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# Brain Connectivity Structure in Spinal Cord Injured: Evaluation by Graph Analysis

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*Abstract*— **The problem of the evaluation of brain connectivity has become a fundamental one in the neurosciences during the latest years, as a way to understand the organization and the interaction of several cortical areas during the execution of cognitive or motor tasks. Following an approach that derives from the graph theory, we analyzed the architectural properties of the networks obtained by the use of DTF measures on the cortical signals estimated from the high resolution EEG recordings. The present work aims at analyse the structure of cortical connectivity during the imagination of a limb movement in spinal cord injured patients, by the computation of the characteristic path length L and the cluster indices Cin and Cout.**

*Keywords*— **Cluster Indices, Path Length, Graph, DTF, high resolution EEG, Spinal Cord Injured**

## I. Introduction

The necessity to describe how different brain areas work together is gaining more and more importance in the neuroscience field [1]. Hence, the concept of functional connectivity is viewed as central for the understanding of the organized behavior of cortical regions beyond the simple mapping of their activity. In this respect, a multivariate spectral technique, called Directed Transfer Function (DTF) , was proposed [2] to determine the directional influences between any given pair of electrodes in a multivariate data set. Such connectivity estimation procedure has been applied to the cortical data estimated from the high resolution EEG recordings. In fact, this EEG techniques include 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 the cortical current densities from the scalp potential measurements [3]. Thus, functional connectivity estimation aims at describing the brain interactions as connectivity patterns which hold the direction and the strength of the information flow between different cortical areas. The structure of these patterns allow us to treat them as real networks and to make several considerations about their architecture by means the "graph" theory.

In fact, recently, a new way to characterize the topographical properties of complex networks has been proposed using the "graph" theoretical approach [4-5]. A graph is a basic representation of a network, which is essentially reduced to nodes and connections [6]. Graphs are characterized by a cluster index C and a characteristic path length L. The cluster index is a measure for the local interconnectedness of the graph, whereas the path length is an indicator of its overall connectedness or level of integration. Watts and Strogatz [7] have shown that graphs with many local connections and a few random long distance connections are characterized by a high cluster index and a short path length; such near optimal networks are designated "small-world" networks. Many types of real networks have been shown to have small-world features [5]; besides, patterns of anatomical connectivity in neuronal networks are particularly characterized by high clustering and a small path length [7]. Networks of functional connectivity based upon recordings in animals, fMRI BOLD signals or MEG recordings have also been shown to have small-world characteristics [8-10]. The present work aims at evaluating the impact of spinal cord injuries on the brain connectivity during the imagination of a motor task. We addressed the question whether the "architecture" of the connectivity evaluated by graph analysis, may differ from an healthy behaviour.

Here we predict that spinal cord injuries will interfere mainly with the "global" structure of the brain functional networks obtained.

## II. Methods

### *High resolution EEG recordings in normal subjects and SCI patients.*

Five healthy subjects and five patients with a spinal cord injury (SCI) participated in the study. Spinal cord injuries were of traumatic etiology and were located at the lesion associated with the trauma leading to the injury. For the EEG data acquisition, subjects were comfortably seated

cervical level (C6 in three cases, C5 and C7 in two cases respectively); patients had not suffered for a head or brain 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 executing (for healthy subjects) or attempting (SCI patients) 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).

*Cortical activity and functional connectivity estimation.*

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. Then, we computed the average activity of the dipoles within twelve ROIs (Region Of Interest) obtained 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 feet (MIF) and lips movement (A4_Lip), the proper supplementary motor area (SMAp), the standard pre-motor area (A6), the cingulated motor area (CMA) and the associative area (A7). The resulting cortical waveforms, one for each predefined ROI, were then processed for the estimation of functional 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. In order to be able to compare the results obtained for data entries with different power spectra, we used the normalized $\underline{\text{DTF}}$ which expresses the ratio of influence of element $j$ to element $i$ with respect to the influence of all the other elements on $i$.

The application of this method to the ROIs waveforms returns a cortical network for each frequency band of interest. (Theta 3-6 Hz, Alpha 7-12 Hz, Beta 13-29 Hz, 30-40 Hz).

*Graph Analysis: Cluster Indices and Path Length*

Informally speaking, a graph is a set of objects called nodes or vertices connected by links called arcs or edges. In a graph proper, which is by default *undirected*, a line from point $A$ to point $B$ is considered to be the same thing as a line from point $B$ to point $A$. In a *digraph*, short for *directed graph*, the two directions are counted as being distinct *arcs* or *directed edges*. A digraph with weighted edges is called a network. As well known it's always possible associate a connection matrix for a finite network of $N$ vertices, that is a $N \times N$ matrix, where the non-diagonal entry $a_{ij}$ is the weight of edge linking vertex $j$ to the vertex $i$, and the diagonal entry $a_{i,i}$ is the number of loops at vertex $i$. In particular the binary matrix associated to a digraph is called adjacent matrix, which is symmetric in the simple graph case. The first step in applying graph theoretical analysis to the connectivity pattern estimated is to convert the cortical network into a digraph. Our connection matrix records DTF values for each directed pair of ROIs and can be converted to an adjacent matrix by considering a threshold $T$. If the weight of the element $\underline{\text{DTF}}_{i,j}$ exceeds $T$ an edge is said to exist from $j$ to $i$; otherwise no edge exists from $j$ to $i$. Here we choose a $T$ value such that we get the 34% more powerful connections, thus neglecting all that edges whose intensity doesn't exceed the average intensity of the network (50%) plus a fixed standard deviation (16%). Anyway, the choice of $T$ is arbitrary. Once the cortical network has been converted, we can characterize the digraph in terms of its cluster index $C$ and its characteristic path length $L$.

*Cluster Indices*. Introduced by Watts and Strogatz (1998) the cluster coefficient of a vertex of a graph indicates how many connections are maintained between a vertex's neighbours. Neighbours, for a simple graph, are all those nodes that are connected to the central vertex. Here, because the digraph, we have to distinguish neighbours-in which are all that nodes connected through an incoming connection to the central vertex and neighbours-out which are the nodes connected through an outgoing connection. According to this remark cluster coefficient had to be split respectively in cluster-in coefficient $c_{in}$ and cluster-out coefficient $c_{out}$. Now the cluster-in coefficient is the ratio of all existing edges between the neighbours-in and the maximal number of such connections possible. It ranges between 0 and 1 and it is computed for all vertices of the digraph.

Let be $k_{in}(i)$ the degree-in of the vertex $i$ that is the number of the incoming connections to the vertex $i$; evidently because the absence of multiple edges it corresponds with the number of nodes transmitting to the central one. Then, remembering that $a_{i,j}$ is the generic element of the adjacent matrix associated with the digraph, the cluster- in coefficient is:

$$c_{in}(i) = \frac{1}{k_{in}(i)^2 - k_{in}(i)} \sum_{j,h} \frac{a_{i,j} + a_{i,h}}{2} \cdot a_{i,j} a_{i,h} a_{j,h} \tag{1}$$

The cluster-in index $C_{in}$ is the average of all these coefficients and represents a measure for the tendency of the digraph elements to form local clusters transmitting information flows.

Likewise the cluster-out coefficient is given as follows:

$$c_{out}(i) = \frac{1}{k_{out}(i)^2 - k_{out}(i)} \sum_{j,h} \frac{a_{i,j} + a_{i,h}}{2} \cdot a_{i,j} a_{i,h} a_{j,h} \tag{2}$$

where $k_{out}(i)$ is the degree-out of the vertex $i$ meaning the number of outgoing connections from it. The cluster-out index $C_{out}$ is the average of the cluster-out coefficients and represents a measure for the presence of local clusters receiving information flows.

*Path Length*. The characteristic path length $L$ is the average shortest path connecting any two vertices of the digraph; the length of a path is indicated by the number of edges of which it exists. It is computed from the distance matrix, obtained by means the Floyd-Warshall algorithm (1962),

that records the length of the shortest path for each pair of nodes belonging to digraph; if a path linking a pair of vertices doesn't exist the value recorded is infinite. The characteristic path length L is the global mean value of finite entries of the distance matrix associated to the digraph.
Let be $p$ the number of finite values of the distance matrix $D$ and $d_{i,j}$ its generic element. Then the path length $L$ can be obtained as follows:

$$L = \frac{1}{p}\sum_{i \neq j} d_{i,j} \tag{3}$$

It is an emergent property of the digraph which indicates how well its elements are interconnected and it is indicative of the global delay for the communication within the network.

## III. Results

In Figure 1 and 2 some of the cortical networks obtained in this study are shown. They represent respectively the average connectivity of the SCI and healthy group in the beta frequency band during the foot-lip task.

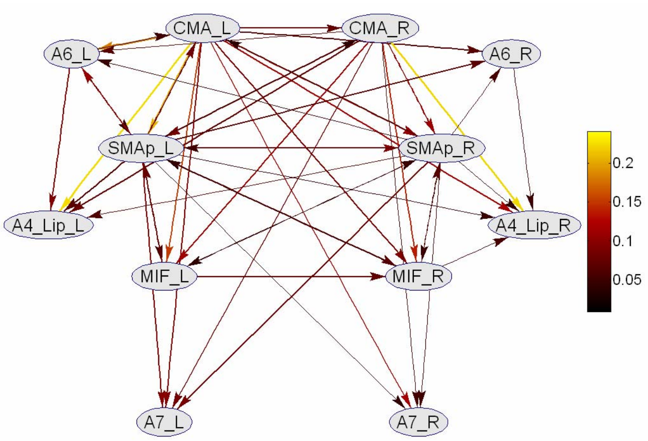


Figure 1. Average network among ROIs of the SCI group obtained from DTF in the beta frequency range during the foot-lip task. It shows the average intensity of the 34 percent most powerful edges belonging to two patients at least. Nodes follow the real disposition of ROIs on the cortex, here seen from above, with nose towards the top of the page; left hemisphere is on the left part of the figure. Flows direction is represented by an arrow while the intensity is coded by its colour and size. Each node is labelled with a ROI acronym.

According to the experimental design, three variables (L, Cin and Cout) for each subject and frequency band were computed and then addressed separately to the ANOVA at the p=0.05 statistical significance level.
Figure 3. shows the scatter plots matrix of the three indices L, Cin and Cout obtained; it is possible to note that the distribution of the SCI group (red-circles) slightly tends to come off from the Healthy one (blue-crosses).

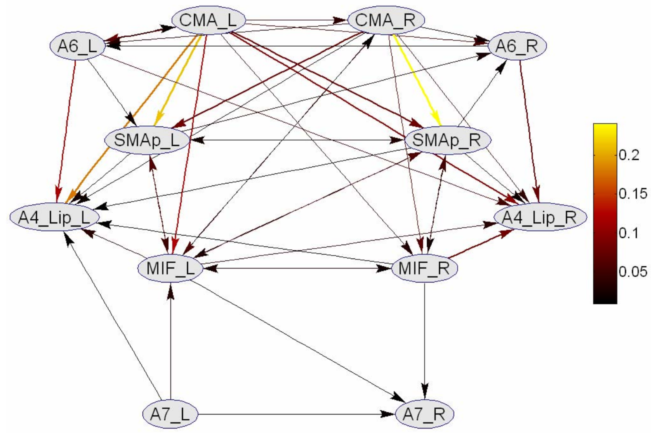


Figure 2. Average network among ROIs of the healthy group obtained from DTF in the beta frequency range during the foot-lip task. It shows the average intensity of the 34 percent most powerful edges belonging to two subjects at least. Same conventions of the Figure 1.

The main factors of the ANOVAs were the "between" factor GROUP (with two levels: Healthy and SCI) and the "within" factor BAND (with four levels: THETA, ALPHA, BETA and GAMMA). Besides, post-hoc analysis with the Duncan's test at the p=0.05 statistical significance level was performed.

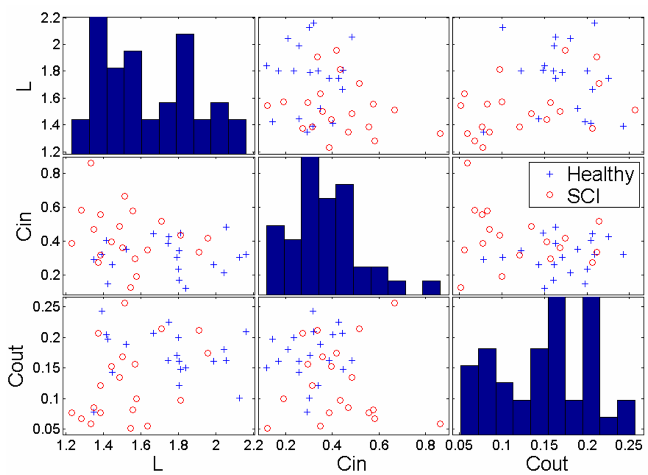


Figure 3. Matrix of scatter plots of the three variable L, Cin, Cout against each other. All plots are grouped by the "between" factor GROUP (blue-cross healthy, red-circle SCI). Along the main diagonal are disposed the histogram of the single variable values.

*Cluster Index Cin.* The ANOVA performed returned no statistical significant differences in the main factors GROUP and BAND. In particular the "between" factor GROUP was found having an F value of 3.23, p<0.11 while the "within" factor BAND was found having an F value of 0.5 and p<0.69.
*Cluster Index Cout.* Statistical results revealed no significant differences in the main factor GROUP (F=2.31 p=0.17); while a significant difference was found between the alpha and beta levels of the main factor BAND (F=3.7, p<0.026).

*Path Length L.* Results revealed a strong influence of the between factor GROUP on the characteristic path length L ($F=10.41$, $p<0.01$), as shown in Figure 4; while the BAND factor and the interaction between GROUP and BAND were found not significant ($F=2.02$ and 1.02 respectively for p values equal to 0.14 and 0.40).

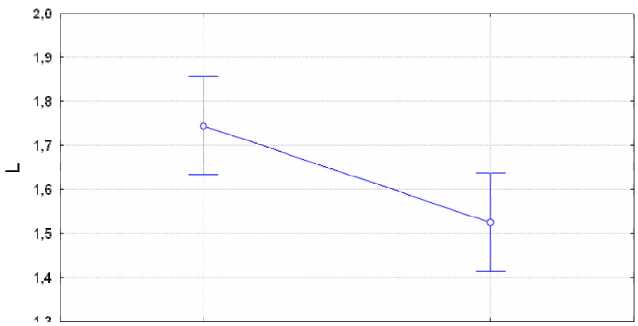


Figure 4. Average values of characteristic path length (L) for the levels (healthy and SCI) of the "between" factor GROUP. A statistical significant difference were noted between healthy subjects and SCI patients. Vertical bars denote 0.95 confidence intervals.

Post hoc tests revealed that the only significant difference between groups (SCI, healthy) is in the beta band ($F=1.92$, $p<0.03$). Last figure 5. presents the average values of the path length L between groups.

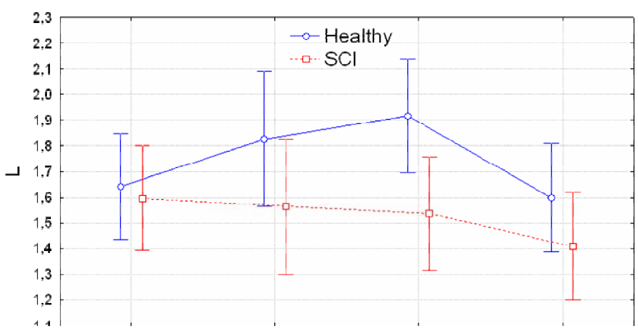


Figure 5. Average values of characteristic path length (L) for the levels of the "within" factor (BAND), grouped by healthy and SCI subjects. A statistical significant difference was noted between Healthy subjects and SCI patients in the BETA band. Vertical bars denote 0.95 confidence intervals.

## IV. Discussion

These results demonstrate that spinal cord injuries affect the functional architecture of the cortical network mainly in its global feature. SCI patients have shown significantly differences from Healthy subjects probably due to the functional reorganization phenomenon, known as brain plasticity [11]. The lower value of the characteristic path length *L* suggests a larger overall connectedness of the networks analyzed. In particular this difference can be observed in the beta frequency band, which is of interest for the attempt/execution of limbs movement. A low path length L means that all ROIs are well connected one to each other; obviously this fact causes an increasing of alternative paths between all nodes within the network. Those paths could represent some supplementary communication channels between the ROIs involved in the experimental task; SCI patients probably use them to improve the behaviour of the motor cortical areas, which is partially altered because the spinal cord injury. Instead, it seems that the level of the integration between the ROIs within the network do not differ significantly from the healthy behaviour, neither for the local clusters receiving information flows (Cout) nor for the transmitting ones (Cin). It could mean that spinal cord injuries do not affect the local interconnectedness of the brain which attempts to preserve the same local property observed during the foot-lip task in the "healthy" cortical networks.

These results suggest that the theoretical graph approach can be a very useful tool able to catch some global and local features in the functional connectivity patterns estimated from the high resolution EEG. Cluster indices and characteristic path length point out some aspects in the structure of the cortical network that can not be easily noticed and that allow us to compare different networks relatively to different task or subjects.

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