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Improved Estimation of Human Cortical Activity and Connectivity with the Multimodal Integration of Neuroelectric and Hemodynamic Data Related to Motor and Cognitive Tasks

F. Babiloni[1,2], D. Mattia[2], A. Basilisco[1], L. Astolfi[1,2], F. Cincotti[2], L. Ding[3], K. Christine[4], J. Sweeney[4], J. C. Edgar[5], G.A. Miller[5,] and B. He[3]

[1]*Department of Human Physiology and Pharmacology, Univ. of Rome "La Sapienza", Rome, Italy*
[2] *IRCCS Fondazione "Santa Lucia", Roma, Italy*
[3] *University of Minnesota, Twin Cities, Minnesota, USA*
[4] *University of Illinois, Chicago, Illinois, USA*
[5] *University of Illinois, Urbana-Champaign, Illinois, USA*

Abstract— **In the last decade, the possibility to noninvasively estimate cortical activity and connectivity has been highlighted by the application of the techniques known as high resolution EEG. These techniques include a subject's multi-compartment head model (scalp, skull, dura mater, cortex) constructed from individual magnetic resonance images, multi-dipole source model, and regularized linear inverse source estimates of cortical current density. More recently, it has proved as the use of information from the hemodynamic responses of the cortical areas as revealed by block-designed (strength of activated voxels) fMRI improves dramatically the estimates of cortical activity and connectivity. Here, we present some applications of such estimation in two set of high resolution EEG and fMRI data, related to the motor (finger tapping) and cognitive (Stroop) tasks. We observed that the proposed technology was able to unveil the direction of the information flow between the cortical regions of interest.**

Keywords— **Linear inverse source estimate, EEG and fMRI integration, Finger tapping, Stroop**

I. INTRODUCTION

It is well known that the high resolution electroencephalography (HREEG) is a brain imaging technique that provides a high temporal resolution adequate to follow the cortical activity. However, such techniques have a relatively modest spatial resolution, on the centimeter scale. In spite of a lack of spatial resolution, neural sources can be localized from HREEG data by making *a priori* hypotheses on their number and extension. On the other hand, the use of *a priori* information from other neuroimaging techniques, like functional magnetic resonance imaging (fMRI) that have higher spatial resolution, may be able to improve the localization of sources from HREEG data [1,2]. This paper deals with the multimodal integration of electromagnetic and hemodynamic data to locate neural sources responsible for the recorded EEG activity related to motor and cognitive tasks. However, in the neuroscience field the necessity to describe how different brain areas communicate one to each other is gaining more and more importance. Many approaches to this problem have been object of study during the years. Kaminski and Blinowska [3] proposed a multivariate spectral measure called the Directed Transfer Function (DTF) to determine the directional influences between any given pair of signals in a multivariate data set. In the following, we reviewed the applications of the DTF to the high-resolution EEG data obtained with the multimodal integration of EEG and fMRI we performed recently [2,4,5] on finger tapping movements, and we provide data related to the application of such connectivity estimation techniques to a set of data obtained during the Stroop task. In the standard color-word Stroop task, subjects must identify the color in which a word is written, while inhibiting the more automatic response of reading the word. The need for attentional selection is high in the so-called 'incongruent condition' in which the meaning of the word conflicts with the color in which it is written. Application of the DTF to estimated cortical activity during the Stroop task aimed to unveil the direction of information flow between several cortical region of interest and functionally differentiate two experimental conditions for congruent and incongruent stimuli.

II. METHODS

High-resolution EEG and fMRI recordings were performed during the execution of motor (finger tapping) as well as cognitive (Stroop) tasks in a group of healthy subjects. The estimation of cortical activity from high-resolution EEG recordings and fMRI information was performed by solving the associated linear inverse problem, as described in [5]. We also estimated the reliability of the cortical activity solutions by solving the multimodal integration problem. Since not all the modeled sources have the same degree of sensitivity to the measurement noise, we had to estimate the projection of such EEG noise onto the cortical surface by using the computed inverse operator. It can be demonstrated that under very general circumstances, the following normally-distributed z score estimator can be obtained for each j-th cortical location and for each time point t

$$\mathbf{z}_j(t) = \frac{\mathbf{G}_{j\cdot} \cdot \mathbf{b}(t)}{\sqrt{\mathbf{G}_{j\cdot}\mathbf{C}(\mathbf{G}_{j\cdot})'}} \qquad (1)$$

where $\mathbf{C}$ is the estimated noise covariance matrix and $\mathbf{G}_{j.}$ is the j-th row of the inverse operator matrix. The uncorrected threshold for the z-score level at 5% is 1.96. Values of z exceeding this threshold represent levels of estimated cortical activity that are unlikely to be due to chance alone but are related to the task performed by the subject.

The Directed Transfer Function (DTF) technique [3] is a full multivariate spectral measure, used to determine the directional influences between any given pair of signals in a multivariate data set. It is computed on a Multivariate Autoregressive model (MVAR) that simultaneously models the whole set of signals. Details of the implementation of the DTF to estimated cortical signals are provided in the literature [4, 5]. The DTF was applied to the cortical signals estimated by the solution of the linear inverse problem in particular regions of interest (ROIs) segmented on the cortical model according to the Brodmann areas.

III. RESULTS

A. *Estimation of cortical activity in finger tapping task*

Hemodynamic fMRI data collected from the experimental subjects during both the motor and the cognitive tasks served as a priori information to constrain the solution of the linear inverse problem [5]. Using the linear inverse procedure, the estimation of the current density waveforms for the selected ROIs was then obtained. In order to define the statistical significance of these cortical estimated waveforms, the z-score transformation was applied following eq 1. The estimated z-score waveforms are represented for some selected ROIs in Figure 1 for the task related to the finger tapping movement. Note that the z-score scale of the waveforms ranges from 0 (the baseline) to 10; this latter value corresponding to a level of statistical significance equal to $p < 10^{-7}$. The use of a high values of z score is appropriate, since the uncorrected level for statistical significance of the estimated waveforms is only equal to 1.96 ($p < 5\ 10^{-2}$). However, we used an increased level of statistical significance to discuss the obtained data ($z = 5$, $p < 10^{-5}$) in order to avoid the risks of the so-called alpha error inflation. This alpha inflation is related to the increase of the probability of obtaining significant results by chance alone, due to the execution of multiple simultaneous univariate tests.

Cortical activity was significantly different from baseline in the left ROIs representing parietal (BA 5), premotor (BA 6A), sensorimotor (BA 3, 2, 1, BA 4) and prefrontal (BA 8 and BA 9) cortical areas, whereas a similar statistical engage has been observed on the right hemisphere only for the ROIs corresponding to premotor (BA 6A) and prefrontal (BA 8) cortical areas.

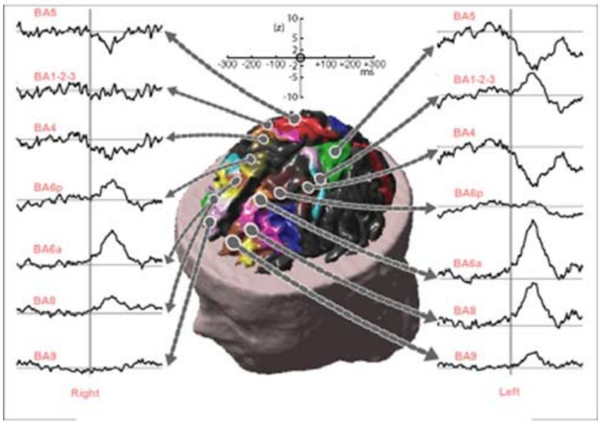

Fig.1. Estimates of the statistical significance of the cortical activity in selected ROIs depicted on the realistic representation of the cortex in Subject #1. The task was the finger tapping of the right hand. Such estimation was performed first by estimating the cortical activity with the use of the a priori information from the hemodynamic measurements during the solution of the linear inverse problem. Then, in order to obtain the statistical significance of cortical estimated waveforms, the z-score transformation was first applied and then represented. Note the z-score scale of the waveforms, ranging from 0 (the baseline) to 10; this latter value corresponding to a level of statistical significance equal to p < 10-7. The figure at the center shows the different ROIs drawn on different colors on the cortical surface reconstruction of Subject #1.

B. *Estimation of cortical connectivity in finger tapping task*

After the solution of the linear inverse procedure, the estimation of the current density waveforms in the employed ROIs were obtained as described in the Methods Section. Connectivity estimations were performed by DTF after the computation of the statistical threshold via the shuffling procedure described previously. Fig. 2 shows the cortical connectivity patterns obtained for the period preceding the movement onset in all the subjects examined during the finger tapping task. Here, we present the results obtained for the connectivity pattern in the alpha band (8-12 Hz), since the ERP data related to the movement preparation and execution are particularly responsive in such frequency interval (for a review, see [4]). The presence of a functional connection is represented with an arrow, moving from a cortical area toward another one. The arrow colors and sizes code the level of strength of the connection. The labels indicate the names of the ROIs employed. Only the cortical connections statistically significant at $p < 0.01$ are represented, after the computation of the shuffling procedure described above. Note that the connectivity patterns during the period preceding the movement in the alpha band involves mainly the parietal and sensorimotor ROIs functionally connected with the left and right premotor cortical ROIs and both the prefrontal ROIs. The stronger functional connections are relative to the link between the premotor and prefrontal areas of both cerebral hemispheres. After the preparation and the beginning of the finger movement light changes in the connectivity patterns can be noted.

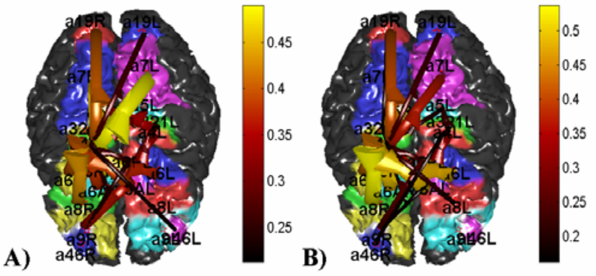

Fig.2. Cortical connectivity patterns obtained for the period preceding and following the movement onset in a representative subject, in the alpha (8-12 Hz) frequency band. Patterns are shown on the realistic cortical envelope of the subject analyzed, obtained from sequential MRIs. The cortex is seen from above, the frontal cortex is located at the bottom, the occipital cortex is located on the top. Cortical functional connections are represented with arrows, that represent movement of information from one cortical area toward another. The arrows' colors and sizes code the level of strengths of the connections. 5A: Connectivity patterns obtained from EP data before the onset of the finger movement (electromyographic onset; EMG), seen from above. 5 B: Connectivity patterns obtained after the EMG onset. Only the cortical connections statistically significant at $p < 0.01$ are represented.

C. *Estimation of cortical connectivity for the Stroop task*

Fig. 3 shows the cortical connectivity patterns obtained for the Stroop task in the time period preceding the subject's response to the visual stimuli in the gamma frequency band. The contrast between the congruent and the incongruent connectivity patterns estimated by solving the associated linear inverse problem mainly highlight bilateral functional links between the prefrontal areas (located on the bottom of the Figure). This is especially evident in some of the individual subjects. Here, all the connectivity estimations presented are statistically significant at $p<0.01$. The colors on the cortex are relative to the particular region of interest analyzed for this particular task. Unlike the cortical segmentation presented in the case of finger movements, here we analyzed also the contribution of anterior cingulate cortex, which is believed to have an important role in the Stroop paradigm.

IV. DISCUSSION

A. *Imaging brain connectivity during motor tasks*

The brain connectivity associated with motor task during visually guided finger tapping movements were studied [4,5]. The main findings obtained with the multimodal integration of ERP and fMRI data [5] are related to the activation of a network involving the right frontoparietal cortical structures. The flow of the connections moves from the parietal and premotor areas toward the right and left prefrontal areas. These results have also been corroborated by the inflow-outflow analysis, indicating how the ROIs located at the parietal (BA 5) and premotor areas (BA 6) could be the source of an activity which spreads and reaches virtually all the other ROIs considered, from the occipital (BA 19) to the prefrontal (BA 9, 46) areas of both hemispheres.

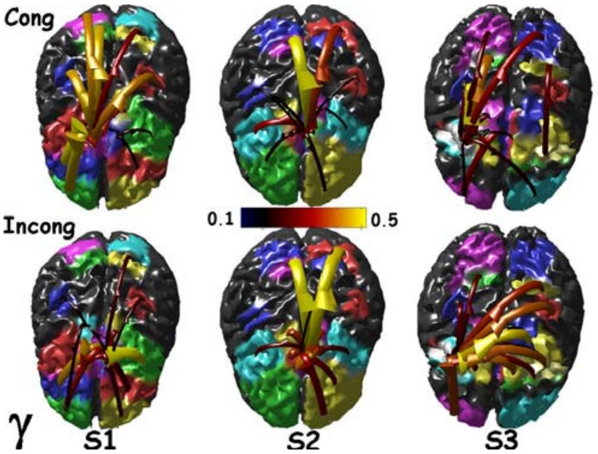

Fig.3. Cortical connectivity patterns obtained for the period preceding and following the movement onset in a representative subject, in the gamma (24-40 Hz) frequency band. Same conventions as in Fig.3. First row is relative to the connectivity estimation for the congruent task evaluated for three healthy subjects (S1, S2, S3). The second row presents the connectivity patterns relative to the incongruent task. Note as the communication between the two hemispheres increases during the incongruent task with respect to the congruent one, especially for the prefrontal areas

Beside the highlight on the technology potential, the physiological features of the reported findings are consistent with and further integrate those already known in the literature on finger tapping movements, expressed by both neuroelectric and hemodynamic measurements. In a previous fMRI study, it has been found that the right-sided dorsal premotor cortex was preferentially activated during left hand finger tapping movements together with the bilateral visual cortex, where the visual pacing stimulus was processed [6]. In addition, the same study described a significant activation of the ventral premotor cortex in conjunction with the parietal cortices. These findings suggest that bilateral visual activation could trigger the timing of finger movements by transferring the sensory pacing codes via the left and right `dorsal' pathways to the prefrontal cortex, where stimulus–response are matched. Of special interest is our observation of the involvement of the occipital area (BA 19) which received information from the ROIs more directly involved in the motor task processing, namely those depicting the premotor and parietal areas. The connectivity patterns of the premotor and prefrontal ROIs reported here are in agreement with earlier electromagnetic findings, suggesting that the dorsolateral and the ventral premotor cortices are the specific candidate for movement execution guided by sensory information as opposed to movements carried out with no sensory control [7]. Finally, the present activity noted in the parietal area (BA 5) could reflect the role for this region in somatosensory-motor integration. Indeed, it has been hypothesized that this area could be regarded as a higher-order somatosensory zone devoted to the analysis of proprioceptive information from joints for appropriate motor control [8].

B. Imaging brain connectivity during cognitive process

The Stroop task is commonly employed in studies of selective attention and has been found to be sensitive to damage in prefrontal regions. For incongruent stimuli, PET and fMRI studies have shown increased activation of a network of anterior brain regions. Most studies report activation of the anterior cingulate cortex (ACC) and the frontal polar cortex, and several authors hint at changes in regional cerebral blood flow (rCFB) in posterior cingulate and other posterior regions [9,10].

The connectivity analysis indicated intense, bilateral ACC activity during the task. The number of directed interactions is similar across the several frequency bands, but there are some differences in the connectivity structure across tasks. The increased activity in the prefrontal cortical regions is in agreement with previous scalp observations. In an EEG study, West and Bell reported increased spectral power for medial (F3, F4) and lateral (F7, F8) frontal sites, as well as for parietal regions (P3, P4) [11]. They suggested that greater activation of the parietal cortex resulted from interaction between prefrontal and parietal regions during the suppression of the influence of the irrelevant word meaning. Interaction between parietal and frontal sites has been advocated as an explanation for the activation of posterior areas [9,11]. Possibly, the minimization of the influence of the irrelevant word information prompts directed interactions from parietal toward frontal sites. In a previous coherence study [12], increased coherences between parietal and frontal sites were also observed for the late time interval. This behaviour is not detectable at the scalp level. With the application of advanced high-resolution EEG methodologies, including realistic cortical modelling, solution of the linear inverse problem, and the application to the estimated cortical signals of the Directed Transfer Function, it became appreciable.

In summary, we have studied brain activity and connectivity assocaiated with the motor task during finger tapping, and during cognitive process of the Stroop task, by using noninvasive methodologies involving the multimodal integration of electrophysiological and hemodynamic measurements. These methodologies provide statistical significance for the estimated cortical activations in the selected ROIs and show the time-varying pattern of connectivity eventually developing during a variety of tasks in humans. This body of methodologies can be suitable for the analysis of simple as well as complex movements or cognitive tasks in humans.

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