Comparison of resting electroencephalogram coherence in patients with mild cognitive impairment and normal elderly subjects

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ABSTRACT

Mild cognitive impairment (MCI) was a condition beginning before more serious deterioration, leading to Alzheimer's dementia (AD). MCI detection was needed to determine the patient's therapeutic management. Analysis of electroencephalogram (EEG) coherence is one of the modalities for MCI detection. Therefore, this study investigated the inter and intra-hemispheric coherence over 16 EEG channels in the frequency range of 1-30 Hz. The simulation results showed that most of the electrode pair coherence in MCI patients have decreased compared to normal elderly subjects. In inter hemisphere coherence, significant differences ($p<0.05$) were found in the FP1-FP2 electrode pairs. Meanwhile, significant differences ($p<0.05$) were found in almost all pre-frontal area connectivity of the intra-hemisphere coherence pairs. The electrode pairs were FP2-F4, FP2-T4, FP1-F3, FP1-F7, FP1-C3, FP1-T3, FP1-P3, FP1-T5, FP1-O1, F3-O1, and T3-T5. The decreased coherence in MCI patients showed the disconnection of cortical connections as a result of the death of the neurons. Furthermore, the coherence value can be used as a multimodal feature in normal elderly subjects and MCI. It is hoped that current studies may be considered for early detection of Alzheimer's in a larger population.

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1. INTRODUCTION

The most prevalent type of dementia was Alzheimer's disease (AD), characterized by a cognitive impairment that has to be more significant for the very elderly than predicted by the usual aging process [1], [2]. Early detection of AD was problematic because many of the signs correlate with those of the regression associated with natural aging. There was no disease-modifying clinical intervention for dementia due to AD, but early diagnosis for complex behavioral and psychological symptoms will allow for improved care and treatment planning.

Mild cognitive impairment (MCI) was mostly the early stage of AD, described as a reduction in mental abilities [3]. MCI detection was important to slow down the deterioration process by providing appropriate treatment management [4]. The modalities that can be used are medical imaging such as magnetic resonance imaging (MRI) scan [5], [6], and positron emission tomography (PET) scan [7], [8]. Their study applies automatic classifier algorithms such as support vector machines (SVM) or artificial neural networks (ANN), which have proven to generate high detection accuracy. However, they are high cost and may not be used in the near future for evaluation. There was an electroencephalogram (EEG) as a solution by considering installation efficiency, cost, and patient safety [9]–[12].

Numerous studies have been conducted in recent years to investigate the effects of MCI and AD on EEG signals. A single-channel EEG-based MCI detection technique for standard home-based patient monitoring was reported by Khatun *et al*. [13]. Using the Montreal cognitive evaluation test, they assessed the cognitive condition and extracted 590 characteristics that achieved classification accuracy of 87.9%. An integrated spectral-temporal analysis-based framework for MCI detection using EEG resting-state signals has been developed [14]. With stationary wavelet transformation and descriptive statistical analysis, a three-dimensional discrete feature space was added, with the SVM classifier achieved a maximum accuracy rate of 96.94%. A machine learning approach to discriminate MCI and normal cases using simple spectral EEG characteristics was suggested and obtained a precision of about 88% [15]. Durongbhan *et al*. [2] developed a supervised classification system that classify healthy controls and AD participants using the K-nearest neighbor method. It can be seen from the aforementioned literatures that their output outcomes were not acceptable and not enough for real world implementation.

Sharma *et al.* [16] reported eight EEG biomarkers for the diagnosis of MCI patients. They were power spectral density, kurtosis, skewness, spectral skewness, spectral crest factor, spectral kurtosis, spectral entropy, and fractal dimension. Normal control and MCI signal classification achieved accuracy ranges from 73.2% to 89.8%. McBride *et al.* [17] conducted spectral and complexity analysis of MCI and early AD scalp EEG characteristics, achieving an average accuracy of 79.2%. Engedal *et al.* [18] observed the EEG power to predict the subjective cognitive decline and MCI. Hagery *et al*. [19] carried out methodological advances in Alzheimer's disease's diagnostic performance using ensemble approaches. Three types of ensemble methods, Boosting, Bagging, and Stacking, used to process the open access series of imaging studies (OASIS) clinical data collection. The methods were combined with the decision tree algorithm. The results of the proposed random forest (Bagging) obtained the highest accuracy of 96.66 %.

The quantitative EEG (qEEG) was performed to identifying patients with subjective cognitive decline (SCD) and MCI who have a high risk of deterioration over a 5-year period to dementia. However, because the method's discriminatory power was mild, it should be applied to other routine diagnostic techniques, such as cognitive assessments and other bio-markers. MCI generally uses power spectral density analysis in the delta, theta, alpha, beta, and gamma bands. It was found that in AD, MCI patients was characterized by an increase of delta and theta frequencies [20]. The disadvantage of the power spectral density approach is that it is biased because the EEG signal is mixed with a large amount of low frequency noise due to blinking artifacts and eye movement. Therefore, another quantitative approach is needed to support the analysis, one of which is the EEG coherence method [21], [22]. Based on the study by Tsolaki *et al*. [20], coherence analysis allows for the characterization of AD. Thus, coherence measurement is thought to be a modality in early detection of AD Coherence is a calculation of the covariation of the two EEG signal spectra. Evidence of structural and functional relations between cortical areas underlying the recording electrodes has been considered to be high coherence between two EEG signals [23], [24].

In this study, we investigated inter and intra-hemispheric coherence over 16 EEG channels in the frequency range of 1-30 Hz EEG in MCI patients and normal elderly subjects. The coherence analysis in this study is expected to complement the spectral analysis which was previously applied to the same dataset in the study [15]. The t-test was conducted to find significant differences between the two groups observed. The proposed method is expected to support clinical diagnosis in early detection of Alzheimer's.

2. MATERIAL AND RESEARCH METHOD

There were three main processes done in this study to observe the EEG coherence in patients with MCI and normal elderly subjects. The first was the artifact removal by applying the bandpass filter using the 4th order of butterworth filter. Channel or electrode pair was arranged following the inter and intrahemispheric location of the brain. There were 16 electrodes used in this process, FP1, FP2, F7, F3, FZ, F4, F8, T3, C3, CZ, C4, T4, T5, P3, PZ, P4, T6, O1, and O2. The coherence value was measured from the electrode pairs, which were then analyzed to see the change between the MCI and the normal subjects. This process was expressed in Figure 1.

2.1. MCI and normal EEG data

This study used EEG recording of 27 subjects from the EEG signals database: *https://misp.mui.ac.ir/en/eegdata*. The data consist of 16 normal elderly subjects and 11 patients with MCI [15]. This dataset was taken from patients admitted to the cardiac catheterization units of the Nour and Sina Hospitals, Isfahan, Iran. The patients were having a history of coronary angiography over the past year in the age range of 60-77 years and minimum elementary school background. Normal and MCI parameters were differentiated based on the mini-mental state examination (MMSE) score diagnosed using neuropsychiatry unit cognitive assessment (NUCOG) tool, where 21-26 scores for MCI and normal scores above 26. Subject demographics are summarized in Table 1.

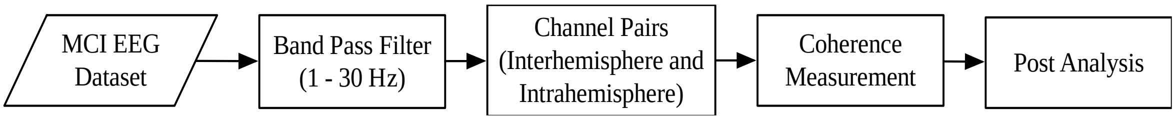


Figure 1. General process of EEG coherence measurement in MCI patients

Table 1. Resume demographics and cognitive scores

Parameter	MCI	Normal
Age (years)	66.4±4.6	65.3±3.9
Education (years)	10.3±3.8	11.1±3
MMSE	27.6±0.9	29±0.8
Cognitive assessment tool	82.4±3.6	91.1±3

This EEG was recorded in the morning for 30 minutes from 19 electrodes using the galileo NT EEG, which 32 digital channels, 256Hz of sampling rate, and electrodes skin impedance was less than 5 kΩ. During the recording, the patients closed their eyes but was prohibited from getting sleepy. All EEG signals were issued from patients with a history of head trauma, major psychiatric disorders, dementia, substance abuse, and serious medical illnesses.

2.2. EEG coherence

The EEG coherence was a normalized measure of the functional connectivity between brain regions [25], namely signal channel x and signal channel y at any given particular frequency band [24]. Generally, EEG coherence analysis was carried out for the traditional four or five frequency bands: gamma (γ=25-50 Hz), beta (β = 13-25 Hz), alpha ($\propto$ = 8-13 Hz)theta (θ = 4-8 Hz), and delta (δ = 0.5-4 Hz) [26], [27]. In this study, coherence was measured in the range 1-30Hz. These are thought to represent the traditional bands. This measurement was investigated by computing the interhemispheric and intrahemispheric cross mutual information [28]. The interhemispheric coherence conducted by computing the functional connectivity between brain hemispheres (left and right) [29]. While the intrahemispheric coherence conducted by computing the functional connectivity between electrodes in the same brain area (left and right) [30]. The EEG coherence values for each frequency band is the extension of the pearson's correlation formulated by (1) [31], [32]:

$$Coh_{xy}(f) = \frac{\left|W_{xy}\right|^2(f)}{W_x(f).W_y(f)} \tag{1}$$

where, $Coh_{xy}\ is$ estimated coherence value in the range of 0-1 [33], f is frequency, $W_x(f)$ is the PSD of signal x, $W_y(f)$ is the PSD of signal y and $W_{xy}(f)$ is cross spectral density between the two brain region. If the coherence value approaches=1, it means that the x and y signals are similar. Since the original EEG record consisted of 19 channels which included three central electrodes (Fz, Cz and Pz), then 16 electrodes were selected to make the symmetrical coherence pair. Coherence was measured on the electrode pairs based on studies [34], [35]. Table 2 shows the measured inter and intrahemispheric electrode pairs.

Table 2. Inter and intrahemispheric electrode pairs investigated in this study

Electrode Pairs		
Interhemispheric	Right Intrahemispheric	Left Intrahemispheric
FP1-FP2, F3-F4, F7-F8, T7-T8, C3-C4, P3-P4, P7-P8, O1-O2	FP2-F4, FP2-F8, FP2-C4, FP2-T4, FP2-P4, FP2-T6, FP2-O2, F4-F8, F4-C4, F4-T4, F4-P4, F4-T6, F4-O2, F8-C4, F8-T4, F8-P4, F8-T6, F8-O2, C4-T4, C4-P4, C4-T6, C4-O2, T4-P4, T4-T6, T4-O2, P4-T6, P4-O2, T6-O2	FP1-F3, FP1-F7, FP1-C3, FP1-T3, FP1-P3, FP1-T5, FP1-O1, F3-F7, F3-C3, F3-T3, F3-P3, F3-T5, F3-O1, F7-C3, F7-T3, F7-P3, F7-T5, F7-O1, C3-T3, C3-P3, C3-T5, C3-O1, T3-P3, T3-T5, T3-O1, P3-T5, P3-O1, T5-O1

3. RESULTS AND DISCUSSION

Raw EEG signals were pre-processed using a digital filter ranging from 1-30 Hz. Low filter and pass filter (IIR Butterworth mode) with a response frequency of 30 Hz and 1 Hz respectively were performed in this stage. Then the coherence value was calculated for all electrode pairs, following the pairing as shown in Table 2.

3.1. Interhemispheric coherence

Interhemispheric coherence represents cortical connectivity between the right and left-brain areas. The coherence of the eight electrode pairs (frontal, parietal, central, temporal, and occipital) was calculated. The results of mean interhemispheric coherence are shown in Figure 2. It showed that the mean interhemispheric coherence in patients with MCI was lower than the normal group. An Independent t-test with a 95% confidence level showed that the FP1-FP2 electrode pair generated a significant difference ($p<0.05$) between MCI and normal.

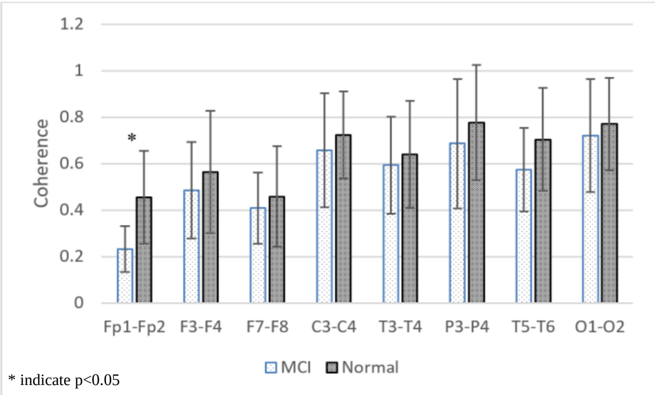


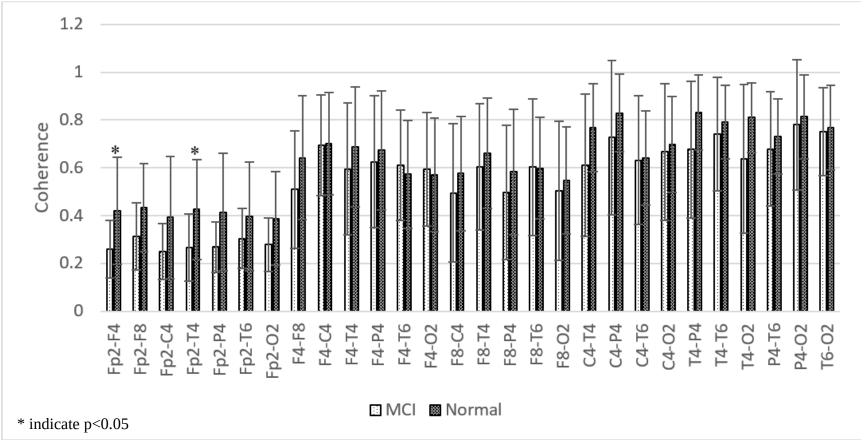
Figure 2. Mean interhemispheric coherence for MCI and normal subjects

3.2. Intrahemispheric coherence

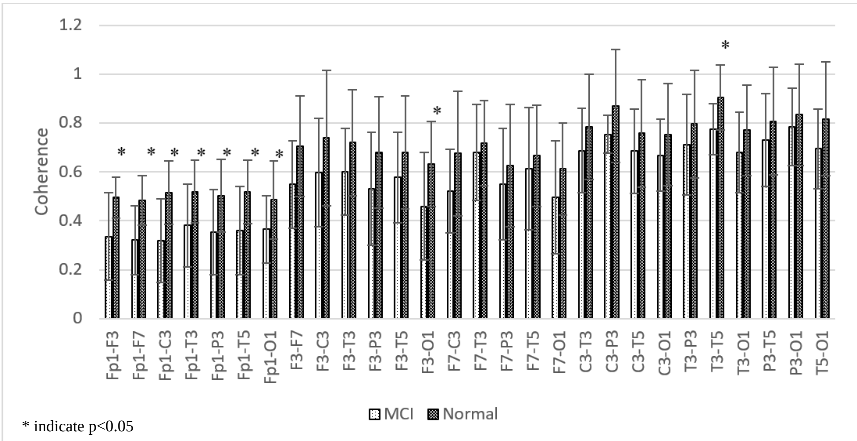
Intrahemispheric coherence conducted by measuring the functional connectivity between electrodes in the same brain area including right and left intrahemispheric. Twenty-eight pairs of electrodes (local and distal) in each right and left region were investigated. The results of right intrahemispheric coherence are shown in Figure 3(a) and the left intrahemispheric coherence are shown in Figure 3(b). These results are consistent with the investigation of interhemispheric coherence where the mean intrahemispheric coherence MCI is lower than normal, found in almost all electrode pairs. In the right intrahemispheric, a significant difference ($p<0.05$) is generated by the FP2-F4 and FP2-T4 pairs while the left intrahemispheric is generated by FP1-F3, FP1-F7, FP1-C3, FP1-T3, FP1-P3, FP1-T5, FP1-O1, F3-O1 and T3-T5 pairs.

Coherence analysis represents the functional connectivity of neurons through the synapse network in response to stimuli. Disruption or decreased connectivity between brain areas indicates a functional abnormality in this case is a cognitive impairment. Generally, MCI patients have a lower coherence value compared to normal subjects. These results are consistent with the analysis of coherence related to the MCI and Alzheimer's as reported in [36]–[38]. In interhemispheric, a significant decrease in coherence was found in the frontal area of the brain. In the Alzheimer's progression analysis, deterioration of function in the frontal area of the brain is strongly presumed as the onset of Alzheimer's [39], [40]. The intrahemispheric coherence analysis showed a significant decrease in frontal-temporoparietal-central-occipital network connectivity, which was significantly found in the FP1 electrode pair. Decreased intrahemispheric coherence in MCI patients is related to disconnection of cortico-cortical connectivity which connects the temporoparietal, occipital areas with the frontal areas [41].

Studies related to EEG coherence have long been reported to analyze the progress of Alzheimer's including early detection through the EEG characterization of MCI patients. The coherence measurement shows a decrease in MCI patients as a marker of decline in connectivity between brain areas. Beta amyloid plaque formation and the death of a number of neurons are closely related to decreased connectivity function [41]. In the practical domain, the method proposed in this study is more efficient than the previous studies, because it does not compute in detail the signal coherence of each band (delta, theta, alpha, beta, and gamma). So, it has less features and will simplify the analysis. However, to support this hypothesis, further simulations are needed, for example performing validation using the classification method. Thus, it can be seen the performance of the proposed method in MCI detection. Moreover, it is also necessary to validate the proposed method in larger dataset.



(a)



(b)

Figure 3. Mean intrahemispheric coherence: (a) right intrahemispheric and (b) left intrahemispheric

4. CONCLUSION

This study investigated the coherence of EEG signals in MCI patients and normal subjects. This study aims to obtain the feature of each group observed so that the coherence value can be a candidate for early Alzheimer's detection based on EEG analysis. We measured the coherence of the electrode pairs, both of interhemispheric and intrahemispheric. The results showed that the mean coherence in MCI patients was lower than in normal subjects. For interhemispheric coherence, significant differences ($p<0.05$) were found in the FP1-FP2 pairs. Meanwhile, for intrahemispheric coherence, a significant difference is generated by FP2-F4, FP2-T4, FP1-F3, FP1-F7, FP1-C3, FP1-T3, FP1-P3, FP1-T5, FP1-O1, F3-O1, and T3-T5 pairs. This indicates a decrease in coherence due to pathological changes in neuronal network connectivity. There was a deterioration of connectivity due to the death of a number of neurons and broken off of the synaptic pathway due to beta-amyloid plaque.

Coherence measurement can provide important information in the analysis of the severity of Alzheimer's and early detection. The coherence measures presented in this study may be more efficient than the detailed coherence calculations on the traditional EEG band. However, the number of extracted features will be less compared to the coherence analysis for each of the traditional EEG bands. We assume that the coherence measurement in the wideband represents the conditions for measuring the coherence of delta, theta, alpha, and beta. Further validation can be observed by simulating an automatic classifier method so that accuracy, sensitivity, and specificity can be known. Finally, it can be seen the performance of the proposed method. This study is expected to be a reference for neurology and medical practitioners, as additional diagnostic criteria for MCI or Alzheimer's. EEG coherence analysis in one frequency band will be more efficient than the detailed analysis of delta, theta, alpha, and beta bands.

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