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Cortical Connectivity Patterns During Imagination Of Limb Movements In Normal Subjects And In A Spinal Cord Injured Patient

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Abstract— **The problem of the definition and evaluation of brain connectivity has become a central one in neuroscience during the latest years, as a way to understand the organization and interaction of cortical areas during the execution of cognitive or motor tasks. In this paper we propose the use of the DTF method on cortical signals estimated from high resolution EEG recordings. An application of the proposed technique to the estimation of cortical connectivity pattern in normal subjects and in one spinal cord injured patient is also provided.**

Keywords— **Directed Transfer Function, High resolution EEG, imagined movement, Spinal Cord Injured patient**

I. INTRODUCTION

The necessity to describe how different brain areas communicate with each other is gaining more and more importance in the neuroscience field [1]. The increase of non-invasive brain imaging methods (like functional Magnetic Resonance Imaging, fMRI; high resolution electroencephalography, EEG, or magnetoencephalography, MEG) that return information about the different cerebral areas activation during a motor or cognitive task makes the concept of brain connectivity a central one. In fact, static images of brain regions activated during particular tasks do not convey the information of how these regions communicate one to each other. Hence, the concept of brain connectivity is viewed as central for the understanding of the organized behavior of cortical regions beyond the simple mapping of their activity. This organization is thought to be based on the interaction between different and differently specialized cortical sites. Cortical connectivity estimation aims at describing these interactions as connectivity patterns which hold the direction and strength of the information flow between cortical areas. To achieve this objective, several methods have been already applied on data gathered from both hemodynamic and electromagnetic techniques [2-3]. The computational methods proposed to estimate how different brain areas are working together typically involve the estimation of some covariance properties between the different time series measured from the different spatial sites during motor and cognitive tasks studied by EEG and fMRI techniques [4]. So far, the estimation of functional connectivity on EEG signals has been addressed by applying either linear and non-linear methods which can both disclose the direct flow of information between scalp electrodes in the time domain, although with different computational demands [5-6]. In addition, due to the evidence that important information in the EEG signals are often coded in the frequency rather than time domain (reviewed in [7]), attention has been focused on detecting frequency-specific interactions in EEG or MEG signals by analyzing the coherence between the activity of pairs of structures [5-6]. Coherence analysis has not however, a directional nature (i.e. it just examines whether a link exists between two neural structures, by describing instances when they are in synchronous activity) and it does not provide directly the direction of the information flow. In this respect, a multivariate spectral technique called Directed Transfer Function (DTF) was proposed [6] to determine the directional influences between any given pair of channels in a multivariate data set. Such connectivity estimation procedure has been applied to the cortical data estimated by high resolution EEG recordings. In fact, this EEG techniques includes the use of a large number of scalp electrodes, realistic models of the head derived from structural magnetic resonance images (MRIs), and advanced processing methodologies related to the solution of the linear inverse problem. These methodologies allow the estimation of cortical current density from sensor measurements [8-9].

The interest in the clinical application of these novel neuroengineering techniques for the estimation of brain connectivity is in the field of the analysis of EEG data related to the imagination of limbs movements, and in the possible use of this technique in the area of brain computer interface. The interest in this field is gaining more and more importance. In fact, only in Europe there are currently 300,000 paralyzed persons, with a mean age of 31 years (a rather low mean age, due to the fact that one of the main causes of paralysis is car crash), and about 5,000 new cases occur every year. Traumatic spinal cord injuries (SCI) can induce sensorimotor dysfunctions (para/tetraplegia) due to a disconnection between paralyzed limbs and supraspinal centers. At present, several hemodynamic neuroimaging

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evidences converge on the position that in stabilized SCIs, the cortical motor areas associated with movements of the body below the damage level can still be activated by mental rehearsal of motor act or even by motor attempt involving paralyzed limbs [10]. However, it is well know that hemodynamic images cannot convey relevant information at the temporal scale necessary to following the brain dynamics (tenths of milliseconds). On the other hand, temporal scales of hundreds of milliseconds are necessary to interact with the external word in an efficient way, and this is a prerequisite for any possible brain-controlled prosthetic devices, i.e. devices that can be controlled without any over muscular movement by the final user. In this respect, the use of particular spectral features from non invasive EEG recordings have been demonstrated to be useful to recognize the user's intentions. The aim of this paper is to present advanced connectivity estimation techniques for the EEG and to suggest a possible use of them in the context of the brain computer interface.

II. Methods

High resolution EEG recordings in normal subjects and in an SCI patient.

Three healthy subjects and one subject with a spinal cord injury (SCI) participated in the study. Informed consent was obtained in each subject after explanation of the study, which was approved by the local institutional ethics committee. The SCI was of traumatic aetiology and located at the cervical level (C7) and the patient had not suffered for a head or brain lesion associated with the trauma leading to the injury. The patient was unable to move his upper and lower limbs. For the EEG data acquisition, subjects were comfortably seated on a reclining chair, in an electrically shielded, dimly lit room. They were asked to perform a brisk protrusion of their lips (lip pursing) while they were performing (for the normal subjects) or attempting (SCI patient) a right foot movement. The task was repeated every 6-7 seconds, in a self-paced manner, and the 100 single trials recorded will be used for the estimate of the Directed Transfer Function (DTF, see below). A 96-channel EEG system (BrainAmp, Brainproducts GmbH, Germany) was used to record electrical potentials by means of an electrode cap, accordingly to an extension of the 10-20 international system. Structural MRIs of the subject's head were taken with a Siemens 1.5T Vision Magnetom MR system (Germany).

Applying the tools for the estimation of cortical activity and connectivity

We estimated the cortical activity from high resolution EEG recordings, by using realistic head models and a cortical surface model with an average of 5,000 dipoles, uniformly disposed. The estimation was obtained by the application of the linear inverse procedure. Cortical activity were then estimated in ROIs generated by the segmentation of the Brodmann areas (B.A.) on the accurate cortical model used. Bilateral ROIs considered in this analysis were the primary motor areas for the foot (MIF) and for the lip movement (A4_Lip), the proper supplementary motor area (SMAp), the standard premotor area (A6) and the cingulated motor area (CMA). The label of the cortical areas have also a postfix characterizing the considered hemisphere (R, right, L, left). Such ROIs were segmented on the basis of Talairach coordinates and anatomical landmarks available. For each time point of the recorded EEG we solved the linear inverse problem, estimated the magnitude for each one of the thousand dipoles used for cortical modelling. Then, we computed the average of the magnitude of such dipoles in each ROI considered, for each time point considered. The resulting cortical waveforms, one for each predefined ROI, were then processed for the estimation of cortical connectivity by using the Directed Transfer Function. The DTF is a full multivariate spectral measure, used to determine the directed influences between any given pair of signals in a multivariate data set. Let be X a set of EEG measurement from k channels at time t: $\underline{X} = [X_1(t), X_2(t), \ldots, X_k(t)]^T$, and suppose that X is adequately described by the following MVAR process:

$$\underline{X} = \sum_{i=1}^{p} -\underline{\underline{A}}(i)\underline{X}(t-i) + \underline{E}(t) \tag{1}$$

which is equal to:

$$\sum_{i=0}^{p} \underline{\underline{A}}(i)\underline{X}(t-i) = \underline{E}(t) \quad \text{with } A(0) = I \tag{2}$$

where E(t) is the vector of multivariate zero-mean uncorrelated white noise process, $A_1, A_2, \ldots A_p$ are the matrices of model coefficients and p is the model order. In order to investigate the spectral properties of the examined process, this equation is transformed to the frequency domain as follows:

$$A(f)\,X(f) = E(f) \tag{3}$$

where A(f) is the Fourier transform of the A(i) process. The Fourier transformed equation could read as

$$X(f) = A^{-1}(f)\,E(f) = H(f)\,E(f). \tag{4}$$

where H(f) is the transfer matrix of the system, whose element Hij represents the connection between j-th input and i-th output of the system. The spectral matrix of the process can be written as:

$$S(f)=X(f)\,X(f)^{*}=H(f)V\,H(f)^{*} \tag{5}$$

where V is the spectral matrix of the white noise input. The DTF from channel j to i , representing the causal influence from j to i, is defined as:

$$\theta_{ij}^{2}(f) = \left|H_{ij}(f)\right|^{2} \tag{6}$$

In order to be able to compare the results obtained for data strings with different power spectra, a normalization is performed by dividing each element by the squared sums of all elements of the relevant row, thus obtaining the *normalized DTF*:

$$\gamma_{ij}^2(f) = \frac{|H_{ij}(f)|^2}{\sum_{m=1}^{k} |H_{im}(f)|^2} \quad (7)$$

which expresses *the ratio of influence of channel j to channel i with respect to the influence of all other channels on i*.

The capability of the DTF to correctly retrieve the connectivity pattern in the standard condition of the EEG recordings was assessed by a simulation study. In the simulations, test signals with predefined connectivity patterns were generated starting from a model of one of the population, based on the equations proposed by Wendling et al. [11]. The statistical analysis performed returns that during simulations, DTF is able to estimate correctly the imposed connectivity patterns under reasonable operative conditions, i.e. when data exhibit a SNR of at least 3 and a length of at least 75 seconds of non-consecutive recordings at 64 Hz of sampling rate, equivalent, more generally, to 4800 data samples.

III. Results

A. Estimated connectivity patterns

After the solution of the linear inverse procedure, the estimation of the current density waveforms in the employed ROIs were obtained as previously described. Statistical significance of the cortical connections was obtained by comparing the estimated cortical connectivities with respect to the mean values of the distribution of the random connectivity values between the cortical signals once the deterministic interdependency between these signals were removed. This was achieved by shuffling the phase of the estimated cortical data. Fig.1 shows the cortical connectivity patterns during the period preceding the lips movement onset, and hence related to the preparation of the foot and lips movement in all the three normal subjects examined. Here, we present the results obtained for the connectivity pattern in the gamma band. The presence of a functional connection is represented with an arrow, moving from a cortical area toward another one. In the inset, the arrow color level and sizes codes the level of strength of the connection. In the labels, the names of the ROIs employed are indicated. Only the cortical connections statistically significant at $p < 0.01$ are represented. Note that the connectivity patterns, estimated in the gamma band, presents strong functional connections between the CMA and the premotor motor areas of both cerebral hemispheres. It can be appreciated the substantial equivalence of the connectivity patterns estimated for the three normal subjects. Hence, the functional directional connections during the preparation of the foot movement are generated in the gamma band from the cingulated areas and spread toward the supplementary motor areas. These patterns have to be compared with that estimated in the SCI patient, during the performance of a similar experimental task.

Cortical connectivity patterns in SCI

The EEG recording and the estimation of the cortical activity and connectivity for the SCI patient during the task was accomplished in the same way already described for the normal subjects. Fig. 2 depicts the connectivity pattern in the gamma frequency band before the execution of the lip movement accompanied to the attempt to move the paralyzed limb. It can be noted how this pattern is similar to those generated by the normal subjects during the preparation to the foot movement. Also in this case the connectivity flow is generated from the cingulated areas and spreads to the supplementary motor areas. Same similarities were observed for the connectivity patterns already generated in the other frequency bands examined between the SCI patient and the group of three normal subjects.

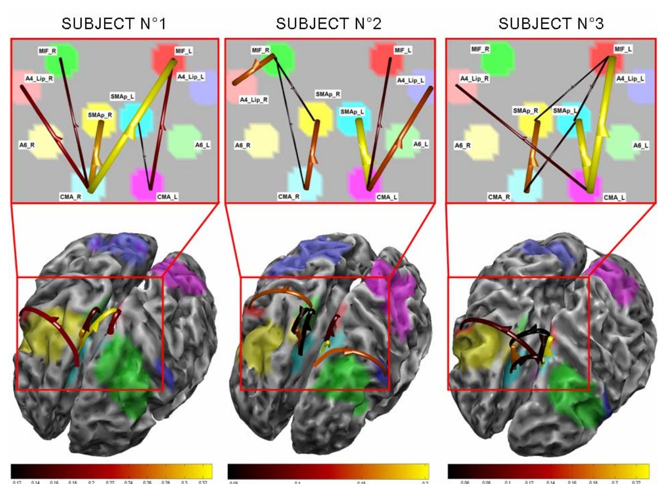

Fig.1 The cortical connectivity patterns obtained for the period preceding the lips movement in three normal subjects, analyzed in the gamma frequency band. Cortical functional connections are represented with arrows, that moves from the source cortical area toward the target one. In the inset, the arrows' colors and sizes code the level of strengths of the connections. Bottom: connectivity patterns obtained from EEG data represented on the realistic cortical reconstruction of each experimental subject, obtained from sequential MRIs, seen from left and above. Top: Details of the connectivity patterns for the central areas. Only the cortical connections statistically significant at $p < 0.01$ are represented.

IV. Discussion

In this paper we propose a study on the application of the DTF technique to the cortical activity estimated by using realistic models of head as volume conductor and high resolution EEG recordings. This has been possible by the actual state of the art of the neural engineering techniques related to the analysis of high resolution EEG data. The main results here provided highlight the possible existence of a common pattern of cortical connectivity during the execution (normal) or the imagination (SCI patient) of a foot limb movement. The activity noted in the cingulated and supplementary motor areas in the present study is consistent with the role that such cortical areas have in the organization and in the performance of simple foot movements. This finding, if confirmed in a larger population of normal subjects as well as SCI patients, could open the way for the use of such feature in a clinical context, for instance in the brain computer interface area. It is worth of note that the presented technology can be applied to retrieve patterns of cortical connectivity during more complex clinically relevant tasks in patients, by using non invasive EEG recordings. Examples in this respect will include the use of the connectivity pattern study in the analysis of the brain damage generated by a stroke, as well as an analysis of the possible recovery of the brain motor areas during the rehabilitation paths.

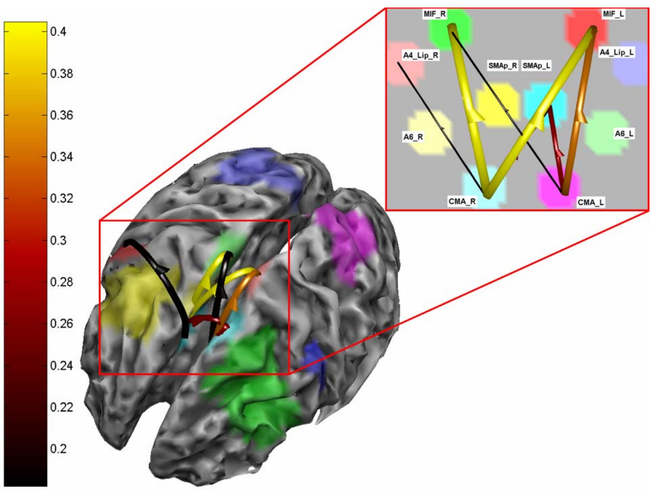

Fig.2 Cortical connectivity patterns obtained for the period preceding the movement onset in a SCI patient, in the gamma frequency band. Same convention than in the previous figure. Only the cortical connections statistically significant at $p < 0.01$ are represented.

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