Neuron
Primer

Magnetoencephalography in Cognitive Neuroscience: A Primer

Joachim Gross[1,2,3,*]
[1]Institute for Biomagnetism and Biosignalanalysis (IBB), University of Muenster, 48149 Muenster, Germany
[2]Otto-Creutzfeldt-Center for Cognitive and Behavioral Neuroscience, University of Muenster, 48149 Muenster, Germany
[3]Centre for Cognitive Neuroimaging (CCNi), University of Glasgow, Glasgow, UK
*Correspondence: joachim.gross@wwu.de
https://doi.org/10.1016/j.neuron.2019.07.001

Magnetoencephalography (MEG) is an invaluable tool to study the dynamics and connectivity of large-scale brain activity and their interactions with the body and the environment in functional and dysfunctional body and brain states. This primer introduces the basic concepts of MEG, discusses its strengths and limitations in comparison to other brain imaging techniques, showcases interesting applications, and projects exciting current trends into the near future, in a way that might more fully exploit the unique capabilities of MEG.

Magnetoencephalography (MEG) allows researchers to study brain activity by recording the magnetic fields generated by the electrical activity of neuronal populations. A key advantage of this approach over other techniques is that it can record brain activity directly and non-invasively with a very high (within milliseconds) temporal resolution. This direct relationship between the recorded magnetic field and the underlying neuronal currents means that MEG is not affected by the problems commonly caused by intermediate processes (such as neurovascular coupling in fMRI [functional magnetic resonance imaging] or fNIRS [functional near-infrared spectroscopy]). MEG can thus generate an information-rich, dynamic representation of large-scale brain activity. These key strengths of MEG entail that it is often used by neuroscientists to study large-scale brain dynamics in health and disease.

MEG was developed in the late 1960s when magnetic fields originating from the brain were first recorded using a single sensor (Cohen, 1968). Since then, MEG systems have developed significantly in their technical sophistication and now routinely feature about 300 sensors that cover the whole scalp in a helmet-shaped design (Figure 1; Box 1). In addition, a new generation of sensors is currently under development that will expand the remit and use of MEG in cognitive neuroscience. Arguably the most exciting developments in the field and its most significant contributions to neuroscience come from the ongoing efforts to make better use of this rich and detailed brain activity signal. These efforts have led to several important transitions in the field. First, the field is moving toward ''single-trial analyses,'' in which the variability of brain responses and their relationship to behavioral changes are explicitly taken into consideration. Second, the rhythmic components of brain activity are increasingly being recognized as being of fundamental importance for brain function and dysfunction; these rhythms can significantly contribute to our understanding of how the brain operates. Third, ''activation studies'' are giving way to ''information and connectivity studies,'' as scientists aim to decode specific information from brain signals and their connectivity instead of simply describing the time course of activation. Together, these technological, methodological, and conceptual developments, combined with MEG's inherent advantages, have created an exciting tool that is ideally placed to make significant contributions to cognitive neuroscience.

This primer is not intended to be a comprehensive review of MEG, given the several excellent recent reviews and books on this topic (Baillet, 2017; Hari and Puce, 2017; Hari et al., 2018; Lopes da Silva, 2013; Supek, 2013; Hansen et al., 2010). For this reason, I also do not discuss best practice in the clinical or fundamental application of MEG but refer readers to other recent reviews (Gross et al., 2013a; Hari et al., 2018; Keil et al., 2014; Pernet et al., 2018). Instead, this primer aims to provide a concise introduction and guide to the most recently reported developments in MEG technologies. My goal is to provide readers with sufficient knowledge to appreciate the role of MEG in neuroscience, to better assess MEG research, and to understand how MEG could contribute to their own research. With this in mind, I explain the fundamental concepts of MEG, including the recording hardware to use, the nature and analysis of the recorded signals, and also MEG's applications to neuroscience research and how it compares with related methods (Figure 2; Box 2). I also consider its potential future applications in the field of cognitive neuroscience.

MEG relies on the fundamental physical principle that electrical currents are always associated with magnetic fields. In the brain, these currents are produced during neural activity by the movement of ions in intra- and extracellular space. Ion currents linked to postsynaptic potentials are the largest contributors to the MEG signal (Lopes da Silva, 2013). Presynaptic neurotransmitter release leads to postsynaptic dendritic transmembrane currents, which cause changes in the local field potential (LFP) at the dendrite and soma of a neuron. This results in a primary intracellular current along the soma-dendritic axis of the neuron (Lopes da Silva, 2013), along with an extracellular return (or volume) current in the opposite direction. When these electrical currents flow simultaneously across neighboring neurons with a similar dendritic orientation, the corresponding individual magnetic fields add up to a detectable field strength that can be recorded by MEG sensors near the scalp (Hämäläinen et al., 1993). Thus,

Figure 1. MEG System
(A) A MEG system inside a magnetically shielded room that consists of several layers of mu-metal. The whole-head MEG system with 275 SQUID sensors inside the helmet-shaped dewar can be seen through the open door.
(B) MEG recordings are obtained from a participant with SQUID sensors in the dewar surrounding the participants head.

postsynaptic currents in neocortical pyramidal neurons are the primary contributors to the MEG, since these neurons have a clear soma-dendritic axis, which is typically locally aligned with neighboring cells and perpendicular to the cortical surface. Modeling studies and invasive recordings suggest that the synchronous activation of a few tens of thousands of neurons leads to robustly detectable signals (Murakami and Okada, 2006). The recorded amplitude of the MEG signal largely depends on three factors: the number of activated neurons, their temporal synchrony, and the degree of their spatial alignment. Thus, a recorded MEG signal provides an approximate representation of the synchronized (also below spiking threshold) fluctuation in the membrane potential of many neurons. However, while synaptic potentials are considered to be the main contributors to the MEG signal, non-synaptic potentials can contribute as well. For example, action potentials and even fast sodium spikes are known to contribute to LFPs, even at frequencies of around 100 Hz (Buzsáki et al., 2012; Pesaran et al., 2018), and they might contribute to the MEG signal if they are temporally precisely synchronized across a local population of neurons (Murakami and Okada, 2006).

Building Blocks of an MEG Study

In this section, I discuss the versatility of MEG along three dimensions: recruitment, recording, and readout (Figure 3).

Recruitment

Most published MEG studies are based on relatively modest participant numbers (about 20). However, larger-scale data collection is possible and should be encouraged in the form of single or multi-center studies, with the results published as open-access data, to improve statistical power (Button et al., 2013) and reproducibility (Poldrack, 2019). Such large, open datasets also help us understand the mechanisms that underlie inter-individual differences in large-scale brain dynamics and behavior. As an example, resting-state MEG studies have investigated heritability and genetic determinants of the amplitude and frequency of brain oscillations and their connectivity (Colclough et al., 2017; Leppäaho et al., 2019). MEG data can also be co-registered and merged with functional and anatomical MRI data allowing to exploit the complementary nature of the signals. In the future, we will hopefully see more large-scale MEG data collection projects and their subsequent open sharing and publication (such as the Human Connectome Project [HCP]; Larson-Prior et al., 2013; Cam-Can; Taylor et al., 2017; MOUS; Schoffelen et al., 2019; or Omega; Niso et al., 2016) and for MEG data to be combined with other data types such as (f)MRI, neuropsychology, and biomaterials (for example, blood, saliva, urine, stool). This will facilitate studies of body-brain interactions and other factors shaping inter-individual differences in brain activity.

Recording

In general, two different MEG recording types are performed: event-based recordings where (often transient) stimuli are repeatedly presented; and continuous recordings, where participants rest or perform a continuous task (such as making hand/finger movements, or processing continuous sensory stimuli). MEG data can also be acquired in combination with other signals, leading to novel applications that can potentially make significant contributions to neuroscience.

Signals. MEG/EEG is an excellent tool to study the dynamics of interactions between body and brain. As described in more detail below, MEG, in combination with source analysis, yields spatiotemporal maps of brain activation with excellent temporal and good spatial resolution. The use of experimental paradigms to probe cognitive functions additionally results in measures of behavioral performance that can be used to identify brain-behavior relationships. This classic approach can be further extended at the data acquisition stage by recording additional signals that capture aspects of body or brain state. In MEG studies, it is common practice to record the electro-oculogram (EOG) to facilitate the identification of artifacts related to eye movements or blinks (Gross et al., 2013a). Eye movements can also be recorded more precisely using MEG-compatible eye-trackers that sample at up to 1–2 kHz. Additionally, they allow recording pupil size as a proxy for arousal (Meindertsma et al., 2017). Another often-used additional signal is the electromyogram (EMG), which records muscle activity. This can be used to measure different aspects of movement also in movement disorders and can be combined with motion tracking devices (Marty et al., 2015). Besides classic examples of recording EMG from arm muscles it can also be used to study swallowing (Suntrup et al., 2013) or speech (Alexandrou et al., 2017). Other signals that can be recorded alongside MEG include electrodermal activity (EDA) (Wessing et al., 2013), the electrocardiogram (ECG) (Park et al., 2014), electrogastrogram (Richter et al., 2017), and blood pressure or respiration (Myllylä et al., 2017). Overall, these additional signals (together with MEG here called MEG$^+$ signals) provide a rich, dynamic, multivariate characterization of the body and brain state and behavior (Figure 3).

Interventions. Interventions are sometimes made during an MEG study to probe and change brain states in a controlled manner and to observe how this change is reflected in MEG$^+$

Box 1. MEG Hardware

MEG systems are based on highly sensitive sensors that non-invasively record—outside of the human head—minute magnetic fields that are generated by neural activity in the brain. Current state-of-the-art, whole-head systems use about 300 sensors that are spatially arranged in a helmet-shaped Dewar (cryogenic storage container). The Dewar is filled with liquid helium at a temperature of about −269°C—just four degrees Celsius above absolute zero temperature. Current commercial, whole-head systems use SQUID sensors (Superconducting QUantum Interference Devices). These sensors operate in the state of superconductivity and allow very weak magnetic fields to be measured in the femto-tesla range (Hämäläinen et al., 1993). More specifically, each SQUID is coupled to a pickup coil and measures the changing magnetic flux through this coil. Superconductivity affords these sensors a high sensitivity; typical MEG signals recorded from the brain have an amplitude in the order of 100 femtoTesla (fT). This is 7–8 orders of magnitude lower than the earth's magnetic field and still about 3 orders of magnitude smaller than the magnetic field generated by the heart. To avoid excessive contamination from ambient magnetic fields, MEG systems are operated in a magnetically shielded room (Figure 1).

MEG systems are relatively expensive to acquire and to maintain. Despite optimal thermal insulation, helium boil-off is unavoidable, which in many of the currently (older) operating systems requires the dewar to be refilled with expensive liquid helium 1–2 times per week, leading to operational downtime and increased costs. The latest-generation MEG systems come with integrated cold-heads that, in a closed system, liquefy most of the boiled-off helium, thereby reducing operating costs and downtime.

In recent years, a new type of sensor has emerged for measuring neuromagnetic signals, called an optically pumped magnetometer (OPM) (Alem et al., 2017). A typical OPM design uses a photodiode to measure the intensity of laser light after it has passed through a gas-filled glass cell. The wavelength of the laser is precisely tuned to the resonance frequency of alkali gas atoms in the cell (Boto et al., 2018). Changes in the magnetic field lead to changes in light transmission that are precisely detected by the photodiode. The sensitivity of OPMs has significantly increased in recent years and is now similar to that of SQUID sensors. However, OPMs do not require the expensive and high-maintenance cryogenic components. Instead, OPMs operate at room temperature (the sensor contains insulation since the alkali gas is heated to about 150°C). An OPM sensor can therefore be integrated into a mobile system (Boto et al., 2018) and can be placed directly onto the scalp. The reduced distance between sensors and the brain leads to a significant increase in signal power, by a factor of 5–7, compared to SQUIDs (Iivanainen et al., 2017). While OPMs are highly promising, they are limited by a relatively low signal bandwidth (about 150 Hz compared to several kilohertz for SQUIDS). In addition, future whole-head multi-channel OPM-based systems will need to account for cross-talk between neighboring OPM sensors.

signals and behavior using online and offline approaches. Online interventions are applied during MEG$^+$ recordings. In a standard cognitive MEG experiment, short sensory stimuli are repeatedly presented to participants who might have received instructions to perform certain tasks on these stimuli (such as detection, discrimination, etc.). Other tasks might not use sensory stimuli (for example, self-paced movements, inner speech, etc.). Cognitive tasks during MEG$^+$ can be combined with transcranial electric stimulation (TES) or deep-brain stimulation (DBS). Recently, the growing interest in brain oscillations has led to an increased use of continuous, and sometimes naturalistic, sensory stimuli (or continuous movement tasks) that can be conveniently analyzed with spectral signal processing methods. Examples are the use of continuous speech (Gross et al., 2013b) or continuous movement (Jerbi et al., 2007). This is of interest for the study of brain rhythms that can be monitored with MEG while they are modulated by or entrain to incoming sensory stimuli (Giraud and Poeppel, 2012; Thut et al., 2012).

Offline interventions are applied between MEG$^+$ sessions. In general, a "baseline" MEG session is recorded, the intervention is performed, and then one or more MEG sessions are recorded to assess the effect of intervention on brain activity. This approach is particularly suited to interventions that are incompatible with online recordings such as TMS, pharmaco- or psychotherapy. The combination of approaches illustrated in Figure 3 leads to versatile applications that have not been fully exploited so far.

Readout

MEG$^+$ signals can be transformed to yield information-rich readouts that help to study the complex multi-directional dependencies between body, brain, and behavior in health and disease. They are typically processed using source analysis (see next section) to reveal how neural activity unfolds across space, time, and frequency and how these activity patterns relate to behavior. More recently, the focus has shifted from the mapping of activation to the mapping of information or representations. For example, information theory can be used to identify brain areas where neural activity measured with MEG or EEG contains information about specific stimulus features (such as the eye in a visually presented face) (Ince et al., 2017; Quian Quiroga and Panzeri, 2009; Schyns et al., 2011). Multivariate analysis enables the mapping of "representations" (Cichy et al., 2014). The following sections will introduce concepts that help understand relevant readouts.

MEG Analysis

In this section, I provide an overview of MEG data analysis and the key concepts involved to equip researchers with the necessary and essential background knowledge they will need to understand MEG data analysis. For more detailed accounts of MEG data analysis in cognitive or clinical studies, I refer readers to several recently published books and articles (Brette and Destexhe, 2012; Cohen, 2014; Gross et al., 2013a; Hari and Puce, 2017; Hari et al., 2018; Keil et al., 2014).

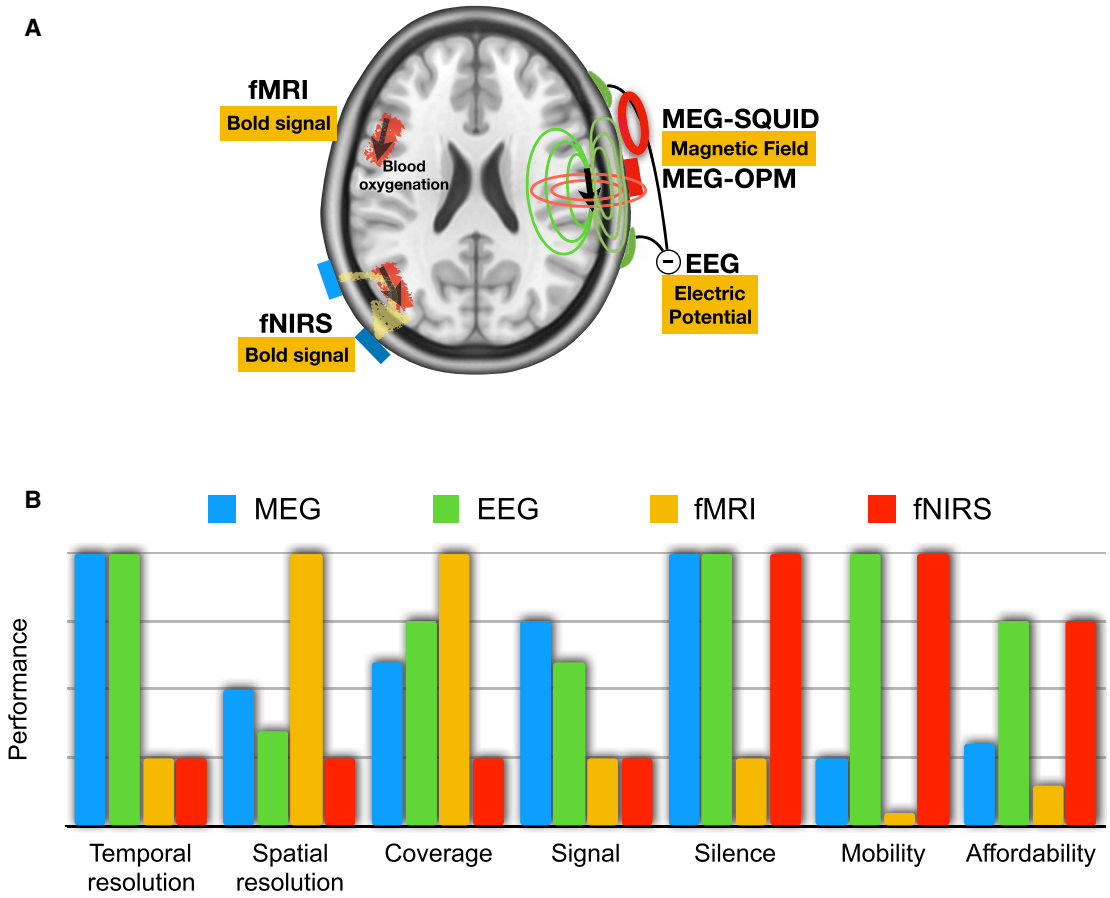

Figure 2. MEG and Other Recording Techniques

(A) Measuring brain activity: this schematic figure illustrates the recording of brain activity with fMRI, fNIRS, MEG, and EEG. Current flow (black arrow) is associated with magnetic fields (red lines) that can be recorded with MEG. SQUID sensors (red coil) operate in liquid helium and need a thermal insulation that leads to a physical separation from the scalp. OPM sensors (red rectangle) operate at near room temperature and in close proximity to the scalp. EEG electrodes (green) are attached to the scalp and record potential differences to a reference electrode. fMRI and fNIRS are sensitive to changes in blood oxygenation that are caused by neural activity.

(B) MEG and other recording techniques. MEG is compared to EEG, fMRI, and fNIRS. The bar graph shows for each aspect a comparative ranking of all four methods. High bars indicate high performance. Temporal resolution: MEG and EEG have the same higher resolution compared to fMRI and fNIRS. Spatial resolution: fMRI has the highest spatial resolution followed by MEG where spatial resolution is less affected by models of head conductivity compared to EEG. Coverage: modern MEG and EEG system have sensors covering most of the scalp (and for EEG sometimes the face) but typically have reduced coverage of prefrontal areas and cerebellum, while fMRI does not have this limitation. fNIRS has limited coverage. Signal: MEG/EEG signals are more directly related to neuronal activity compared to fNIRS and fMRI. MEG signals are less distorted by changes in tissue conductivities compared to EEG. Silence: MEG, EEG, and fNIRS are silent recording techniques in contrast to fMRI where gradient coils produce noise during data acquisition. Mobility: mobile systems exist for EEG and fNIRS but not for fMRI. New MEG-OPM sensors can be integrated in more mobile MEG systems. Affordability: fMRI systems are most expensive, followed by MEG and more affordable EEG and fNIRS systems. Please note that this graph is not the result of a quantitative, precise assessment.

MEG Source Analysis

MEG source analysis aims to identify the neural generators of the recorded magnetic fields. It is a central part in most MEG studies, motivated by the fact that interpretation of functional data is typically more meaningful when they can be assigned to the underlying anatomical brain areas. Source localization is based on two fundamental concepts: the forward and the inverse problem (Figure 4). Solutions to the forward problem model the magnetic fields at known sensor locations that are generated by a current with known location and orientation in a specified head model (see below). By contrast, solutions to the inverse problem identify the location and orientation of currents based on the recorded magnetic field. Practically, identifying the location of a source current from measured MEG signals starts with solving the forward problem. This requires the construction of a head model that specifies the spatial distribution of tissue conductivities. Individual anatomical MRIs are used to produce two types of state-of-the-art, realistic head models: boundary element models (BEMs), which model tissue surfaces; and finite element models (FEM), which model tissue volumes of the entire head. Currently, advanced FEM models differentiate between several tissue types and their associated conductivities such as skin, skull compacta, skull spongiosa, cerebrospinal fluid (CSF), and gray and white matter (Vorwerk et al., 2014). The head model is used to compute solutions of the forward problem at known sensor locations, typically for a single, infinitesimally

Box 2. MEG Compared to Other Non-invasive Neuroimaging Methods

A number of methods for recording brain activity exist. Here, I discuss advantages and limitations of MEG in comparison to EEG, fMRI, and fNIRS (Figure 2).

MEG VERSUS EEG

As a non-invasive recording technique, MEG is most closely related to electroencephalography (EEG) (Biasiucci et al., 2019). Both techniques measure the consequences of transmembrane currents (Buzsáki et al., 2012; Pesaran et al., 2018) but in different ways. Whereas MEG measures the extracranial magnetic fields predominantly related to primary dendritic currents, EEG records potential differences that reflect volume currents across different locations on the scalp. Therefore, the distortive effect of especially skull and skin compartments is larger in EEG than in MEG (Figure 2A). As a result, the spatial distribution of measurements across sensors, arising from a specific active neuronal population, is less distorted for MEG than it is for EEG (Vorwerk et al., 2014). For the same reason, the localization of the activated neuronal populations in EEG is much more sensitive to errors in modeling the distribution of tissue conductivities in the head, compared to MEG. This problem is exacerbated by the fact that these tissue conductivities, which are required for accurate head models, are notoriously difficult to measure. MEG and EEG signals also differ in their sensitivity to the orientation of neuronal currents. In contrast to EEG, MEG is less sensitive to radial currents than to tangential currents. This complementarity means that researchers may opt to use simultaneous EEG and MEG recordings to localize the underlying generators (Aydin et al., 2015; Sharon et al., 2007).

MEG VERSUS BLOOD-FLOW IMAGING TECHNIQUES

Both fMRI and fNIRS signals are only indirectly related to neural activity because they record associated changes in blood oxygenation levels (Figure 2A). Instead, and as already discussed, MEG signals are directly coupled to neural activity via the generated magnetic fields, which travel at the speed of light and undergo minimal distortion by the tissues they pass through. Another key advantage of MEG (and of EEG) compared to fMRI and fNIRS is the excellent temporal resolution of under 1 ms they provide (Figure 2B). Thus, MEG is the preferred method for studying the fast dynamics of brain activity and connectivity. However, fMRI has significantly higher spatial resolution compared to MEG while providing full brain coverage. Instead, spatial resolution in MEG is inhomogeneous across the brain, decreases with distance from the sensors, and depends on the signal-to-noise ratio, the location, orientation, and spatial extent of the activated neuronal population. MEG can have a spatial resolution in the millimeter range for cortical brain areas (Barnes et al., 2004) especially if head movements are restricted with a flexible headcast (Bonaiuto et al., 2018). However, MEG registers neural activity in subcortical areas with lower sensitivity and spatial resolution compared to cortical areas. Nevertheless, there is converging evidence that MEG can record activity from deep-brain structures such as hippocampus, amygdala, thalamus, and the brainstem (Pizzo et al., 2019; Pu et al., 2018; Ruzich et al., 2019).
In summary, compared to other commonly used non-invasive recording techniques in cognitive neuroscience, MEG's strengths lie in its ability to directly, silently, and non-invasively record neural activity with full-brain coverage at high temporal and good spatial resolution. It is therefore ideally suited for studying the dynamics of large-scale neural activation and connectivity throughout the brain.

MULTI-MODAL STUDIES

Interestingly, MEG can be combined with other complementary techniques to obtain either a multi-modal readout of brain activity, or to modulate brain activity before or during MEG recordings. An obvious and standard example is the simultaneous recording of MEG and EEG, which is motivated by their partial complementarity, as described earlier. This setup can be further extended by the simultaneous acquisition of invasively recorded EEG data from implanted depth electrodes in patients (Dalal et al., 2009; Gavaret et al., 2016). Similarly, LFPs can be recorded from patients using implanted DBS electrodes (Hirschmann et al., 2011; Litvak et al., 2011). A key strength of these setups is that they can be used to obtain precise recordings from a few target locations using an invasive approach, as well as non-invasive recordings from the whole brain. Surprisingly, it is even possible to record MEG signals during DBS, for example, to investigate how DBS modulates cortical activity (Abbasi et al., 2018; Oswal et al., 2016). Since fNIRS is an optical technique it can be simultaneously recorded with MEG to enable electrophysiological signals to be related to blood-oxygen-level-dependent (BOLD) signals (Mackert et al., 2008).

MEG AND NEUROSTIMULATION

Non-invasive neurostimulation techniques such as TMS and TES offer exciting applications for potential treatment of neurological and mental health disorders or for probing the causal relevance of specific neural activity patterns (such as brain oscillations) for cognitive processes (Thut et al., 2017). Although MEG can be combined with TES one limitation of this approach is that TES

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Box 2. *Continued*

generates very strong artifacts during MEG recordings. Nevertheless, modern SQUID sensors can tolerate the currents that are typically applied through electrodes on the scalp during TES (about 4 mA). Indeed, several studies have reported the use of electric stimulation during MEG, using alternating (tACS) or constant (tDCS) currents (Herring et al., 2019; Ruhnau et al., 2016). However, removing the corresponding artifacts from the MEG signals is not trivial because the amplitude of the artifact is modulated by a number of rhythmic and non-rhythmic processes, such as heartbeat, respiration, head movement, and changes in electrode impedance (Noury and Siegel, 2018). Another important consideration for MEG-TES studies is the optimization of the stimulation parameters, including electrode location (Dmochowski et al., 2011; Opitz et al., 2018; Wagner et al., 2016). Stimulation of a specific target area is only possible with the use of computational models that are based on realistic volume conductor models (Huang et al., 2017; Wagner et al., 2014) ideally derived from individual anatomical MRIs (Liu et al., 2018). Modern multi-channel TES systems offer further degrees of freedom to control the path, focality, and orientation of induced currents to optimally stimulate a target area (Baltus et al., 2018). This is a promising and active research area driven by the exciting prospect of combining spatio-temporally detailed electrophysiological recordings with a versatile neurostimulation technique.

small current segment with a specified location and orientation (called the equivalent current dipole) (Figure 4). The solution of the forward problem therefore relates a single current source to the expected magnetic fields at the sensor locations. Importantly, the magnetic fields generated by more complex and spatially extended currents can also be computed (as a linear superposition of magnetic fields) from these elementary sources. Solutions to the inverse problem make use of this relationship and aim to identify the locations and orientations of elementary current sources in the brain that explain components of the recorded magnetic field. There is no unique solution to the inverse problem, and different inverse methods impose different constraints that lead to different representations of the underlying generators (Baillet et al., 2001; Wipf and Nagarajan, 2009).

All inverse methods require the specification of a source model that approximates the underlying continuous current density distribution with a finite number of parameters. The choice of source model therefore constrains the result. The classic source model is the multi-dipole model, which aims to explain the measured magnetic field with a small number (typically <10) of equivalent current dipoles. More recently, distributed source models have become increasingly popular. These models describe currents as vector fields across the brain at a pre-defined spatial resolution (between about 4 and10 mm). The source estimation can be constrained, for example, by restricting currents to the gray matter. An orientation constraint can also be incorporated when solving the inverse problem to locate sources perpendicular to the local cortical surface according to the preferred orientation of pyramidal neurons. Several open-source software packages exist to perform MEG source analysis (Baillet et al., 2011; https://www.biomagcentral.org).

In summary, MEG source analysis can be used to reconstruct the brain's neural activity with relatively high fidelity in space and time. This ability to observe and study large-scale brain dynamics in a non-invasive and regionally specific manner is a key strength of MEG, which also translates directly into two further advantages: its use in the study of brain rhythms and functional connectivity.

MEG Spectral Analysis

MEG spectral analysis utilizes the high temporal resolution of MEG data to study brain rhythms. A standard MEG spectral analysis involves performing a source analysis (i.e., solving the inverse problem) to identify regions of interest (ROIs) and estimating the neural activity with millisecond temporal resolution. Methods based on the Fourier or wavelet transform are then used to create time-frequency representations (TFRs) that quantify the temporal modulation of frequency-specific brain rhythms over time (Cohen, 2014). With suitable experimental paradigms, this is a versatile and powerful approach to identifying brain-behavior relationships (Figure 3).

MEG is also an excellent tool for functional connectivity analysis that studies how different brain areas interact to process information. The whole-brain coverage provided by MEG and its excellent temporal and good spatial resolution generate rich data that are well suited for investigating statistical dependencies between brain areas (Bastos and Schoffelen, 2016; Pesaran et al., 2018; Schoffelen and Gross, 2009). Yet, in interpreting estimates of MEG (or EEG) connectivity, one needs to be aware of some important limitations (Gross et al., 2013a; Palva et al., 2018): the main limitation is that each activated brain area is recorded by all MEG sensors, albeit at different amplitudes that depend on the location and orientation of the activated neuronal population. Therefore, even a single activated brain area will lead to a common signal component in all sensors, which results in spurious "connectivity" between these sensor recordings. The hallmark of this spurious connectivity is that it is due to a common signal with no delay across different sensors. This makes the interpretation of connectivity results—at the level of sensor recordings—very difficult if not impossible. This problem can be partly addressed by using source analysis. But even source analysis does not achieve a perfect un-mixing of the signals (Schoffelen and Gross, 2009). Directed connectivity measures such as Granger causality can alleviate this problem because they are insensitive to these spurious zero-lag interactions (Bastos and Schoffelen, 2016). However, other factors such as signal-to-noise ratio, the source localization method, or inaccuracies in the head model will still affect the quality of the connectivity estimate and need to be considered (Cho et al., 2015; Mahjoory et al., 2017; Palva et al., 2018).

A complementary approach for functional connectivity analysis is dynamic causal modeling (DCM), which are discussed in more detail in Emerging Topics. While Granger causality is data driven and makes few assumptions about the observed system, DCM is model based and allows hidden states and

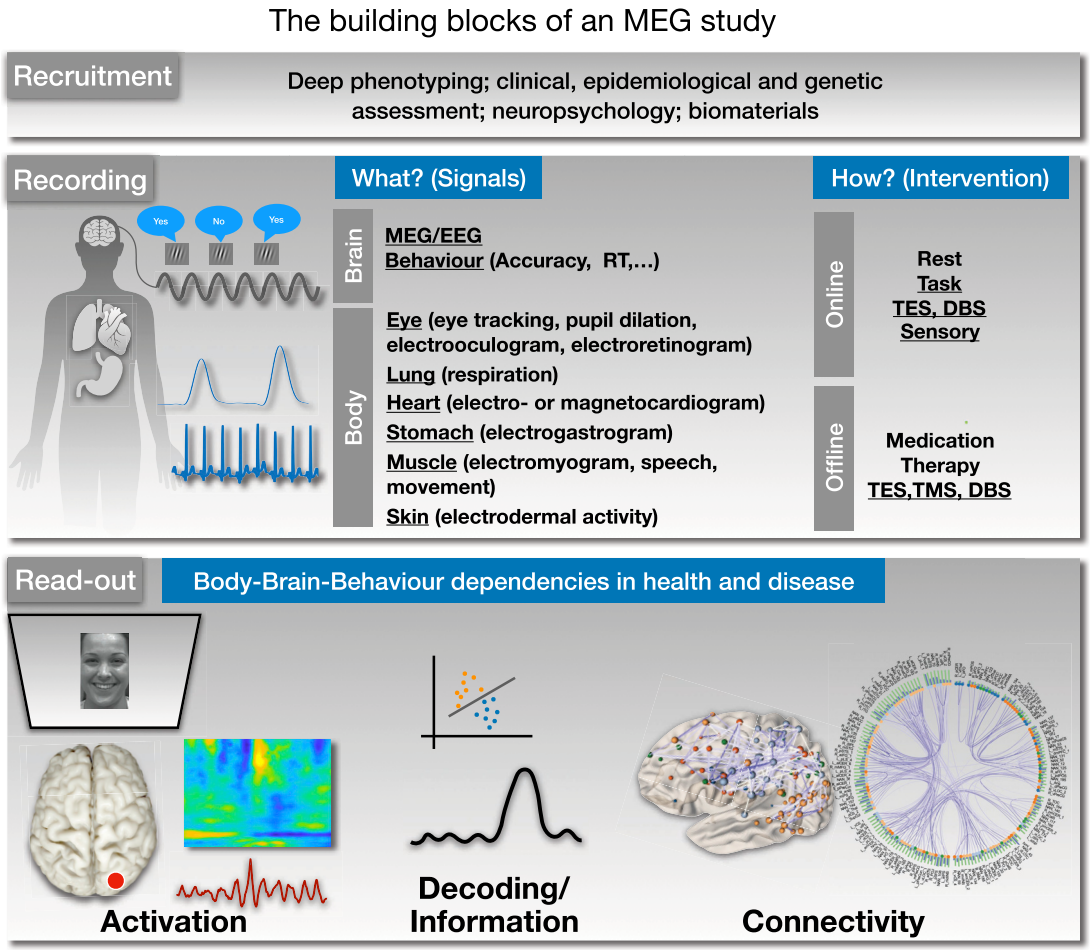

Figure 3. The Building Blocks of an MEG Study

The figure shows the different parts of an MEG study that can be adapted according to the specific purpose of the study.

Recruitment: especially in large-scale cohort studies, the rich MEG data can be complemented with detailed clinical and epidemiological data but also with other imaging data such as (f)MRI.

Recording: typical MEG studies record MEG/EEG and behavioral data (such as accuracy and reaction time [RT]). In addition, peripheral signals can be recorded simultaneously to allow for a more detailed analysis of body-brain interactions. A range of online or offline interventions can be employed such as continuous tasks (e.g., movements or isometric contraction), sensory stimulation, TES, TMS (transcranial magnetic stimulation), DBS, medication, or other forms of therapy. Underlined interventions can also be applied in a rhythmic mode with the aim to interact with intrinsic brain oscillations.

Readout: MEG source analysis leads to spatiotemporal functional maps that are characterized by excellent temporal and good spatial resolution. This can be used to characterize the activation of specific brain areas in response to sensory stimulation, or in relation to a specific task (red line). The activation time series can be transformed to the time-frequency domain to study the relationship between brain rhythms and behavior. Combining MEG data with decoding or information analysis can result in a time series representing the decoding performance over time or the information about a certain stimulus feature that is coded in the MEG signal (illustrated by the black line representing decoding of two conditions [blue versus red dots]). MEG connectivity analysis quantifies statistical dependencies with applications in the study of brain-brain coupling, body-brain coupling, or brain-environment coupling. (Connectivity plots were created with https://immersive.erc.monash.edu/neuromarvl/.)

variables to be estimated. In general, connectivity analysis is an exciting tool when performed with the required caution and interpreted with an awareness of its limitations.

MEG Applications

In this section, I draw on examples from the recent literature to provide a selective overview of how MEG and its applications are making significant contributions to cognitive neuroscience. I also discuss challenges in the field, interesting developments, and their potential applications in the near future. We start with the general topic of temporal dynamics and then focus mostly on studies of brain rhythms, which have received increasing interest in recent years.

Temporal Dynamics of Information Processing

The main strength of MEG compared to other neuroimaging methods is that the silently recorded MEG signals allow neural activity to be reconstructed across the brain with excellent temporal and good spatial resolution. These information-rich data are thus ideally suited for studying large-scale neural dynamics in the information-processing brain. Indeed, from the beginning, the excellent temporal resolution of MEG has been exploited to identify different stages of

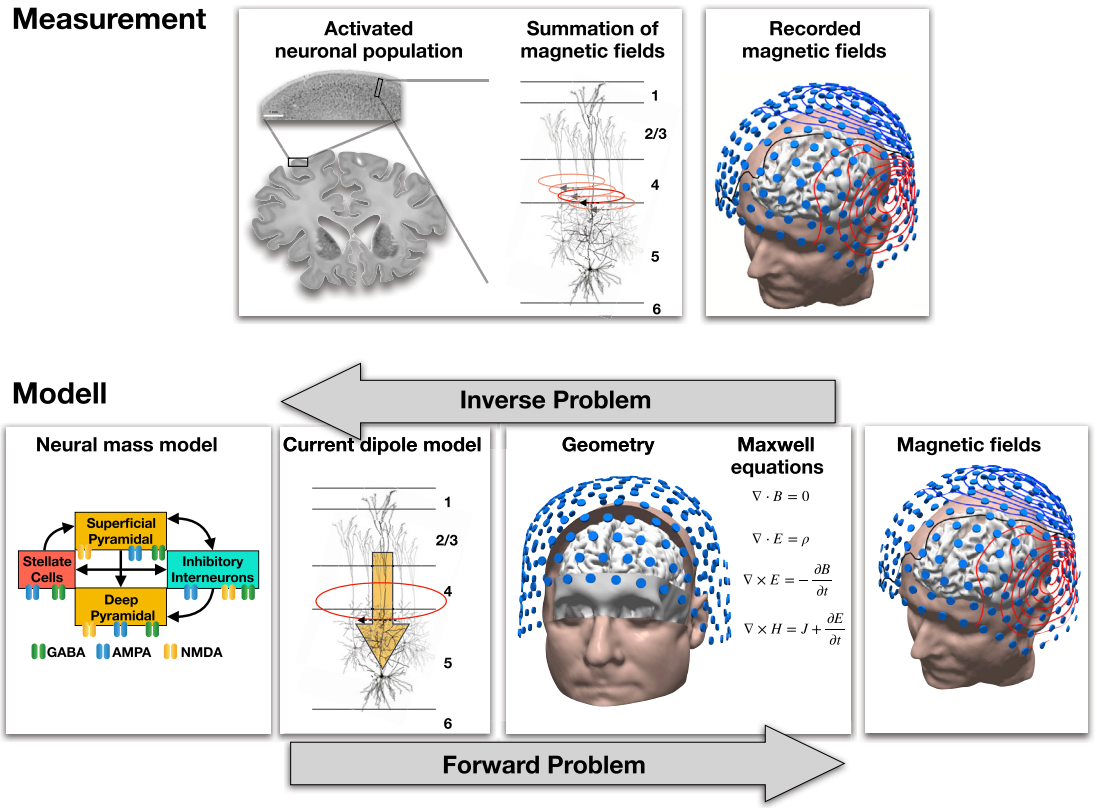

Figure 4. Forward and Inverse Problem

The forward and inverse problem are based on models of the MEG measurement process.

Top: an activated neuronal population leads to the summation of magnetic fields associated with electrical currents. These magnetic fields (displayed with isocontour lines) are detected non-invasively outside the head with MEG sensors (plotted as blue disks).

Bottom: regional brain activity arising from interacting excitatory and inhibitory neurons across the different cortical layers can be modeled with a neural mass model (NMM, e.g., Symmonds et al., 2018). NMMs can account for different receptor types. The primary currents representing the accumulated currents of several tens of thousands of neurons are modeled with single current dipole. Solving the forward problem requires precise knowledge of the measurement geometry. This is modeled with a 3D head model and sensor positions obtained during the recording. The Maxwell equations can then be used to compute magnetic fields at the sensor locations for a current dipole with a given orientation at a certain location in the head model. The inverse problem describes the process of inverting this model. Recorded magnetic fields are used to estimate parameters of the generative model such as parameters of the NMM or location and orientation of currents associated with activated neuronal populations. (The high-resolution brain slice is from big brain atlas; Amunts et al., 2013; the layer 5 pyramidal neuron is from http://opensourcebrain.org/; Hay et al., 2011.)

information processing (e.g., Nishitani and Hari, 2002; Ploner et al., 2002).

More recently, multivariate analysis methods have been used to better understand the specific cognitive processes that are reflected in the recorded MEG signal. One of these methods, representational similarity analysis (RSA), quantifies the similarity of stimuli, behavioral responses, or brain responses across conditions (Kriegeskorte et al., 2008). In MEG, this similarity can be computed on a sample-by-sample basis time-locked to the onset of a stimulus. RSA can thus provide—when applied to source-localized MEG data—insights into the spatiotemporal evolution of stimulus representations in the brain, as well as into brain-behavior relationships and the explanatory power of computational models (Hebart et al., 2018; Klimovich-Gray et al., 2019). Similarly, multivariate decoding has been used to elucidate dynamic brain correlates of conscious perception and dual task interference (King et al., 2016). Here, decoding algorithms identify where and when brain activity contains information that can be used to identify the corresponding sensory stimulus or experimental condition. In the context of decoding, the high temporal resolution of MEG is particularly advantageous for two reasons. First, it helps to characterize the spatiotemporal progression of stimulus-related neural processes throughout the brain. Second, it can be used to study how a decoding algorithm, trained using data from a certain latency after stimulus onset, leads to significant decoding performance when applied to temporally neighboring data points. This "generalization" of a decoder may allow inferences to be made about the temporal dynamics of distinct stages of information processing (King and Dehaene, 2014).

Another appealing way to capitalize on the rich MEG signal is based on information theory and is complementary to decoding approaches (Quian Quiroga and Panzeri, 2009). It also offers a mathematically rigorous way to quantify linear and non-linear dependencies in data using mutual information (Ince et al., 2017). Mutual information has recently been complemented

with measures that quantify the representation, or transfer, of a specific feature of a stimulus (such as the mouth of a happy face) more directly (Schyns et al., 2011; Zhan et al., 2019). Interestingly, current developments that aim to decompose statistical dependencies between three signals (such as auditory stimulus, visual stimulus, and brain activity) make it possible to compute brain maps that represent unique information about each stimulus, as well as their synergistic or redundant interactions (Ince et al., 2017). Redundancy quantifies the information about the MEG signal that is common to or shared between the two stimulus signals and synergy quantifies the extra information that arises when both signals are considered together.

Generally, these recent developments in this area of MEG research focus on better characterizing the "meaning" of large-scale neural activity instead of simply describing the time course of activation in each brain area. These and similar approaches have also been used to investigate brain rhythms, as I discuss next.

Brain Rhythms and Spectral Signatures

Rhythmicity in brain activity is a fundamental and defining property of neural dynamics in humans and animals (Buzsáki et al., 2013; Wang, 2010), and neural rhythms form an important component of the MEG signal. Rhythmicity arises through precisely timed interactions of neuronal excitation and inhibition, leading to rhythmic changes in LFPs that can be recorded throughout the human brain. Neuronal firing rates are modulated by the phase of oscillations (Lakatos et al., 2007), and the dynamic evolution of LFP phases contains information that is complementary to that contained in spikes (Kayser et al., 2009). These cyclic excitability changes make brain rhythms a suitable mechanism for supporting information processing with accurate temporal coordination, a prerequisite for human behavior. Buzsáki and colleagues summarize this by stating that brain oscillations "form a hierarchical system that offers a syntactical structure for the spike traffic within and across circuits at multiple timescales" (Buzsáki et al., 2013). This dynamic functional structure complements the more static anatomical structure and allows the flexible task-dependent routing and gating of information flow within anatomically constrained networks. It is therefore not surprising that brain oscillations and their task-dependent modulations have been linked to a wide range of cognitive tasks, such as working memory, attention, perception, and language (Wang, 2010). In addition, evidence exists that these brain oscillations reflect brain states, encode stimulus and task-relevant information, are expressed by individual brain areas in a characteristic manner, and cause rhythms in action and perception (Buzsaki, 2006; VanRullen, 2016). Furthermore, pathologically altered brain rhythms are associated with a variety of neurological and mental health disorders (Schnitzler and Gross, 2005; Uhlhaas et al., 2018). For more detailed information on the importance of brain rhythms, I refer readers to relevant reviews (Buzsáki and Draguhn, 2004; Fries, 2015; Schnitzler and Gross, 2005; Siegel et al., 2012; Thut et al., 2012; Wang, 2010). Across this research field the concept of spectral signatures is an emerging topic that has received significant interest. In this context, the term spectral signature (or spectral fingerprint) refers to a characteristic organization of brain rhythms or their coupling across space, time, and frequency that is reliably associated with a cognitive process, behavioral state, or neural dysfunction (including dysfunctions arising from neurological diseases or mental health disorders). Some examples are discussed below.

Resting-State Spectral Signatures

Many MEG (and EEG) studies have investigated resting-state activity in healthy participants and patients (e.g., Cabral et al., 2017; Engels et al., 2017; Mandal et al., 2018; Uhlhaas et al., 2018). The spatiospectral structure of brain activity in this state is shaped and constrained by anatomical connectivity and by the area-specific anatomical substrate (Mars et al., 2018), and it leads to functional correlations between brain areas that are reported as resting-state networks in fMRI studies (Park and Friston, 2013). These fMRI resting-state networks have an electrophysiological correspondence, namely, resting-state amplitude correlations especially in the alpha (7–13 Hz) and beta (15–30 Hz) frequency band that can be observed in MEG recordings (Brookes et al., 2011; Florin and Baillet, 2015). In addition to these band-specific long-range connectivity patterns, the anatomical microstructure of each brain region also produces characteristic local spectral signatures (Keitel and Gross, 2016). More recently, the concept of spectral signatures in rest has been extended. Vidaurre and colleagues used hidden Markov models (HMMs) to describe resting-state MEG data as a sequence of a finite number of states (Vidaurre et al., 2018). These states correspond to brain networks that have specific spectral properties (power spectra) but also specific functional connectivity and are consistent with fMRI resting-state networks. State transitions were found on relatively fast timescales of about 100–200 ms. Consistent with the previously reported spectral signatures (Keitel and Gross, 2016), this suggests that resting-state brain activity recorded with MEG shows a regionally specific organization in spectral power and spectral connectivity that can be characterized by a finite number of states. This begs the question how these spectro-temporal signatures of resting-state activity shape human behavior and are in turn modulated by behavior.

Spectral Signatures in Perception and Spatial Attention

Already in a simple target-detection task, the state of brain oscillations at stimulus presentation is related to detection performance (van Dijk et al., 2008). MEG and EEG studies have demonstrated that near-threshold stimuli are more likely to be detected when the amplitude of "alpha" (about 10 Hz) oscillations is low in parietal-occipital brain areas compared to when the amplitude is high. Recently, it was suggested that this is caused by changes in the perceptual experience (Iemi and Busch, 2018). In general, this indicates that the brain state—as it is reflected in ongoing brain oscillations—determines the fate of a near-threshold stimulus (that is, whether and how a target is seen). These findings can be explained with the above-mentioned fact that brain oscillations represent excitability changes in neuronal populations (Haegens et al., 2011; Romei et al., 2008). Similar results have been reported in studies of spatial attention. Instructing participants to covertly shift visual attention to one hemifield leads to a sustained decrease in the amplitude of alpha oscillations in contralateral occipito-parietal brain areas (Bauer et al., 2014; Foxe and Snyder, 2011; Thut et al., 2006). The amount of alpha modulation is related to

behavioral performance (of detecting a subsequent target) indicating a functional role of alpha oscillations in the gating of target-related stimulus information.

Spectral Connectivity Signatures

Distinct functional roles of brain rhythms in different frequencies might have an anatomical basis. Feedforward projections typically start in supragranular layers and terminate in layer 4 of the cortex, whereas feedback projections predominantly start in infragranular layers and terminate in layers other than layer 4 (Markov et al., 2014). A recent study capitalizes on the specific strength of MEG for non-invasively studying large-scale brain activity and demonstrated that anatomical feedforward and feedback connections are associated with connectivity (quantified with Granger causality) in different frequency bands (Michalareas et al., 2016). Feedforward signals are mediated in the gamma frequency band, whereas feedback signals are predominantly conveyed in the alpha/beta frequency bands. This model of frequency-specific communication channels suggests that directed connectivity derived from source-localized MEG data might potentially be used as a functional "marker" to disambiguate feedforward and feedback processes that often occur simultaneously and are notoriously difficult to separate—especially in non-invasively recorded data. Overall, the empirical anatomical and functional data largely support a computational model that builds on predictions and prediction errors in a hierarchically organized neural architecture (Friston et al., 2015). This has important implications for our understanding of pathological mechanisms underlying various neurological and mental health disorders (Friston et al., 2014). Within this predictive coding model, it has been suggested that pathological changes in the precision of predictions or the processing of predictions or prediction errors can possibly explain symptoms observed in autism (Lawson et al., 2014), schizophrenia (Limongi et al., 2018), chronic pain (Ploner et al., 2017), and tinnitus (Sedley et al., 2016).

In general, MEG is an excellent tool to study spectral connectivity signatures and the sophistication of these studies has increased over recent years. Schoffelen and colleagues recently used Granger causality analysis to identify spectral connectivity signatures during reading (Schoffelen et al., 2017). They report Granger causality effects from middle temporal areas to anterior temporal and frontal areas in line with information flow along the auditory cortical hierarchy. In addition, several studies have uncovered spectral connectivity signatures that rely on cross-frequency coupling (CFC). The hallmark of CFC is a significant statistical dependence of phase or amplitude between two time series at different frequencies and has been implicated in inter-area communication (Bonnefond et al., 2017). CFC signatures across large areas of cortex are evident in resting-state recordings (Florin and Baillet, 2015) might be pathologically altered in patients (Antonakakis et al., 2016) and support coordinated information processing during cognitive tasks such as working memory (Siebenhühner et al., 2016).

Spectral Entrainment Signatures

Spectral signatures in the brain are not only evident in rest and modulated during tasks but they also interact with rhythmic signals in the environment in a way that establishes a brain-environment connectivity. An excellent example is human communication. Despite the seemingly continuous nature of connected speech, the auditory and visual speech signals received by our senses contain rhythmic components, for example, corresponding to the syllable rate (Ding et al., 2017). Recent MEG studies have shown that frequency-specific brain activity becomes temporally aligned to these partly rhythmic amplitude variations in continuous speech (Gross et al., 2013b). This temporal alignment is most strongly observed at frequencies below 10 Hz and is thought to be initiated by acoustic edges in the speech waveform that lead to a phase reset of ongoing oscillations in auditory cortex (Giraud and Poeppel, 2012). As a result of the phase reset, brain activity will be temporally aligned to the quasi-rhythmic structure in speech. Since low-frequency brain oscillations represent cyclic excitability changes in underlying neuronal populations, this entrainment leads to preferential processing of attended stimuli (Ding and Simon, 2012; Lakatos et al., 2013). This is likely the result of top-down effects of higher-order brain areas (left inferior frontal gyrus and left motor areas) on auditory areas as reported in a recent MEG study (Park et al., 2015). Taken together, these and other studies suggest that brain rhythms play a significant role in processing continuous quasi-rhythmic signals from the environment.

Emerging Topics

In this section, I will discuss interesting emerging applications of MEG that might attract more attention in the future. I will present this by highlighting individual recent studies that sample the range of novel applications. This is not intended to be a comprehensive overview of new applications and not even of these particular topics. I rather intend to showcase individual studies that are representative of emerging topics.

Connecting Body and Brain

In this primer, I promote the idea that MEG is an excellent tool to study the brain. However, the typical neuroimaging approach of studying the brain in isolation is inherently flawed because it ignores the fact that the brain is part of the whole body. This is important because there are continuous bidirectional interactions between the brain and the rest of the body. The dynamically changing state of the human body influences brain activity; the body is, in turn, controlled by the brain, and their mutual interactions and states affect cognition and are altered in disease. MEG recordings combined with peripheral recordings of body states are thus ideally suited to study these dynamic interactions (see Figure 3). MEG can record top-down signals from the brain that dynamically shape autonomic functions. Recordings of body signals, such as respiration, heartbeat, pupil dilation, etc. can be used to characterize certain aspects of the body's physiological state, which is continuously conveyed to the brain. Such recordings could help to uncover the principles and mechanisms that underlie brain-body interactions in health and disease, which as yet remain largely unknown and virtually unstudied with MEG or EEG. For example, peripheral infections (which constitute a change in body state) lead to the production of pro-inflammatory cytokines that modulate brain function by inducing sickness behavior such as reduced motor activity and social withdrawal (Dantzer et al., 2008). In addition, several studies have demonstrated that information processing in the brain also transiently depends on dynamically changing body

states—such as the phase of the cardiac cycle (Critchley and Garfinkel, 2018; Park et al., 2014). Similarly, the respiratory rhythm is known to modulate motor and cognitive functions (Varga and Heck, 2017; Zelano et al., 2016).

The need to take into account physiological signals is particularly important when studying brain rhythms because several body signals are also (quasi-) rhythmic over a wide range of frequencies (Klimesch, 2018) (such as the piper rhythm in muscle ~40 Hz; Brown, 2000; some eye movements ~5 Hz; Otero-Millan et al., 2008; heartbeat ~1 Hz and breathing ~0.25 Hz; Fleming et al., 2011; and gastric basal rhythm ~0.05 Hz; Rebollo et al., 2018). Importantly, even low-frequency (and non-rhythmic) peripheral signals can modulate the amplitude of higher-frequency brain activity. These peripheral signals are typically treated as a confounding signal (if considered at all); instead, they represent an interesting target for studying mutual dependencies between body and brain signals and behavior. Relevant analytical approaches have already been developed over the last 20 years in MEG studies of communication between brain and muscles. For example, continuous isometric muscle contraction is associated with a temporal coupling of oscillations in the recordings of muscle activity (EMG) and brain activity (MEG) at frequencies of about 15–30 Hz (Salenius and Hari, 2003). In combination with source analysis, functional maps of cerebromuscular coupling have been computed and revealed that this 15–30 Hz coupling represents efficient driving of spinal motor neurons from primary motor cortex (Gross et al., 2001; Schoffelen et al., 2005). In summary, these studies illustrate the ubiquitous and continuous dependencies between (rhythmic) body signals, brain rhythms, and sensory and cognitive processing. It is of great interest to study this trivariate relationship between body, brain, and behavior in health and disease using MEG.

Computational Models

Combining MEG/EEG data with computational models has a long history and holds great promise to further our mechanistic understanding of brain dynamics. A notable recent example is a study where MEG, computational modeling, and laminar recordings in animals were combined to identify a generative mechanism for local beta (15–30 Hz) oscillations (Sherman et al., 2016). Going beyond modeling of local activity, DCM allows inference on hidden neural network states within a Bayesian framework based on recordings of brain activity such as MEG data (Friston et al., 2013). Recently, DCM has been extended with a neural mass model that reflects the structure of cortical canonical microcircuits (Symmonds et al., 2018). This model includes parameters for different receptors such as NMDA, GABA, and AMPA. The generative model relates receptor-specific time constants and connection strengths to membrane potentials and ultimately to MEG/EEG signals. Bayesian inversion of the model based on non-invasively recorded MEG or EEG data therefore allows inference on these parameters and their selective change in disease (Heinzle and Stephan, 2018). This opens up the exciting possibility to use MEG (and EEG) to study receptor (dys-)function in health and disease. Interestingly, this modeling can be combined with "pharmaco-MEG" where MEG recordings are obtained before and during administration of pharmacological substances, for example, to study the relationship between neurotransmitters, brain activity, and behavior (Bauer et al., 2012; Lozano-Soldevilla et al., 2014; Moran et al., 2011; Muthukumaraswamy, 2014).

Another type of computational models that has recently gained interest can be referred to as brain network models (BNM) (Breakspear, 2017; Stephan et al., 2015). Similar to DCM, brain activity in each brain area is described by a neural mass model that aims to model the behavior of local neuronal populations with a small set of equations. However, unlike DCM, BNMs can be constructed as whole-brain models. Individual neural mass models are connected based on anatomical connectivity information—for example, acquired with diffusion-tensor imaging (DTI). The local activity at each node is shaped by input from other nodes and the specific parameters of the local neural mass model. These local neural mass models are combined with a forward model that can estimate fMRI, EEG or MEG recordings from the dynamics of neural mass models. One example of this approach is implemented in the Virtual Brain software (https://thevirtualbrain.org/tvb/zwei; Deco et al., 2017; Sanz-Leon et al., 2015; Schirner et al., 2018). BNMs can be used to study how changes in parameters of neural mass models or their connectivity might lead to changes in recorded brain activity. Similarly, the effect of neurostimulation (such as TMS or TES) can be modeled with BNMs (Kunze et al., 2016), for example, to identify the effect of local stimulation on brain networks in comparison with empirical data. In summary, computational models provide an interesting and complementary path for the analysis and interpretation of MEG data.

Conclusions

MEG is a powerful tool with highly versatile applications in the field of cognitive neuroscience. Its main strength lies in non-invasively recording a signal that is closely related to neuronal population activity. When combined with source localization techniques, it yields a rich representation of brain activity with millisecond temporal resolution throughout the brain. Whereas MEG cannot compete with fMRI or invasive recordings with regards to spatial resolution, it is uniquely suited to study large-scale electrophysiological whole-brain activity. The main features of MEG, qualifying it for the study of large-scale brain dynamics are whole-brain coverage, silent and non-invasive recording, excellent temporal resolution, good spatial resolution, low sensitivity to uncertainties about tissue conductivities, and direct coupling of the recorded signal to neural activity independent of neurovascular coupling. These advantages notwithstanding, users need to be aware of strengths and weaknesses of MEG as a recording technique and of the different analysis methods. Seeking converging evidence across analysis pipelines combined with open science principles will be key to ensure that MEG studies will have an increasingly relevant impact in cognitive neuroscience. In the past, MEG has already made significant contributions to our understanding of the relationship between the (rhythmic) dynamics of large-scale brain activity and behavior in health and disease. However, the full potential of MEG has not yet been fully exploited. I envisage that in coming years currently emerging trends in the field will merge and transform the way we use MEG in cognitive neuroscience. Specifically, I foresee the following developments: multi-center cohort studies will collect MEG data on large numbers of participants

and patients together with deep phenotyping and multi-modal imaging and will make these data publicly available. These studies would greatly benefit from standardized task batteries and analysis pipelines that are currently unavailable. In the future, combined MEG and EEG recordings might be complemented with simultaneous recordings of a range of body signals (Figure 3). This will enable novel applications such as studying body-brain interactions, attributing task-related changes in brain activity more directly to cognitive processes or simultaneous changes in body state and identifying body-brain changes in disease. Machine learning and deep neural networks will likely play an important role in the analysis of these large datasets. Furthermore, we can expect to see an integrated multi-modal framework where these MEG$^+$ cohort data are combined with computational brain network modeling and neurostimulation to gain mechanistic insights in brain function and dysfunction. The next years will also see new generations of OPM sensors combined into powerful multi-channel systems that will further expand the remit of MEG and might even allow simultaneous TMS stimulation. Together, these MEG-assisted approaches will likely help to identify spectral signatures of specific disorders to assist with early diagnosis and inform therapy (van Diessen et al., 2015; Schnitzler and Gross, 2005; Uhlhaas et al., 2018). This clinical approach can complement endeavors in cognitive neuroscience where MEG and EEG is used to identify individual spectral signatures of cognitive processes constrained by individual anatomy, shaped by phenotype and decoded with the help of cohort studies, machine learning, and computational models. There is well-founded hope that in the near future all this might lead to a comprehensive taxonomy of brain rhythms and a better understanding of the main principles that govern information processing in the brain in health and disease.

ACKNOWLEDGMENTS

The author thanks Jan-Mathijs Schoffelen, Markus Butz, Markus Ploner, Hyojin Park, and colleagues from the IBB, Muenster, and CCNi, Glasgow, for valuable comments on the manuscript. Thanks to Marios Antonakakis and Andreas Nüßing for contributing material to Figures 3 and 4. The author acknowledges funding by the Wellcome Trust (098433).

DECLARATION OF INTERESTS

The author declares no competing interests.

REFERENCES

Abbasi, O., Hirschmann, J., Storzer, L., Özkurt, T.E., Elben, S., Vesper, J., Wojtecki, L., Schmitz, G., Schnitzler, A., and Butz, M. (2018). Unilateral deep brain stimulation suppresses alpha and beta oscillations in sensorimotor cortices. Neuroimage *174*, 201–207.

Alem, O., Mhaskar, R., Jiménez-Martínez, R., Sheng, D., LeBlanc, J., Trahms, L., Sander, T., Kitching, J., and Knappe, S. (2017). Magnetic field imaging with microfabricated optically-pumped magnetometers. Opt. Express *25*, 7849–7858.

Alexandrou, A.M., Saarinen, T., Mäkelä, S., Kujala, J., and Salmelin, R. (2017). The right hemisphere is highlighted in connected natural speech production and perception. Neuroimage *152*, 628–638.

Amunts, K., Lepage, C., Borgeat, L., Mohlberg, H., Dickscheid, T., Rousseau, M.-É., Bludau, S., Bazin, P.-L., Lewis, L.B., Oros-Peusquens, A.-M., et al. (2013). BigBrain: an ultrahigh-resolution 3D human brain model. Science *340*, 1472–1475.

Antonakakis, M., Dimitriadis, S.I., Zervakis, M., Micheloyannis, S., Rezaie, R., Babajani-Feremi, A., Zouridakis, G., and Papanicolaou, A.C. (2016). Altered cross-frequency coupling in resting-state MEG after mild traumatic brain injury. Int. J. Psychophysiol. *102*, 1–11.

Aydin, Ü., Vorwerk, J., Dümpelmann, M., Küpper, P., Kugel, H., Heers, M., Wellmer, J., Kellinghaus, C., Haueisen, J., Rampp, S., et al. (2015). Combined EEG/MEG can outperform single modality EEG or MEG source reconstruction in presurgical epilepsy diagnosis. PLoS ONE *10*, e0118753.

Baillet, S. (2017). Magnetoencephalography for brain electrophysiology and imaging. Nat. Neurosci. *20*, 327–339.

Baillet, S., Mosher, J.C., and Leahy, R.M. (2001). Electromagnetic brain mapping. IEEE Signal Process. Mag. *18*, 14–30.

Baillet, S., Friston, K., and Oostenveld, R. (2011). Academic software applications for electromagnetic brain mapping using MEG and EEG. Comput. Intell. Neurosci. *2011*, 972050.

Baltus, A., Wagner, S., Wolters, C.H., and Herrmann, C.S. (2018). Optimized auditory transcranial alternating current stimulation improves individual auditory temporal resolution. Brain Stimul. *11*, 118–124.

Barnes, G.R., Hillebrand, A., Fawcett, I.P., and Singh, K.D. (2004). Realistic spatial sampling for MEG beamformer images. Hum. Brain Mapp. *23*, 120–127.

Bastos, A.M., and Schoffelen, J.-M. (2016). A Tutorial Review of Functional Connectivity Analysis Methods and Their Interpretational Pitfalls. Front. Syst. Neurosci. *9*, 175.

Bauer, M., Kluge, C., Bach, D., Bradbury, D., Heinze, H.J., Dolan, R.J., and Driver, J. (2012). Cholinergic enhancement of visual attention and neural oscillations in the human brain. Curr. Biol. *22*, 397–402.

Bauer, M., Stenner, M.-P., Friston, K.J., and Dolan, R.J. (2014). Attentional modulation of alpha/beta and gamma oscillations reflect functionally distinct processes. J. Neurosci. *34*, 16117–16125.

Biasiucci, A., Franceschiello, B., and Murray, M.M. (2019). Electroencephalography. Curr. Biol. *29*, R80–R85.

Bonaiuto, J.J., Meyer, S.S., Little, S., Rossiter, H., Callaghan, M.F., Dick, F., Barnes, G.R., and Bestmann, S. (2018). Lamina-specific cortical dynamics in human visual and sensorimotor cortices. eLife *7*, 7.

Bonnefond, M., Kastner, S., and Jensen, O. (2017). Communication between Brain Areas Based on Nested Oscillations. eNeuro *4*. Published online October 22, 2018. https://doi.org/10.7554/eLife.33977.

Boto, E., Holmes, N., Leggett, J., Roberts, G., Shah, V., Meyer, S.S., Muñoz, L.D., Mullinger, K.J., Tierney, T.M., Bestmann, S., et al. (2018). Moving magnetoencephalography towards real-world applications with a wearable system. Nature *555*, 657–661.

Breakspear, M. (2017). Dynamic models of large-scale brain activity. Nat. Neurosci. *20*, 340–352.

Brette, R., and Destexhe, A. (2012). Handbook of Neural Activity Measurement (Cambridge University Press).

Brookes, M.J., Woolrich, M., Luckhoo, H., Price, D., Hale, J.R., Stephenson, M.C., Barnes, G.R., Smith, S.M., and Morris, P.G. (2011). Investigating the electrophysiological basis of resting state networks using magnetoencephalography. Proc. Natl. Acad. Sci. USA *108*, 16783–16788.

Brown, P. (2000). Cortical drives to human muscle: the Piper and related rhythms. Prog. Neurobiol. *60*, 97–108.

Button, K.S., Ioannidis, J.P.A., Mokrysz, C., Nosek, B.A., Flint, J., Robinson, E.S.J., and Munafò, M.R. (2013). Power failure: why small sample size undermines the reliability of neuroscience. Nat. Rev. Neurosci. *14*, 365–376.

Buzsaki, G. (2006). Rhythms of the Brain (Oxford University Press).

Buzsáki, G., and Draguhn, A. (2004). Neuronal oscillations in cortical networks. Science *304*, 1926–1929.

Buzsáki, G., Anastassiou, C.A., and Koch, C. (2012). The origin of extracellular fields and currents–EEG, ECoG, LFP and spikes. Nat. Rev. Neurosci. *13*, 407–420.

Buzsáki, G., Logothetis, N., and Singer, W. (2013). Scaling brain size, keeping timing: evolutionary preservation of brain rhythms. Neuron *80*, 751–764.

Cabral, J., Kringelbach, M.L., and Deco, G. (2017). Functional connectivity dynamically evolves on multiple time-scales over a static structural connectome: Models and mechanisms. Neuroimage *160*, 84–96.

Cho, J.-H., Vorwerk, J., Wolters, C.H., and Knösche, T.R. (2015). Influence of the head model on EEG and MEG source connectivity analyses. Neuroimage *110*, 60–77.

Cichy, R.M., Pantazis, D., and Oliva, A. (2014). Resolving human object recognition in space and time. Nat. Neurosci. *17*, 455–462.

Cohen, D. (1968). Magnetoencephalography: evidence of magnetic fields produced by alpha-rhythm currents. Science *161*, 784–786.

Cohen, M.X. (2014). Analyzing Neural Time Series Data: Theory and Practice (MIT Press).

Colclough, G.L., Smith, S.M., Nichols, T.E., Winkler, A.M., Sotiropoulos, S.N., Glasser, M.F., Van Essen, D.C., and Woolrich, M.W. (2017). The heritability of multi-modal connectivity in human brain activity. eLife *6*. Published online July 26, 2017. https://doi.org/10.7554/eLife.20178.

Critchley, H.D., and Garfinkel, S.N. (2018). The influence of physiological signals on cognition. Curr. Opin. Behav. Sci. *19*, 13–18.

Dalal, S.S., Baillet, S., Adam, C., Ducorps, A., Schwartz, D., Jerbi, K., Bertrand, O., Garnero, L., Martinerie, J., and Lachaux, J.-P. (2009). Simultaneous MEG and intracranial EEG recordings during attentive reading. Neuroimage *45*, 1289–1304.

Dantzer, R., O'Connor, J.C., Freund, G.G., Johnson, R.W., and Kelley, K.W. (2008). From inflammation to sickness and depression: when the immune system subjugates the brain. Nat. Rev. Neurosci. *9*, 46–56.

Deco, G., Kringelbach, M.L., Jirsa, V.K., and Ritter, P. (2017). The dynamics of resting fluctuations in the brain: metastability and its dynamical cortical core. Sci. Rep. *7*, 3095.

Ding, N., and Simon, J.Z. (2012). Neural coding of continuous speech in auditory cortex during monaural and dichotic listening. J. Neurophysiol. *107*, 78–89.

Ding, N., Patel, A.D., Chen, L., Butler, H., Luo, C., and Poeppel, D. (2017). Temporal modulations in speech and music. Neurosci. Biobehav. Rev. *81* (Pt B), 181–187.

Dmochowski, J.P., Datta, A., Bikson, M., Su, Y., and Parra, L.C. (2011). Optimized multi-electrode stimulation increases focality and intensity at target. J. Neural Eng. *8*, 046011.

Engels, M.M.A., van der Flier, W.M., Stam, C.J., Hillebrand, A., Scheltens, P., and van Straaten, E.C.W. (2017). Alzheimer's disease: The state of the art in resting-state magnetoencephalography. Clin. Neurophysiol. *128*, 1426–1437.

Fleming, S., Thompson, M., Stevens, R., Heneghan, C., Plüddemann, A., Maconochie, I., Tarassenko, L., and Mant, D. (2011). Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. Lancet *377*, 1011–1018.

Florin, E., and Baillet, S. (2015). The brain's resting-state activity is shaped by synchronized cross-frequency coupling of neural oscillations. Neuroimage *111*, 26–35.

Foxe, J.J., and Snyder, A.C. (2011). The Role of Alpha-Band Brain Oscillations as a Sensory Suppression Mechanism during Selective Attention. Front. Psychol. *2*, 154.

Fries, P. (2015). Rhythms for Cognition: Communication through Coherence. Neuron *88*, 220–235.

Friston, K., Moran, R., and Seth, A.K. (2013). Analysing connectivity with Granger causality and dynamic causal modelling. Curr. Opin. Neurobiol. *23*, 172–178.

Friston, K.J., Stephan, K.E., Montague, R., and Dolan, R.J. (2014). Computational psychiatry: the brain as a phantastic organ. Lancet Psychiatry *1*, 148–158.

Friston, K.J., Bastos, A.M., Pinotsis, D., and Litvak, V. (2015). LFP and oscillations-what do they tell us? Curr. Opin. Neurobiol. *31*, 1–6.

Gavaret, M., Dubarry, A.-S., Carron, R., Bartolomei, F., Trébuchon, A., and Bénar, C.-G. (2016). Simultaneous SEEG-MEG-EEG recordings Overcome the SEEG limited spatial sampling. Epilepsy Res. *128*, 68–72.

Giraud, A.-L., and Poeppel, D. (2012). Cortical oscillations and speech processing: emerging computational principles and operations. Nat. Neurosci. *15*, 511–517.

Gross, J., Kujala, J., Hamalainen, M., Timmermann, L., Schnitzler, A., and Salmelin, R. (2001). Dynamic imaging of coherent sources: Studying neural interactions in the human brain. Proc. Natl. Acad. Sci. USA *98*, 694–699.

Gross, J., Baillet, S., Barnes, G.R., Henson, R.N., Hillebrand, A., Jensen, O., Jerbi, K., Litvak, V., Maess, B., Oostenveld, R., et al. (2013a). Good practice for conducting and reporting MEG research. Neuroimage *65*, 349–363.

Gross, J., Hoogenboom, N., Thut, G., Schyns, P., Panzeri, S., Belin, P., and Garrod, S. (2013b). Speech rhythms and multiplexed oscillatory sensory coding in the human brain. PLoS Biol. *11*, e1001752.

Haegens, S., Nácher, V., Luna, R., Romo, R., and Jensen, O. (2011). α-Oscillations in the monkey sensorimotor network influence discrimination performance by rhythmical inhibition of neuronal spiking. Proc. Natl. Acad. Sci. USA *108*, 19377–19382.

Hämäläinen, M., Hari, R., Ilmoniemi, R.J., Knuutila, J., and Lounasmaa, O.V. (1993). Magnetoencephalography—theory, instrumentation, and applications to noninvasive studies of the working human brain. Rev. Mod. Phys. *65*, 413–497.

P. Hansen, M. Kringelbach, and R. Salmelin, eds. (2010). MEG: An Introduction to Methods (Oxford University Press).

Hari, R., and Puce, A. (2017). MEG-EEG Primer (Oxford University Press).

Hari, R., Baillet, S., Barnes, G., Burgess, R., Forss, N., Gross, J., Hämäläinen, M., Jensen, O., Kakigi, R., Mauguière, F., et al. (2018). IFCN-endorsed practical guidelines for clinical magnetoencephalography (MEG). Clin. Neurophysiol. *129*, 1720–1747.

Hay, E., Hill, S., Schürmann, F., Markram, H., and Segev, I. (2011). Models of neocortical layer 5b pyramidal cells capturing a wide range of dendritic and perisomatic active properties. PLoS Comput. Biol. *7*, e1002107.

Hebart, M.N., Bankson, B.B., Harel, A., Baker, C.I., and Cichy, R.M. (2018). The representational dynamics of task and object processing in humans. eLife. Published online January 31, 2018. https://doi.org/10.7554/eLife.32816.

Heinzle, J., and Stephan, K.E. (2018). Dynamic causal modeling and its application to psychiatric disorders. In Computational Psychiatry, A. Anticevic and J.D. Murray, eds. (Elsevier), pp. 117–144.

Herring, J.D., Esterer, S., Marshall, T.R., Jensen, O., and Bergmann, T.O. (2019). Low-frequency alternating current stimulation rhythmically suppresses gamma-band oscillations and impairs perceptual performance. Neuroimage *184*, 440–449.

Hirschmann, J., Özkurt, T.E., Butz, M., Homburger, M., Elben, S., Hartmann, C.J., Vesper, J., Wojtecki, L., and Schnitzler, A. (2011). Distinct oscillatory STN-cortical loops revealed by simultaneous MEG and local field potential recordings in patients with Parkinson's disease. Neuroimage *55*, 1159–1168.

Huang, Y., Liu, A.A., Lafon, B., Friedman, D., Dayan, M., Wang, X., Bikson, M., Doyle, W.K., Devinsky, O., and Parra, L.C. (2017). Measurements and models of electric fields in the *in vivo* human brain during transcranial electric stimulation. eLife. Published online February 15, 2018. https://doi.org/10.7554/eLife.35178.

Iemi, L., and Busch, N.A. (2018). Moment-to-Moment Fluctuations in Neuronal Excitability Bias Subjective Perception Rather than Strategic Decision-Making. eNeuro *5*, 5.

Iivanainen, J., Stenroos, M., and Parkkonen, L. (2017). Measuring MEG closer to the brain: Performance of on-scalp sensor arrays. Neuroimage *147*, 542–553.

Ince, R.A.A., Giordano, B.L., Kayser, C., Rousselet, G.A., Gross, J., and Schyns, P.G. (2017). A statistical framework for neuroimaging data analysis based on mutual information estimated via a gaussian copula. Hum. Brain Mapp. *38*, 1541–1573.

Jerbi, K., Lachaux, J.-P., N'Diaye, K., Pantazis, D., Leahy, R.M., Garnero, L., and Baillet, S. (2007). Coherent neural representation of hand speed in humans revealed by MEG imaging. Proc. Natl. Acad. Sci. USA *104*, 7676–7681.

Kayser, C., Montemurro, M.A., Logothetis, N.K., and Panzeri, S. (2009). Spike-phase coding boosts and stabilizes information carried by spatial and temporal spike patterns. Neuron *61*, 597–608.

Keil, A., Debener, S., Gratton, G., Junghöfer, M., Kappenman, E.S., Luck, S.J., Luu, P., Miller, G.A., and Yee, C.M. (2014). Committee report: publication guidelines and recommendations for studies using electroencephalography and magnetoencephalography. Psychophysiology *51*, 1–21.

Keitel, A., and Gross, J. (2016). Individual Human Brain Areas Can Be Identified from Their Characteristic Spectral Activation Fingerprints. PLoS Biol. *14*, e1002498.

King, J.R., and Dehaene, S. (2014). Characterizing the dynamics of mental representations: the temporal generalization method. Trends Cogn. Sci. *18*, 203–210.

King, J.-R., Pescetelli, N., and Dehaene, S. (2016). Brain mechanisms underlying the brief maintenance of seen and unseen sensory information. Neuron *92*, 1122–1134.

Klimesch, W. (2018). The frequency architecture of brain and brain body oscillations: an analysis. Eur. J. Neurosci. *48*, 2431–2453.

Klimovich-Gray, A., Tyler, L.K., Randall, B., Kocagoncu, E., Devereux, B., and Marslen-Wilson, W.D. (2019). Balancing prediction and sensory input in speech comprehension: the spatiotemporal dynamics of word recognition in context. J. Neurosci. *39*, 519–527.

Kriegeskorte, N., Mur, M., and Bandettini, P. (2008). Representational similarity analysis - connecting the branches of systems neuroscience. Front. Syst. Neurosci. *2*, 4.

Kunze, T., Hunold, A., Haueisen, J., Jirsa, V., and Spiegler, A. (2016). Transcranial direct current stimulation changes resting state functional connectivity: A large-scale brain network modeling study. Neuroimage *140*, 174–187.

Lakatos, P., Chen, C.-M., O'Connell, M.N., Mills, A., and Schroeder, C.E. (2007). Neuronal oscillations and multisensory interaction in primary auditory cortex. Neuron *53*, 279–292.

Lakatos, P., Musacchia, G., O'Connel, M.N., Falchier, A.Y., Javitt, D.C., and Schroeder, C.E. (2013). The spectrotemporal filter mechanism of auditory selective attention. Neuron *77*, 750–761.

Larson-Prior, L.J., Oostenveld, R., Della Penna, S., Michalareas, G., Prior, F., Babajani-Feremi, A., Schoffelen, J.M., Marzetti, L., de Pasquale, F., Di Pompeo, F., et al.; WU-Minn HCP Consortium (2013). Adding dynamics to the Human Connectome Project with MEG. Neuroimage *80*, 190–201.

Lawson, R.P., Rees, G., and Friston, K.J. (2014). An aberrant precision account of autism. Front. Hum. Neurosci. *8*, 302.

Leppäaho, E., Renvall, H., Salmela, E., Kere, J., Salmelin, R., and Kaski, S. (2019). Discovering heritable modes of MEG spectral power. Hum. Brain Mapp. *40*, 1391–1402.

Limongi, R., Bohaterewicz, B., Nowicka, M., Plewka, A., and Friston, K.J. (2018). Knowing when to stop: Aberrant precision and evidence accumulation in schizophrenia. Schizophr. Res. Published online January 10, 2018. https://doi.org/10.1016/j.schres.2017.12.018.

Litvak, V., Jha, A., Eusebio, A., Oostenveld, R., Foltynie, T., Limousin, P., Zrinzo, L., Hariz, M.I., Friston, K., and Brown, P. (2011). Resting oscillatory cortico-subthalamic connectivity in patients with Parkinson's disease. Brain *134*, 359–374.

Liu, A., Vöröslakos, M., Kronberg, G., Henin, S., Krause, M.R., Huang, Y., Opitz, A., Mehta, A., Pack, C.C., Krekelberg, B., et al. (2018). Immediate neurophysiological effects of transcranial electrical stimulation. Nat. Commun. *9*, 5092.

Lopes da Silva, F. (2013). EEG and MEG: relevance to neuroscience. Neuron *80*, 1112–1128.

Lozano-Soldevilla, D., ter Huurne, N., Cools, R., and Jensen, O. (2014). GABAergic modulation of visual gamma and alpha oscillations and its consequences for working memory performance. Curr. Biol. *24*, 2878–2887.

Mackert, B.-M., Leistner, S., Sander, T., Liebert, A., Wabnitz, H., Burghoff, M., Trahms, L., Macdonald, R., and Curio, G. (2008). Dynamics of cortical neurovascular coupling analyzed by simultaneous DC-magnetoencephalography and time-resolved near-infrared spectroscopy. Neuroimage *39*, 979–986.

Mahjoory, K., Nikulin, V.V., Botrel, L., Linkenkaer-Hansen, K., Fato, M.M., and Haufe, S. (2017). Consistency of EEG source localization and connectivity estimates. Neuroimage *152*, 590–601.

Mandal, P.K., Banerjee, A., Tripathi, M., and Sharma, A. (2018). A comprehensive review of magnetoencephalography (MEG) studies for brain functionality in healthy aging and alzheimer's disease (AD). Front. Comput. Neurosci. *12*, 60.

Markov, N.T., Vezoli, J., Chameau, P., Falchier, A., Quilodran, R., Huissoud, C., Lamy, C., Misery, P., Giroud, P., Ullman, S., et al. (2014). Anatomy of hierarchy: feedforward and feedback pathways in macaque visual cortex. J. Comp. Neurol. *522*, 225–259.

Mars, R.B., Passingham, R.E., and Jbabdi, S. (2018). Connectivity fingerprints: from areal descriptions to abstract spaces. Trends Cogn. Sci. *22*, 1026–1037.

Marty, B., Bourguignon, M., Jousmäki, V., Wens, V., Op de Beeck, M., Van Bogaert, P., Goldman, S., Hari, R., and De Tiège, X. (2015). Cortical kinematic processing of executed and observed goal-directed hand actions. Neuroimage *119*, 221–228.

Meindertsma, T., Kloosterman, N.A., Nolte, G., Engel, A.K., and Donner, T.H. (2017). Multiple Transient Signals in Human Visual Cortex Associated with an Elementary Decision. J. Neurosci. *37*, 5744–5757.

Michalareas, G., Vezoli, J., van Pelt, S., Schoffelen, J.-M., Kennedy, H., and Fries, P. (2016). Alpha-Beta and Gamma Rhythms Subserve Feedback and Feedforward Influences among Human Visual Cortical Areas. Neuron *89*, 384–397.

Moran, R.J., Symmonds, M., Stephan, K.E., Friston, K.J., and Dolan, R.J. (2011). An in vivo assay of synaptic function mediating human cognition. Curr. Biol. *21*, 1320–1325.

Murakami, S., and Okada, Y. (2006). Contributions of principal neocortical neurons to magnetoencephalography and electroencephalography signals. J. Physiol. *575*, 925–936.

Muthukumaraswamy, S.D. (2014). The use of magnetoencephalography in the study of psychopharmacology (pharmaco-MEG). J. Psychopharmacol. (Oxford) *28*, 815–829.

Myllylä, T., Zacharias, N., Korhonen, V., Zienkiewicz, A., Hinrichs, H., Kiviniemi, V., and Walter, M. (2017). Multimodal brain imaging with magnetoencephalography: A method for measuring blood pressure and cardiorespiratory oscillations. Sci. Rep. *7*, 172.

Nishitani, N., and Hari, R. (2002). Viewing lip forms: cortical dynamics. Neuron *36*, 1211–1220.

Niso, G., Rogers, C., Moreau, J.T., Chen, L.-Y., Madjar, C., Das, S., Bock, E., Tadel, F., Evans, A.C., Jolicoeur, P., and Baillet, S. (2016). OMEGA: the open MEG archive. Neuroimage *124* (Pt B), 1182–1187.

Noury, N., and Siegel, M. (2018). Analyzing EEG and MEG signals recorded during tES, a reply. Neuroimage *167*, 53–61.

Opitz, A., Yeagle, E., Thielscher, A., Schroeder, C., Mehta, A.D., and Milham, M.P. (2018). On the importance of precise electrode placement for targeted transcranial electric stimulation. Neuroimage *181*, 560–567.

Oswal, A., Jha, A., Neal, S., Reid, A., Bradbury, D., Aston, P., Limousin, P., Foltynie, T., Zrinzo, L., Brown, P., and Litvak, V. (2016). Analysis of simultaneous MEG and intracranial LFP recordings during Deep Brain Stimulation: a protocol and experimental validation. J. Neurosci. Methods *261*, 29–46.

Otero-Millan, J., Troncoso, X.G., Macknik, S.L., Serrano-Pedraza, I., and Martinez-Conde, S. (2008). Saccades and microsaccades during visual fixation, exploration, and search: foundations for a common saccadic generator. J. Vis. *8*, 21.1–21.18.

Palva, J.M., Wang, S.H., Palva, S., Zhigalov, A., Monto, S., Brookes, M.J., Schoffelen, J.-M., and Jerbi, K. (2018). Ghost interactions in MEG/EEG source space: A note of caution on inter-areal coupling measures. Neuroimage *173*, 632–643.

Park, H.-J., and Friston, K. (2013). Structural and functional brain networks: from connections to cognition. Science *342*, 1238411.

Park, H.-D., Correia, S., Ducorps, A., and Tallon-Baudry, C. (2014). Spontaneous fluctuations in neural responses to heartbeats predict visual detection. Nat. Neurosci. *17*, 612–618.

Park, H., Ince, R.A.A., Schyns, P.G., Thut, G., and Gross, J. (2015). Frontal top-down signals increase coupling of auditory low-frequency oscillations to continuous speech in human listeners. Curr. Biol. *25*, 1649–1653.

Pernet, C.R., Garrido, M., Gramfort, A., Maurits, N., Michel, C., Pang, E., Salmelin, R., Schoffelen, J.M., Valdes-Sosa, P.A., and Puce, A. (2018). Best Practices in Data Analysis and Sharing in Neuroimaging using MEEG. Published online August 9, 2018. https://doi.org/10.31219/osf.io/a8dhx.

Pesaran, B., Vinck, M., Einevoll, G.T., Sirota, A., Fries, P., Siegel, M., Truccolo, W., Schroeder, C.E., and Srinivasan, R. (2018). Investigating large-scale brain dynamics using field potential recordings: analysis and interpretation. Nat. Neurosci. *21*, 903–919.

Pizzo, F., Roehri, N., Medina Villalon, S., Trébuchon, A., Chen, S., Lagarde, S., Carron, R., Gavaret, M., Giusiano, B., McGonigal, A., et al. (2019). Deep brain activities can be detected with magnetoencephalography. Nat. Commun. *10*, 971.

Ploner, M., Gross, J., Timmermann, L., and Schnitzler, A. (2002). Cortical representation of first and second pain sensation in humans. Proc. Natl. Acad. Sci. USA *99*, 12444–12448.

Ploner, M., Sorg, C., and Gross, J. (2017). Brain rhythms of pain. Trends Cogn. Sci. *21*, 100–110.

Poldrack, R.A. (2019). The costs of reproducibility. Neuron *101*, 11–14.

Pu, Y., Cheyne, D.O., Cornwell, B.R., and Johnson, B.W. (2018). Non-invasive Investigation of Human Hippocampal Rhythms Using Magnetoencephalography: A Review. Front. Neurosci. *12*, 273.

Quian Quiroga, R., and Panzeri, S. (2009). Extracting information from neuronal populations: information theory and decoding approaches. Nat. Rev. Neurosci. *10*, 173–185.

Rebollo, I., Devauchelle, A.-D., Béranger, B., and Tallon-Baudry, C. (2018). Stomach-brain synchrony reveals a novel, delayed-connectivity resting-state network in humans. eLife. Published online March 21, 2018. https://doi.org/10.7554/eLife.33321.

Richter, C.G., Babo-Rebelo, M., Schwartz, D., and Tallon-Baudry, C. (2017). Phase-amplitude coupling at the organism level: The amplitude of spontaneous alpha rhythm fluctuations varies with the phase of the infra-slow gastric basal rhythm. Neuroimage *146*, 951–958.

Romei, V., Rihs, T., Brodbeck, V., and Thut, G. (2008). Resting electroencephalogram alpha-power over posterior sites indexes baseline visual cortex excitability. Neuroreport *19*, 203–208.

Ruhnau, P., Neuling, T., Fuscá, M., Herrmann, C.S., Demarchi, G., and Weisz, N. (2016). Eyes wide shut: Transcranial alternating current stimulation drives alpha rhythm in a state dependent manner. Sci. Rep. *6*, 27138.

Ruzich, E., Crespo-García, M., Dalal, S.S., and Schneiderman, J.F. (2019). Characterizing hippocampal dynamics with MEG: A systematic review and evidence-based guidelines. Hum. Brain Mapp. *40*, 1353–1375.

Salenius, S., and Hari, R. (2003). Synchronous cortical oscillatory activity during motor action. Curr. Opin. Neurobiol. *13*, 678–684.

Sanz-Leon, P., Knock, S.A., Spiegler, A., and Jirsa, V.K. (2015). Mathematical framework for large-scale brain network modeling in The Virtual Brain. Neuroimage *111*, 385–430.

Schirner, M., McIntosh, A.R., Jirsa, V., Deco, G., and Ritter, P. (2018). Inferring multi-scale neural mechanisms with brain network modelling. eLife. Published online January 8, 2018. https://doi.org/10.7554/eLife.28927.

Schnitzler, A., and Gross, J. (2005). Normal and pathological oscillatory communication in the brain. Nat. Rev. Neurosci. *6*, 285–296.

Schoffelen, J.-M., and Gross, J. (2009). Source connectivity analysis with MEG and EEG. Hum. Brain Mapp. *30*, 1857–1865.

Schoffelen, J.-M., Oostenveld, R., and Fries, P. (2005). Neuronal coherence as a mechanism of effective corticospinal interaction. Science *308*, 111–113.

Schoffelen, J.-M., Hultén, A., Lam, N., Marquand, A.F., Uddén, J., and Hagoort, P. (2017). Frequency-specific directed interactions in the human brain network for language. Proc. Natl. Acad. Sci. USA *114*, 8083–8088.

Schoffelen, J.-M., Oostenveld, R., Lam, N.H.L., Uddén, J., Hultén, A., and Hagoort, P. (2019). A 204-subject multimodal neuroimaging dataset to study language processing. Sci. Data *6*, 17.

Schyns, P.G., Thut, G., and Gross, J. (2011). Cracking the code of oscillatory activity. PLoS Biol. *9*, e1001064.

Sedley, W., Friston, K.J., Gander, P.E., Kumar, S., and Griffiths, T.D. (2016). An integrative tinnitus model based on sensory precision. Trends Neurosci. *39*, 799–812.

Sharon, D., Hämäläinen, M.S., Tootell, R.B.H., Halgren, E., and Belliveau, J.W. (2007). The advantage of combining MEG and EEG: comparison to fMRI in focally stimulated visual cortex. Neuroimage *36*, 1225–1235.

Sherman, M.A., Lee, S., Law, R., Haegens, S., Thorn, C.A., Hämäläinen, M.S., Moore, C.I., and Jones, S.R. (2016). Neural mechanisms of transient neocortical beta rhythms: Converging evidence from humans, computational modeling, monkeys, and mice. Proc. Natl. Acad. Sci. USA *113*, E4885–E4894.

Siebenhühner, F., Wang, S.H., Palva, J.M., and Palva, S. (2016). Cross-frequency synchronization connects networks of fast and slow oscillations during visual working memory maintenance. eLife. Published online September 26, 2016. https://doi.org/10.7554/eLife.13451.

Siegel, M., Donner, T.H., and Engel, A.K. (2012). Spectral fingerprints of large-scale neuronal interactions. Nat. Rev. Neurosci. *13*, 121–134.

Stephan, K.E., Iglesias, S., Heinzle, J., and Diaconescu, A.O. (2015). Translational perspectives for computational neuroimaging. Neuron *87*, 716–732.

Suntrup, S., Teismann, I., Wollbrink, A., Winkels, M., Warnecke, T., Flöel, A., Pantev, C., and Dziewas, R. (2013). Magnetoencephalographic evidence for the modulation of cortical swallowing processing by transcranial direct current stimulation. Neuroimage *83*, 346–354.

Supek, S. (2013). Magnetoencephalography: From Signals To Dynamic Cortical Networks (New York: Springer).

Symmonds, M., Moran, C.H., Leite, M.I., Buckley, C., Irani, S.R., Stephan, K.E., Friston, K.J., and Moran, R.J. (2018). Ion channels in EEG: isolating channel dysfunction in NMDA receptor antibody encephalitis. Brain *141*, 1691–1702.

Taylor, J.R., Williams, N., Cusack, R., Auer, T., Shafto, M.A., Dixon, M., Tyler, L.K., Cam-Can, and Henson, R.N. (2017). The Cambridge Centre for Ageing and Neuroscience (Cam-CAN) data repository: Structural and functional MRI, MEG, and cognitive data from a cross-sectional adult lifespan sample. Neuroimage *144*, 262–269.

Thut, G., Nietzel, A., Brandt, S.A., and Pascual-Leone, A. (2006). Alpha-band electroencephalographic activity over occipital cortex indexes visuospatial attention bias and predicts visual target detection. J. Neurosci. *26*, 9494–9502.

Thut, G., Miniussi, C., and Gross, J. (2012). The functional importance of rhythmic activity in the brain. Curr. Biol. *22*, R658–R663.

Thut, G., Bergmann, T.O., Fröhlich, F., Soekadar, S.R., Brittain, J.-S., Valero-Cabré, A., Sack, A.T., Miniussi, C., Antal, A., Siebner, H.R., et al. (2017). Guiding transcranial brain stimulation by EEG/MEG to interact with ongoing brain activity and associated functions: A position paper. Clin. Neurophysiol. *128*, 843–857.

Uhlhaas, P.J., Grent-'t-Jong, T., and Gross, J. (2018). Magnetoencephalography and translational neuroscience in psychiatry. JAMA Psychiatry *75*, 969–971.

van Diessen, E., Numan, T., van Dellen, E., van der Kooi, A.W., Boersma, M., Hofman, D., van Lutterveld, R., van Dijk, B.W., van Straaten, E.C.W., Hillebrand, A., and Stam, C.J. (2015). Opportunities and methodological challenges in EEG and MEG resting state functional brain network research. Clin. Neurophysiol. *126*, 1468–1481.

van Dijk, H., Schoffelen, J.-M., Oostenveld, R., and Jensen, O. (2008). Prestimulus oscillatory activity in the alpha band predicts visual discrimination ability. J. Neurosci. *28*, 1816–1823.

VanRullen, R. (2016). Perceptual Cycles. Trends Cogn. Sci. *20*, 723–735.

Varga, S., and Heck, D.H. (2017). Rhythms of the body, rhythms of the brain: Respiration, neural oscillations, and embodied cognition. Conscious. Cogn. *56*, 77–90.

Vidaurre, D., Hunt, L.T., Quinn, A.J., Hunt, B.A.E., Brookes, M.J., Nobre, A.C., and Woolrich, M.W. (2018). Spontaneous cortical activity transiently organises into frequency specific phase-coupling networks. Nat. Commun. *9*, 2987.

Vorwerk, J., Cho, J.-H., Rampp, S., Hamer, H., Knösche, T.R., and Wolters, C.H. (2014). A guideline for head volume conductor modeling in EEG and MEG. Neuroimage *100*, 590–607.

Wagner, S., Rampersad, S.M., Aydin, Ü., Vorwerk, J., Oostendorp, T.F., Neuling, T., Herrmann, C.S., Stegeman, D.F., and Wolters, C.H. (2014). Investigation of tDCS volume conduction effects in a highly realistic head model. J. Neural Eng. *11*, 016002.

Wagner, S., Burger, M., and Wolters, C.H. (2016). An Optimization Approach for Well-Targeted Transcranial Direct Current Stimulation. SIAM J. Appl. Math. *76*, 2154–2174.

Wang, X.-J. (2010). Neurophysiological and computational principles of cortical rhythms in cognition. Physiol. Rev. *90*, 1195–1268.

Wessing, I., Rehbein, M.A., Postert, C., Fürniss, T., and Junghöfer, M. (2013). The neural basis of cognitive change: reappraisal of emotional faces modulates neural source activity in a frontoparietal attention network. Neuroimage *81*, 15–25.

Wipf, D., and Nagarajan, S. (2009). A unified Bayesian framework for MEG/EEG source imaging. Neuroimage *44*, 947–966.

Zelano, C., Jiang, H., Zhou, G., Arora, N., Schuele, S., Rosenow, J., and Gottfried, J.A. (2016). Nasal respiration entrains human limbic oscillations and modulates cognitive function. J. Neurosci. *36*, 12448–12467.

Zhan, J., Ince, R.A.A., van Rijsbergen, N., and Schyns, P.G. (2019). Dynamic construction of reduced representations in the brain for perceptual decision behavior. Curr. Biol. *29*, 319–326.e4.