainment") to quasi-rhythmic visual input and "frequency-tagging" experiments employing strictly rhythmic stimulation. We propose that sustained EEG-stimulus locking can be considered as a continuous neural signature of processing dynamic sensory input in early visual cortices. Accordingly, EEG-stimulus locking traces the temporal evolution of rhythmic as well as quasi-rhythmic stimulation and can be subject to attentional bias.

Visual gamma frequency reflects behavioral differences in visual sensitivity.

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Sensory hypersensitivity is frequently observed in autism spectrum disorders (ASD) and may reflect over-excitation of sensory cortices. Animal studies suggest that the frequency of gamma oscillations reflects excitation of inhibitory neurons and the excitation/inhibition balance in neural networks. Therefore, both gamma frequency and sensory sensitivity may depend on partly the same underlying mechanisms. We investigated the putative link between visual gamma frequency, as recorded with MEG, and normal variations in sensory sensitivity, as assessed with the adult Sensory Profile, in 'neurotypical' adult participants. To measure gamma we presented high-contrast circular gratings moving with velocities of 1.2 (V1), 3.6 (V2), or 6.0 (V3)°/s to 17 typical males (19-40 years). The gamma frequency (e.g., fV1) is defined as the maximal reliable stimulus-induced increase of sensor power between 40-100Hz. We also calculated the sensitivity and sensory avoidance scores (SSAS) across sensory modalities and separately for each modality.

The gamma frequency increased with increasing velocity of visual motion (fV1:55.5Hz, fV2:65Hz, fV3:74Hz, $p<0.00001$). After correcting for age, the higher gamma frequency in V2 and V3 conditions, as well as the greater velocity-related frequency growth (fV3-fV1) correlated with lower general and visual SSAS. No correlations with the SSAS for other modalities were found, suggesting modal specificity of the effect. Gamma power did not correlate with any of the SSAS measures.

The greater increase of gamma frequency in response to the fast motion may reflect stronger excitatory capacity of the visual inhibitory neurons that in turn are capable of more effectively inhibiting principle cells, thus preventing over-excitation. The negative correlation between gamma frequency and visual sensitivity may therefore be mediated by individual differences in excitability of visual inhibitory neurons. These results may have important implications for ASD research.

Neural temporal dynamic of global/local visual processing: a MEG study

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Visual scenes contain local and global properties. Numerous behavioral studies demonstrate that the global features are processed more rapidly than local features, namely global precedence effect. Specifically, the holistic structure of visual scene is extracted before fine details are analyzed, known as a coarse-to-fine model in visual perception. However, the neuronal temporal dynamics underlying the global and local processing as well as their interactions remains largely unknown.To address the issue, we recorded MEG from 20 human subjects as they viewed 5-sec long glass pattern stimuli, the luminance of which was randomly modulated continuously. Critically, the form coherence of the glass pattern was also randomly and independently modulated simultaneously. Based on the two random sequences (luminance and form coherence) within one trial, we were able to calculate and separate the brain response that specifically tracks changes in local (luminance) and global (global form) property from the same MEG responses, by employing a temporal response function technique (TRF). The TRF for local and global property processing showed quite distinct spatiotemporal patterns. Specifically, local feature changes elicited activations in early visual area (EVA), including V1, V2, and V3, around 100 msec. Global features, on the other hand, elicited much earlier responses (< 50 msec), which first developed in orbitofrontal area (OFA), then in V3A, V1, and TPJ. We further examined the interactions between global and local processing and found a two-stage course. In particular, within 100~200 msec, the OFA activations in global processing negatively correlated with EVA activities in local processing, suggesting a global-local competition relationship, whereas within 200-300 msec, OFA and TPJ responses in global processing and EVA responses in local processing showed a positive relationship, implicating a global-local integration process.Our experiments, by employing a new technique, successfully enables the dissociation of global and local processing within the same trial response. Commensurate with previous findings, our results support that OFA initiates the coarse-to-fine process in visual perception. The global and local process undergoes competition (100-200 msec) and then integration (200-300 msec).

Parietal gamma-band activity reflects individual performance in the 3-D mental rotation

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Recent electrophysiological studies indicate that the gamma-band spontaneous brain activities in the parietal areas play a crucial role in manipulating mental representation of 3-D objects, however, it is not fully characterized whether individual changes in these activities are correlated with the individual difference in the performance of mental image processing. In this study, we measured MEG responses to investigate neural correlates of the individual variability in the performance of 3-D mental image processing.Fifteen subjects performed mental rotation task with 4 different rotation angles (0, 30, 60, 120 deg). Subjetcs\' task was to discern whether presented pair of objects was either identical or mirror reversed and to react by lifting their index of middle finger. MEG signals were measured using 122-channel neuromagnetometers.Based on the measured performance (percent correct of the subjects\' response averaged over all conditions, subjects were divided into two groups, namely, (a) high-performers (HP) and (b) low performers (LP). Results of the MEG-RMS analysis showed that the activities in the primary visual area were significantly increased in the low-performer compared to the high-performer at around 200 ms after the onset of the stimuli. Results of the MEG time-frequency analysis showed that the gamma-band activities around 30 Hz measured at the occipital and the parietal sensors were significantly increased in the HP compared to LP.The current results show significant increase in gamma-band power at primary visual area and the superior parietal area in the high-performers, which suggests that the efficient binding of visual features for mental image manipulation in these regions leads to better performance in the mental rotation task. Increase in the event-related responses observed in the primary visual area in the low-performers might indicate the subjects\' dependence on the presented visual object in performing mental rotation task.

Visual gamma oscillations across the UK: Comparability of UK MEG Partnership data recorded with different MEG scanners

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The UK MEG Partnership is a collaborative research programme across eight MEG centres in the UK, supported by the Medical Research Council. The collaboration was established in 2013, with the aim to build a normative MEG database of 640 datasets recorded with CTF, Neuromag, and 4D MEG scanners. Here we present a comparability study of data recorded while participants performed a visual task known to induce gamma oscillations (30-90 Hz) in the visual cortex. The visual stimulus consisted of a vertical, stationary, maximum contrast, three cycles per degree, square-wave grating subtending 4° of visual angle, presented in the lower left visual field for 1.5-2 s. By using a standardised paradigm across sites, we controlled for the influence of the sensory parameters that are known to affect both the amplitude and the frequency of visual gamma responses (e.g., size, contrast, spatial frequency, eccentricity, etc.). Using a common analysis pipeline, we reconstructed virtual sensors in early visual cortex to measure peak gamma amplitude and peak gamma frequency in each participant. We then used a within-subject bootstrapping approach to estimate the robustness of the peak gamma frequency, measured by the width of the bootstrapped peak frequency distribution around the distribution mode [1]. This measure was used to compare data quality across MEG centres and scanners. Our preliminary results showed that peak gamma frequency, a parameter that could represent an index of individual synaptic function, was highly comparable across sites. In contrast, physical differences in sensor type may need to be controlled for, before combining gamma amplitude measures from different scanners. These results have implications for large-sample or clinical studies aiming to combine data collected at different research centres, or recorded with MEG from different scanner manufacturers. [1] Magazzini, Muthukumaraswamy, Hamandi, Lingford-Hughes, Myers, Nutt, Wilson & Singh (2016). *Under review*.

Saccadic eye movements are phase-locked to posterior alpha oscillations during successful memory formation – evidence from MEG and intracranial data

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The sampling of visual information is assumed to be discrete rather than continuous (VanRullen & Koch, 2003). Empirical work suggests that the visual system samples the environment at 7-12 Hz, possibly clocked by alpha oscillations (VanRullen et al., 2011). This relatively slow sampling period at 80-140 ms seems at odds with the remarkably fast processing speed of the visual system. For instance, it has been demonstrated that the visual system can distill meaning from images presented for only 13 ms (Potter et al., 2014). This conundrum could partly be resolved if saccades are locked to the phase of ongoing visual oscillations, as investigated in this study.

We simultaneously recorded MEG and eye tracking data from 36 healthy participants during a free viewing encoding task of natural pictures. A memory test was subsequently provided in order to classify the encoding trials as 'later remembered' versus 'later forgotten'. MEG data were aligned to the onset of saccades. Analyses of inter-trial coherence revealed significantly higher phase-locking in the alpha (8-12 Hz) band prior to saccades for later remembered vs. later forgotten pictures. The source of this effect was localized to the parieto-occipital cortex. Intracranial data recorded directly from the occipital and parietal cortex of epilepsy patients provided converging results.

The study provides evidence that saccadic eye-movements and brain oscillations are coordinated, and demonstrates that this coordination determines what the brain encodes. Specifically, our results suggest that saccades are timed to the dynamical state of the brain, such that the new retinal inputs are temporally aligned to the 'optimal' phase of the alpha rhythm.

A Simultaneous EEG/MEG Study for Stereoscopic Depth Perception

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Neuroergonomics provides neural understandings on designing work environment and opens a way for development of state-of-art technologies to maximize the safety and efficiency in various work environments. Recently, stereoscopic three-dimensional contents including 3D movies, 3D TV,head mounted display (HMD), and augmented reality have become more compelling. Studies for stereoscopic depth perception in the neuroergonomic view are rare. To understand neural oscillatory responses for stereoscopic depth, we conducted single trial based experiments and introduced simultaneous EEG/MEG acquisition. Eight participants were stimulated by subject-specific four different depth levels within visual comfort zone. We found saturation point of cognitive neural responses within visual comfort zone and observed cortical processing behaviors over various depth perception. Amplitudes of N100 and P300 showed peaks at depth level 3. Beta oscillation (16 - 25 Hz) was attenuated as depth level increased at visual cortex around 500 - 1000 ms after the stimulus onset. Therefore, it is expected that cognitive response may have a cognitive limit in the comfort zone, while cortical process may increase as depth level increases. We hope that our findings will be quite helpful in designing stereoscopic contents and predicting their brain effects.

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Face-selective neuromagnetic responses to fast periodic presentation of natural images

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Recent electroencephalographic studies have used a fast periodic visual stimulation approach to identify an objective and high signal-to-noise ratio signature of face categorization in the human brain. Here we extended this approach to magnetoencephalography (MEG).Twenty-six right-handed adults (13 F, 29.4 ± 4.5 year sold) were tested with a 160 channel whole head MEG system (Yokogawa, Japan). They were presented with natural images of objects at a rate of 6 images/s (6 Hz) for 60s. Natural and highly variable images of faces were presented on every fifth stimulus (1.2 Hz). Phase-scrambled versions of the same images were presented in a separate 60s block (*scrambled periodic condition*). Each participant viewed four blocks each of periodic and scrambled periodic stimuli, presented in random order. Beyond a common response to faces and objects recorded at 6 Hz and harmonics (12 Hz,etc.), Fourier analyses showed peaks corresponding to the 1.2 Hz face rate and significant harmonics (2.4 Hz, etc. until 8.4 Hz). Overall, this"face-selective response" had a highly focal scalp topography, with three foci over right anterior temporal, and right and left lateral occipital lobes. All subjects showed a significant face-selective response in ten minutes of recordings only, and the topography of this response was highly consistent across participants. Phase-scrambled versions of the same images produced only a negligible (6%) face-selective response.Time-domain analysis revealed two main face-selective responses: a bilateral temporal response peaking at around 210 ms; and a dorsal temporal-occipital response at around 300 ms, with the latter manifested a right hemispheric advantage. These data provide the first neuromagnetic category-selective response in a rapid visual stream. The objective definition and high signal-to-noise ratio of the response open new perspectives for developmental studies in MEG as well as objective comparison of multiple brain recording modalities.

Evoked and induced responses to oriented contrast edges share a common representational structure

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The human visual brain is highly efficient in binding simple features into complex coherent wholes. One prominent neural marker of bottom-up feature binding is induced gamma oscillations. However, a number of recent multivariate pattern analysis studies have also demonstrated the encoding of simple visual features in MEG evoked responses. Up until now the relationship and respective roles of the evoked and induced responses in the encoding of simple visual features remains under debate.

Here we combined multivariate pattern analysis with representational similarity analysis to systematically compare evoked and induced responses during the encoding of oriented contrast edges. We recorded human MEG data while participants viewed 6 grating stimuli with different orientations (0-150° in 30° steps; 800 ms presentation time; 3 cycles/degree of visual field). We then applied a support vector machine classifier to decode all pairwise combinations of stimuli, and used the resulting decoding accuracies to populate time-resolved 6x6 representational dissimilarity matrices (RDMs).

Our findings confirmed we could decode orientation information from evoked and induced responses in two dominant frequencies (25 and 50 Hz). We found consistent cardinal (higher decoding for horizontal/vertical versus oblique orientations) and angle (increased decoding at progressively disparate angles) effects in both evoked and induced components. Comparison (Spearman's R) between the 6x6 evoked and induced RDMs showed that the two responses share representations.

Taken together, our results show that both evoked and induced responses encode simple visual features and even though they have discrete temporal dynamics, they largely encode the same information with a shared representational structure. While this offers evidence for redundant coding or even a common neural basis, follow up experiments with more extensive stimulus sets will be essential in corroborating these findings.

Temporal dynamics of face identity and eye gaze recognition revealed by pattern analysis of MEG signals

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Extensive neuroimaging and electrophysiological evidence confirms the existence of two distinct processing pathways of face perception, one involving invariant face features (face identity), and another change ableaspects of faces (eye gaze, expression). While the cortical locus of these networks has been well described, their dynamics overlap considerably in time, making their characterization challenging.

Here we characterized the temporal dynamics of face identity and eye gaze following a two-pronged approach: a) we revealed processing-specific neural activity as it is modulated by attention to either face identity or eye gaze, and b) we applied multivariate pattern analysis to overcome limitations of traditional event-related responses such as M170 or M250, and obtain a more sensitive and holistic description of the neural dynamics.

We recorded MEG data from 15 human subjects while they performed a 1-back task on either face identity (face task) or gaze direction (gaze task) in alternating blocks of trials. The stimuli comprised images of 3 individual faces in 3 eye gaze directions each (left, direct and right). Using support vector machine classifiers, we decoded identity or gaze conditions in each task.

Our results show the time series of face identity decoding peaked at approximately 150ms, in line with literature highlighting the N170 face selective response. Moreover, identity decoding was sustained for several hundred milliseconds with comparable dynamics for both tasks. In contrast, the time series of gaze decoding peaked later at approximately 300-400ms and was significantly stronger for the gaze than the identity task.

Taken together, multivariate pattern analysis proved powerful in dissociating task-specific face perception dynamics. Our work compliments a multitude of studies following the seminal work of Haxby (2000) in adding the crucial temporal dimension in human face perception, showcasing the temporal distinctness between two processing pathways.

FEF-controlled Alpha Delay Activity Predicts Stimulus-induced Gamma Band Activity in Visual Cortex

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Recent findings in the visual system of non-human primates have demonstrated an important role of gamma band activity (40 – 100 Hz) in the feed-forward drive of sensory information, whereas feedback control appears to be dynamically established by oscillations in the alpha and beta bands. It is not clear, however, how alpha oscillations are controlled and how they interact with the flow of visual information mediated by gamma band activity. Using non-invasive human magnetoencephalographic recordings in subjects performing a visuo-spatial attention task, we show that fluctuations in alpha power during a delay period in a spatial attention task predicted subsequent stimulus-driven gamma band activity. Importantly, these interactions correlated with behavioral performance. Using a Granger analysis we further show that the frontal-eye field (FEF) exerted feedback control of the visual alpha oscillations. Our findings suggest that alpha oscillations controlled by the FEF route cortical information flow by modulating gamma band activity.

Adaptation of sustained visual gamma oscillations to moving annular grating stimuli, at 4 temporal frequencies of movement, using MEG.

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Modulation of neural oscillations in the gamma band (>40Hz), in response to specific visual stimuli, has been consistently reported, and thought to indicate information processing in local cortical networks [1,2]. Using MEG, we investigated gamma band changes to a full-field moving annular-grating stimulus [3]. We used relatively long stimulus durations (30 seconds) to allow for future comparison with fMRI data. Participants(n=13) viewed the stimulus at 4 temporal frequencies of movement: 0, 4, 8 and 12Hz.The peak amplitude and frequency of the response in the gamma band was extracted from the visual cortex, averaged over six 5-second time periods, using a beam-former analysis. Peak amplitude showed a systematic decrease over time in all conditions, suggesting that the gamma response is subject to adaptation over time. A lower frequency of response was found for static versus moving stimuli, but for moving stimuli we did not see any clear tuning of either gamma amplitude or frequency with stimulus temporal frequency. fMRI data collected from the same subjects, using the same experimental paradigm, will be used to compare the gamma band with BOLD and CBF responses to this class of stimuli. [1]Schnitzler & Gross (2005). *Nat. Rev. Neurosci.*, 6(4) [2] Jerbi et al.(2009). *Hum. Brain Mapp.*, 30(6) [3]Muthukumaraswamy & Singh (2013). *Neuroimage*, 69

High-frequency retinal rhythms drive corresponding activity in visual cortex

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The retina is known to substantially preprocess visual stimuli, and many consider it to be an extension of the brain due to the sophistication of its neural circuitry. The electrical activity of the retina, or the electroretinogram (ERG), can be measured using special electrodes placed on or near the eye. Although ERG is a widely used diagnostic technique in ophthalmology, it is nearly unknown in human neuroscience research. Studies examining information transfer between retina and cerebral cortex in humans remain particularly rare.

Visual stimuli induce occipital gamma band activity in visual cortex that is measurable with MEG, with some considering this as a reflection of local information processing. However, visual stimuli also evoke retinal "oscillatory potentials" in similar frequency bands. We therefore hypothesized that a substantial portion of the visual cortical gamma band response may follow directly from retinal responses.

Stimuli consisted of light flashes of 16.7 ms duration. ERG responses were examined with respect to the corresponding responses of visual cortex reconstructed with MEG. We furthermore implemented a novel neuroimaging strategy, combining beamforming with Hilbert analytic amplitude and phase. The filtered and source-reconstructed data were then used to examine neural connectivity between ERG and MEG-derived cortical maps in further detail, yielding what we term *retinocortical coherence*.

Visual cortex responses typically mirrored those of the retina with a delay of ~35 ms. The profile of high gamma band activity was similar between the two recordings, centered at approximately 110 Hz. Significant retinocortical coherence was found in the same frequency band, mapping to visual cortical areas slightly contralateral to the measured retina.

Our results suggest that gamma band activity in visual cortex can be directly driven by retinal output, either in addition to or perhaps instead of local processing within visual cortex. Phase variability across stimuli can be introduced already at the retina, possibly changing the interpretation of what such variability in cortex may signify. Further investigations are in progress with more complex imagery such as photographic stimuli.

Neurodynamics and connectivity during compound threat cue perception

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Studies of facial threat cues employing fMRI have revealed greater amygdala responses to clear facial cues of threat source during rapid presentation (~300 ms), and greater amygdala responses to ambiguous threat cues during longer presentations (1s/1.5s). The goal of this study was to elucidate the temporal evolution of neural activity and interregional connectivity using MEG during perception of compound threat cues conveyed by facial emotion and eye gaze direction. Observers (N=60) viewed images of fearful faces with direct or averted gaze for brief (255 ms) or longer (880 ms) exposures. MEG activity was source-localized using MNE and extracted from a set of anatomically and functionally constrained regions of interest: early visual cortex (EVC), fusiform face area (FFA), periamygdaloid cortex (PAC) and orbitofrontal cortex (OFC). Clear threat cues elicited an early (120 ms) increase in β-band (13-30 Hz) phase-locking in the right PAC. Simultaneously, greater interregional phase-locking occurred in the β-band between right PAC and OFC in response to ambiguous threat. For brief exposures, stimulus removal elicited increased right PAC activation amplitude for ambiguous threat. Conversely, for longer exposures, left PAC exhibited stronger θ-band (4-7 Hz) phase-locking to clear threat within this period that became greater for ambiguous threat later in the trial. These findings suggest that both left and right PAC are initially more sensitive to clear threat cues, while ambiguous cues trigger increased connectivity between right PAC-OFC and phase-locking to ambiguous threat cues in right and left PAC dependent upon exposure duration. Taken together, our results elucidate the temporal dynamics during visual threat perception: We find early reflexive processing of clear threat cues, with faster right PAC processing and sensitivity to rapid exposure, and later recruitment of additional processing resources needed to reflect on and resolve ambiguous threat stimuli.

REAL TIME RETINOTOPIC MAPPING OF PRIMARY VISUAL CORTEX IN MEG

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Retinotopic mapping of the primary cortex in MEG imaging is possible, and although not as spatially fine grained as fMRI there are numerous applications for MEG retinotopy. These range from basic research to clinical applications (e.g. research on visual perception, or possible usage in glaucoma). In the present study we aimed to perform retininotopic mapping in real time. With an advanced digital signal processing (DSP) system, and new CTF MEG electronics we are now able to interrogate the MEG signal within a latency of 1msec. Participants viewed a checkerboard annulus at various visual locations and eccentricities, intended to elicit retionotically specific activations of primary visual cortex. To gain further signal power, and with the benefit of the real time latency, we utilized the steady-state response with both the fundamental (9Hz) and the first-harmonics(18Hz) of the checkerboard alternation frequency being projected to source space in simulated real-time. Preliminary results indicate an ability to track primary visual cortex retinotopy in real-time, with a spatial resolution akin to offline processing. Thus, confirming the ability of MEG to be used in retinotopic mapping, and showing proof of real-time MEG.

Neural dynamics underlying reading of crowd emotion

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Reading crowd emotion from a group of faces is crucial for our social interactions and deficits in this ability are related to anxiety and social malfunctioning. However, neural dynamics underlying this process have not been investigated. We used source-localized MEG to characterize for the first time the neurodynamics of reading crowd emotion and compare it with single emotional face perception. Twenty-four subjects viewed stimuli containing two emotional (happy or angry), bilaterally presented single faces or groups of different faces, and chose rapidly which face or which crowd they would most avoid. We assessed the latencies of MEG activity in our regions of interest (ROIs): V1, V2, fusiform face area (FFA), periamygdaloid cortex (PAC), orbitofrontal cortex (OFC), superior temporal sulcus (STS), and precuneus. The ROIs were first anatomically extracted from MNI coordinates then functionally constrained. First, we found STS was more activated for single faces, while V1, V2, and precuneus were more activated for crowd stimuli (all p's< 0.01). The other ROIs were activated by both single faces and crowds, varying as a function of emotional valence. However, we found both earlier peak of activation to an angry face (200-350ms) and later activation for a happy face (550-900ms) in bilateral FFA, PAC, and OFC whereas we found hemispheric lateralization for crowd stimuli: Left FFA, PAC, and OFC showed higher early activation for angry crowds (200-450ms) and right FFA, PAC, and OFC showed higher activation for happy crowds (550-950ms). Our findings suggest that single face and crowd perception employ distinct neurodynamic patterns, with STS and visual areas (V1, V2, and precuneus) preferentially responding to single faces, and crowd stimuli, respectively. Moreover, while we found bilateral activity discriminating between two single faces, the face network showed hemispheric lateralization for discriminating the emotion of two crowds of faces.

Temporal variability along the visual pathway during face processing

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The hierarchical organization of the visual system was first proposed based on physiological data in animals (Hubel and Wiesel, 1962, Felleman and Van Essen, 1991). Using MEG and a visuomotor task, Tang et al. (1999) found that early responses showed smaller variability and late responses showed larger variability within the human primary visual cortex. We hypothesized that increasing variability would be found across functional areas along the functional hierarchy. To test this hypothesis, we showed faces and scrambled faces (Kanwisher et al., 1997) to subjects and compared differences in variability along the ventral pathway of visual processing.

MEG signals from seven adult subjects were recorded with a 306-channel MEG system. Source activity was calculated using minimum norm estimates. Template waveforms were created using the average source activity across subjects. Single-epoch waveforms were estimated by averaging over 30 randomly selected trials. Relative latency was then defined using cross-correlations between the template waveform and the estimated single-epoch waveforms. With these relative latencies, the intra-subject, inter-subject, and total variability were calculated.

When faces were presented, significantly larger variability was found in the fusiform gyrus compared to calcarine fissure. In the right calcarine fissure and fusiform gyrus, the total variability was larger for the scrambled faces than faces condition. Our results suggest that differences in variability between functional areas could be related to the functional hierarchy along the visual pathway in which the earlier the processing stage, the smaller the variability. In addition, differences in variability between conditions could reflect functional specification of a given cortical area. The close correspondence between temporal variability and functional hierarchy should be further tested with other complex stimuli and stimuli in other modalities.

The sex differences in brain activity ofprocessing emotional faces in early processes

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Thepresent study investigates the brain activities in processing male and femaleemotional faces in identity and emotion tasks. It was suggested that there are twopathways for the visual analysis of faces, one processes the changeable facialproperties(e.g., expression), the other processes the invariant facialproperties (e.g., identity) (Haxby, Hoffman & Gobbini, 2000; Duchaine,Parker, & Nakayama, 2005; Tamietto & de Gelder, 2010). In the presentstudy, we included seven emotions and collected data of Magnetoencepalographyfor comparisons of temporal and brain activity. Twenty participants (10 malesand 10 females) were recruited and completed both identity and emotionrecognition tasks using the same set of Caucasian adult faces. There were 10runs and 560 trials in total of each task. The tasks were presented in separateruns and in counter-balanced order. In the identity task, participants wereasked to identify if the two faces in a pair the same person. They pressed abutton for the same face identity and pressed another button for a different identity.In the emotion task, the participants were asked to judge if the second face isshowing the same emotion of the first face and pressed a button accordingly. Ineach trial, the first face and second faces were each presented for 1000±100ms in sequence, a response question was presentedfor 400ms, and finally the screen went dark during the ISI for 1600±200ms. Magnetic brain activity was recorded witha 160-channel whole-head MEG system in a continuous mode sampled at 1000 Hz,with acquisition between 0.03 and 200 Hz. The results found that the brainactivation of person identity task was significant higher than those of theemotion task. The Identity task was found with higher activation in three areasat 60-90ms. Compared to in the emotion task, female participants had higheractivity in processing male faces in identity task at ventral anterior cingulatecortex and angular gyrus at 60-90ms, at BA7 and caudate at 240-275ms, and atBA44 at 300-500ms. Male participants exhibited higher activity in processingfemale faces at inferior temporal gyrus at 300-500ms. It is suggested taskspecificity brain activations with emotion information implemented in variousbrain structures with sex differences in the early processes.

Study of MEG measurements of the Visual Evokedmagnetic fields for Arithmetic Logic Formula Response

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Superconducting quantum interference device (SQUID),which is a very sensitive magnetic sensor, has been widely used to detect theultra-small magnetic signals in many different territories, especially in thebiomagnetic measurement. In this study, a 128-channel SQUID first-order axial gradiometersystem for whole-head magnetoencephalography (MEG) measurements was setup to characterizethe visual evoked magnetic fields (VEFs) for arithmetic logic formula response.We can observe receptor geologic fault image of three-dimensional. Normallyapply on medicine field. In addition, when subjects get the different stimulatemay get image from MRI. Make use of the equipment and brainwave image arecombined. Using arithmetic to compute, arithmetic formula of digits to hundredsdigits.

How far does visual frequency tagging above 60 Hztravel?

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Frequency tagging is a tool often used to study the engagement of sensory regions. The idea is to drive the system at a given frequency and then measure cortical steady-state visual evoked potentials or fields using respectively EEG or MEG. However, the driving frequencies used are often in the 5-20 Hz range, which interferes with cortical rhythms in similar bands such as the alpha rhythm (8-12 Hz). As such tagging at higher frequencies could be highly advantageous. New developments in projector technology allows for using frequency tagging by presenting complex stimuli presented at higher frequencies.

In the current MEG study we investigated the feasibility of using complex stimuli presented at high frequencies to investigate stimulus processing beyond early visual cortex. To this end we presented participants (n=8) with lateralized face and house stimuli driven at 63 Hz, and 78 Hz respectively (randomly intermingled). This was done using the PROPixx projector at a refresh rate at 1440 Hz. In each trial participants were asked to attend to either the left, or the right stimulus and respond by button-press if the stimulus was flipped vertically (25% flip trials, cue 80% valid).

We found the early visual regions were driven at the tagged frequency in the hemisphere contralateral to the driven stimulus. Furthermore, attention towards the cued stimulus enhanced the stimulus response. Importantly we also found indications showing activity at the tagged frequencies in areas beyond visual cortex. Preliminary source modelling suggests activity in areas linked to respectively face and house processing.

Our study demonstrates that is it possible to drive earlier visual regions at frequencies beyond 60 Hz in a spatial specific manner. In future we aim to establish if we can engage face and house specific regions by the tagged frequencies. Importantly we will also quantify how the phase and attention driven power of the cortical alpha oscillations modulate the tagged signals.

Dynamics and properties of mental modelsof spinning 3D objects: an M/EEG study.

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Object perception relies at least on twoaspects: the state of the object at a given time (e.g. spatial configuration)and its identity/category. Previous studies have shown that brain activitydistinguishes these two levels for two spatial properties: at first, the brain signal isspecific to the size and location of an object's view, then the informationbecomes position-/size-invariant, and identity-specific. This distinction issubtler for different angles of view of an object, since they can have completelydifferent low-level representations, while still being associated with the samesystem. Are there two different stages, view-specific and view-invariant, inthe processing of the representation of an object? If so, how are these tworepresentations being employed during dynamic perception and mentalmanipulation of objects? We investigated the properties of these two levels ofrepresentation in 20 subjects, who watched 1) static images of cardinal anglesof view of two objects, 2) perceptual rotation and 3) performed a mentalrotation of these two objects, while M/EEG data were collected. By applyingmachine-learning techniques on the brain data associated with the staticimages, we built view-specific and view-invariant classifiers based on logisticregression. We show that object perception indeed presents a first stage ofview-specific content, followed by a view-invariant representation(view-specific classifiers generalize later to other views). However, theserepresentations could barely be decoded during the physical and mentalrotation. Only the identity of the objects could still be decoded followingunexpected events during these phases. These results argue for a qualitativedifference in the way the content is encoded depending on the transient vs.stationary nature of a process. We propose that prediction violations areencoded by ERF/ERP, while stationary processes are based on oscillatoryprocesses. Further analyses will deepen this hypothesis.