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Consistency of EEG source localization and connectivity estimates

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ABSTRACT

As the EEG inverse problem does not have a unique solution, the sources reconstructed from EEG and their connectivity properties depend on forward and inverse modeling parameters such as the choice of an anatomical template and electrical model, prior assumptions on the sources, and further implementational details. In order to use source connectivity analysis as a reliable research tool, there is a need for stability across a wider range of standard estimation routines. Using resting state EEG recordings of N=65 participants acquired within two studies, we present the first comprehensive assessment of the consistency of EEG source localization and functional/effective connectivity metrics across two anatomical templates (ICBM152 and Colin27), three electrical models (BEM, FEM and spherical harmonics expansions), three inverse methods (WMNE, eLORETA and LCMV), and three software implementations (Brainstorm, Fieldtrip and our own toolbox). Source localizations were found to be more stable across reconstruction pipelines than subsequent estimations of functional connectivity, while effective connectivity estimates where the least consistent. All results were relatively unaffected by the choice of the electrical head model, while the choice of the inverse method and source imaging package induced a considerable variability. In particular, a relatively strong difference was found between LCMV beamformer solutions on one hand and eLORETA/WMNE distributed inverse solutions on the other hand. We also observed a gradual decrease of consistency when results are compared between studies, within individual participants, and between individual participants. In order to provide reliable findings in the face of the observed variability, additional simulations involving interacting brain sources are required. Meanwhile, we encourage verification of the obtained results using more than one source imaging procedure.

Introduction

Two major methodological challenges in noninvasive neuroimaging concern the determination of task-specific cortical areas and the determination of their interactions from functional data.

Functional magnetic resonance imaging (fMRI) measures changes in blood flow induced by neuronal activity. While being able to distinguish brain activations even a few millimeters apart, fMRI suffers from poor temporal resolution with sampling rates typically lower than 1 Hz.

Compared to fMRI, electro- and magnetoencephalography (EEG/MEG) provide much higher temporal resolution thus making them attractive techniques for studying interactions between different brain structures.

Yet, EEG and MEG suffer from low spatial resolution since only superpositions of brain signals originating from the entire cortical gray matter can be recorded. Sensor space analyses in general are not suitable to infer the involvement of brain structures in interaction even in such broad terms as 'frontal-to-occipital' (Haufe, 2011; Van de Steen et al., 2016). The interpretation of EEG/MEG data in neuroanatomical terms therefore requires a reconstruction of the sources from the recorded data. This, however, requires a solution of an 'ill-posed' inverse problem, for which infinitely many solution exists. To select a unique solution, prior knowledge of the source characteristics needs to be employed. Consequently, there is a host of methods estimating sources under specific assumptions.

The choice of an inverse method is a factor that heavily influences

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the reconstructed brain activity, as well as subsequent analyses relying on the recovered sources. Other important factors are the specifics of the physical model of electrical current flow in the head and the choice of an anatomical template with which to perform the source reconstruction. In practice, researchers typically resort to one of the publicly available toolboxes for source analysis such as Brainstorm (Tadel et al., 2011), FieldTrip (Oostenveld et al., 2010), EEGLAB (Delorme and Makeig, 2004) and MNE (Gramfort et al., 2014). These toolboxes typically provide ready-made anatomical templates, methods for electrical forward calculations, and implementations of inverse solutions. While the methods portfolios provided by different toolboxes are in general similar, the different possible combinations of forward and inverse models, as well as the differences in their implementations and the choice of their numerous parameters (such as tissue conductivities, segmentation and meshing parameters for forward models, and regularization and depth weighting constants for inverse models) may lead to a substantial variability of possible source location and connectivity estimates.

Numerous studies have quantified biases in the localization of brain sources (e.g., Darvas et al. (2004), Haufe (2011), Gramfort et al. (2013)), as well as in the determination of brain connectivity (e.g., Schoffelen and Gross (2009), Haufe et al. (2010), Haufe et al. (2013), Ewald et al. (2013), Rodrigues and Andrade (2015), Haufe and Ewald (2016)) for specific methods. The error of a statistical measure depends however not only on its estimation bias but also on its variance. Large variability in combination with the small sample sizes that are common in neuroimaging studies have been identified as the major cause of the lack of reproducibility that is generally observed (Button et al., 2013). A recent study by Colclough et al. (2016) consequently assessed the consistency of MEG source connectivity metrics across different datasets.

When working with EEG/MEG source estimates, another source of variability to be considered is the choice of the forward and inverse modeling parameters. Intuitively, we would consider results based on reconstructed sources only meaningful if they are reasonably consistent across a range of widely accepted estimation procedures (pipelines) when applied to the same data. An investigation of this latter factor would help to assess the reliability of EEG and MEG based brain connectivity estimation as a research tool, but has not yet been provided.

With this work, we present the first comprehensive assessment of the consistency of EEG source location and connectivity analyses across common forward and inverse models. Our data is based on reconstructions performed in three different analysis packages using combinations of three different inverse methods, three different electrical modeling approaches, and two different template anatomies. We investigated the sources and communication patterns of alpha-band (8–13 Hz) oscillations using resting-state recordings acquired within two different studies (N=65). We chose to use alpha oscillations because: 1) they have high signal-to-noise ratio – thus ameliorating the problem of noisy recordings and 2) these oscillations have relatively stable spatial patterns across subjects corresponding to sources in occipito-parietal and central areas of the cortex.

Our main goal was to bring the attention of the neuroimaging community to the problem of identifying interacting neuronal sources on the basis of the multichannel EEG recordings. We wanted to illustrate pitfalls in obtaining measures of connectivity due to different stages of the data analysis including selection of the toolbox, forward/inverse models and connectivity estimates. By making researchers aware of multiple problems in connectivity analysis, we hope to help them with the validation of the results and consequently in establishing reliable findings about the brain functioning.

The paper starts by introducing the data, preprocessing steps, forward and inverse modeling approaches, and robust connectivity measures. In the experimental part we first demonstrate that the choice of the reference electrode dramatically influences EEG sensor-space connectivity maps, making sensor-space analysis unsuitable for the study of brain connectivity. Using pairwise correlations, we quantified the similarity of inverse solutions and source connectivity matrices when different source reconstruction pipelines are applied to the same data. We also quantified the within-participant, between-participant and between-study variability. We conclude the paper with a discussion of the different sources of variability and their impact on the reliability of results, strategies to deal with variability, general validation strategies, and the perhaps counter-intuitive relationship between robustness and consistency of connectivity measures.

Methods

Definition of alpha-band SNR

Alpha activity between 8 and 13 Hz is predominantly observed in occipital EEG channels. Its peak frequency and range can differ across participants. Following (Nolte et al., 2008), we define an individual alpha band for each participant covering a symmetric 5 Hz range (2.5 Hz left and right of the peak) around the participant's alpha peak frequency, where the peak is determined by maximum spectral power at electrodes O1 and O2, and is constrained to the interval $[8.5, 12.5]$ Hz. Alpha-band signal-to-noise ratio (SNR) of an EEG sensor or reconstructed source is defined as the ratio between the spectral power at the alpha peak and the average spectral power in 2 Hz wide side bands to the left and right of the individual alpha band. Spectral power is computed using the Welch method using non-overlapping Hanning windows of 200 samples length, where we assume a sampling frequency of 100 Hz.

Spatio-spectral decomposition (SSD)

We apply spatio-spectral decomposition (SSD, Nikulin et al. (2011)) in order to remove brain activity without strong alpha peaks. SSD seeks spatial filters $\mathbf{w}$ that maximize the signal power of the projected data in a frequency band of interest (here, the alpha band) while simultaneously suppressing the power in the left and right side (flanking) bands. We use the same alpha and side bands as in the definition of alpha-band SNR. Alpha band power was defined as the sum of the squared signal after 2nd order Butterworth bandpass filtering. The power in the side bands was computed analogously after application of an appropriate bandpass filter and a subsequent notch filter. Apart from these minor differences, SSD thus directly optimizes the alpha-band SNR of the projected components as defined above.

The first SSD spatial filter is given by

$$\mathbf{w}_1 = \arg\max_{\mathbf{w}} \frac{\mathbf{w}^\top \mathbf{C}_s \mathbf{w}}{\mathbf{w}^\top \mathbf{C}_n \mathbf{w}} , \tag{1}$$

where $\mathbf{C}_s \in \mathbb{R}^{M \times M}$ is the covariance of the sensor data filtered in the alpha band, and $\mathbf{C}_n$ is the covariance of the data filtered in the side bands as outlined above. A complete SSD decomposition matrix can be computed by solving a generalized eigenvalue problem (Nikulin et al., 2011).

To identify the number of SSD components, a heuristic based on the achieved alpha-band SNR of each component is employed, where only components with SNR values larger than 2 are retained for further analysis.

EEG source modeling

The generative model of EEG data is given by

$$\mathbf{x}(t) = \sum_{\mathbf{u}_i \in \beta} \mathbf{L}_i \mathbf{j}_i(t) + \boldsymbol{\epsilon}(t) , \tag{2}$$

where $\mathbf{x}(t) \in \mathbb{R}^M$ is the signal measured at M EEG electrodes at time t, $\mathbf{j}_i(t) \in \mathbb{R}^3$ is the activity of a single source at a brain location $\mathbf{u}_i$, and