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Clinical Neurophysiology 117 (2006) 1610–1622

www.elsevier.com/locate/clinph

Effects of fMRI–EEG mismatches in cortical current density estimation integrating fMRI and EEG: A simulation study

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Accepted 30 March 2006

Abstract

Objective: Multimodal functional neuroimaging by combining functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) has been studied to achieve high-resolution reconstruction of the spatiotemporal cortical current density (CCD) distribution. However, mismatches between these two imaging modalities may occur due to their different underlying mechanisms. The aim of the present study is to investigate the effects of different types of fMRI–EEG mismatches, including fMRI invisible sources, fMRI extra regions and fMRI displacement, on the fMRI-constrained cortical imaging in a computer simulation based on realistic-geometry boundary-element-method (BEM) model.

Methods: Two methods have been adopted to integrate the synthetic fMRI and EEG data for CCD imaging. In addition to the well-known 90% fMRI-constrained Wiener filter approach (Liu AK, Belliveau JW, Dale AM. PNAS 1998;95:8945–8950.), we propose a novel two-step algorithm (referred to as ‘Twomey algorithm’) for fMRI–EEG integration. In the first step, a ‘hard’ spatial prior derived from fMRI is imposed to solve the EEG inverse problem with a reduced source space; in the second step, the fMRI constraint is removed and the source estimate from the first step is re-entered as the initial guess of the desired solution into an EEG least squares fitting procedure with Twomey regularization. Twomey regularization is a modified Tikhonov technique that attempts to simultaneously minimize the distance between the desired solution and the initial estimate, and the residual errors of fitness to EEG data. The performance of the proposed Twomey algorithm has been evaluated both qualitatively and quantitatively along with the lead-field normalized minimum norm (WMN) and the 90% fMRI-weighted Wiener filter approach, under repeated and randomized source configurations. Point spread function (PSF) and localization error (LE) are used to measure the performance of different imaging approaches with or without a variety of fMRI–EEG mismatches.

Results: The results of the simulation show that the Twomey algorithm can successfully reduce the PSF of fMRI invisible sources compared to the Wiener estimation, without losing the merit of having much lower PSF of fMRI visible sources relative to the WMN solution. In addition, the existence of fMRI extra sources does not significantly affect the accuracy of the fMRI–EEG integrated CCD estimation for both the Wiener filter method and the proposed Twomey algorithm, while the Twomey algorithm may further reduce the chance of occurring spurious sources in the extra fMRI regions. The fMRI displacement away from the electrical source causes enlarged localization error in the imaging results of both the Twomey and Wiener approaches, while Twomey gives smaller LE than Wiener with the fMRI displacement ranging from 1–2 cm. With less than 2 cm fMRI displacement, the LEs for the Twomey and Wiener approaches are still smaller than in the WMN solution.

Conclusions: The present study suggests that the presence of fMRI invisible sources is the most problematic factor responsible for the error of fMRI–EEG integrated imaging based on the Wiener filter approach, whereas this approach is relatively robust against the fMRI extra regions and small displacement between fMRI activation and electrical current sources. While maintaining the above advantages possessed by the Wiener filter approach, the Twomey algorithm can further effectively alleviate the underestimation of fMRI invisible sources, suppress fMRI spurious sources and improve the robustness against fMRI displacement. Therefore, the Twomey algorithm is expected to improve the reliability of multimodal cortical source imaging against fMRI–EEG mismatches.

Significance: The proposed method promises to provide a useful alternative for multimodal neuroimaging integrating fMRI and EEG.

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1388-2457/$30.00
doi:10.1016/j.clinph.2006.03.031

Keywords: Multimodal neuroimaging; EEG; fMRI; Lead-field normalized minimum norm; Point spread function; Twomey regularization; Wiener estimation; Boundary element method

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1. Introduction

In the past decade, tremendous efforts have been made to integrate information across multiple neuroimaging modalities during the same task with the aim to characterize brain function with high-resolution in both spatial and temporal domains. Electroencephalography (EEG), as well as magnetoencephalography (MEG), can detect the rapid change of neurophysiologic processes but they suffer from limited spatial resolution due to their inherent mathematical difficulties. Functional magnetic resonance imaging (fMRI), by measuring hemodynamic responses related to brain activation, has the advantage of revealing anatomical details of neural activation but is limited by its low temporal resolution on the order of seconds (Bandettini et al., 1992; Kwong et al., 1992; Ogawa et al., 1992). Hence, combining the complementary information from EEG (or MEG) and fMRI holds potential for high-resolution spatiotemporal mapping of brain activity (Dale and Halgren, 2001; He and Lian, 2002).

A common strategy for fMRI–EEG integration is to use the results of fMRI analysis as a priori knowledge for imaging the continuous distribution of EEG sources over the entire cortical surface, namely fMRI-constrained cortical current density estimation (which we shall call cortical imaging subsequently) (Babiloni et al., 2003; Liu et al., 1998). This approach implies that cortical electrical sources can be modeled by hundreds or thousands of current dipoles evenly disposed over a triangulated cortical surface with the dipole orientation perpendicular to its local patch (Dale and Sereno, 1993). The problem of EEG-based cortical imaging is thus to estimate the strengths of these dipoles from the recorded electrical potentials over the scalp (He et al., 2002). Considering the close coupling between local hemodynamic response and neural activity as observed in animal and human experimental studies (Logothetis et al., 2001; Puce, 1995), it is expected that an enhanced spatial resolution of EEG-based cortical imaging should be achieved by incorporating the information from fMRI. However, the physical and physiological basis that accounts for the correlation between fMRI signal and neural electrical activity is not yet well understood, and the existing approaches for fMRI–EEG data fusion are mainly based on variations of weighted minimum norm methods. Typically, the fMRI 'hotspots' (locations with significant hemodynamic change) are preferred in the fMRI-constrained cortical imaging, which can be accomplished, for example, by encoding the fMRI spatial information into the source covariance matrix and constructing an optimal linear estimator in the form of Wiener filter (Dale and Sereno, 1993; Liu et al., 1998). Previous simulation and experimental studies have discussed the efficacy of using fMRI constraints to enhance the spatial resolution of EEG- or MEG-based cortical imaging (Ahlfors and Simpson, 2004; Babiloni et al., 2003; Liu et al., 1998), and applications of this method have already advanced our understanding of the spatiotemporal pattern of brain activity and connectivity underlying perception, motion and cognition (Babiloni et al., 2005; Bonmassar et al., 2001; Dale et al., 2000; Jaaskelainen et al., 2004).

However, since EEG (or MEG) and fMRI measure physically different aspects of brain activities and they usually involve a variety of experimental setup and complicated mathematical procedures, it is important to consider possible misspecifications between multimodal signals, such as the presence of fMRI extra sources, fMRI invisible (missing) sources and displacement of fMRI activation from electrical current sources. The fMRI extra sources are the regions that are deemed as fMRI activations but produce no observable EEG/MEG signals, which may likely happen as some of the EEG sources are activated at certain time window while some others are activated at other time windows, but the fMRI activation map may include all of them together as it pools the activity over time due to its inherent lack of temporal resolution. The fMRI invisible (missing) sources are the generators of bioelectromagnetic signals that are not detected by fMRI. Typically, the fMRI invisible sources may happen if neurons are not activated long enough to induce a detectable increase of cerebral blood flow; or they may also happen if a cortical patch generates an EEG signal simply by increasing the firing synchronicity of a small percentage of neurons with little modification of its metabolic consumption (Babiloni and Cincotti, 2004). Also fMRI, by applying statistical methods, is assumed to reflect the integral energy consumption of local neural firing during an entire time period, while cortical imaging can actually be performed instant-by-instant since EEG is, in principle, capable of monitoring brain function virtually at every single time point. A cortical patch of little hemodynamic response can be interpreted as non-active in fMRI in the sense that the mean power of local electrical activity during the time course of the 'event' is too small to induce significant BOLD change. But one can hardly say such a cortical region must be always 'silent' during the whole process; it is likely that its instantaneous activity can give rise to signals observable in EEG. Additionally, the possible difference in the locations of neurons and the involved blood vessels can cause slight displacement of fMRI 'hotspots' away from neural electrical generators.