ARTICULATION OF CORTICAL CONNECTIVITY

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ABSTRACT

The brain is the most complex part of the human body. Some brain diseases are Alzheimer's disease, Epilepsy, and Parkinson's disease. The samples are taken for normal people (Nold), Mild Cognitive Impairment (MCI) and Parkinson's disease (PD). The difference between the normal person and patients are identified by the variations in path length, clustering coefficient, small world with the support of different band levels.

Keywords-path length, small world, clustering coefficient, Parkinson's disease

I. INTRODUCTION

The brain is the control center of the body. It controls thoughts, memory, speech, and movement. It regulates the function of many organs. When the brain is healthy, it works quickly and automatically. However, when problems occur, the results can be devastating. Inflammation in the brain can lead to problems such as vision loss, weakness and paralysis. Loss of brain cells, which happens if you suffer a stroke, can affect your ability to think clearly. Brain tumors can also press on nerves and affect brain function. Some brain diseasesare genetic. Electroencephalographic (EEG) helps to measure the values in both eyes-open and eyes-closed condition [4]. The symptoms of brain diseases vary widely depending on the specific problem. In some cases, damage is permanent. In other cases, treatments such as surgery, medicines, or physical therapy can correct the source of the problem or improve symptoms.

According to Graph Theory, structural brain networks can be described as graphs that are composed of nodes (vertices) denoting neural elements (neurons or brain regions) that are linked by edges representing physical connections (synapses or axonal projections) [3].

Here Neurons are considered as vertices, connections between neurons are considered as edges. Graph Theory is made up of vertices and edges. Swiss Mathematician Euler who invented Graph Theory in 18th century [5].

Through Graph Theory, the differences in brain connectivity for Nold, MCI, PD patients with the help of Path Length, Clustering Coefficient, and Small world has been found [1]. By identifying these problems can be rectifying by taking Medicines and treatment with the help of doctors.

II. PRELIMINARIES

Definition 2.1: A linear graph consists of a set of objects $V = \{v_1, v_{2.....}\}$ called vertices and another set $E = \{e_1, e_2.....\}$ whose elements are called edges. The vertices are representedas points and each edge as a line segment joining its end vertices [2].

Definition 2.2: In graph theory, a Clustering Coefficient is a measure of the degree to which nodes in a graph tend to cluster together [1].

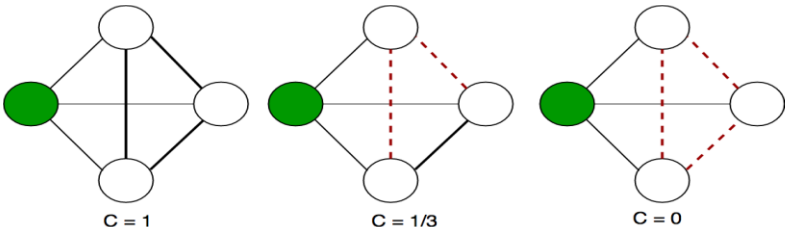


Figure 2.2 Clustering Coefficient

Definition 2.3: In a graph, a Path is a sequence of nodes in which each node is connected by an edge to the next. The path length corresponds to the number of edges in the path [1].

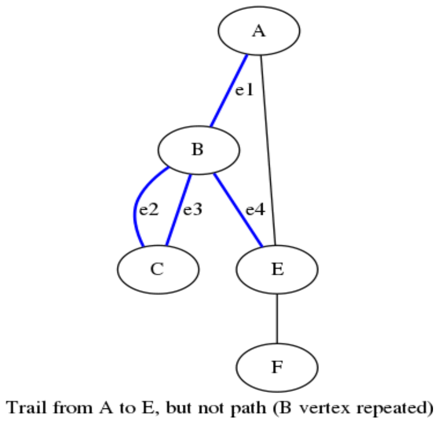


Figure 2.3 Path Length

Definition 2.4: A small-world network is in which most nodes are not neighbors of one another,but the neighbors of any given node are likely to be neighbors of each other and most nodescan be reached from every other node by a small number of hops or steps. Specifically, a small world network is defined to be a network where the typical distance L betweentwo randomly chosen nodes (the number of steps required) grows proportionally to the logarithm of the number of nodes N in the network [1].

Figure 2.4 Small world

Definition 2.5: A weighted graph is a graph in which each branch is given a numerical weight. A weighted graph is therefore a special type of labeled graph in which the labels are numbers (which are usually taken to be positive) [5].

Definition 2.6: If edges in a graph have weights then the graph is said to be a weighted graph, if the edges do not have weights, the graph is said to be unweighted. A weight is a numerical value attached to each individual edge [5].

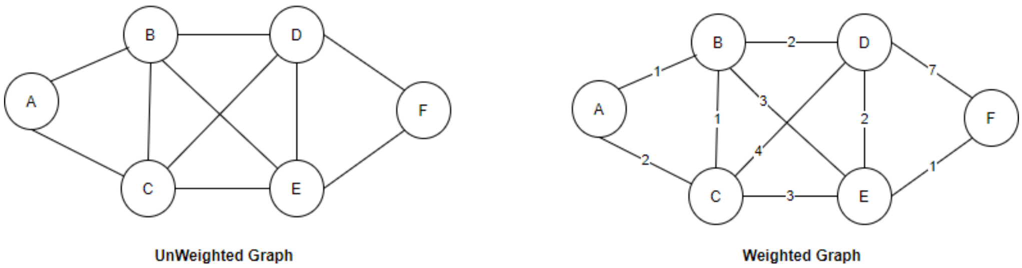
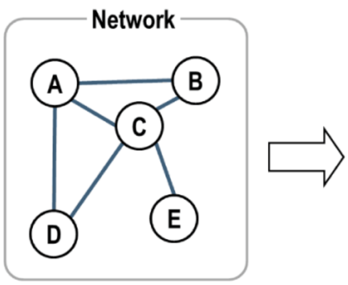


Figure 2.5 Unweighted and Weighted graph

Definition 2.7: The connection matrix is considered as a square array where each row represents the out-nodes of a graph and each column represents the in-nodes of a graph. Entry 1 represents that there is an edge between two nodes. The adjacency matrix for an undirectedgraph is symmetric [2].



Connectivity Matrix

	A	B	C	D	E
A	0	1	1	1	0
B	1	0	1	0	0
C	1	1	0	1	1
D	1	0	1	0	0
E	0	0	1	0	0

Figure 2.6 Connection Matrix

Definition 2.8: Two vertices *u* and *v* of G are said to be connected if there is a (u,v)-path in G. Connection is an equivalence relation on the vertex set V. Thus there is a partition of V into nonempty subsets V_1, $V_{2...}$, V_w such that two vertices u and u are connected if and only if both *u* and *v* belong to the same set V_i. The subgraphs $G[V_1]$, $G[V_2]$, ..., $G[V_w]$ are called the components of G. If G has exactly one component, G is connected; otherwise Gis disconnected and the number of components of G is denoted by w(G) [5].

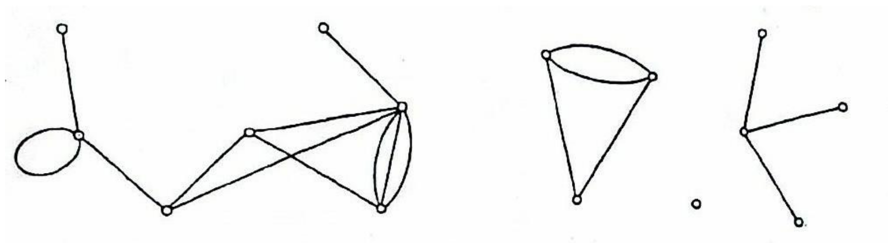


Figure 2.7 Connected and disconnected graph

Definition 2.9: The brain is a complex organ that controls thought, memory, emotion, touch, motor skills, vision, breathing, temperature, hunger and every process that regulates our body. Together, the brain and spinal cord that extends from it make up the central nervous systemor CNS [6].

Definition 2.10: A disorder of the central nervous system that affects movement, often including tremors. Nerve cell damage in brain causes dopamine levels to drop leading to the symptoms of Parkinson's [7].

III. A GRAPH THEORITICAL ANALYSIS OF CORTICAL CONNECTIVITY FROM EEG DATA

Graph theory aims to concisely quantify the properties of complex networks. It has been proposed that a detailed understanding of structural connectivity between cortical areas (i.e., the 'human connectome'), particularly in their dynamics and hierarchies, will provide a mechanistic explanation of different brain functions. It has been mainly used to describe brain graphs deriving from anatomical, morphological, and functional neuroimaging techniques, because a detailed description of the human connectome is difficult to obtain.

Measurements of path length have been also associated with disease severity as measured by the Mini-Mental State Examination (MMSE) and more complex neuropsychological tests. Electroencephalographic (EEG) studies showed that a higher MMSE correlated with a higher clustering coefficient and smaller characteristic path length. The results were interpreted in terms of a less optimal, that is less small world like network organization in the PD group.

A. Data recordings and Preprocessing

EEG recordings were performed at rest, with closed eyes and in a "no task" conditions (at least 5 minutes); subjects were seated and relaxed in a sound attenuatedand dimly lit room. EEG signals were recorded from 19 scalp electrodes (Fp1, Fp2, F7, F8, F3, F4, T3, T4, C3, C4, T5, T6, P3, P4, O1, O2, Fz, Cz and Pz) positioned accordingto the International 10–20 system. The monitoring of the eye movements was obtained with two different channels, vertical and horizontal electrooculography; skin/electrode impedances were lowered below 5 KΩ. The EEG recordings were band-pass filtered from 0.1 to 47 Hz using a finite impulse response filter and the sampling rate frequency was set up at 256 and 512 Hz. Imported EEG data were fragmented in 2 second duration epochs, identifying and extracting visible artifacts (i.e., eye movements, cardiac activity, and scalp muscle contraction) using an independent component analysis (ICA) procedure. ICA is a blind source decomposition algorithm that enables the separation of statistically independent sources from multichannel data. It has been proposed as an effective method for separating ocular movement and blink artifacts from EEG data. ICA was performed using the Infomax ICA algorithm as implemented in the EEGLAB.

B. Graph analysis

A network is a mathematical representation of a real world complex system and is defined by a collection of nodes (vertices) and links (edges) between pairs of nodes. Nodes in large-scale brain networks usually represent brain regions, while links represent anatomical, functional, or effective connections, depending on the dataset. Two core measures of graph theory were computed: characteristic path length (L) and clustering coefficient (C). Based on the insights they deliver, they can be classified into measures reporting on aspects of integration and segregation of the network, respectively. Segregation (or specialization) refers to the degree to which a network's elements form separate clusters. Integration refers to the capacity of the network as a whole to become interconnected and exchange information. L is reported in the following:

$$L = \frac{1}{n}\sum_{i \subset N} L_i$$

$$= \frac{1}{n}\sum_{i \subset N} \frac{\sum_{j \subset N, j \neq i} d_{ij}}{n-1}$$

Where L_i is the average distance between nodes i and all other nodes.

Measures of integration are generally based on the concept of communication paths and their path lengths. A path is any unique sequence of edges that connects two nodes with one another, and its length is given by the number of steps (in a binary graph) or the sum of the edge lengths (in a weighted graph). The length of the shortest path between each pair of nodes corresponds to their distance (also often referred to as the "shortest path length"), and the global average of all distances across the entire network is called the network's characteristic path length. Short path lengths promote functional integration since they allow communication with few intermediate steps, and thus minimize effects of noise or signal degradation. In non-mathematical terms, the functional integration in the brain is the ability to rapidly combine specialized information from distributed brain regions. Lengths of paths estimate the potential for functional integration between brain regions, with shorter paths implying stronger potential for integration. The clustering coefficient C of a node is reported in the following:

$$L = \frac{1}{n}\sum_{i \subset N} C_i$$

$$= \frac{1}{n}\sum_{i \subset N} \frac{2t_i}{k_i(k_i - 1)}$$

Where C_i is the clustering coefficient of node i ($C_i = 0$ for $k_i < 2$).

IV. GRAPH THEORY APPLICATIONS IN FUNCTIONAL BRAIN NETWORK ARCHITECTURE

Network science and graph theory methods can significantly contribute tounderstand age-related brain function and dysfunction and in particular, to map brain from structure to function, to explore how cognitive processes emerge from their morphological substrates, and to better evaluate the linkage between structural changes and functional derangement in the near future, this approach might even help to develop new individualized therapeutic/rehabilitative strategies.

A. Graph Theory approach

The human brain is probably the most complex container of interconnected networks in nature, and the "network science of the brain". It defines the connection matrix of the human brain as the human "Connectome." Previous studies have applied graph theory to EEG datafor the investigation of brain network organization during aging and, in particular, alongthe continuous line that connects normal aging (Nold), mild cognitive impairment (MCI),and PD.

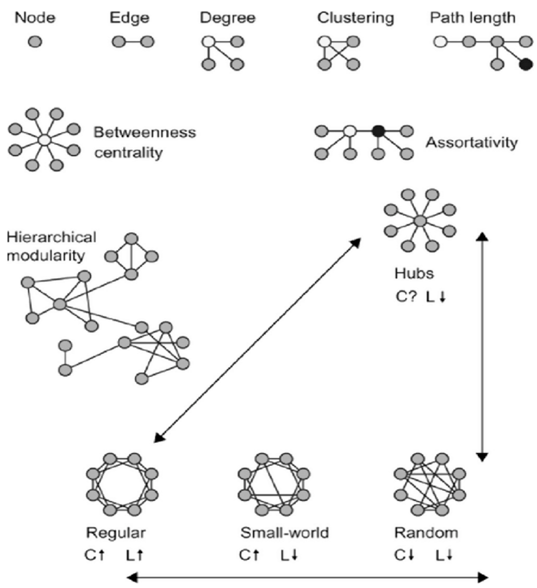


Figure 4.1 Comprehension of Graph Theory concepts

By performing an individual analysis, brain connectivity was computed by eLORETA software in the regions of interest (ROIs) defined according to the available Brodmann areas for left and right hemispheres. Intracortical LagR, extracted by “all nearest voxels” or those in a sphere of 19mm radius, selected on the basis of the number of considered nodes, was individually computed between all possible pairs of ROIs for each EEG frequency band : delta (2–4 Hz), theta (4–8 Hz), alpha 1 (8–10.5 Hz), alpha 2 (10.5–13 Hz), beta 1 (13–20 Hz), beta 2 (20–30 Hz), and gamma (30–45 Hz).

B. Parameters derived by Graph Theory

Segregation refers to the degree to which network elements form separate clusters and correspond to clustering coefficient (C), while integration refers to the capacity of network to become interconnected and exchange information, and it is defined by the characteristic path length (L) coefficient.

The mean clustering coefficient is computed for all the nodes of the graph and then averaged. It is a measure of the tendency of network elements to form local clusters. Starting by the definition of L, the weighted characteristic path length L^w represents the shortest weighted path length between two nodes.

Small-world (SW) parameter is defined as the ratio between normalized C and L – C^w And L^w respect to the frequency bands. The SW coefficient describes the balance between local connectivity and global integration of a network. Small-world organization is intermediate between that of random networks, the overall shortest path length which is associated with a low level of local clustering, and that of regular networks or lattices and the high level of clustering which is accompanied by a long path length. This implies that nodes are linked through relatively few intermediate steps, and most nodes maintain few direct connections.

V. EEG STUDY FOR PARKINSON’S DISEASE

The recording of the first human EEG was performed in 1924 by German physician Hans Berger. Since then relative band power has become an established measure to quantify deviations from normal oscillatory brain activity. Several minutes of EEG signal, usually recorded under resting state condition and in an ’eyes closed’ (EC) setting, are filtered into four to seven non-overlapping frequency bands covering a range from 0.5Hz up to 70Hz. Then, for each of those bands, the relative signal power is calculated.

High density EEG machines available today provide up to 256 individual electrodes recording brain activity at a frequency of 1000Hz or higher.

Parkinson’s disease (PD) is the second most common age-related neurodegenerative disorder after Alzheimer’s disease. It is estimated to affect nearly 2 percent of those over age 65. Diagnosing Parkinson’s disease especially in its early stages requires experienced practitioners. Thus providing tools for detecting early changes in brain activity that are as easy to use as taking one’s own blood pressure is an important first step.

	1	2	3	4	5	6
AGE	65	66	72	68	65	66
BASELINE	0.98	1.03	0.96	0.97	0.98	0.965
T_0	0.97	1.04	0.975	0.956	0.98	0.997
T_1	0.985	1.06	0.985	0.93	0.978	0.98
T_2	0.97	1.06	0.985	0.991	0.997	0.98

Table 5.1 Small World parameter for Parkinson’s disease (PD)

	1	2	3	4	5	6
AGE	65	66	72	68	65	66
NOLD	1.005	1.002	1.02	0.998	1.01	0.99
MCI	1.001	1.003	1	1	1.02	0.99
PD	1.001	1.003	1	1	1.01	0.99

Table 5.2 Small world parameter for Parkinson's disease in Eyes open condition

	1	2	3	4	5	6
AGE	65	66	72	68	65	66
NOLD	1.025	1.025	0.99	0.998	1.002	1.001
MCI	1.02	1.02	0.99	0.999	1.002	1.001
PD	1.001	1.003	1	1	1	0.99

Table 5.3 Small world parameter for Parkinson's disease in Eyes close condition

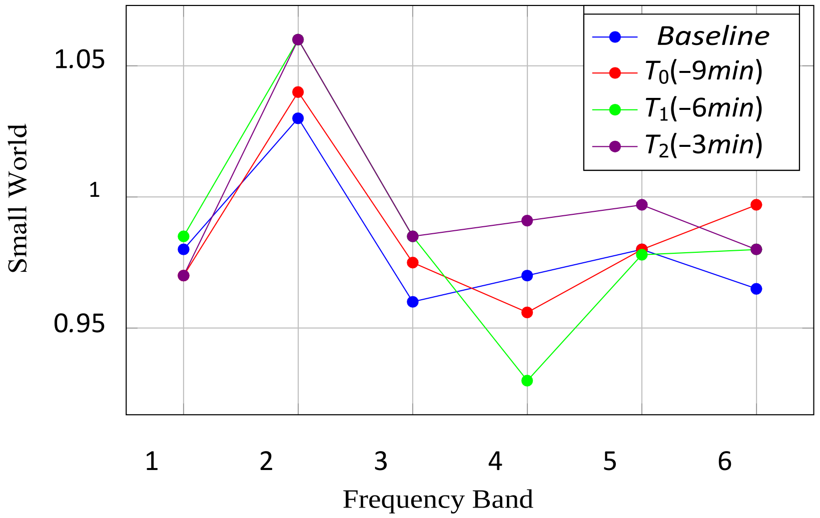


Figure 5.1 [x axis (1 as Delta, 2 as Theta, 3 as Alpha 1, 4 as Alpha 2, 5 as Beta 1, 6 as Beta 2)]

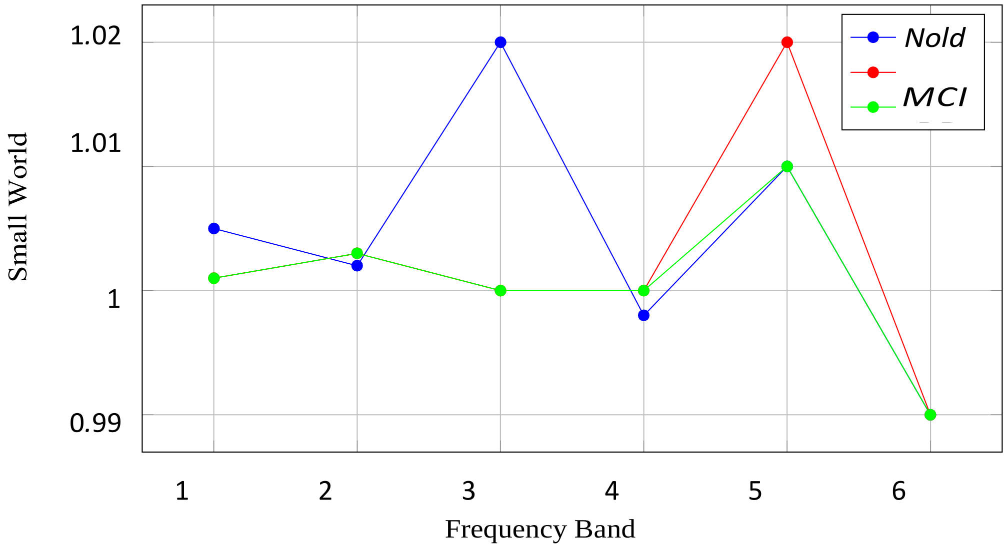


Figure 5.2 [x axis (1 as Delta, 2 as Theta, 3 as Alpha 1, 4 as Alpha 2, 5 as Beta 1, 6 as Beta 2)] Eyes opened

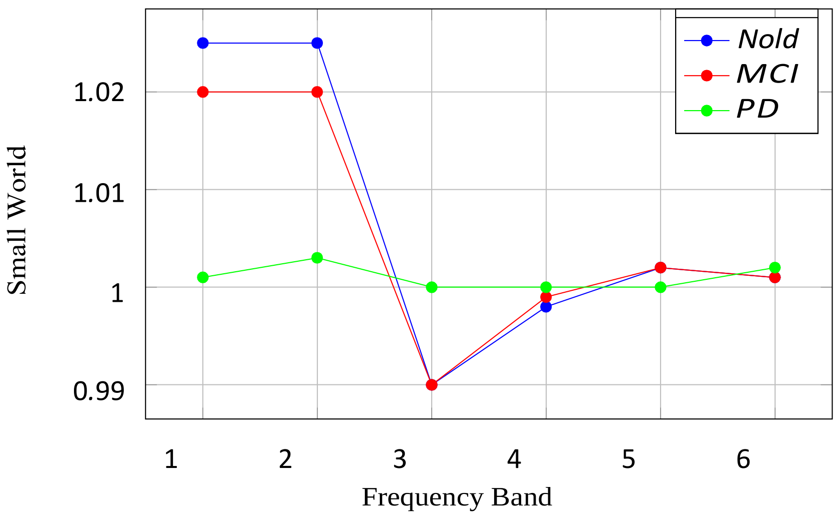


Figure 5.3 [x axis (1 as Delta, 2 as Theta, 3 as Alpha 1, 4 as Alpha 2, 5 as Beta 1, 6 as Beta 2)] Eyes closed

Data comparisons were analyzed by the statistical analysis of variance (ANOVA) design for the SW index between the factors Group (PD, Nold) and Band (delta, theta, alpha 1, alpha 2, beta 1, beta 2, and gamma).

The ANOVA for the evaluation of the SW index showed a statistically significant interaction between both factors, Group (PD, MCI, Nold) and Band (delta, theta, alpha 1, alpha 2, beta 1, beta 2, gamma), as reported in Figure 5.1, 5.2 5.3. In particular, the SW index in Parkinson's showed lower values (more structured network) in theta and higher (less organized network) in alpha 2 compared to controls.

The results showed that PD patients presented a more ordered low-frequency EEG rhythm structure (lower value of SW) than age-matched healthy subjects, particularly in the theta band (4–8 Hz). Conversely, in the high-frequency alpha band (10.5–13 Hz), PD patients presented more random organization (higher value of SW) than age-matched healthy subjects.

EEG spectral analysis in the resting state in PD patients increased in slower and decreased in faster frequency bands, suggesting a slowing of PD patient's cortical activity.

Others have revealed that the EEG cortical sources in the theta frequencies are associated with a pathological synchronization of the brain motor systems related to tremor or sensorimotor integration.

For the higher-frequency bands, the SW increase in the alpha 2 band in PD patients could be interpreted as a possible biomarker of a cognitive decline in the early phase of PD. High alpha rhythm (10.5–13 Hz) reflects the physiological modalities of the thalamo–cortical and cortico–cortical loops, which facilitate and inhibit the transmission of impulses and the processing of sensorimotor information flow.

Several studies have demonstrated that a decrease in alpha power is correlated with reduced brain region synchronization and integration, namely a more randomized network, which reflects cognitive dysfunction.

In general, the alpha band constitutes an important characteristic of normal EEG activity at rest; a disruption of these rhythms might be interpreted as an EEG marker of altered cortical functioning and impaired information processing. Vecchio and colleagues have revealed that an increase in the alpha SW parameter, derived from EEG data, can distinguish between a neurodegenerative status, as Alzheimer's disease, and a healthy elderly brain condition. In fact, they observed that the SW index in the alpha band increased in the pathological condition rather than the physiological one.

An increase in terms of SW in alpha 2, which means more random network organization, might be an early sign of motor dysfunction in PD patients. Decrease in the path length parameter in the alpha 2 band in PD patients compared to healthy subjects, which could be associated with a more random network organization.

Therefore a lower SW value in the theta band and a higher value in the alpha band represent functional disconnections that could be interpreted as biomarkers of motor impairments typical of PD and a reduction in the performance of cortical network.

VI. CONCLUSION

This study shows that resting brain exhibit a different small word between Parkinson's patients and control subjects. The result suggests that Parkinson's disease globally modulates the cortical connectivity of the brain, modifying the underlying functional organization, and that this modulation could be linked to changes in the synaptic efficiency of the motor network and related areas of the brain. Evaluating this parameter could be helpful for the early diagnosis and treatment of Parkinson's disease (PD). Through small world and band signals the problem in brain can be detected. According to finding small world is lower in theta band and a higher value in alpha band represent functions disconnections. This may contribute to understanding whether Parkinson's disease (PD) forms such as tremor dominant and non-tremor dominant.

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