A Novel Method of Early Diagnosis of Alzheimer's Disease based on EEG Signals

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Abstract

Studies have reported that electroencephalogram signals in Alzheimer's disease patients usually have less synchronization than those of healthy subjects. Changes in electroencephalogram signals start at early stage but clinically, these changes are not easily detected. To detect this perturbation, three neural synchrony measurement techniques; phase synchrony, magnitude squared coherence and cross correlation are applied on three different databases of mild Alzheimer's disease patients and healthy subjects. We have compared the right and left temporal lobe of the brain with the rest of the brain area (frontal, central and occipital), as temporal regions are relatively the first ones to be affected by Alzheimer's disease. Moreover, electroencephalogram signals are further classified into five different frequency bands (delta, theta, alpha beta, and gamma) because each frequency band has its own physiological significance in term of signal evaluation. A new approach using principal component analysis before applying neural synchrony measurement techniques has been presented and compared with Average technique. The simulation results indicated that applying principal component analysis before synchrony measurement techniques show significantly better results as compare to the lateral one. At the end, all the aforementioned techniques are assessed by a statistical test (Mann-Whitney *U* test) to compare the results.

1. Introduction

Mild Cognitive Impairment (MCI) is characterized by impaired memory state of brain probably leading towards mild Alzheimer's disease (MiAD) or Alzheimer's disease (AD). This prodromal stage of AD is under a great influence of research since long time [1-3]. Statistics reported that 6-25% of MCI are transformed to AD annually and 0.2-4% from healthy person to AD [2, 4], revealing the fact that MCI is a transition state of MiAD and AD.

Loss of functional connectivity between cortical and hippocampus has long been an important focus of researches to examine the cause of cognitive dysfunction in AD [5, 6]. Statistical analysis of interdependence among times series recorded from different brain areas, to study the functional interaction, is called "functional connectivity" [7]. Due to destructive characteristics of AD, it has also been characterized as a neocortical "disconnection syndrome" [8]. The brain's visualization as a complex network of subsystems has led us to find out the factors that can best identify functional disorders in brain [9]. There is now ample evidence that formation of dynamic links in term of synchronization constitutes the functional integration of the brain [10-12].

Electroencephalogram (EEG) signals are considered functional examples to evaluate cognitive disturbances and a diagnostic tool, especially when a diagnostic doubt exists even after the initial clinical

procedures [13, 14]. A great deal of research has already been conducted to detect the fluctuations in (EEG) signals [2, 5, 15]. Alteration in the regional cerebral blood flow (rCBF) has been considered one of the causes of abnormality in EEG signals of AD [16, 17]. Studies on MCI have shown a decrease of alpha power [18, 19] and an increase of theta (4-8 Hz) power [20, 21] in cortio-cortical and subcortical parts of the brain. Babiloni et al [2] claimed that the reduction of the synchronization likelihood occurs both at inter-hemispherical (delta-beta2) and fronto-parietal (delta-gamma) electrodes.

Topographically analyzing the EEG signals, Micheal et al [22] reported a less synchronization of upper alpha band between central and temporal cortex. In line, a correlation between higher low-frequency amplitude and alpha-beta activity at frontal region may reflect an early sign of cortical atrophy during the course of AD [23]. Similarly, perturbation in cholinergic inputs from the basal forebrain to cortex and hippocampus indicates a decrease in cortical EEG coherence [24] that can be considered a biomarker for the early detection of AD [2]. Moreover, a combination of multi-linear interaction within the tensor formed by multiplying the *subject x frequency x regions* also provides a simple set of features for the interpretation and classification of AD at its early stage [25]. The concept of *local* and *global* methods is used to analyze synchronization between pairs of signals and entire EEG channels at the same time, respectively [15].

The studies, so far, have provided a very limited regional comparison of brain; for instance less synchronization has been reported between temporal and central regions [22] and also in fronto-parietal region [2]. Similarly, functional coupling of EEG rhythms by sensorimotor events is presented only in centro-parietal regions of brain [26]. A wider range of study is still required to analyze the synchronization likelihood in all parts of brain (right temporal, left temporal, frontal, central and occipital) at the same time, on different sets of data for AD.

Synchronization, precisely speaking, is a coordination of "rhythmic oscillators" [27] for a repetitive functional activity. Whereas, neural synchronization is putatively considered a mechanism where brain regions simultaneously communicate with each other to complete a specific task such as perception, cognition, and action [28, 29]. Any disturbance in the brain, caused by a disease or any other infection, can highly affect the synchronization of brain. Quantitative analysis of EEG signals provides a better insight of synchronization between different parts of brain. For instance, less synchrony has been detected in the EEG signals of AD patients as compare to healthy persons [15].

Various synchrony measurement techniques have already been discussed to detect any perturbation in the EEG signals of AD patients [30]. Both linear such as coherence and nonlinear such as phase synchronization methods are widely used to quantify synchronization in electroencephalographic signals [6, 31, 32]. A comparison of occipital inter-hemispheric coherence (IHCoh) for normal older adults and AD patients reveals a reduced occipital IHCoh for both lower and higher bands of alpha [33]. Almost similar findings reported by Locatelli et al. [34] where a significant increase in delta coherence is noticed between frontal and posterior regions in AD patients while a decrease in alpha coherence is shown in temporo-parieto-occipital areas. Spontaneous phase synchronization of different brain regions is calculated by Kuramoto's parameter (ρ), which is particularly useful to measure multi-channel data [6].

Despite the considerable success of the above mentioned techniques to analyze disruption in the EEG signals of Alzheimer's patients, further investigations are still required to fulfill the clinical requirements. For instance, in order to detect Alzheimer's at its earlier stages we need to focus on those areas where

Alzheimer's attack at first and then we need to check its synchronization with the rest of the brain regions. Furthermore, additional novel and comprehensive methods are still required to check the validity of aforementioned techniques on EEG signals.

The above overview suggests that, first, Spatial-Spectral Analysis of EEG signals can provide a measure of memory visualization. Second, neural synchrony measurement techniques have a potential to discriminate between AD patients and healthy subjects. What is still missing or ambiguous in the literature survey is the simultaneous comparison of all parts of brain with the right and left temporal (the most affected parts of brain) to analyze synchronization and also the implementation of new methods to apply synchrony measurement techniques. In this research work, the following novel contributions are considered:

- We have filtered a dataset of MiAD patients into five different frequency bands (delta, theta, alpha, beta and gamma). For each frequency band we have computed neural synchronization to compare all parts of brain (frontal, occipital and central) with left and right temporal.
- Furthermore, three different sets of MiAD patients are compared to check the validity of our methodology. A high inter-subject variability has been seen in the EEG signals of AD patients, especially with different level of severity and comorbidities [25, 35, 36]. Most of the existing studies focus on a single synchrony measure with a single set of data [37]. Also, they apply different measures to different datasets. In this case it is hard to compare the results to conclude a single hypothesis. To extract a general set of feature we have analysed three different databases, each from one hospital at a time.
- In order to remove the ambiguity of biased results due to "features redundancy" we have applied PCA (Principal Component Analysis) technique before applying synchrony measurement techniques. Reducing features vector dimension, commonly known as feature reduction, will help to get accuracy results, and avoid over-fitting classification [38]. We compare the results with simple Average technique to analyze the pros and corns of the new proposed methodology.

Besthorn et al [39] applied PCA technique in the quantitative analysis of EEG signals to compress a group of predictor variables to a small set of factors or principle components. Later they applied linear discriminant classifier on these variables to discriminate AD patients from healthy subjects. Similarly, Peter et al [40] applied PCA to remove the artifacts from EEG signals that were generated by eye-blink. To the best of our knowledge and the literature we have surveyed so far, we could not find the application of PCA to remove the redundant features from the data that can generate a biased result to check the synchronization of brain areas.

Given the exploratory nature of the study, our a priori hypothesis is, the proposed methodology would provide a better insight to investigate the decline in the neural synchronization of AD patients. It would provide a better topographical and spectral analysis of the brain regions eliminating the probability of biased result due to feature redundancy.

The rest of this paper is structured as follows. Section 2 provides an overview of our synchrony measurement techniques, the utilized data and the filtering process using five frequency bands, methodology of the proposed technique, and statistical analysis of the results. Sections 3 and 4 are dedicated for discussion and conclusion, respectively.

2. Methods

2.1. Synchrony Measurement Techniques

In this section, we briefly review the synchrony measurement techniques that we have implemented on our datasets which include phase synchrony, cross correlation and coherence.

2.1.1. Phase Synchrony (Hilbert Transform)

Synchronization of two periodic non-identical oscillators refers to the adjustment of their rhythmicity, i.e. the phase locking between the two signals [41, 42]. It refers to the interdependence between the instantaneous phases $\varphi_1(t)$ and $\varphi_2(t)$ of the two signals $s_1(t)$ and $s_2(t)$, respectively. It is usually written as:

$$\varphi_{n,m} = n\varphi_1(t) - n\varphi_2(t) = constant \quad (1)$$

Where n and m are integers indicating the ratio of possible frequency locking, and $\varphi_{n,m}$ is their relative phase or phase difference. To compute the phase synchronization, the instantaneous phase of the two signals should be known. This can be detected using analytical signals based on Hilbert Transform [9].

$$z(t) = x(t) + i\tilde{x}(t) \quad (2)$$

Here *z(t)* is complex value with *x(t)* is a real time series and $\tilde{x}(t)$ is its Hilbert transform.

2.1.2. Cross Correlation

Cross correlation is a mathematical operation used to measure the extent of similarity between two signals. If a signal is correlated to itself, it is called auto-correlated. If we suppose that *x(n)* and *y(n)* (why not S1(t) and S2(t) make a uniform signals suggestion) are two time series then the correlation between is calculated as [43]:

$$\hat{R}_{xy}(m) = \begin{cases} \sum_{n=0}^{N-m-1} x_{n+m} y_n & m \geq 0 \\ \hat{R}_{yx}(-m) & m < 0 \end{cases} \quad (3)$$

Cross correlation returns a sequence of length 2*M−1 vector, where *x* and *y* are of length N vectors (N>1). If *x* and *y* are not of the same length then the shorter vector is zero-padded. Cross correlation returns value between −1 and +1. If both signals are identical to each other the value will be 1, otherwise it would be zero [15].

2.1.3. Magnitude Squared Coherence

The coherence functions estimates the linear correlation of signals in frequency domain [15]. The magnitude squared coherence is defined as the square of the modulus of the mean cross power spectral density (PSD) normalized to the product of the mean auto PSDs [44]. The coherence $C_{xy}(f)$ between two channel time series is computed as:

$$C_{xy}(f) = \frac{|P_{xy}(f)|}{P_{xx}(f)P_{yy}(f)} \quad (4)$$

$P_{xy}(f)$ is the cross PSD estimate of x and y. $P_{xx}(f)$ and $P_{yy}(f)$ are the PSD estimates of x and y respectively.

2.2. Data Description and Data Filtering

2.2.1. Data Description

The datasets we are analyzing, have been recorded from three different countries of European Union . Specialist at the memory clinic referred all patients to the EEG department of the hospital. All patients passed through a number of recommended tests; Mini Mental State Examination (MMSE) [45], The Rey Auditory Verbal Learning Test [46], Benton Visual Retention test [47] and memory recall tests [48]. The results are scored and interpreted by psychologists and a multidisciplinary team in the clinic. After that, each patient is referred to hospital for EEG assessment to diagnose the symptoms of AD. Patients were advised to be in a resting state with their eyes closed is this during the test. The sampling frequency and number of electrodes for three datasets are all different. Detailed information is as follows:

2.2.2. Database A

The EEG *dataset A* contains 17 MiAD patients (10 males; aged 69.4 ± 11.5 years) while 24 healthy subjects (9 males; aged 77.6 ± 10 years). They all are of British nationality. This data was obtained using a strict protocol from Derriford Hospital, Plymouth, U.K. and has been collected using normal hospital practices. EEG signals were obtained using the modified Maudsley system which is similar to the traditional 10-20 international system [49]. EEGs were recorded for 20 sec at a sampling frequency of 256 Hz (later on sampled down to 128 Hz) using 21 electrodes.

2.2.3. Database B

This EEG dataset composed of 5 MiAD patients (2 males; aged 78.8 ± 5.6 years) as well as 5 healthy subjects (3 males; aged 76.6 ± 10.0 years). They all are of Italian nationality. Several tests, for instance; MMSE, the clinical dementia rating scale (CDRS) and the geriatric depression scale (GDS) were conducted to evaluate the cognitive state of the patients. The MMSE result for healthy subjects is (29.3 ± 0.7) while for MiAD patients is (22.3 ± 3.1). EEGs were recorded for 20 sec at a sampling frequency of 128 Hz using 19 electrodes at the University of Malta, Msida MSD06, Malta.

2.2.4. Database C

This dataset consists of 8 MiAD patients (6 males; aged 75 ± 3.4 years) and 3 healthy subjects (3 males; aged 73.5 ± 2.2 years). They all are of Romanian Nationality. The AD patients have been referred by a neurologist for EEG recordings. All subjects are diagnosed with AD by means of psychometric tests (MMSE, CDR, OTS), neuroimaging (CT) and clinical examination (gender, age, disease, duration, education and medication). The MMSE result for healthy subjects is (28-30) while for MiAD patients it is (20-25). EEG data is recorded using a large equidistant 22-channel arrangement conforming to the international federation of clinical neurophysiology (IFCN) standards [50] for digital recording of clinical EEG from the Ecological University of Bucharest. The time series are recorded for 10 to 20 minutes at a sampling frequency of 512 Hz using 22 electrodes. The signals are notch filtered at 50 Hz. Further details about the data can be found in [51].

For current research work, we have obtained a version of the data that is already preprocessed of artifacts by using Independent Component Analysis (ICA), a blind source separation technique (BSS). Details of these procedures can be found in [52]. For ICA processed data, the least corrupted 20s recordings have been selected for further analysis.

2.2.5. Data filtering into five frequency bands

EEG time series are classified into five frequency bands. Each frequency band has its own physiological significance [6] [53].

- Delta (δ: $1 \leq f \leq 4$ Hz): these are characterized for deep sleep and are correlated with different pathologies.
- Theta (θ: $4 \leq f \leq 8$ Hz): play an important role during childhood. High theta activities in adults are considered abnormal and associated with brain disorders.
- Alpha (α: $8 \leq f \leq 12$ Hz): usually appear during mental inactive conditions and under relaxation. They are best seen during eye closed and mostly pronounced in occipital location.
- Beta (β: $12 \leq f \leq 25$ Hz): are visible in central and frontal locations. Their amplitude is less than alpha waves and they mostly enhance during tension.
- Gamma (γ: $25 \leq f \leq 30$ Hz): are best characterized for cognitive and motor functions.

Bandpass filter is applied to each EEG channel to extract the EEG data in specific frequency band [F:(F+W)] Hz. Butterworth filters were used (of 2nd order) as they offer good transition band characteristics at low coefficient orders; thus, they can be implemented efficiently [54].

2.3. Methodology

In this research work, a novel methodology using PCA and neural synchrony measurement of the brain is proposed. We have compared our proposed method with other methods which takes the average of synchrony measures for all channels in one region of the brain. As mentioned previously, we are comparing the right and left temporal lobe with the frontal, central and occipital so there are total 7 comparisons of the brain ((left temporal-right temporal (LT-RT)), (left temporal-frontal (LT-F)), (left temporal-central (LT-C)), (left temporal-occipital (LT-O)), (right temporal-frontal (RT-F)), (right temporal-central (RT-C)), and (right temporal-occipital (RT-O))) for all frequency bands (δ, θ, α, β, γ). A brief description of these methods is given below.

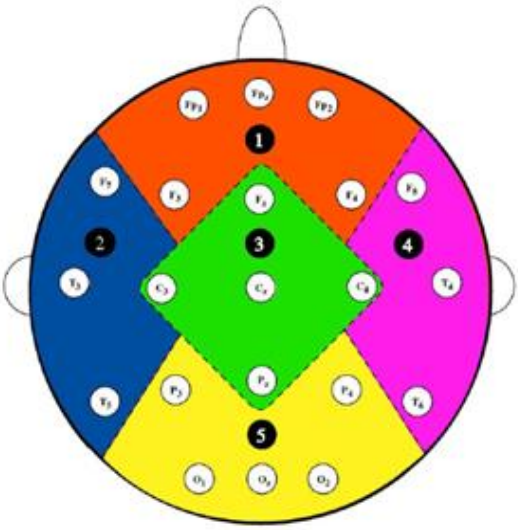

Fig.1. The 21 Channels used for EEG recording

2.3.1. First Method (Taking average of synchrony measures for all channels of one region)

First we apply neural synchrony measurement techniques on each channel pair (time series of two channels) of two different regions for all frequency bands and then we take the average of those results. For instance, we apply phase synchrony measure on each channel pair of right and left temporal ((F_7-F_8), (F_7-T_4), (F_7-T_6), (T_3-F_8), (T_3-T_4), (T_3-T_6), (T_5-F_8), (T_5-T_4), (T_5-T_6) and then we take the average result of right temporal-left temporal. We compare the left temporal lobe with the frontal (FP_1, FP_2, FP_z, F_3, F_4), central (F_z, C_3, C_z, C_4, P_z) and occipital (P_3, P_4, O_1, O_2, O_z). Similarly, we compare the right temporal lobe (F_8, T_4, T_6) to rest of the brain area. The same technique has been used for rest of the synchrony measures i.e. cross correlation and coherence.

After getting the results, we compare the neural synchronization of AD patients and healthy subjects, for all three measurement techniques (phase synchronization, cross correlation and coherence), by Mann-Whitney U test. Figure 2 shows all the steps of our Average method.

2.3.2. Second Method (PCA based neural synchrony measure)

In this method, instead of applying synchrony measurement techniques directly on the filtered data, first we apply Principal Component Analysis (PCA) technique on all channels of one. This eliminates any redundant information that a region could provide. For instance, we apply PCA on all three channels of left temporal lobe (F_7, T_3, T_5) and consequently it provides a single signal without any redundant information. Then we apply PCA on all channels of right temporal lobe (F_8, T_4, T_6). After that, we apply synchrony measure on these two regions. Similarly, we apply PCA on all other channels of a region; frontal (FP_1, FP_2, FP_z, F_3, F_4), central (F_z, C_3, C_z, C_4, P_z) and occipital (P_3, P_4, O_1, O_2, O_z) and compute the synchrony measure with left and right temporal. The rest of the procedure is similar to the first proposed method.

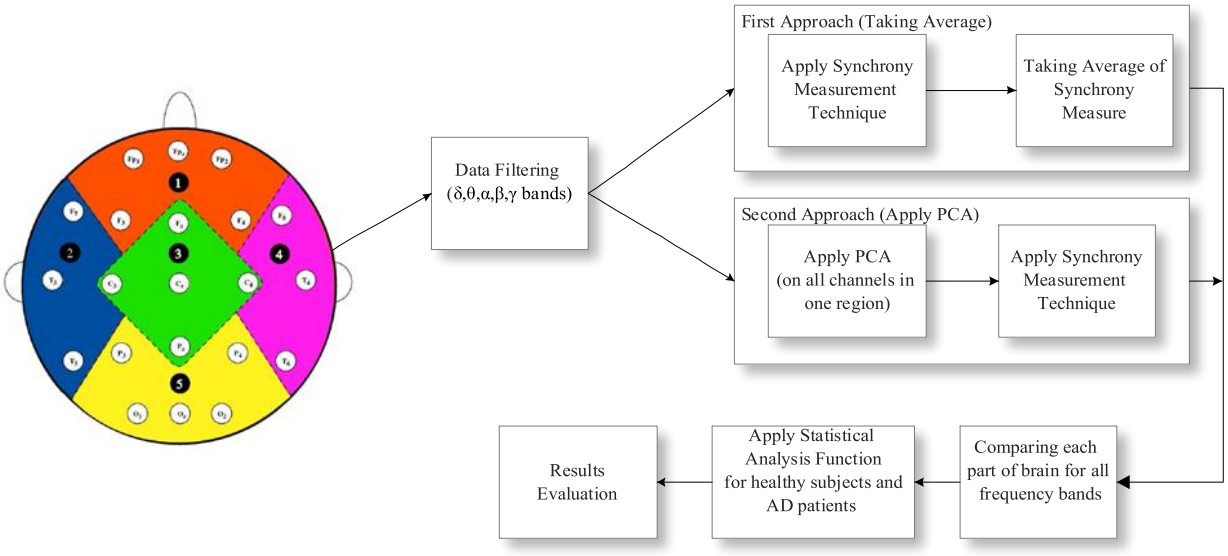

Fig.2. Average and PCA Methods

2.3.3. Principal Component Analysis (PCA)

The basic purpose of PCA is to reduce the dimensionality of a dataset to convert it to uncorrelated variables providing maximum information about a data while eliminating interrelated variables. In other words it transforms the highly dimensional dataset (of *m* dimensions) into low dimensional orthogonal features (of *n* dimension) where $n<m$ [55].

In our case we apply PCA on all channels in one particular region, for instance, the application of PCA for the left temporal lobe as is shown in Fig.3 (a) using channel (F_7, T_3, T_5) are converted into a single signal as shown in Fig. 3(b). The generated temporal signal contains almost all information from the left temporal lobe while eliminating any redundant information.

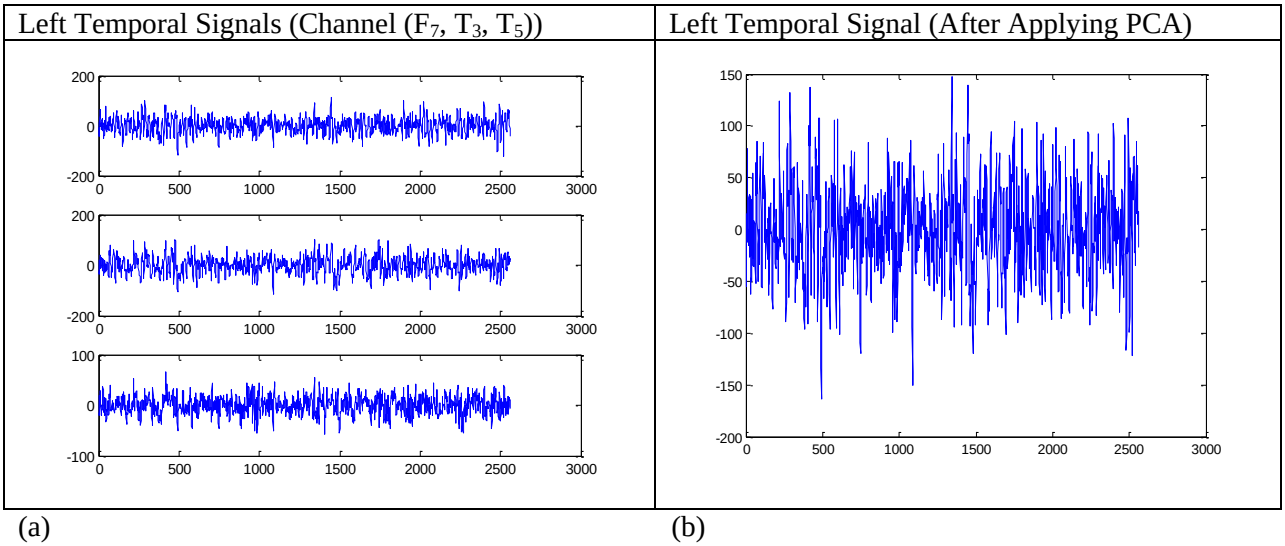

Fig.3. Application of PCA on left temporal lobe channels signals

2.4. Statistical Analysis

To investigate whether there is a significant difference between the EEG signals of MiAD patients and the control subject and also to prove the probable significance of our proposed methodology, we apply Wilcoxon ranksum (Mann-Whitney) test [reference] on our datasets. A ranksum function is a non-parametric test which allows us to check whether the statistics at hand, in our case synchrony results, take different values from two different populations. Lower p-values indicate higher significance in term of large difference in medians of two populations [15].

Since we are applying three different synchrony measures on three different sets of data, first we consider our first proposed method (Taking average of synchrony values) to compute the synchrony measure. We apply all three measures for all 7 different comparisons of brain for all frequency bands and compute the results by Mann-Whitney test. Then we apply the same techniques on all, above mentioned, three datasets using the second proposed method (PCA based synchrony measures). This will enable us to compare our results in two different perspectives:

i. Investigating three different synchrony measures at a time will help us to compare which measure works better for EEG signals.
ii. Secondly, we are able to compare two different methods for three synchrony measures using three different datasets.

In addition to evaluating the statistical significance of our proposed method, this will also help us to differentiate the MiAD patients from healthy subjects.

3. Results and Discussions

The aim of the present study is to find the relationship of EEG synchronization with AD and thus to explore further dimensions in disconnection theorem of cognitive dysfunction in AD. And also, to investigate a better method to detect any changes in EEG synchrony that can be considered a biomarker for the early detection of AD. Here we investigate and discuss results in two different angles. First, we discuss the role of synchrony measures to examine a change in EEG synchrony in MiAD patients and later we confer the significance of applying PCA before synchrony measures.

3.1. Functional disconnection of brain regions due to lower synchronization

We have observed that all of the synchrony measures, tested in this paper, show a decrease in EEG synchrony for MiAD patients as compare to healthy subjects. However, cross correlation shows a higher number of significant results at the p=0.01 level as compare to phase synchrony and coherence. We have examined mostly the areas that have shown less functional connectivity for all three synchrony measures are right temporal- central (RT-C) for delta, theta and alpha bands and also left temporal-occipital (LT-O) for delta and alpha bands. The rest of this paper discusses these two regions where we find highly significant results compared to the rest of the regions.

First we discuss *dataset A* for all three synchrony measures with PCA based method. The p-values for cross correlation in RT-C region are 2.47×10^{-4}, 1.46×10^{-4}, 0.009 for delta, theta and alpha bands respectively. In LT-O region the smallest p-vales for delta and theta bands are 8.50×10^{-5} and 6.8×10^{-5} respectively. The 2nd best measure which has given us remarkable results is phase synchrony, where we

get 0.0067, 0.0403, and 0.0585 p-values for delta, theta and alpha bands respectively in RT-C region. We get 0.0041 and 0.0271p-values for delta and alpha bands in LT-O region. Lastly, the coherence function shows significant results in RT-C region for delta band, p-vale=0.0378 and in LT-O 9.8x10-4 and 0.05 for delta and alpha bands respectively. Coherence function does not provide significant results and hence contradicts Bahar theory [56] where control group showed higher values of evoked coherence in delta, theta and alpha bands in the left fronto-parietal electrode pairs as compare to AD patients.

Lower p values at delta and alpha bands are shown by Babiloni et al [2] at fronto-parietal couplings of electrodes which indicates a lower synchronization in MCI and AD subjects. Further to the previous findings, our results show a higher difference of synchronization for temporal, occipital and central areas in MiAD patients at delta, theta and alpha level. They show lower magnitudes of delta, theta and alpha bands in temporal, central and occipital areas in MiAD patients than the compared healthy subjects. Temporal regions are characterized for short term and long term memory and any neuronal change on these sites is a clear indication of progression of AD.

Interestingly, we find a decrease in alpha band synchronization for all three synchrony measures in almost all regions. For instance, for cross correlation p-value<0.01 in almost all parts of the brain, for phase synchrony the p-values are 0.058, 0.0038, 0.011, and 0.027 in RT-C, RT-O, RT-F and LT-O respectively. This shows the importance of alpha rhythm for the early detection of AD which is in accordance with the phenomena that alpha rhythms are mainly modulated by thalamo-cortical and cortio-cortical systems [57]. Alpha band is mainly related to a subjects global attentional readiness and engagement of specific neural channels for the elaboration of sensorimotor or semantic information [2].

As aforementioned, mostly the areas that show lower dysfunctional connectivity are right temporal-central and left temporal-occipital. A lower synchronization in these connections, especially in RT-C region, for alpha band indicates a disturbance in the perception and integration of somatosensory information, visuospatial processing, and cognitive disorder. This information is in line with clinical findings presented in [58] for increasing visual and spatial deficits in MCI and MiAD patients. Table 1 shows the significant p-values in different parts of the brain in different frequency bands for *dataset A*.

Synchrony Measure	Brain-Connections	Frequency regions	P-values
Cross Correlation	RT-C	Delta (δ)	$2.47x10^{-4}$
		Theta(θ)	$1.46x10^{-4}$
		Alpha(α)	0.009
	RT-O	Delta (δ)	$6.9\ x10^{-5}$
		Theta(θ)	$2.7\ x10^{-5}$
		Alpha(α)	0.0029
	RT-F	Delta (δ)	$5.01x10^{-4}$
		Theta(θ)	$6.8\ x10^{-5}$
		Alpha(α)	0.0062
	LT-C	Delta (δ)	$4.3\ x10^{-5}$
		Theta(θ)	$3.8\ x10^{-5}$
		Alpha(α)	0.0192
	LT-O	Delta (δ)	$8.5\ x10^{-5}$
		Theta(θ)	$6.8\ x10^{-5}$
		Alpha(α)	0.0052
	LT-F	Delta (δ)	$2.2\ x10^{-4}$
		Theta(θ)	$5.4\ x10^{-5}$
		Alpha(α)	0.0091
	LT-RT	Delta (δ)	$3.3\ x10^{-4}$
		Theta(θ)	$6\ x10^{-5}$
		Alpha(α)	0.0253
Phase Synchrony	RT-C	Delta (δ)	0.0067
		Theta(θ)	0.0403
		Alpha(α)	0.05
	RT-O	Delta (δ)	0.0041
		Alpha(α)	0.0271
Coherence	RT-C	Delta (δ)	0.0378
	RT-O	Delta (δ)	0.0378
		Alpha(α)	0.0192

Table.1. P-values for dataset A, different frequency bands in different brain connections

Similarly, for *dataset B* and *dataset C* we found low p-values in the same regions for same frequency bands but not as much significant as for the *dataset A*. One thing in common in all three datasets is they show lower p-values in alpha frequency bands in the RT-C region.

3.2. Significance of PCA approach over Average approach

Our second hypothesis was to show the significance of using PCA techniques to eliminate the redundant information from the data that can give biased results, before applying synchrony measures. As expected, we found a big difference in results with and without PCA method. We have found that more than 90% of the values are better in case of *PCA* method as compare to *Average* method for all of three datasets.

For instance, for *dataset A*, in case of PCA method, we have found 8 significant values below 0.01 ($p<0.01$) and 11 significant values below 0.05 ($p<0.05$) while only 2 values below 0.01 ($p<0.01$) and 8 values below 0.05 ($p<0.05$) in case of Average method for phase synchrony measure. Similarly, for cross

correlation measures, although the difference is not very high yet the PCA method has shown more significant values. For example, the number of p-values below 0.01(P<0.01) are 26 while almost all 35 values below 0.05 (p<0.05) while for Average method 22 values are below 0.01 while 30 values below 0.05 (p<0.05). As aforementioned, coherence function doesn't perform better as compare to other two synchrony measures but again we found more significant results in case of *PCA* method as compare to the *Average* method.

Synchrony Measure	Method	P<0.01 (Total Values)	P<0.05 (Total Values)
Cross correlation	PCA	26	35
	Average	22	30
Phase Synchrony	PCA	8	11
	Average	2	8

Table.2. Total number of Significant Values in case of PCA and Average method

The reults are also shown by boxplot in Fig 4 that show the difference of p-values for all three synchrony measures in all 7 brain comparsion for *dataset A*. They compare the results of synchrony measures for PCA and Average methods.

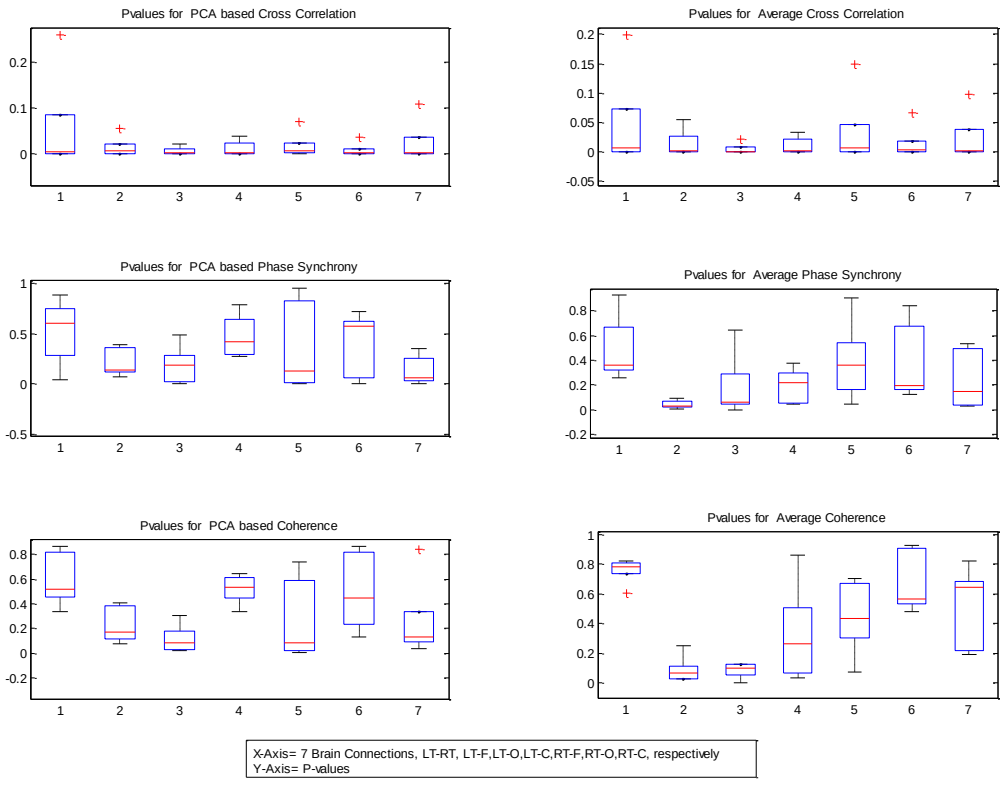

Fig.4. Boxplots show the results of three synchrony measures for PCA and Average methods

Similarly, for *dataset B* and *dataset C*, the results of *PCA* method are more significant as compare to *Average* method. This clearly shows that using PCA method before synchrony measures has two advantages:

- As the redundant information is eliminated from the datasets, the results are not biased and are more reliable.
- Secondly, it proves that application of PCA generates more significant results as compare to obsolete methods.

4. Conclusion

The aim of the current study was to show the significance of applying PCA method to eliminate redundant information from the datasets to get more reliable results. In this study, three different datasets where selected with different specifications and three different synchrony measures are applied to prove the significance of our approach. Moreover we have compared our proposed method with Average methods to compute synchronization in MiAD patients as well as in control subjects.

Results revealed that cross correlation measure showed higher difference in synchronization of MiAD and control subjects as compare to phase synchrony while coherence function did not perform very well. They have also indicated that alpha and theta bands play a major role in identifying the change in synchronization from MiAD and control subjects especially in right temporal-central region (RT-C) and also in left temporal-occipital (LT-O) region.

Furthermore, the original contribution of this research work is the comparison of previous methods of applying synchrony measures with PCA based method. Our proposed method proved the importance of eliminating redundant information, from EEG time series, that may come from consecutive electrodes. It should be noted that comparison with previous findings is problematic due to the significant differences in the utilized methodology and the utilization of different kinds of synchrony measures on different kinds of datasets. However, our results are consistent with most of the studies on the loss of average EEG synchrony in different parts of the brain for MiAD patients and also in accordance with the clinical findings.

Furthermore, we have successfully shown the importance and significance of our proposed method, to detect lower synchronization in MiAD patients, as compare to the Average method for all three datasets.

Future work will involve the study of much significant results of lower synchronization in case of *datasets B* and *datasets C* as compare to *dataset A*.

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