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Time-significant Wavelet Coherence for the Evaluation of Schizophrenic Brain Activity using a Graph theory approach

Vangelis Sakkalis, Theofanis Oikonomou, Ellie Pachou, Ioannis Tollis, Sifis Micheloyannis, and Michalis Zervakis, *member IEEE*

Abstract—**Among the various frameworks in which Electroencephalographic (EEG) signal synchronization has been traditionally formulated, the most widely studied and used is the coherence that is entirely based on frequency analysis. However, at present time it is possible to capture information about the temporal profile of coherence, which is particularly helpful in studying non-stationary time-varying brain dynamics, like the Wavelet Coherence (WC). In this paper we propose a new approach of studying brain synchronization dynamics by extending the use of WC to include certain statistically significant (in terms of signal coherence) time segments, to study and characterize any disturbances present in the functional connectivity network of schizophrenia patients. Graph theoretical measures and visualization provide the tools to study the "disconnection syndrome" as proposed for schizophrenia. Specifically, we analyzed multichannel EEG data from twenty stabilized patients with schizophrenia and controls in an experiment of working memory (WM) using the gamma band (i.e., the EEG frequency of ca. 40 Hz), which is activated during the connecting activity (i.e., the "binding" of the neurons). The results are in accordance with the disturbance of connections between the neurons giving additional information related to the localization of most prominent disconnection.**

I. INTRODUCTION

ELECTROENCEPHALOGRAPHIC (EEG) coherence measures have been successfully used in the past as indices of cerebral engagement in cognitive tasks using linear [1] and non-linear [2] methods.

Coherence has been a well-established and traditionally used tool to investigate the linear relation between two signals or EEG channels, by means of examining periodicities in frequency domain using classical Fourier analysis. This method actually neglects time resolution for the sake of perfect frequency resolution (Heisenberg uncertainty principle) and assumes stationary processes in the time domain. However, EEG signals reflect the underlying brain dynamics and in principle convey information on dynamically evolving channel interdependencies. Thus, measuring the dynamic behavior of EEG channels coupling, while different cognitive tasks are happening, is possible only if temporal resolution is conserved. Towards the latter direction, several Fourier-based adaptations [3] have been attempted, but still require stationarity within each window for which coherence is calculated.

In this study the aforementioned limitations are addressed by adopting the Continuous Wavelet Transform (CWT). The CWT is able to examine whether regions in time frequency space with large common power have a consistent phase relationship and therefore are suggestive of causality between EEG channels. In addition, CWT makes use of complex basis functions (wavelets) that are able to capture the amplitude and phase information from the analyzed EEG signals, as well as time information [4]. Using the CWT is possible to compute the WC, which has already been successfully used in EEG analysis [5]. Motivated by the additional "time profile" information gained from the use of CWT, this paper proceeds one step further and utilizes statistics to identify only those EEG signal time segments where significant coherence occurs.

In this study two different situations are considered: the control (rest) and the cognitive activation during working memory (WM), testing both control subjects and schizophrenia patients. The testing hypothesis suggests that WM task requires considerable mental effort and the disconnection on neuronal assemblies in patients could be visible by reduced "binding" expressed by the gamma band (30-45 Hz). The disconnection hypothesis [6] and WM deficits [10][11] are well established in the literature on schizophrenia.

Both local and long distance functional connectivity in complex networks is evaluated using measures and visualizations derived from graph theory. Special interest in using graph theory to study neural networks has been in focus recently, since it offers a unique perspective of

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V. Sakkalis is with the Department of Electronic and Computer Engineering, Technical University of Crete, Chania 73100 and the Institute of Computer Science, Foundation for Research and Technology, Heraklion 71110, Greece (+30-281-0391448; fax: +30-281-0391609; e-mail: sakkalis@ics.forth.gr).

T. Oikonomou and I. Tollis are with the Institute of Computer Science, Foundation for Research and Technology, Heraklion, Greece and the Department of Computer Science, University of Crete, Heraklion 71409, Greece (e-mail:thoikon@ics.forth.gr , tollis@ics.forth.gr).

M. Zervakis is with the Department of Electronic and Computer Engineering, Technical University of Crete, Chania 73100, Greece (e-mail: michalis@systems.tuc.gr).

E. Pachou and S. Micheloyannis are with the Clinical Neurophysiology Laboratory (L. Widen), Faculty of Medicine, University of Crete, Heraklion 71409, Greece (e-mail: michelogj@med.uoc.gr).

studying local and distributed brain interactions [12][13].

The paper proceeds as follows. Section II provides a brief background of the proposed methods. Section III presents the results obtained followed by a discussion of the findings (Section IV). Finally, Section V concludes this paper.

II. Methods

A. Data Acquisition

The EEG signals in both groups (20 controls and 20 stabilized patients with schizophrenia) were recorded from 30 cap electrodes, according to the 10/20 international system, referred to linked A1+A2 electrodes (Fig. 2). The signals were digitized at 500 Hz.

B. Experimental setting and Test Description

Continuous EEGs were recorded in an electrically shielded, sound and light attenuated, room while participants sat in a reclined chair. EEG data were visually inspected for artifacts and epochs of 8 sec were chosen for analysis. We analyzed epochs at rest i.e., while each individual had the eyes fixed on a small point on the computer screen and during a two-back WM test using capital Greek letters.

C. The Continuous Wavelet Transform (CWT)

Over the past decade, the WT has been developed into an important tool for time series analysis that contains non-stationary power (such as the EEG signal) at many different frequencies [14]. The CWT of a discrete sequence x_n with time spacing δt and N data points ($n = 0 \ldots N-1$) is defined as the convolution of x_n with consecutive scaled and translated versions of the wavelet function $\psi_0(\eta)$:

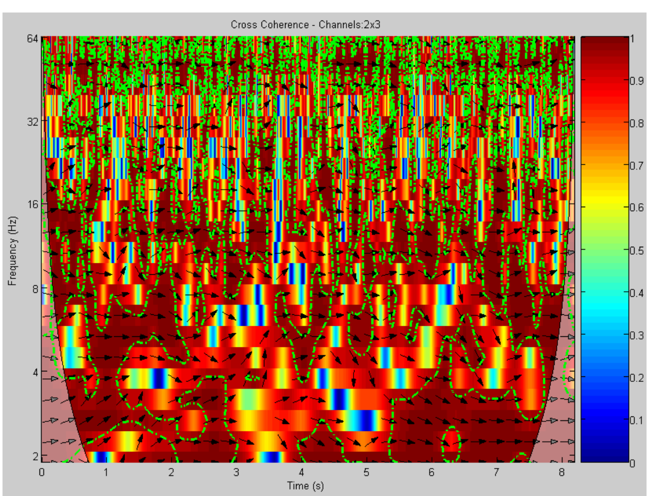

Fig. 1: The squared WC time-frequency transformed scalogram. The 5% significant regions over the time-scale transform are indicated by the contours (green dashed outline). The outer elliptical region at the edges of the second graph indicates the cone of influence in which errors (edge effects) may be apparent due to the transformation of a finite-length series EEG signal [4]. The relative phase relationship is shown as arrows (with in-phase pointing right, anti-phase pointing left).

$$W_n^X(s) = \sqrt{\delta t/s}\sum_{n'=0}^{N-1} x_{n'}\psi_0 * \left[(n'-n)\delta t/s\right] \quad (1)$$

$$\psi_0(\eta) = \pi^{-1/4} e^{i\omega_0\eta} e^{-\eta^2/2} \quad (2)$$

where η and ω_0=6 is a non-dimensional "time" parameter and frequency, respectively. $\psi_0(\eta)$ describes the most commonly used wavelet type for spectral analyses: the *normalized complex Morlet wavelet* (2). The *power spectrum* of the WT is defined by the square of coefficients (1) of the wavelet series as $\left|W_n^X(s)\right|^2$. The notion of scale s is introduced as an alternative to frequency [14]. Thus, we may define frequency bands of interest, such as *gamma* band, capable of encapsulating the different functional frequencies of the brain.

D. Wavelet Coherence

Assuming two ergodic and stationary signals x and y, then the traditional *coherence* γ_{xy}^2 is defined as follows:

$$\gamma_{xy}^2(f) = \frac{\left|S_{xy}(f)\right|^2}{S_{xx}(f)\cdot S_{yy}(f)} \quad (3)$$

where S_{xx}, S_{yy} denote the Fourier transform of the respective autocorrelation function and S_{xy} the Fourier transform of the cross-correlation function. In a similar way, given two time series X and Y, with wavelet transforms $W_n^X(s)$ and $W_n^Y(s)$, one can initially define the *cross-wavelet spectrum* as $W_n^{XY}(s) = W_n^X(s)W_n^{Y*}(s)$, where * denotes the complex conjugate. The cross-wavelet power is given by $\left|W_n^{XY}(s)\right|$. If one closely resembles (3) then the WC R_n^2 of two signals may be defined as:

$$R_n^2(s) = \frac{\left|S(s^{-1}W_n^{XY}(s))\right|^2}{S\left(s^{-1}\left|W_n^X(s)\right|^2\right)\cdot S\left(s^{-1}\left|W_n^Y(s)\right|^2\right)} \quad (4)$$

where S is a smoothing operator in time S_t and scale S_s such as $S(W) = S_s(S_t(W_n(s)))$ which for the Morlet wavelet is given by a Gaussian and a boxcar filter of width equal to 0.6, (the scale-decorrelation length) respectively [4][15]:

$$S_t(W,s) = \left(W_n(s) * c_1^{-t^2/2s^2}\right) \quad (5)$$

$$S_s(W,n) = \left(W_n(s) * c_2 \prod(0.6s)\right) \quad (6)$$

where c_1 and c_2 are normalization constants and $\prod$ is the rectangle function. The squared WC time-frequency transformed scalogram is depicted in Fig.1.

Additionally, we are able to gain confidence in causal relationships of the coherence findings by estimating the statistical level of significance against a background spectrum using Monte Carlo methods [15]. The background spectrum is defined as the mean time-averaged wavelet power spectrum over all healthy subjects performing the control task. A large set of surrogates (1000 datasets) was generated for each channel pair from the average WC of the healthy subjects and used to estimate the significance level for each scale. Our aim is to map the WC scalogram (Fig. 1) into a feature vector that best characterizes each channel pair coupling. One may think of this step as an attempt to crop up the most significant (in terms of coherence) regions out of the bulk initial signal. Fig. 1 depicts the WC scalogram of two EEG channel signals of a schizophrenic patient. The significant regions (over the time-frequency transformed domain) that are strongly coupled while the subject is performing the WM task against the background spectrum are indicated by closed contours. Hence, one is able to form *Significant Coherency* features, which encapsulate the time and "band-scaled" coherence information, over those time regions where apparent significant differentiation is indicated (contours in Fig. 1). Such features are constructed for each channel pair in both tasks and populations. As a result a 30x30 coherence matrix (CM) with elements ranging from 0 to 1 is formulated per task and subject.

E. Measures & Signatures of Graph Topology

In order to obtain a graph from a CM we need to convert it into an *N*x*N* binary adjacency matrix, *A*. To achieve that we define a variable called *threshold T*, such that $T \in [0,1]$. The value *A(i,j)* is either 1 or 0, indicating the presence or absence of an edge between nodes *i* and *j*, respectively. Namely, $A(i,j)=1$ if $C(i,j)\geq T$, otherwise $A(i,j)=0$. Thus we define a graph for each value of *T*. For the purposes of our work, we defined 1000 such graphs, one for every thousandth of *T*. After constructing *A*, we compute various properties of the resulting graph. These include the average degree *K*, the clustering coefficient *C* and the average shortest path length *L* of our graph. For statistical analysis we compared the graph properties using t-tests. The significant results (according to *p*-value) are concentrated in the region of $0.75\leq T\leq 0.85$ (with step 0.001 and $0.001\leq p\leq 0.02$). We define a graph in terms of a set of *n* nodes $V=v_1,v_2,..,v_n$ and a set of edges *E*, where e_{ij} denotes an edge between nodes v_i and v_j. The neighborhood N_i of a node v_i is defined as the set of vertices that have an edge to v_i, namely $N_i=\{v_j\}:e_{ij}\in E$.

The degree k_i of a node is the number of vertices in its neighborhood, i.e., $|N_i|$. The average degree of a graph is the average of the degrees of all nodes, i.e., $K=\sum_{i\in V} k_i / n$.

The clustering coefficient C_i of a node v_i is the fraction of the existing edges between the nodes in v_i's neighborhood over the number of all possible edges between them. For an undirected graph, if a node v_i has k_i neighbors, then $k_i(k_i-1)/2$ is the number of all possible edges in its neighborhood. Thus, $C_i=2|\{e_{jk}\}|/k_i(k_i-1):v_j,v_k\in N_i$. This measure is 1 if every neighbor connected to v_i is also connected to every other node within the neighborhood, and 0 if no node connected to v_i connects to any other node connected to v_i. The clustering coefficient for the whole graph is the average of C_i for each node, $C=\sum_{i=1}^{n} C_i / n$, and is a measure of the tendency of graph nodes to form local clusters [16].

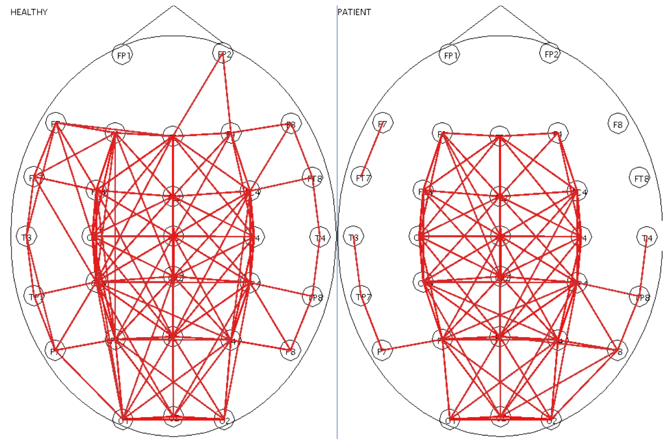

Fig. 2: A "healthy" network (left graph) (WM task and selected threshold) appears to have higher K, C values and lower L values compared to the "schizophrenic" one (right graph). These disturbances are more prominent for the connections of the frontal lobes as well as the temporal lobes.

The shortest path (distance) d_{ij} between two nodes v_i and v_j is the minimum number of edges we need to traverse in order to go from node v_i to node v_j. The average shortest path length $L=\sum_{i,j\in V,i\neq j} d_{ij} / n(n-1)$ is a measure of interconnectedness of the graph. Note that, in our experiments, the absence of a path between v_i and v_j implies $d_{ij}=1000$.

III. Results

Our study focuses on gamma band coherence analysis. Significant coherent time-regions are transformed to the aforementioned binary matrix *A* served as input to the graph analysis algorithm. The average values of *K*, *C* and *L* for $0.75\leq T\leq 0.85$ with step 0.005 during WM were computed (three selected values shown in Table I). We concentrated in different values of *T*, where the values of *K* and *C* of schizophrenic patients were equal to those of control subjects. For the above values of *T*, the respective values of *L* for patients were much greater than those for controls. A

TABLE I

HEALTHY				PATIENTS			
T	K	C	L	T	K	C	L
0.8	11.03	0.71	100.95	0.755	11.35	0.7	163.55
0.805	10.2	0.68	100.99	0.765	10.05	0.64	163.71
0.84	5.11	0.43	224.78	0.815	5.08	0.43	383.99

detailed view of the network topology is depicted in Fig. 2.

IV. Discussion

The proposed wavelet coherence analysis in combination with the graph analysis methodology indicated significant task differentiation in gamma band more prominent in frontal, frontal-central and temporal regions. Such disturbances of integration of brain function in schizophrenic processes have been suspected from the first detailed descriptions of the disease and are reinforced by clinical findings. Anatomical, biochemical brain mapping and electrophysiological findings support this hypothesis. Such clinical methods, using gamma band evaluation, further support the "disconnection" hypothesis i.e., the disturbance of the integrative processes. Various alternative studies relating gamma band and schizophrenia indicate that there is an overall reduction of the amount of the connected nodes and synchronization strength of this frequency band in schizophrenics. Additionally, there are differences between the gamma activity on the left and right hemispheres among patients and controls, as well as indices of less frontal integration as expressed by this band [6][7][8].

The three graph measures K, C, L actually represent an overall signature of the graph topology. Our experiments indicated that K, C and L are getting lower while moving from healthy to schizophrenics (in the whole threshold range). But instead of studying each measure independently, we attempt to quantify their interaction. Towards this direction we determined in three different values of T (Table I), where the values of K and C of patients are equal to those of healthy. The physical meaning of this maneuver addresses the following question: Assuming both healthy and schizophrenic populations have the same average degree and clustering coefficient, is the network proportionally efficient? According to Table I the answer is no, which means that for the above values of T the respective values of L of the patients are much greater than those of healthy. This is also evident by observing Fig. 2. The latter syllogism leads to the suggestion that schizophrenic patients need significantly more direct node (channel) connections in order to perform the same WM task.

V. Conclusion

The algorithmic approach presented illustrates the idea of using statistically-based feature vectors in the time-scale WT domain in order to select the most significant time segments capable of revealing the most prominent task changes out of the background signal. Results suggest that the proposed methodology is capable of identifying regions of cerebral synchrony during the specified tasks. Using the graph theoretical analysis we found that the integration, as expressed by the high frequency gamma band, related to the "binding" phenomenon i.e., the integration on neuronal activity, and the related parameters is overall reduced in schizophrenics. This is evident at rest but more prominent during a cognitive task, the WM. Additionally, these disturbances are more prominent for the connections of the frontal lobes as well as the temporal lobes.

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