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Describing Relevant Indices from the Resting State Electrophysiological Networks

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***Abstract*— The "Default Mode Network" concept was defined, in fMRI field, as a consistent pattern, involving some regions of the brain, which is active during resting state activity and deactivates during attention demanding or goal-directed tasks. Several fMRI studies described its features also correlating the deactivations with the attentive load required for the task execution. Despite the efforts in EEG field, aiming at correlating the spectral features of EEG signals with DMN, an electrophysiological correlate of the DMN hasn't yet been found. In this study we used advanced techniques for functional connectivity estimation for describing the neuroelectrical properties of DMN. We analyzed the connectivity patterns elicited during the rest condition by 55 healthy subjects by means of Partial Directed Coherence. We extracted some graph indexes in order to describe the properties of the resting network in terms of local and global efficiencies, symmetries and influences between different regions of the scalp. Results highlighted the presence of a consistent network, elicited by more than 70% of analyzed population, involving mainly frontal and parietal regions. The properties of the resting network are uniform among the population and could be used for the construction of a normative database for the identification of pathological conditions.**

I. Introduction

Recent studies in fMRI field highlighted the existence of a "Default Mode network" (DMN) characterizing the brain functions during the rest condition [1,2]. The DMN concept was defined as a consistent pattern of deactivation of some regions (precuneus/posterior cingulate cortex (PCC), medial prefrontal cortex (MPFC) and medial, lateral and inferior parietal cortex) which occurs during the initiation of task-related activity. Such network is active during the resting state activity in which an individual is awake and alert, but not actively involved in an attention demanding or goal-directed task [1]. Moreover, the deactivation is correlated with the attentive load required for the task execution. In fact, the more demanding the task, the stronger the deactivation appears to be [3,4]. Some DMN abnormalities could be also put in relation with a number of different mental disorders [5].

Several electroencephalographic (EEG) studies tried to describe some electrophysiological properties of DMN by correlating the spectral activity in a specific band with a specific group of brain areas belonging to the highlighted network [6,7]. Despite these efforts, an electrophysiological correlate of the DMN discovered in fMRI field hasn't yet been found.

For this reason, the aim of this study is to describe the electrophysiological properties of DMN by means of advanced techniques of functional connectivity estimation applied on EEG signals acquired during the resting state. The idea is to extract some salient indices borrowed from graph theoretical approach for characterizing the connectivity networks elicited during the rest condition by a population of 55 healthy subjects. Once evaluating their uniformity among the population, the values achieved for such indices could be included in a normative database to be used as a baseline in the identification of pathological conditions.

II. Methods

A. Partial Directed Coherence

The PDC [8] is a full multivariate spectral measure, used to determine the directed influences between any given pair of signals in a multivariate data set. This estimator was demonstrated to be a frequency version of the concept of Granger causality [9].

It is possible to define PDC as:

$$\pi_{ij}(f) = \frac{\Lambda_{ij}(f)}{\sqrt{\sum_{k=1}^{N} \Lambda_{ki}(f)\Lambda_{ki}(f)}}, \quad \sum_{n=1}^{N} \left|\pi_{ni}(f)\right|^2 = 1 \qquad (1)$$

where $\Lambda(f)$ is a matrix containing the coefficients of associated Multivariate Autoregressive (MVAR) model.

In this study we used the square formulation of PDC due to its higher accuracy and stability [10].

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B. Statistical Assessment of Connectivity Estimates: Asymptotic Statistic

The assessment of the significance of the estimated causal links was performed by means of asymptotic statistic method [11], whose accuracy has been demonstrated in [12]. Such method is based on the assumption that PDC in the null case follows a χ^2 distribution. The statistical threshold is achieved by means of a χ^2 distribution obtained by applying a Monte Carlo method. The percentile related to the significance level imposed is then computed. Due to the high number of comparisons between PDC values and statistical thresholds, a correction for multiple comparisons issue is needed to avoid the occurrence of type I errors (false positives). The statistical theory provides different correction algorithms. We considered here the more recently introduced False Discovery Rate (FDR).

C. Graph Theory

A graph consists of a set of vertices (or nodes) and a set of edges (or connections) indicating the presence of some sort of interaction between the vertices. The adjacency matrix A contains the information about the connectivity structure of the graph. When a directed edge exists from the node i to j, the corresponding entry of the adjacency matrix is $A_{ij} = 1$, otherwise $A_{ij} = 0$. Several indices based on the elements of such matrix can be extracted for the characterization of the main properties of investigated networks [13].

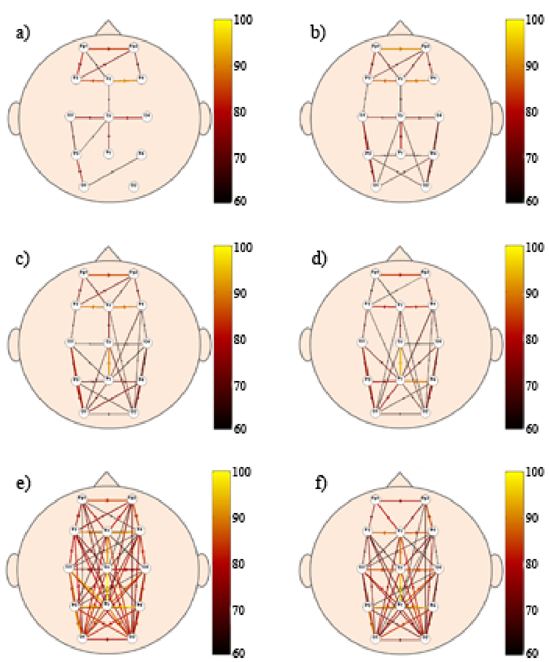

Figure 1. Grand Average of functional connectivity patterns elicited during the eyes-closed condition by 55 healthy subjects in 6 frequency bands defined according to IAF: a) Theta Band (IAF-6, IAF-4), b) Lower1-Alpha Band (IAF-4, IAF-2), c) Lower2-Alpha Band (IAF-2, IAF), d) Upper Alpha Band (IAF, IAF+2), e) Beta Band (IAF+2, IAF+15), f) Gamma Band (IAF+15, IAF+30). Connectivity patterns are represented on a scalp model seen from above with the nose pointing the upper part of the page. Color and size of each arrow code the percentage of subjects who elicited the correspondent connection.

Global Efficiency. The global efficiency is the average of the inverse of the geodesic length (shortest path between two nodes in the network) and represents the efficiency of the communication between all the nodes in the network [14].

Local Efficiency. The local efficiency is the average of the global efficiencies computed on each sub-graph belonging to the network and represents the efficiency of the communication between all the nodes around the node i in the network [14].

In order to describe symmetries and influences between different regions of the scalp, in this study we defined two new indices. Before the computation of these indices it is necessary to arrange the adjacency matrix by disposing in the first N1 rows and N1 columns the connectivity values related to the nodes belonging to the first scalp area and in the second N2 rows and N2 columns the connectivity values related to the nodes belonging to the second scalp area.

Symmetry. The symmetry index is the difference in the number of internal connections between two different spatial regions. It could assume values in the range [-1 ; 1] and it is defined as follows

$$S = \frac{\sum_{i=1}^{N_1}\sum_{j=1}^{N_1} A'_{ij}}{N_1(N_1-1)} - \frac{\sum_{i=N_1+1}^{N_2}\sum_{j=N_1+1}^{N_2} A'_{ij}}{N_2(N_2-1)} \quad (2)$$

where A' is the arranged version of A.

Influence. The influence index represents the difference in the number of inter connections between two different spatial regions. It could assume values in the range [-1 ; 1] and it is defined as follows

$$I = \frac{\sum_{i=1}^{N_1}\sum_{j=N_1+1}^{N_2} A'_{ij} - \sum_{i=N_1+1}^{N_2}\sum_{j=1}^{N_1} A'_{ij}}{N_1 \cdot N_2} \quad (3)$$

The last two indices were used in the study for investigating the symmetries and influences between the two hemispheres and between frontal and parietal areas.

D. Experimental Design

55 healthy subjects (age: 27.5±5 years; 25 female) participated in the study. The experiment consisted in 2 minutes of recording session during which the subjects were asked to stay in a rest condition for one minute with their eyes closed and one minute with their eyes opened, without moving or performing any mental activities. A 64-channel system with a sampling frequency of 200 Hz (BrainAmp, Brainproducts GmbH, Germany) was used to record EEG data.

EEG signals were band-pass filtered (1-45 Hz + 50 Hz Notch filter) and ocular artifacts were removed by means of Independent Component Analysis. EEG traces were segmented in epochs of 1s each in order to increase the robustness of methodologies applied in the following and

TABLE I. RESULTS OF ANOVA STUDY

GRAPH INDEXES	TYPE		TYPE x BAND	
	F	p	F	p
Global efficiency	**78.1**	**< 0.00001**	**12.01**	**< 0.00001**
Local efficiency	**10.5**	**0.00201**	1.16	0.323
$S_{Left\text{-}Right}$	1.34	0.25	0.46	0.81
$I_{Left\text{-}Right}$	3.75	0.58	0.52	0.76
$S_{Anterior\text{-}Posterior}$	0.12	0.73	**12.03**	**< 0.00001**
$I_{Anterior\text{-}Posterior}$	**16.5**	**0.00016**	**19.76**	**< 0.00001**

residual artifacts were removed. The whole dataset couldn't be subjected to PDC computation due to the limitation, typical of multivariate approach, on the number of signals to be considered contemporary in the estimation. Thus a subset of 12 channels (spatially distributed on the scalp) among the 64 channels used for the recording (Fp1, Fp2, F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, O2) were selected and used for PDC estimation. The achieved connectivity patterns were statistically validated by means of asymptotic statistic method for a significance level of 5% FDR corrected and subjected to graph indices computation.

Thus in order to characterize the features of the networks elicited during the rest condition we computed a statistical study as described in the follow:

1) Generation of 100 random graphs for each network without varying the total number of connections of the corresponding real network.

2) Extraction of all the graph indexes described above from each generated random network and average of the achieved values across all the iterations.

3) Application of a statistical test, repeated measures ANOVA, for comparing the indexes extracted from real and random networks under different conditions.

III. RESULTS

After the pre-processing described in Sec. IID, the EEG traces related to resting condition of 55 healthy subjects were subjected to functional connectivity estimation. The optimal order of the correspondent MVAR model was estimated by means of Akaike Information Criterion (AIC) for each subject. The achieved estimations were averaged within six frequency bands defined according to Individual Alpha Frequency (IAF) [15] (IAF = 10.25 ± 0.86). Fig. 1 showed the Grand Average of functional connectivity patterns elicited during the eyes-closed condition by 55 healthy subjects in 6 frequency bands: a) Theta Band (IAF-6, IAF-4), b) Lower1-Alpha Band (IAF-4, IAF-2), c) Lower2-Alpha Band (IAF-2, IAF), d) Upper Alpha Band (IAF, IAF+2), e) Beta Band (IAF+2, IAF+15), f) Gamma Band (IAF+15, IAF+30). Connectivity patterns are represented on a scalp model seen from above with the nose pointing the upper part of the page. Color and size of each arrow code the percentage of subjects who elicited the correspondent connection. The figure highlighted the existence of a consistent pattern elicited by more than 70% of the analyzed population. Such pattern was characterized by a sub-network between electrodes in frontal regions in theta, lower1 and lower2 alpha, by a role of Cz as source of information in all bands and by a sub-network between electrodes located in parietal areas in upper alpha, beta and gamma bands.

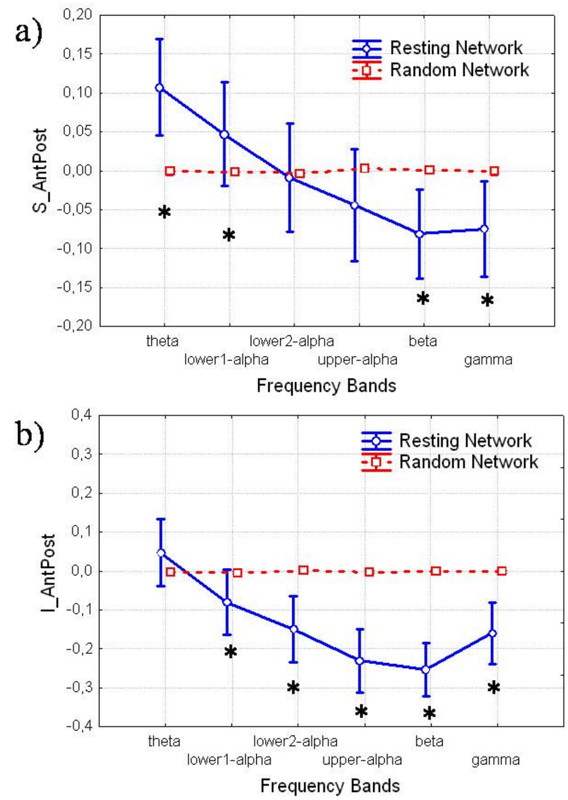

Figure 2. Results of ANOVA performed on the indexes Symmetry (a) and Influence (b) between anterior and posterior parts of the scalp computed on resting and random network: plot of means with respect to the factors TYPE and BAND. ANOVA shows a high statistical significance ($F=12.03$, $p<0.0001$) for the case a) and ($F=19.76$, $p<0.0001$) for the case b) respectively. The bar on each point represents the 95% confidence interval of the mean errors computed across the subjects. The symbol * codes a significant difference between resting and random networks revealed by Duncan's post-hoc test.

In order to extract salient properties for describing the achieved connectivity patterns, we computed graph theory indices on their associated adjacency matrices. The adjacency matrices were extracted by means of the statistical validation method of connectivity patterns. In fact, the asymptotic statistic method allowed to build an adjacency matrix whose entries were 1 if the connection resulted significantly different from the null case and 0 if not. Once extracted the correspondent adjacency matrix for each subject and for each band, several indices, such as global and local efficiencies, symmetries and influences between the two hemisphere or between the anterior and posterior parts of the scalp, were computed. In order to validate the values achieved for the graph indices, 100 random graphs with the same number of connections were generated for each adjacency matrix. On each random graph indices described above were computed and averaged among the iterations.

Then a statistical comparison between indices' values achieved on real and random graphs was computed.

In particular, for each index, a two way ANOVA was computed considering as main factors the type of graph (TYPE: real, random) and the band (BAND: theta, lower1-alpha, lower2-alpha, upper alpha, beta, gamma). The results of each ANOVA were reported in Table1. In the first column the dependent variables are reported. In the other two columns the results (F and p) related to the effect of main factors TYPE and TYPE x BAND were showed. The table showed a significant influence of factor TYPE on global and local efficiencies and of factor TYPE x BAND only on global efficiencies. In particular, the Duncan's post-hoc analysis revealed that the global efficiency of the network elicited during the rest condition is lower than those achieved with random graph for all bands. Instead an higher local efficiency was showed in resting network in respect to random patterns for all bands. No effects of factors TYPE and TYPE x BAND on symmetry and influence between the two hemispheres resulted from the ANOVA. Both indices remained around zero for both resting and random networks, indicating a complete symmetry between the two hemispheres. Fig.2 showed the influence of the different levels of the main factors TYPE and BAND on the indexes Symmetry (panel a) and Influence (panel b) computed between the anterior and posterior parts of the brain. The bar on each point represents the 95% confidence interval of the mean errors computed across the subjects. In panel a Duncan's post hoc analysis (* symbol) revealed differences between resting and random networks in theta, lower1-alpha, beta and gamma bands. In particular, in theta and lower1-alpha bands an higher number of connections in the anterior part of the scalp resulted in respect to the posterior part (S>0). The opposite situation was showed in beta and gamma bands (S<0). In panel b Duncan's post hoc analysis revealed differences in influence index between resting and random networks for all the bands except theta band. The negative values achieved for such index revealed an high influence of the posterior part on the anterior part of the scalp for all the bands.

IV. Discussion

The application of advanced methods for functional connectivity estimation to EEG signals allowed to reconstruct the electrophysiological properties of DMN. The use of PDC, its relative statistical validation and graph theoretical approach led to the definition of a consistent neuroelectrical network elicited by a population of 55 healthy subjects during the rest condition. Such network, characteristic of more than 70% of the population, involved mainly the frontal part of the scalp in the lower bands (theta, lower1 and lower2 alpha) and the parietal part of the scalp in the higher bands (beta, gamma) as highlighted by means of grand average connectivity patterns. This result was confirmed by the statistical comparison between resting and random networks in terms of influences and symmetries between anterior and posterior part of the scalp. The same statistical study stated also the existence of a perfect symmetry between the two hemispheres during the rest condition. The ANOVA study highlighted also the small worldness properties of the network elicited during the rest condition, characterized by an high local efficiency and a low global efficiency in respect to random graph.

The consistent results of statistical analysis, in particular the values achieved for all the indexes computed on resting networks are uniform among the population, thus they could be used to build a normative database to be considered in the identification of pathological conditions.

Moreover, the methodological steps performed for the analysis of DMN and the new graph indexes, defined for the purposes of this work, has been revealed as valid procedure for the description of the neuroelectrical properties of any condition.

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