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The impact of MEG source reconstruction method on source-space connectivity estimation: A comparison between minimum-norm solution and beamforming

Ana-Sofía Hincapié[a,b,c,d,*,1,2,3,4], Jan Kujala[b,e,2,5], Jérémie Mattout[b,2], Annalisa Pascarella[f,6], Sebastien Daligault[g,7], Claude Delpuech[b,g,2,7], Domingo Mery[c,3], Diego Cosmelli[d,4], Karim Jerbi[a,b,1,2]

[a] Psychology Department, University of Montreal, Quebec, Canada
[b] Lyon Neuroscience Research Center, CRNL, INSERM, U1028 – CNRS – UMR5292, University Lyon 1, Brain Dynamics and Cognition Team, Lyon, France
[c] Department of Computer Science, Pontificia Universidad Católica de Chile, Santiago de Chile, Chile
[d] Escuela de Psicología, Pontificia Universidad Católica de Chile and Interdisciplinary Center for Neurosciences, Pontificia Universidad Católica de Chile, Santiago de Chile, Chile
[e] Department of Neuroscience and Biomedical Engineering, Aalto University, Espoo, Finland
[f] Consiglio Nazionale delle Ricerche (CNR – National Research Council), Rome, Italy
[g] MEG Center, CERMEP, Lyon, France

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ABSTRACT

Despite numerous important contributions, the investigation of brain connectivity with magnetoencephalography (MEG) still faces multiple challenges. One critical aspect of source-level connectivity, largely overlooked in the literature, is the putative effect of the choice of the inverse method on the subsequent cortico-cortical coupling analysis. We set out to investigate the impact of three inverse methods on source coherence detection using simulated MEG data. To this end, thousands of randomly located pairs of sources were created. Several parameters were manipulated, including inter- and intra-source correlation strength, source size and spatial configuration. The simulated pairs of sources were then used to generate sensor-level MEG measurements at varying signal-to-noise ratios (SNR). Next, the source level power and coherence maps were calculated using three methods (a) L2-Minimum-Norm Estimate (MNE), (b) Linearly Constrained Minimum Variance (LCMV) beamforming, and (c) Dynamic Imaging of Coherent Sources (DICS) beamforming. The performances of the methods were evaluated using Receiver Operating Characteristic (ROC) curves. The results indicate that beamformers perform better than MNE for coherence reconstructions if the interacting cortical sources consist of point-like sources. On the other hand, MNE provides better connectivity estimation than beamformers, if the interacting sources are simulated as extended cortical patches, where each patch consists of dipoles with identical time series (high intra-patch coherence). However, the performance of the beamformers for interacting patches improves substantially if each patch of active cortex is simulated with only partly coherent time series (partial intra-patch coherence). These results demonstrate that the choice of the inverse method impacts the results of MEG source-space coherence analysis, and that the optimal choice of the inverse solution depends on the spatial and synchronization profile of the interacting cortical sources. The insights revealed here can guide method selection and help improve data interpretation regarding MEG connectivity estimation.

* Corresponding author at: Psychology Department, University of Montreal, Pavillon Marie-Victorin, 90, avenue Vincent d'Indy, Quebec, Canada.
E-mail addresses: ashincap@uc.cl (A.-S. Hincapié), jan.kujala@aalto.fi (J. Kujala), jeremie.mattout@inserm.fr (J. Mattout), a.pascarella@iac.cnr.it (A. Pascarella), daligault@cermep.fr (S. Daligault), claude.delpuech@inserm.fr (C. Delpuech), dmery@ing.puc.cl (D. Mery), dcosmelli@uc.cl (D. Cosmelli), karim.jerbi@umontreal.ca (K. Jerbi).
[1] Postal address: Pavillon Marie-Victorin, 90, avenue Vincent d'Indy, Montreal, Québec, Canada.
[2] Postal address: INSERM U1028, 69675 Bron Cedex, France.
[3] Postal address: Av. Vicuña Mackenna 4860 (143), Macul, Santiago de Chile, Chile.
[4] Postal address: Av. Vicuña Mackenna 4860, Macul, Santiago de Chile, Chile.
[5] Postal address: P.O. Box 15100, FI-00076 Aalto, Finland.
[6] Postal address: Via dei Taurini, 19, 00185 Roma, Italy.
[7] Postal address: INSERM U1028, 69675 Bron Cedex, France.

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Introduction

Interactions between neural assemblies in different brain structures are a hallmark of healthy brain function (Mesulam, 1990; Varela et al., 2001; Luo et al., 2010; Mišić and Sporns, 2016). The ability to reliably measure the dynamics of cerebral networks is therefore of utmost importance when it comes to elucidating the neural basis of large-scale integration in health and monitoring its breakdown in disease (Schnitzler and Gross, 2005; Lopes da Silva, 2013; Pittau and Vulliemoz, 2015; Alamian et al., 2017). Given the diversity of available neuroimaging and brain recording techniques, numerous functional brain connectivity measures have been used (e.g. Schoffelen and Gross, 2009; Friston et al., 2013; Engel et al., 2013; O'Neill et al., 2015). One technique that is particularly well suited for the detection of large-scale interactions among neural assemblies is magnetoencephalography (MEG) (Hämäläinen et al., 1993; Dalal et al., 2009; Baillet et al., 2001; Gross et al., 2013; O'Neill et al., 2015). The millisecond-range temporal resolution of MEG allows us to probe the electrophysiological mechanisms that underlie functional brain connectivity (Schölvinck et al., 2013), and its role in sensory, motor and higher-order cognitive tasks (Lopes da Silva, 2013; Jerbi et al., 2007; Gross et al., 2003; Schnitzler and Gross, 2005; Meeren et al., 2013; Simanova et al., 2015) as well as in the resting-state (Cabral et al., 2014; de Pasquale et al., 2012; Hipp et al., 2012; Schölvinck et al., 2013; O'Neill et al., 2015; Henson et al., 2007; van Diessen et al., 2015; Garcés et al., 2016; Colclough et al., 2016).

Although sensor-level analyses of MEG recordings have provided important insights into brain function, the estimation of neuronal interactions at the source level is key to elucidating the role of large-scale brain networks in health and disease. To achieve this goal, one needs, first of all, to reconstruct the source time series that underlie the sensor-level measurements.

This is an ill-posed inverse problem since there is no unique solution (an infinite number of current density distributions result in zero magnetic field outside the head) and furthermore there is no continuous dependency of the solution from the data (i.e. small variations in source space can lead to large perturbations in data space). Given that the Maxwell equations are linear, it is impossible to choose between an infinite number of equally good solutions, without prior knowledge, additional constraints or both. Numerous methods have been proposed to tackle this inverse problem (Baillet et al., 2001; Küçükaltun-Yildirim et al., 2006; Gross et al., 2013). The specificity of each technique depends on the assumption that is made about the properties of the neural sources and on the way it incorporates various forms of a priori information, if any is available. One of the earliest and most widely used inverse methods is the Minimum Norm Estimate (MNE) (Dale and Sereno, 1993; Hämäläinen and Ilmoniemi, 1984, 1994; Sarvas, 1987; Matsuura and Okabe, 1995; Wang et al., 1993; Baillet et al., 2001; Hauk, 2004; David et al., 2002; Attal and Schwartz, 2013; Lin et al., 2006; Liu et al., 1998; Grave de Peralta Menendez et al., 1997; Hsiao et al., 2015; Cheng et al., 2015; Stenroos and Hauk, 2013; Meeren et al., 2013; Palva et al., 2010; Mattout et al., 2005; Chang et al., 2015; Simanova et al., 2015; Kanamori et al., 2013). In principle, MNE searches for a source distribution with the minimum (L2-norm) current that gives the best account of the measured data. Another popular family of MEG inverse methods is the beamformer approach (Van Veen et al., 1997; Gross et al., 2001; Hadjipapas et al., 2005; Küçükaltun-Yildirim et al., 2006; Barnes and Hillebrand, 2003; Barnes et al., 2004; Ikezawa et al., 2011; Sekihara et al., 2001; Quraan et al., 2011; Hillebrand and Barnes, 2005; Kujala et al., 2012, 2008; Darvas et al., 2004; Popescu et al., 2008; Litvak et al., 2010; Laaksonen et al., 2012; Gross et al., 2003; Spaak et al., 2014; Rossiter et al., 2012; Muthuraman et al., 2015; Hui et al., 2010; Diwakar et al., 2011). Beamformers scan the source space through a set of spatial filters designed to pass the brain activity from a specified location while attenuating activity originating at other locations. Interestingly, although beamformers and MNE are among the most commonly used methods in MEG source level analysis (Sorrentino and Pascarella, 2011; Hansen et al., 2010; Baillet et al., 2001), these techniques have primarily been compared in terms of source localization accuracy, but their effect on subsequent source-level connectivity reconstruction is only poorly understood and has been largely overlooked in the literature.

The differences between available methods are largely driven by the assumptions they make on the sources or on the character of the noise. While MNE assumes a Gaussian distribution for the noise, beamformers assume that the noise is uncorrelated with the sources. One theoretical difference regarding connectivity analysis is that beamformers assume the sources underlying the measurements to be uncorrelated (Van Veen et al., 1997) while MNE does not (Hämäläinen and Ilmoniemi, 1984, 1994). Several studies have sought to assess the effect of method selection on source localization and power mapping (Liljeström et al., 2005; Darvas et al., 2004; Küçükaltun-Yildirim et al., 2006; Mattout et al., 2006; Sekihara et al., 2005; Hauk et al., 2011; Lin et al., 2006; Haufe et al., 2011), yet there are hardly any studies that have directly assessed the impact of method selection on the subsequent source-level coupling analysis (cf. Schoffelen and Gross, 2009; Hui et al., 2010).

Because MNE and spatial filters are widely used inverse solutions in MEG, it would be helpful to understand whether they differentially impact source-level connectivity estimations and, in particular, what parameters affect their potential difference in performance. Although beamformers are by construction tuned to work with uncorrelated sources, they have been shown to be stable to moderately correlated sources and to even localize completely correlated point-like sources in the presence of noise (Van Veen et al., 1997; Gross et al., 2001; Hadjipapas et al., 2005; Sekihara et al., 2005; Küçükaltun-Yildirim et al., 2006; Kujala et al., 2008; Quraan and Cheyne, 2010). Given that this assumption about uncorrelated sources is embedded in beamformer reconstructions, one may ask how it affects the identification of coherent sources, compared to inverse solutions that do not make such an assumption (for instance MNE)? Furthermore, how do the connectivity-detection performances of MNE and beamforming compare when the coupled sources vary in size, or in coupling strength? And how does the noise level affect the performance of both methods when it comes to detecting interacting sources? These are all open questions which we address here via extensive data simulations.

More specifically, the goal of the current study is to investigate the effect of the inverse method selection on the quality of subsequent source-space connectivity analyses. In particular, we evaluated the difference in the ability to correctly uncover oscillatory coupling in source-space following an initial source estimation step that is either performed with (a) Minimum Norm Estimate (MNE), (b) Linearly Constrained Minimum Variance (LCMV) beamformer or (c) Dynamic Imaging of Coherent Sources (DICS) beamformer. This was achieved using numerous simulations of oscillatory signals where we varied a range of parameters, including source size, inter-patch and intra-patch coherence strengths and signal-to-noise ratio (SNR).

Methods and materials

Although our main objective is to evaluate the effect of using different methods to estimate coherence between cortical areas, we also compare the performance of the methods to localize active sources by evaluating their accuracy in determining the levels of oscillatory power. This power estimation also allows us to compare our results with other studies. For the analysis with MNE and LCMV, the time-series of the signals are first reconstructed and then spectral coherence and power can be calculated. DICS operates in the frequency domain allowing for a direct reconstruction of coherence and power. As shown in *LCMV Beamforming* and *DICS Beamforming*, LCMV and DICS beamformers are based on the same filtering principle, but DICS was especially