NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 37 (2007) 731 – 748

A novel integrated MEG and EEG analysis method for dipolar sources

Ming-Xiong Huang,[a,b,c,*] Tao Song,[a] Donald J. Hagler Jr.,[a] Igor Podgorny,[d] Veikko Jousmaki,[e] Li Cui,[a] Kathleen Gaa,[a] Deborah L. Harrington,[a,c] Anders M. Dale,[a,d] Roland R. Lee,[a,b] Jeff Elman,[f] and Eric Halgren[a,d]

[a]Department of Radiology, University of California, San Diego, San Diego, CA, USA
[b]Radiology Service, VA San Diego Healthcare System, San Diego, CA, USA
[c]Research Service, VA San Diego Healthcare System, San Diego, CA, USA
[d]Department of Neuroscience, University of California, San Diego, San Diego, CA, USA
[e]Brain Research Unit, Low Temperature Laboratory, Helsinki University of Technology, FIN-02015 HUT, Finland
[f]Department of Cognitive Science, University of California, San Diego, San Diego, CA, USA

Received 22 November 2006; revised 2 May 2007; accepted 3 June 2007
Available online 14 June 2007

The ability of magnetoencephalography (MEG) to accurately localize neuronal currents and obtain tangential components of the source is largely due to MEG's insensitivity to the conductivity profile of the head tissues. However, MEG cannot reliably detect the radial component of the neuronal current. In contrast, the localization accuracy of electroencephalography (EEG) is not as good as MEG, but EEG can detect both the tangential and radial components of the source. In the present study, we investigated the conductivity dependence in a new approach that combines MEG and EEG to accurately obtain, not only the location and tangential components, but also the radial component of the source. In this approach, the source location and tangential components are obtained from MEG alone, and optimal conductivity values of the EEG model are estimated by best-fitting EEG signal, while precisely matching the tangential components of the source in EEG and MEG. Then, the radial components are obtained from EEG using the previously estimated optimal conductivity values. Computer simulations testing this integrated approach demonstrated two main findings. First, there are well-organized optimal combinations of the conductivity values that provide an accurate fit to the combined MEG and EEG data. Second, the radial component, in addition to the location and tangential components, can be obtained with high accuracy without needing to know the precise conductivity profile of the head. We then demonstrated that this new approach performed reliably in an analysis of the 20-ms component from human somatosensory responses elicited by electric median-nerve stimulation.

Keywords: MEG; EEG; Integration; Conductivity; Skull; Tangential; Radial; Median-nerve stimulation; Somatosensory evoked field; Somatosensory evoked potential; Inverse problem

Introduction

MEG and EEG are functional imaging techniques that directly detect neuronal activity with millisecond temporal resolution. Previous studies have shown that integrating MEG and EEG is more beneficial than using each modality alone (Cohen and Cuffin, 1983, 1987; Baillet et al., 1999; Huizenga et al., 2001; Goncalves et al., 2003a; Babiloni et al., 2004). Many studies indicate that MEG's ability to accurately locate neuronal sources is primarily due to its insensitivity to the conductivity profile of the head tissues. MEG localization accuracy is typically about 3 mm in spherical phantom studies (Barth et al., 1986; Janday and Swithenby, 1987; Hansen et al., 1988; Yamamoto et al., 1988). While early studies using skull phantoms suggested that MEG localization accuracy was in the range of 4–8 mm (Barth et al., 1986; Weinberg et al., 1986; Janday and Swithenby, 1987; Yamamoto et al., 1988), a more rigorously designed human skull phantom study using 32 dipoles reported that MEG localization accuracy was about 3 mm (Leahy et al., 1998), similar to spherical phantoms. In contrast, EEG localization accuracy is about 8–10 mm using phantoms (Henderson et al., 1975; Leahy et al., 1998)

* Corresponding author. Radiology Imaging Laboratory, Department of Radiology, University of California, San Diego, 3510 Dunhill Street, San Diego, CA 92121, USA. Fax: +1 858 552 7404.
E-mail address: mxhuang@ucsd.edu (M.-X. Huang).
Available online on ScienceDirect (www.sciencedirect.com).

1053-8119/$ - see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2007.06.002

and 10–20 mm using implanted electrodes in epilepsy patients (Smith et al., 1983, 1985; Cuffin et al., 1991; Cuffin, 1996; Krings et al., 1999). In all these studies, the number of MEG sensors and/or EEG electrodes was sufficiently larger than that of the dipole parameters. In empirical studies, EEG's localization accuracy is mainly affected by the errors of the estimated conductivity profile of the head. If the conductivity profile was precisely known, the EEG localization accuracy could be at least as good as that of the MEG (Liu et al., 2002).

MEG can also accurately obtain the tangential components of the neuronal current (Cohen and Cuffin, 1983, 1987; Leahy et al., 1998; Huizenga et al., 2001; Goncalves et al., 2003a), but cannot reliably obtain the radial component of neuronal current that is perpendicular to the inner skull surface. In contrast, EEG is sensitive to both the tangential and radial components of the neuronal current. However, as noted above, accurate estimation of these components with EEG depends on precise knowledge of the source location and conductivity profile of the head tissues, particularly the skull (Pohlmeier et al., 1997; van den Broek et al., 1998; Ollikainen et al., 1999).

Usually, a piece-wise homogeneous approximation is adopted in EEG head models (based on a spherical model or more realistic Boundary Element Method (BEM) model), in which effective conductivities of the scalp, skull, and brain must be estimated (Mosher et al., 1999). The conductivities of the scalp and brain cannot be determined independently from extracranial measures (an ill-posed problem) and hence, they are usually assumed to be the same in most investigations (Nicholson, 1965; Geddes and Baker, 1967; Kosterich et al., 1983; Oostendorp et al., 2000; Goncalves et al., 2003a,b; Lai et al., 2005), and the conductivity of the skull is assigned to be much lower than those of the scalp and the brain. In the case of MEG, a single layer that models the inner skull surface is quite accurate without knowledge of the conductivity profile of the skull and scalp (Hamalainen and Sarvas, 1989).

There are several approaches to analyzing simultaneous recordings from MEG and EEG (Brenner et al., 1978; Cohen and Cuffin, 1983; Cohen and Cuffin, 1987; Baillet et al., 1999; Huizenga et al., 2001; Goncalves et al., 2003a; Babiloni et al., 2004). In studies of somatosensory responses (Brenner et al., 1978; Cohen and Cuffin, 1983), the dipole locations in a spherical head model were separately obtained from MEG and EEG, and MEG showed better localization than EEG. Tangential dipole components can be obtained from MEG reliably whereas the radial component can be obtained from EEG with one set of pre-assigned conductivity values (Cohen and Cuffin, 1983). Several studies have also investigated different approaches of integrating MEG and EEG. Babiloni et al. (2004) have shown that with a variable signal-to-noise ratio, the combined MEG and EEG analysis performed better than each modality alone (Babiloni et al., 2004). The integrated MEG and EEG analysis suggested by Huizenga et al. (2001) used a noise covariance matrix and estimated conductivities. The main concern, though, has been that the less-accurate EEG localization and unreliable MEG radial moment may systematically spoil the performance of the other imaging modality without any consequent improvement. Baillet et al. (1999) suggested a method for a cooperative processing of MEG and EEG in a distributed source model, which minimizes the mutual information between these two modalities. Goncalves et al. (2003a), on the other hand, treated the dipole location and tangential dipole moments obtained from MEG as known parameters when fitting the EEG data by adjusting the conductivities of the brain (σ_{brain}), scalp (σ_{scalp}), and skull (σ_{skull}).

The major challenge remaining for combining MEG and EEG is the large variation in the estimated σ_{brain}, σ_{scalp}, and particularly σ_{skull}. Published values for σ_{brain} range from 0.12 to 0.48 S/m (Nicholson, 1965; Goncalves et al., 2003a,b), and for σ_{skull} range from 0.006 to 0.015 S/m (Geddes and Baker, 1967; Kosterich et al., 1983; Oostendorp et al., 2000; Goncalves et al., 2003a.b). It is generally accepted that the $\sigma_{\text{brain}}/\sigma_{\text{skull}}$ ratio is the key factor in EEG source analysis (for a review see Lai et al., 2005). However, the impact of less-accurate estimations of the conductivity profile for an integrated MEG and EEG analysis is largely unclear. For example, in two integrated MEG and EEG studies from median-nerve responses in human, the $\sigma_{\text{brain}}/\sigma_{\text{skull}}$ ratio in one study was about 80 (Cohen and Cuffin, 1983); whereas in another study the ratio fell considerably, ranging between 43 and 86 in five human cases (average 72, SD = 48%) (Goncalves et al., 2003a). This finding raises three questions that have not been addressed systematically: (1) Why there is a wide range of $\sigma_{\text{brain}}/\sigma_{\text{skull}}$ ratios across subjects and studies that all appear to fit integrated MEG and EEG data equally well? (2) With such a discrepancy in the $\sigma_{\text{brain}}/\sigma_{\text{skull}}$ ratios in the literature, is it still possible to accurately obtain the source moments in an integrated MEG and EEG analysis? (3) Does the outcome of an integrated MEG and EEG analysis only depend on the ratio of $\sigma_{\text{brain}}/\sigma_{\text{skull}}$, or actually, does it depend on the individual values of σ_{brain} and σ_{skull}?

The real situation can be even more complicated with the sandwich-like substructure of the skull which contains two layers of compact bones with very low conductivity and one layer of spongiform tissue with higher conductivity (Leahy et al., 1998; Akhtari et al., 2003). If one treats the skull as a single layer, the effective conductivity of the skull may be inhomogeneous and anisotropic (Leahy et al., 1998). Furthermore, the effective conductivity of the scalp can also vary with skin conditions (e.g., bald, sweating), skin preparation procedures used for EEG, electrode contact sizes, and EEG gels and pastes. These factors raise two more questions that need consideration when integrating MEG and EEG data: (4) Will the results of an integrated approach be accurate if we model the complicated substructure of the skull with one layer of homogeneous and isotropic conductor? (5) If the conductivities of the scalp and brain are not the same, but are set equal in a model, will that arrangement affect the accuracy of the integrated MEG and EEG approach?

In the present study, we addressed the above five key questions using computer simulations to test a new approach for combining simultaneously acquired MEG and EEG data, which uses a comprehensive analysis of the conductivity dependence to accurately derive the location and both the tangential and radial components of neuronal currents. In our approach, the source location and tangential components are first estimated from MEG alone, and the optimal combinations of conductivity values are obtained not only from best fitting to the EEG signal, but also by precisely matching the tangential components of sources from EEG to those from MEG. Then, the radial components of the source are obtained from EEG using the previously obtained optimal conductivity combinations. We hypothesized that: (1) A three-layered conductor model with scalp, skull, and brain (the effective conductivity of the scalp equals that of the brain, i.e., $\sigma_{\text{scalp}} = \sigma_{\text{brain}}$), can adequately model a variety of conductivity distributions of the head including the substructure of the skull, the existence of the cerebrospinal fluid (CSF), and situations in which the $\sigma_{\text{scalp}} \neq \sigma_{\text{brain}}$;