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Community structure of cortical networks in spinal cord injured patients

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Abstract— **In the present study, we estimated the cortical networks were from high-resolution EEG recordings in a group of spinal cord injured patients and in a group of healthy subjects, during the preparation of a limb movement. Then, we use the Markov Clustering method to analyse the division of the network into community structures. The results indicate large differences between the injured patients and the healthy subjects. In particular, the networks of spinal cord injured patient exhibited a higher density of clusters. In the Alpha (7-12 Hz) frequency band, the two observed largest communities were mainly composed by the cingulate motor areas with the supplementary motor areas, and by the pre-motor areas with the right primary motor area of the foot. This functional separation could reflect the partial alteration in the primary motor areas because of the effects of the spinal cord injury.**

I. INTRODUCTION

Finding the communities within a cerebral network allows identifying the hierarchy of functional connections within a complex architecture. This opportunity would represent an interesting way to improve the basic understanding of the brain functioning. Indeed, some cortical regions are supposed to share a large number of functional relationships during the performance of several motor and cognitive tasks. This characteristic leads to the formation of highly connected clusters within the brain network. These functional groups consist in a certain number of different cerebral areas that are cooperating more intensively in order to complete a task successfully.

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Methods to detect the community structures in a graph, i.e. tightly connected group of nodes are now available in the market [1]. Communities (or clusters or modules) are groups of vertices that probably share common properties and/or play similar roles within the graph [2]. Hence, communities may correspond to groups of pages of the World Wide Web dealing with related topics [3], to functional modules such as cycles and pathways in metabolic networks [4,5], to groups of affine individuals in social networks [6,7], to compartments in food webs [8,9] and so on.

In the present paper, we present a study of the structural properties of functional networks estimated from high-resolution EEG signals in a group of spinal cord injured patients during the preparation of a limb movement. Then we analyse the networks by studying their structure in communities, and we compare the results with those obtained from a group of healthy subjects.

II. METHODS

A. Experimental Design

All experimental subjects participating in the study were recruited by advertisement. The spinal cord injured (SCI) group consisted of five patients (age, 22-25 years; two females and three males). Spinal cord injuries were of traumatic etiology and located at the cervical level (C6 in three cases, C5 and C7 in two cases, respectively). The control (CTRL) group consisted of five healthy volunteers (age, 26–32 years; five males). Informed consent was obtained in each subject after the explanation of the study, which was approved by the local institutional ethics committee. For 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 (healthy subjects) or attempting (SCI patients) a right foot movement. The choice of this joint movement was suggested by the possibility to trigger the SCI’s attempt of foot movement. A 96-channel system (BrainAmp, Brainproducts GmbH, Germany) was used to record EEG electrical potentials by means of an electrode cap. The electrode cap was built accordingly to an extension of the 10-20 international system to 64 channels. Structural MRIs of the subject’s head were taken with a Siemens 1.5T Vision Magnetom MR system (Germany). 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 functional connectivity by means of the Directed Transfer Function (DTF, see following paragraph).

B. Cortical Activity and Functional Connectivity

Cortical activity from scalp EEG recordings was estimated by using realistic head models. The head compartments were modeled from MRI images. The estimation of the current density strength on the cerebral cortex was obtained by solving the Linear Inverse problem, according to techniques described in previous papers [10,11]. By using the passage through the Tailairach coordinates system, twelve Regions Of Interest (ROIs) were then obtained by segmentation of the Brodmann areas on the accurate cortical model utilized for each subject. The ROIs considered for the left (_L) and right (_R) hemisphere are: the primary motor areas for foot (MF_L and MF_R) and lip movement (ML_L and ML_R); the proper supplementary motor area (SM_L and SM_R); the standard pre-motor area (6_L and 6_R); the cingulated motor area (CM_L and CM_R) and the associative Brodmann area 7 (7_L and 7_R). Then, the average activity of dipoles within each ROI was computed. In order to study the preparation to an intended foot movement, a time segment of 1.5 seconds before the lips pursing was analyzed; lips movement was detected by means of an EMG. The resulting cortical waveforms, one for each predefined ROI, were then simultaneously processed for the estimation of functional connectivity by using the Directed Transfer Function, a full multivariate spectral measure, used to determine the causal influences between any given pair of signals in a multivariate data set [12]. In the present study, we selected four frequency bands of interest (Theta 4-7 Hz, Alpha 8-12 Hz, Beta 13-29 Hz and Gamma 30-40 Hz) and we gathered the respective cortical networks by averaging the values within the respective range. In order to consider only the functional links that are not due to chance, we adopted a Montecarlo procedure. In particular, we contrasted each DTF value with a surrogate distribution of one thousand DTF values obtained by shuffling the signals' samples in the original EEG dataset. Then, we considered a threshold value by computing the 99th percentile of the distribution and we filtered the original DTF values by removing the edges with intensity below the statistical threshold.

C. Network Community Structures

In order to detect the community structures, we used the Markov Clustering (MCl) algorithm [13]. The algorithm is based on the properties of the dynamical evolution of random walkers moving on the graph. This approach is useful since it manages to achieve reliable results in the case of weighted and directed graphs, and also when the graph contains self-loops, i.e. edges connecting a node to it. Since a community is a group of densely connected nodes, a random walker that started in a node of a given community will leave this cluster only after having visited a large number of the community's nodes. Hence, the basic idea implemented in the algorithm is to favour the random motion within nodes of the same community. This is obtained by alternating the application of two operators on the transition matrix of the random walk: the expansion operator and the inflation one. The expansion operator applied on a given matrix returns its square power, while the inflation operator corresponds to the Hadamard power of the same matrix, followed by a scaling. In practice, the algorithm works as follows:

1. Take the adjacency matrix A and add a self-loop to each node, i.e. set A_{ii}=1 for i=1,2,…N.

2. Obtain from A the transition probability matrix W, that describes the random motion: $$W_{ij} = \frac{A_{ij}}{\sum_k A_{kj}}$$ Every element W_{ij} expresses the probability to go from j to i in one step. W is a stochastic matrix i.e. a matrix of non-negagtive elements and where the sum of elements of each column is normalized to one: $\sum_{i=1}^{N} W_{ij} = 1$;

3. Take the square of W (expansion step);

4. Take the rth power ($r>1$) of every element of W^2 and normalize each column to one to obtain a new stochastic matrix W '(inflation step): $$W' = \frac{\left[\left(W^2\right)_{ij}\right]^r}{\sum_k \left[\left(W^2\right)_{kj}\right]^r};$$

5. Go back to step 3.

Step 3 corresponds to computing random walks of "higher-lengths", that is to say random walks with many steps. Step 4 will serve to enhance the elements of a column having higher values. This means, in practice, that the most probable transition from node j will become even more probable compared to the other possible transitions from node j. The algorithm converges to a matrix invariant under the action of expansion and inflation. The graph associated to such matrix consists of different star-like components; each of them constitutes a community (or cluster) and its central node can be interpreted as the basin of attraction of the community.

III. Results

Figure 1 shows the realistic head model obtained for a representative subject. The twelve ROIs used in the present study are illustrated in colour on the cortex model that is grey coloured. At the bottom side of the figure 1, we report the adjacency matrices representing the cortical networks estimated, in the Alpha frequency band, from the two analyzed populations during the movement preparation. The level of grey within each matrix in figure encodes the number of subjects that hold the functional connection identified by row *i* and column *j*.

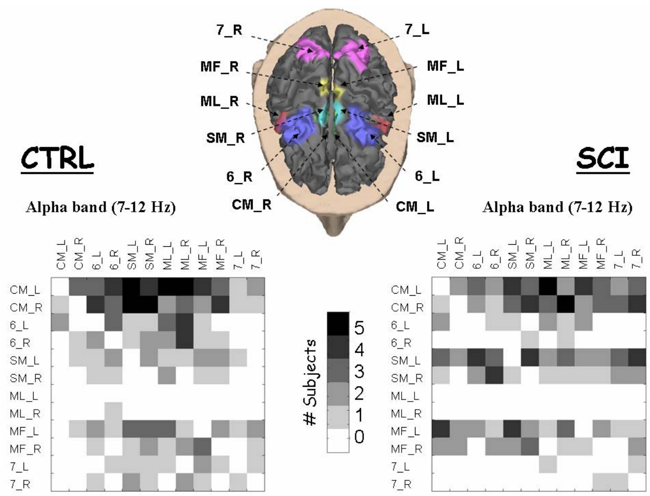

Fig. 1. *Top* – Reconstruction of the head model from magnetic resonance images. The twelve regions of interest (ROIs) are illustrated in colour on the grey cortex and labelled according to previously defined acronyms. *Bottom Left* – Adjaceny matrix for the control group (CTRL) in the Alpha (7-12 Hz) band. The level of grey encodes the number of subjects that hold the functional connection identified by the row *i* and column *j*. *Bottom Right* – Adjacency matrix for the patients group (SCI) in the Alpha band. Same conventions as above.

The identification of functional clusters within the cortical networks estimated in the control subjects and in the spinal cord injured patients during the movement preparation was addressed through the MCl algorithm (see Methods – *C. Network Community Structures*). For the case under study here, we have decided to adopt the granularity *r* =1.5, that is a value in the plateau. Usually good values of *r* are in the range (1.3) [13].

For this value of *r,* the average number of clusters in the Alpha band is equal to 3.2 for the cortical networks of the control subjects, while it is equal to 5 for the the spinal cord injured patients. In the Beta band, the average number of cluster is 3.4 for the CTRL networks and 4.6 for the SCI networks, as can be observed at the bottom of the figure 3.

Figure 2 illustrates the partitioning of the cortical networks estimated in the Alpha band for a representative subject of the control (CTRL) group and for a representative patient of the spinal cord injured (SCI) group. Functional networks are represented as three-dimensional graphs on the realistic head model of the experimental subjects. The colour of each node, located in correspondence to each cortical area (ROI), encodes the cluster to which the node belongs.

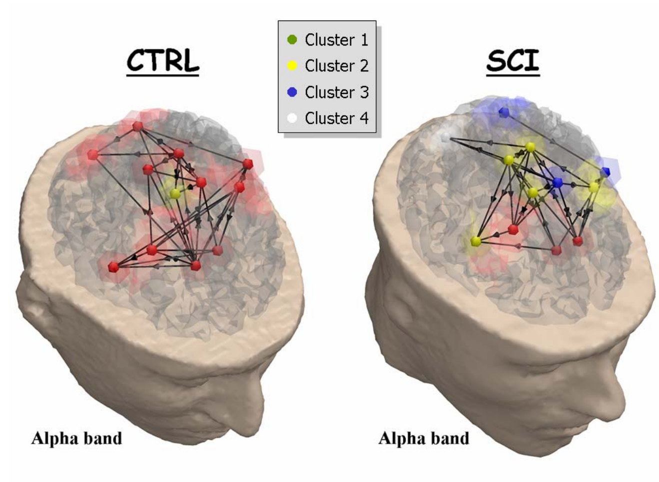

Fig 2. Graphical representation of the identified clusters of ROIs within the functional networks estimated from a representative control (CTRL) subject and spinal cord injured (SCI) patient during the movement preparation in the Alpha band. The functional network is illustrated as a three-dimensional graph on the realistic cortex model. Spheres located at the barycentre of each ROI represent nodes. Black directed arrows represent edges. The graph partitioning is illustrated through the nodes colouring. Nodes with same colours belong to the same cluster.

In the following, the functional clusters detected within the cortical networks in all the subjects and patients participating in the present study are summarized.
In the Alpha band, the CTRL networks do not present a particularly complicate division into clusters, since for each subject the large part of the cortical areas belong to a unique large community. In general, the SCI networks are organized in a larger number of clusters more clustered, and two main communities can be observed. The first community is mostly composed by the cingulate motor areas (CM_L and CM_R), the supplementary motor areas (SM_L and SM_R) and the left primary motor area (MF_L). The second community is predominantly composed by the left pre-motor areas (6_L) and the right primary motor area of the foot (MF_R). The remaining ROIs tend to form isolated groups.
In the Beta band both the cortical networks of the control and spinal cord injured group tend to get organized in two main modules. In particular, while for both the populations the first cluster is principally composed by the cingulate motor areas CM_ L and CM_R, the SM_L and SM_R and the MF_L and MF_R, the second cluster does not present a common set of ROIs across the experimental subjects neither in the CTRL and SCI group.

IV. Discussion

The obtained results reveal a different average number of clusters for the functional networks of the spinal cord injured patients and the control subjects in both the main spectral contents. In particular, in the Alpha band the SCI network presents an average number of modules equal to five, while the CTRL network appears to be divided in three main groups. In the same band, the cortical areas of control subjects do not present a clear partitioning in different modules. They rather appear to belong to a unique community, meaning that they are all involved, in the same way, in the exchange of information during the movement preparation. The analysis of the functional communities within the networks obtained for the spinal cord patients revealed a higher tendency to form separate clusters. The pre-motor areas (Brodmann 6_L and 6_R), the associative regions (Brodmann 7_L and 7_R) and the right primary motor area of the foot (MF_R) break away from the large module that was found in the networks of the CTRL group. In particular, the area MF_R and the region 6_L belong to the same cluster in at least three experimental patients. This result reveals that the SCI networks exhibit a high communication between their frontal pre-motor areas and primary motor areas, which are already known to be active during the successful execution of a simple movement [14].

In the Beta band, the average number of identified clusters in the SCI networks and in the CTRL networks is similar. The ROIs that appeared to belong to different clusters in the Alpha band are in this case functionally tied in the same community.

Summing up, the present study focused on the identification of the functional communities within cortical networks estimated in a group of healthy subjects and in a group of spinal cord injured patients. In particular, in the Alpha band the SCI networks exhibited a higher density of clusters with respect to the CTRL networks. The two largest communities are mainly composed by the cingulate motor areas with the supplementary motor areas and by the pre-motor areas with the right primary motor area of the foot. This functional separation could reflect the partial alteration in the primary motor areas because of the effects of the spinal cord injury.

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