Whole-head OPM-MEG enables non-invasive assessment of functional connectivity

Mainak Jas*[1,2], Stephanie R. Jones[3, 4], and Matti S. Hämäläinen[1,2,5]

[1]Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, MA, USA

[2]Harvard Medical School, Boston, MA, USA

[3]Department of Neuroscience, Brown University, Providence, RI, USA

[4]Center for Neurorestoration and Neurotechnology, Providence VAMC, Providence, RI, USA

[5]Department of Neuroscience and Biomedical Engineering, School of Science, Aalto University, Espoo, Finland.

*Correspondence: mjas@mgh.harvard.edu (Mainak Jas)

Keywords

On-Scalp MEG; Resting-State Networks; Task-Based Connectivity

Abstract

A recent paper by Boto et al. established reliability of non-invasive functional connectivity measurements with a new whole-head optically pumped magnetometer magnetoencephalography (OPM-MEG) system. This rapidly developing technology enables a conformal the sensor array to accommodate different head sizes and opens up new avenues for experiments in more naturalistic settings.

Whole-head OPM-MEG enables non-invasive assessment of functional connectivity

Mainak Jas*[1,2], Stephanie R. Jones[3, 4], and Matti S. Hämäläinen[1,2,5]

[1]Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, MA, USA

[2]Harvard Medical School, Boston, MA, USA

[3]Department of Neuroscience, Brown University, Providence, RI, USA

[4]Center for Neurorestoration and Neurotechnology, Providence VAMC, Providence, RI, USA

[5]Department of Neuroscience and Biomedical Engineering, School of Science, Aalto University, Espoo, Finland.

*Correspondence: mjas@mgh.harvard.edu (Mainak Jas)

Keywords

On-Scalp MEG; Resting-State Networks; Task-Based Connectivity

Abstract

A recent paper by Boto et al. established reliability of non-invasive functional connectivity measurements with a new whole-head optically pumped magnetometer magnetoencephalography (OPM-MEG) system. This rapidly developing technology enables a conformal the sensor array to accommodate different head sizes and opens up new avenues for experiments in more naturalistic settings.

Magnetoencephalography (MEG) is a well-established non-invasive electrophysiological method for measuring neuronal activity with high temporal resolution [2]. A traditional MEG device employs an array of Superconducting Quantum Interference Devices (SQUIDs) submerged in liquid Helium inside a dewar. Due to the dewar wall thickness and variable head sizes, the head-to-sensor spacing in SQUID-MEG is between 20 and 40 mm in adults, limiting the obtainable spatial resolution (Figure 1). Optically pumped magnetometers (OPMs) are an exciting new sensor technology that has the potential to reduce this distance to as little as 3 mm. OPMs use a laser to excite Rubidium atoms to an energy state where atoms precess coherently around the magnetic field, and this polarization is detected using a light beam and photodiode setup. The dimensions of the sensors can be as small as 3 x 3 x 3 mm^3 [3]. OPM-MEG has two important advantages. First, due to the smaller sensor-scalp distance, OPM sensor arrays can detect higher spatial frequencies of the electromagnetic field distributions thus providing improved detection and localization of complex distributions of cortical activity. Second, the sensor array can conform to the individual head shape, further improving spatial resolution and signal-to-noise ratio (SNR), and enabling more naturalistic experimental designs in adults, children, and infants without restrictions for head movements. Fully integrated OPM-MEG systems are still in early stages of development but the technology is rapidly advancing. The utility of OPM-MEG in generating novel scientific discoveries beyond current SQUID-MEG technology are withstanding. However, there is a definite promise for OPM-MEG to help advance our understanding of the human brain in health and disease. Figure 1 summarizes key characteristics of existing SQUID-MEG vs. OPM-MEG systems, as well as some of the future goals for OPM-MEG.

On the path to establishing the utility of OPMs, a recent paper by Boto et al. [1] showed for the first time that cortical functional connectivity can be assessed with OPM-MEG. Functional connectivity (FC) measures statistical associations between the activities in two or more distinct regions of the brain. FC analysis can be applied to any brain signals, and is a common approach to define biomarkers of healthy and pathological human brain function, so far typically conducted using fMRI and/or MEG/EEG [4, 5].

Employing a whole-head ~50-channel (subject dependent) OPM-MEG system, Boto and colleagues were able to estimate FC in a visuomotor task as well as in resting state. The authors compared the reliability of the connectivity estimates against those obtained from a standard 275-channel SQUID-MEG system with established methods. Such connectivity analysis was not possible with earlier OPM systems, which recorded from a smaller number of sensors over a targeted brain region related to the task (Figure 1). During the visuomotor experiment, an inward moving circular grating was presented, and participants were asked to perform continuous abductions of their right index finger. During resting state, subjects were asked to fixate on a red cross and relax. The sensor-space signals were localized to 78 active brain regions using a source estimation method known as beamforming. This parcellation was based on the automated anatomical labeling (AAL) atlas. FC was estimated between all pairs of regions as Pearson's correlation of the amplitude envelope in the alpha (8--13 Hz), beta (13--30 Hz), and gamma (52--80 Hz) bands.

The authors assessed whether it was possible to distinguish the identity of a subject based on the connectivity matrices estimated from their OPM data. The FC values within subjects were found to be more similar to each other than between subjects. This indicated that OPM-MEG has matured far enough to measure subject-level connectivity and to identify a subject based on FC.

To examine the quality of OPM-MEG based FC estimates, the authors compared them to those obtained using SQUID-MEG. They found that both for within-subject and between-subjects comparisons, FC values were more similar between SQUID-MEG measurements than between OPM/SQUID or OPM/OPM. This suggests that, at least for the settings in the current study, SQUID-MEG measurements are more reproducible than those with OPM. The authors hypothesize that this could be due to inhomogeneous coverage of the OPM and SQUID sensors. Many subjects tend to rest their head against the back of the SQUID helmet, whereas OPM helmets may have had a noticeable gap in that region, even though the helmets are well fitted at the top of the head. This could potentially inflate the correlations, as the largest connectivities for the alpha band are observed in the occipital region for the SQUID system but are more widespread in the OPM sensors. These limitations could be addressed with future OPM-MEG systems that have denser and conformal sensor placement. Importantly, the authors also point out that existing integrated OPM systems are still made in-house, which could potentially cause reliability issues that negatively affect the results.

The study by Boto et al. also illustrates the importance of carefully designing data analysis pipelines in neuroimaging studies, particularly to improve SNR by minimizing non-brain activity. Specifically, the authors used beamformers for source localization, a method which effectively suppresses environmental noise and physiological non-brain activity such as heartbeats. As OPM-MEG systems become more widely available and commercially manufactured, it will be essential to concurrently establish analysis pipelines that can be applied to this new sensor technology and to share them through open-source code and data repositories [6]. There are number of methods that are well-established and widely distributed for SQUID-MEG processing, but still need to be optimized for OPM-MEG. Specifically, this includes methods for artifact removal, reduction of cross-talk, signal processing and forward modeling to maximize the information extracted.

Boto and colleagues have shown that OPM-MEG has the potential to replicate SQUID-MEG FC results with a relatively sparse sensor array. While validating concurrence with SQUID systems is a valuable step, the transformative promise of OPM technology lies in its potential to lead to new neuroscientific discoveries. Since the spatial resolution that can be obtained using on-scalp OPM-MEG is expected to be higher than that of SQUID-MEG, the potential to uncover previously unobservable features of human brain signals is evident. This could include, for instance, subtle features of transient or nonsinusoidal oscillations [7], which will in turn enable more accurate modeling of their underlying neural mechanisms [8]. Several groups are making fast progress in OPM development [9, 10] and commercial entities have also entered the field (e.g., Kernel, QuSpin, FieldLine, and Cerca Magnetics). Some of the considerations in the design of improved OPM systems include, for instance, enhancing bandwidth and sensor density, while improving reliability and minimizing cost. These goals will be most effectively reached through close partnership between academic scientists and industry, and by focusing engineering and analytical-development efforts according to scientific needs and research questions that are difficult to address using existing tools.

Figure legend

Figure 1. Current MEG technologies and future promise of OPM-MEG. Left: Schematic of current SQUID-MEG and OPM-MEG systems together with their critical characteristics. In a recent study [1], the authors employed a whole-head ~50-channel OPM-MEG system, and demonstrated functional connectivity (FC) capabilities similar to those of typical SQUID-MEG (functional connectivity images modified from [1]). Right: future OPM-MEG systems may include a high number of densely packed sensors, which can be operated in a lightly-shielded environment. Such systems could provide better assessment of FC in terms of signal-to-noise ratio (SNR) and spatial resolution, while adding the capability to conduct experiments in more naturalistic settings.

Declaration of Interests

The authors declare no competing interests in relation to this work.

Acknowledgements

This work was supported by NIH grants 5R01NS104585, 1P41EB030006, and 5P20GM103645.

References

[1] Boto, E., et al. (2021) Measuring functional connectivity with wearable MEG. NeuroImage. 230. 117815.

[2] Hämäläinen, M., et al. (1993) Magnetoencephalography—theory, instrumentation, and applications to noninvasive studies of the working human brain. Rev. Mod. Phys. 65.2. 413.

[3] Boto, E., et al. (2018) Moving magnetoencephalography towards real-world applications with a wearable system. Nature. 555.7698. 657–661.

[4] Biswal, B., et al. (1995) Functional connectivity in the motor cortex of resting human brain using echo- planar MRI. Magn. Reson. Med. 34.4. 537–541.

[5] Brookes, M.J., et al. (2011) Measuring functional connectivity using MEG: methodology and comparison with fcMRI. NeuroImage 56.3. 1082–1104.

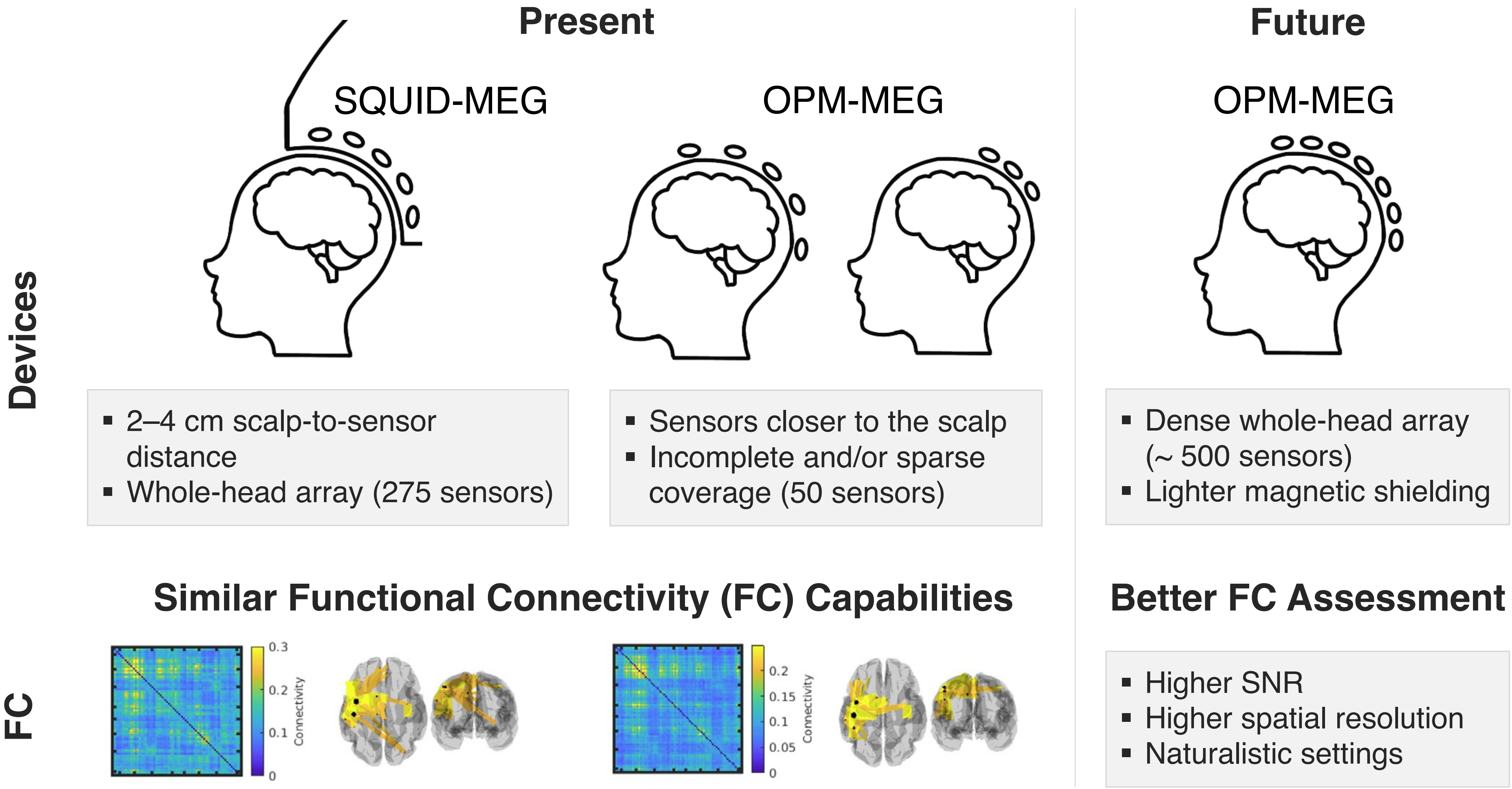
[6] Jas, M., et al. (2018) A reproducible MEG/EEG group study with the MNE software: recommendations, quality assessments, and good practices. Front. Neurosci. 12. 530.

[7] Jones, S.R. (2016) When brain rhythms aren't ‘rhythmic’: implication for their mechanisms and meaning. Curr. Opin. Neurobiol. 40. 72–80.

[8] Neymotin, S.A., et al. (2020) Human Neocortical Neurosolver (HNN), a new software tool for interpreting the cellular and network origin of human MEG/EEG data. Elife. 9. e51214.

[9] Iivanainen, J., et al. (2019) On-scalp MEG system utilizing an actively shielded array of optically-pumped magnetometers. NeuroImage. 194. 244–258.

[10] Sander, T. H., et al. (2012) Magnetoencephalography with a chip-scale atomic magnetometer. Biomed. Opt. Express. 3.5. 981–990.


Present
Future
SQUID-MEG
OPM-MEG
OPM-MEG
Devices
▪ 2–4 cm scalp-to-sensor distance
▪ Whole-head array (275 sensors)
▪ Sensors closer to the scalp
▪ Incomplete and/or sparse coverage (50 sensors)
▪ Dense whole-head array (~ 500 sensors)
▪ Lighter magnetic shielding
FC
Similar Functional Connectivity (FC) Capabilities
Better FC Assessment
0.3
0.2
0.1
0
Connectivity
0.2
0.15
0.1
0.05
0
Connectivity
▪ Higher SNR
▪ Higher spatial resolution
▪ Naturalistic settings