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Three-Dimensional Source Imaging from Simultaneously Recorded ERP and BOLD-fMRI

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Abstract

We present the three-dimensional (3-D) EEG source images reconstructed by using the minimum norm least square (MNLS) method in combination with the fMRI statistical parametric mapping. For a group of five normal subjects, EEG and fMRI signals responding to the full-view checkerboard pattern-reversal visual stimulation were recorded simultaneously and separately. The electrical activities in V1/V2 and V5 were successfully imaged in the N75-P100-N145 and P100-N145 components, respectively. The present results demonstrate the merits of high-resolution spatiotemporal functional neuroimaging by integrating the simultaneously recorded fMRI and EEG data.

Index Terms

Three-dimensional source imaging; EEG; ERP; fMRI; simultaneous EEG/fMRI; VEP; MNLS

I. Introduction

Integration of electroencephalogram (EEG) or magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI) is motivated by their complementary advantages in imaging the temporal and spatial aspects of the brain function [1]-[3]. In the past decade, great strides have been made in developing the fMRI-EEG (or MEG) integration methods [4]-[10], [37], which have led to novel findings in neuroscience and clinical settings, such as [7], [11].

fMRI and EEG/MEG measure fundamentally different biophysical signals related to brain hemodynamics and electrophysiology. In regard to the cross-modal relationship, agreements have been reached in general [38], [39], but not in details [30]. As quantitative modeling and

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experimental investigation of the neurovascular coupling are still under active research, most of existing fMRI-EEG/MEG integrated neuroimaging approaches are based upon an empirical assumption of co-localized fMRI responses and electrical source activities. Although this assumption sounds valid, it remains to be demonstrated quantitatively and experimentally. Towards this end, previous studies have been conducted to assess the spatial correspondence between the results obtained from EEG/MEG source imaging and fMRI statistical parametric mapping [12]-[14]. However, the conclusions in most of these related studies were confounded by the facts that the EEG/MEG and fMRI data were acquired separately rather than simultaneously [12], or that the EEG/MEG source space was confined to the cortical surface whereas the fMRI data were collected in the three-dimensional (3-D) brain volume [14].

In line with these existing studies [7]-[14], the present study focuses on the comparison between three-dimensional (3-D) electrical source imaging and fMRI statistical parametric mapping. Briefly, we recorded the EEG and fMRI data, both simultaneously and separately, in response to pattern-reversal visual stimuli. A minimum norm least square (MNLS) method [15] was used to estimate the 3-D current density distribution, which was in turn compared with the fMRI activation map. The effect of simultaneous vs. separate recordings was addressed. In addition, we compared the source estimates with and without applying the fMRI spatial constraints, assessing the possible benefits of the fMRI-EEG integration in probing the temporal dynamics of visual-evoked cortical responses, as well as in revealing weak EEG sources that might be hidden by strong source activities if using the EEG alone.

II. Materials and methods

A. Subjects and stimuli

Five healthy subjects (male, right-handed, age: 19-29) participated in the study. All subjects gave written and informed consent before the study. The visual stimuli were checkerboard patterns reversing at 2 Hz (rectangular, full-screen, 7×7 black/white contrast, average luminance: 20 cd/m²) (Fig. 1). The visual stimuli were presented on a LCD monitor in a dimly lit shielding room, or through the rear-projection onto a mirror inside the MRI scanner. Under both conditions, the visual angles of the checkerboard pattern (horizontal: 40°, vertical: 30°) were kept identical. After a few sessions of training, all subjects were able to fixate at a cross-mark at the screen center during the experiment.

B. MRI and fMRI

Both the anatomical and functional MR images were collected in a 3-T magnet (Siemens Trio, Siemens, Germany) with a phase array head volume coil. For the anatomical scans, 256 sagittal T1-weighted slices covering the whole head were acquired by using a Turboflash sequence (TR/TE: 20/5 ms, matrix size: 256×256, slice thickness: 1 mm). For the functional scans, 10 axial T2*-weighted images covering the entire occipital cortex were acquired using a gradient echo planar imaging (EPI) sequence (TR/TE: 1000/35 ms, matrix size: 64×64, slice thickness: 5 mm). The functional study used a block design consisting of three 30-sec blocks with visual stimuli separated by four 30-sec control blocks with a black screen (Fig. 1).

C. EEG with and without simultaneous fMRI acquisition

The EEG data were collected, both simultaneously with the fMRI acquisition and in a separate session outside the MRI room, by using the same 64-channel MR compatible EEG system (BrainAmp MR 64 Plus, BrainProducts, Germany). The scalp potentials were referred to FCz and sampled at 1000 Hz for the EEG-alone recordings or at 5000 Hz for the simultaneous recordings. For the simultaneous fMRI-EEG acquisition, the EEG signals were locally amplified and digitized by two shielded and non-magnetic preamplifiers (16-bit) placed inside the magnet. The digitized EEG signals were transmitted to a PC in the control room via optical

fibers. The onsets of EPI volume acquisition were recorded in the EEG recordings by connecting the TTL output from the MRI scanner to the PC. A unipolar electrode was placed on the subject's back to record ECG signals. The locations of all electrodes and 5 landmark points (nasion, preauricular left, preauricular right,inion, and vertex) were determined by radiofrequency localizer (Polhemus Fastrak, VT).

D. fMRI data analysis

The fMRI data were analyzed using BrainVoyager QX (BrainInnovation, Netherlands). The EPI volumes underwent preprocessing including 3-D motion correction, slice scan time correction and linear trend removal. After preprocessing, the EPI volumes were aligned with the anatomical MR images for co-registration and visualization. The fMRI activation map was obtained by using a period cross correlation (CC) method. The statistical threshold was set as $CC > 0.5$.

E. EEG data analysis

The EEG data recorded inside the MRI scanner with concurrent EPI acquisition underwent the MR artifact correction by using BrainVision Analyzer (BrainVision, Germany). The gradient artifact (GA) and cardiac ballistic artifact (CBA) were removed by using the methods based on template subtraction. After the artifact correction, both the EEG data recorded with and without simultaneous EPI acquisition were filtered (0.5-40 Hz) and segmented (-100 to 400 ms around the stimulation onsets). Then EOG artifact rejection, linear trend removal and baseline correction were sequentially applied to the segmented epochs. The visual evoked potentials (VEP) were obtained by averaging 250-300 preprocessed epochs [16], [17].

F. Source imaging

The EEG source analysis was conducted in Curry 5.0 (Neuroscan, TX, USA). The EEG electrodes were co-registered with the anatomical MRIs by matching the digitized landmarks with their corresponding voxels identified in the MR images. The three-compartment (skin, skull and brain) boundary element (BE) head model was constructed from anatomical MRIs of each individual subject [18]. The conductivities of the skin, skull and brain were assumed to be 0.33, 0.0165 and 0.33 S/m respectively [19]. The 3-D distributed dipole grid was generated inside the brain volume with a 5-mm inter-dipole distance. The MNLS method was applied to reconstruct the 3-D source distribution, which can provide a unique inverse solution that is the best estimate in the least-squares sense [6], [15], [20]. The chi-square criterion method was performed to determine the optimal value of the lamda in the MNLS method (Neuroscan, TX, USA). The fMRI data were used to bias the EEG inverse solution towards those locations deemed statistically significant in the view of fMRI [6]. In the source imaging analysis, the source locations inside the fMRI activations were favored by a factor of 1.4 relative to those outside [6]. We further pinpointed the estimated source activity to specific visual areas, by visually inspecting the anatomical landmarks related to known visual areas, as well as by transforming the individual structural MRI to the Brodmann Areas atlas (BrainVoyager QX) and comparing the spatially transformed source locations with the known ranges of different visual areas. All 3D source results are displayed with a threshold set at 50% of the maximum current density [41]-[44].

III. Results

Fig. 2a and b show an example of EEG collected before and after removing MR-related artifacts, respectively. The EEG spectrogram is shown in Fig. 2c. The artifact removal algorithms appeared to be effective, since the EEG waveforms and spectrograms resembled those if collected in a clear EEG recording environment. For a single subject, Fig. 2d shows the VEP waveforms at occipital electrode Oz obtained from the EEG recorded outside and

inside the MRI scanner. A similar temporal behavior was observed in both waveforms, regardless of observable difference in amplitudes and peak latencies.

Fig. 3 summarizes the results of the fMRI activation maps and the 3-D source images for the P100 VEP component (around 100 ms) for all 5 subjects. The fMRI activation map revealed the significant BOLD responses ($CC > 0.5$) at the primary visual cortex (V1/V2), the extra-striate cortex (V3/V3A and V4) and the lateral occipito-temporal area (around V5). Without applying the fMRI spatial constraints, the 3-D source reconstructions for the P100 component based on the separate EEG recordings (Fig. 3b) were similar to those based on the EEG recordings with the concurrent fMRI acquisition (Fig. 3c), although a slight difference between them was observable. The source images also appeared to be more consistent with the fMRI activation map when the EEG and fMRI were recorded simultaneously. Compared to the low spatial specificity shown in the source estimates by using the VEP alone, the use of fMRI spatial constraints significantly improved the spatial resolution of the source reconstruction (Fig. 3d). The source regions close to V5 were revealed only when the fMRI spatial priors were applied (Fig. 3d). These findings were consistent among all five subjects as shown in Fig. 4 (I-V).

Similarly, improved source imaging results were obtained for all three VEP components (N75, P100 and N145) by integrating fMRI and EEG as compared to the EEG-alone solutions. Two typical examples for Subject #1 and Subject #4 were shown in Fig. 4 and Fig. 5 respectively. The temporal evolution of activated source regions could be further seen as follows: 1) N75 component: early V1/V2 activation; 2) P100 component: maximal V1/V2 and early V5 activations; 3) N145 component: late V1/V2 and maximal V5 activations. Particularly the noticeable was the imaged source close to V5 and its clear temporal evolution, which was not seen in the EEG-alone solutions.

IV. Discussions

From the above results, the simultaneous fMRI-EEG and separate EEG recordings had subtle difference on the extracted VEP signals as well as the resulting 3-D source reconstruction. This was mainly because the well-studied visual stimuli were adopted in the present study and the elicited neural activations were highly reproducible. For other multimodal investigations on human cognitive function or pathology, it is still desirable to acquire fMRI and EEG simultaneously to ensure that two modalities are monitoring the exact same neural processes.

The locations and temporal sequence of the imaged 3-D current density distribution were consistent with the findings reported in the previous literatures [25]-[29]. The N75-P100-N145 and P100-N145 components are known to be associated with generators in V1/V2 [26], [28], [29] and V5 [27]-[29], respectively. As demonstrated from the present results, the use of EEG provided additional temporal information to the neural activations localized in the fMRI; on the other hand, the use of fMRI improved the specificity of EEG source imaging. Under the pattern-reversal visual stimulation, the source in V5 was considerably weaker than the sources in V1/V2, probably because that V5 was much smaller in size than V1/V2 [29]; as a result, the source in V5 was often underestimated if the EEG is used alone [29]. As the V5 was deemed as activated in view of fMRI, incorporating the spatial information from fMRI into the EEG source imaging effectively revealed the V5 area as an active EEG sources at the latencies of P100 and N145.

In the present study, the fMRI-constrained 3-D current density estimation was based upon a "weighted minimum norm" inverse algorithm that allows for the incorporation of fMRI spatial information as a weighting matrix [6], [8]. This algorithm is equivalent to a Wiener filter algorithm [22], in which the fMRI information can be used to construct the source covariance

matrix [3], [5], [7]. In these algorithms, an fMRI weighting factor needs to be chosen to determine the degree of fMRI constraints. Previous computer simulation studies have suggested the fMRI weighting factor to be 10 [5], 3 [8] or 1.4 [6]. Since we used the same software, algorithm and modeling settings as in [6], a weighting factor of 1.4 was used in the present study. Future studies should be conducted to identify the optimal weighting factor, but we believe it is beyond the scope of the present investigation.

The fMRI-EEG/MEG integration may also be implemented under the empirical [24] and hierarchical [23] Bayesian frameworks. In these frameworks, the fMRI information can be incorporated to defining the prior distribution of source activity [24] or its variance [23]. An advantage of these implementations lies in its ability to estimate the degree of fMRI weighting in a data driven manner. Alternatively, the fMRI constraints may be applied in a two-step Twomey algorithm [10]. In the first step, a hard fMRI constraint is applied to confine the source space to the regions highlighted in fMRI. In the second step, the inverse solution obtained in the first step is re-entered as the initial solution to the minimum norm estimation without any spatial weighting or constraints derived from the fMRI data. Such an algorithm also avoids using any empirically determined fMRI weighting factor.

In fact, all of these algorithms attempt to deal with possible mismatches between the locations of instantaneous EEG sources and fMRI activations. Fundamentally, fMRI and EEG signals are related to different aspects of brain responses (i.e. hemodynamics and electrophysiology) [30]. Although previous investigations have demonstrated a close coupling between hemodynamic and electrophysiological responses, one cannot simply equate the activated areas viewed in fMRI as the sources of EEG signals at specific time point [3], [10]. This is mainly because of the fact that fMRI and EEG responses are generated and collected in highly different time scales [37]. Quantitative modeling of the interaction between stimuli, electrophysiological responses and fMRI signals may provide crucial insight to the relationship between cross-modal data, as well as the multimodal integration in a principled way, such as in [37]. In the present study, the fMRI analysis was based on the period cross correlation method [40], because the fMRI block-design only involves the repetition of a single stimulus condition. General linear model (GLM) may be more effective for more complex experiment designs involving multiple tasks [32]-[34]. More advanced methods are also available for choosing the threshold in fMRI statistic parametric mapping as well as EEG/MEG source imaging [35], [36].

V. Conclusions

In the present study, we have demonstrated the feasibility of fMRI-EEG simultaneous recordings and their integration for 3-D multimodal neuroimaging with enhanced spatial and temporal resolutions. Two commercial software packages (BrainVoyagerTM QX and Curry 5.0TM) are used for the data analysis; the reported procedures can be applied, without modification, to analysis of other event-related potential (ERP) studies.

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Biographies

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published by Kluwer Academic Publishers, 2005, and an associate or guest editor of over ten international journals in biomedical engineering.

Fig. 1.

Experimental design. The functional study consisted of three 30-sec blocks with visual stimuli separated by four 30-sec control blocks with a black screen. The visual stimuli were checkerboard patterns (Pattern 1 and Pattern 2) reversing at 2 Hz.

Fig. 2.

An example of the EEG spikes, the spectrogram of EEG recording and VEP waveforms after averaging. a) EEG prior to artifact removal; b) EEG after artifact removal; c) the spectrogram of EEG recording; d) VEP waveforms of Subject #1 at occipital electrode Oz.

Fig. 3.

Results of the 3-D source images at the P100 component and the fMRI activation maps for five subjects. (I) Subject #1, (II) Subject #2, (III) Subjects #3, (IV) Subjects #4 and (V) Subjects #5. (a) fMRI activation map ($CC \geq 0.5$), (b) using the MNSL method without fMRI prior knowledge from the separately recorded EEG, (c) using the MNLS method without fMRI prior knowledge from the simultaneously recorded EEG, (d) using the MNLS method with fMRI prior knowledge from the simultaneously recorded EEG. The white line shown in Fig. 3 (a) was the location of the axial view plane. The three dimensional current density was denoted as 3DCD. All results are displayed with a threshold set at 50% of the maximum current density (A/mm^2).

Fig. 4.

Results of the 3-D source images at N75, P100, N145 components and fMRI activation maps for Subject #1. (1) fMRI activation map; (2) 3-D current density; (A) using the MNLS method with fMRI prior knowledge from the simultaneously recorded EEG, (B) using the MNLS method without fMRI prior knowledge from simultaneously recorded EEG. The color bars of fMRI and 3-D current density images have been shown in Fig. 3.

Fig. 5.

Results of the 3-D source images at N75, P100, N145 components and fMRI activation maps for Subject #4. (1) fMRI activation map; (2) 3-D current density; (A) using the MNLS method with fMRI prior knowledge from the simultaneously recorded EEG, (B) using the MNLS method without fMRI prior knowledge from simultaneously recorded EEG. The color bars of fMRI and 3-D current density images have been shown in Fig. 3.