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QEEG as a Novel Parameter of Neuroplasticity in Elderly with Mild Cognitive Impairment

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ABSTRACT

Neuroplasticity is the ability of the brain to change structurally and functionally in compensation for changes related to age or disease. In elderly people, the most common neuroplasticity problem is mild cognitive impairment (MCI). MCI is a syndrome defined as a decrease in cognitive function that is not appropriate for a person's age and educational level. One way to minimize the progress of deterioration in MCI is by doing physical exercise, such as walking. In this study, participants did physical activity by walking at least 4000 steps/day for 3 months. Cognitive function was measured by brain wave parameters with Quantitative Electroencephalography (QEEG). Electroencephalography (EEG) signals were recorded before and after the intervention. The EEG results showed that the QEEG wave parameters after the intervention increased in the alpha frequency band and decreased in the delta frequency band.

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1. INTRODUCTION

Neuroplasticity is the ability of the brain to change structurally and functionally which results in stability or compensation for changes related to age or disease.[1] Neuroplasticity of the brain can occur when a person engages in social interactions, meditation, repetitive learning, focusing on the same thing over and over, a particular diet/food habit, physical exercise, and new life experiences. In elderly people, the most common neuroplasticity problem is MCI. Mild cognitive impairment is a syndrome defined as a decrease in cognitive function that is not in accordance with a person's age and level of education.[2] According to the World Health Organization (WHO), there is an increase number of people suffering from cognitive disorders at 10 million each year. MCI is estimated to occur at the age of 65 years in 10-30% of the population. In Indonesia, it was reported that cognitive impairment not yet demented was 53% in type II diabetes mellitus patients aged 45-75 years.[3] Measurable cognitive function can be demonstrated by several things, including forgetfulness. It is estimated that 39% of elderly people aged 50-59 years complain of forgetfulness, increasing to more than 85% in the elderly over 80 years.[4]

Patients with MCI will have difficulty carrying out daily activities, so this will make their quality of life decline. The decline in the quality of life will cause the elderly to depend on others. In addition, they can feel lonely, depressed, or in severe cases even cause death. It is necessary to reduce the decline in cognitive function, one of which is by increasing physical activity. Physical activity that is very easy and safe to do in the elderly is walking for a certain time and long enough to affect neuroplasticity.[5]

Assessment of cognitive function can use several assessments, one of which is by using the HKND assessment that has been developed by Martina WS Nasrun.[2] In this study, there were two models of HKND assessment carried out by examining the condition of the presence or absence of depressive disorders, diabetes, and dyslipidemia as well as the good or bad results of the psychometric evaluation of the ROCF test, TMT B, and backward digits. In addition to using assessments, cognitive function can be assessed from brain signals using QEEG parameters. The signal of the human brain in conscious and resting conditions has a dominant frequency value in the alpha frequency band. In a study conducted by Sugondo Hadiyoso, et al [6], it was found that MCI patients experienced a slowdown in the EEG rhythm as indicated by the high power value in the delta frequency band and a decrease in the power value at the alpha frequency. Delta rhythms are commonly seen in deep sleep in the frotocentral head area. The delta rhythm is pathologically present in the awake state in cases of generalized encephalopathy and cerebral dysfunction.

In a previous study conducted by Sauliyusta and Ekawati, it was stated that the level of physical activity affects cognitive functions in the elderly. This study uses a questionnaire method to compare the elderly who have high physical activity with low physical activity.[7] Furthermore, there are other studies [8,9] using the method of activity with a treadmill which is done acutely. The results of this study are an increase in short-term memory executive function in the elderly who perform activities acutely.

However, there are weaknesses in the previous study where the effects of acute physical activity were only temporary. In addition, the measurement of cognitive function using a questionnaire can lead to measurement bias. Therefore, this study is proposed to carry out physical activity by walking, measuring at least 4000 steps every day for 3 months to improve cognitive function in the elderly, and measuring cognitive function using QEEG and brain-derived neurotrophic factor (BDNF).

2. RESEARCH METHOD

The methods (Figure 1) in this study include subject recruitment, HKND screening, recording of EEG signals before intervention, intervention of walking 4000 steps/day for 3 months, recording of EEG signals after intervention, pre-processing of EEG signals, quantification of EEG signals into QEEG and analysis. Subject recruitment was carried out at *Rumah Sakit Cipto Mangunkusumo - Fakultas Kedokteran Universitas Indonesia* (RSCM-FKUI). After recruitment, the subjects were screened first using the HKND instrument. It aims to determine the subjects who experienced MCI and passed the research criteria. Furthermore, the EEG signal was recorded before the intervention. The recording was done for 20 minutes with 10 minutes eyes open and 10 minutes eyes closed. Then a walking intervention of 4000 steps/day was performed for 3 months. Subjects were given a pedometer and checked for the number of steps each week. After the intervention was completed, the EEG signal was recorded again. After the EEG signal is obtained, pre-processing of the EEG signal is carried out to eliminate grid noise and eliminate data offsets. Furthermore, EEG quantification and analysis were performed.

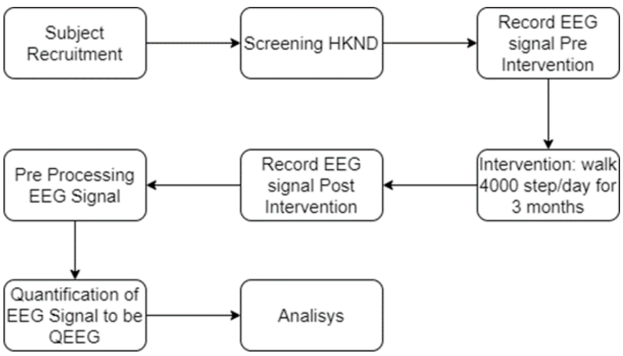

Figure 1. Research method

Subjects must pass several research inclusion criteria, which are 1) male or female aged 60-74 years, 2) having mild cognitive impairment who was examined using the HKND (with a score of >120 for model I and <-110 for model III), 3) being able to understand the instructions given, 4) minimum education is Junior High School or the equivalent, 5) can speak Indonesian, and 6) independent ambulation is not sedentary (physical activity <1.4). Subject recruitment was done by distributing posters and inviting patients to the Department of Medical Rehabilitation *Rumah Sakit Cipto Mangunkusumo - Fakultas Kedokteran Universitas Indonesia* (RSCM-FKUI). If the subject is willing to participate, then the inclusion examination is carried out.

This research was approved by the ethical clearance committee of the Faculty of Medicine Universitas Indonesia number KET-451/UN2.F1/ETIK/PPM.00.02/2020 and protocol number 20-03-0283.
The minimum number of subjects was 8 people, using the comparative sample size formula in pairs with repeated measurements twice. The number of subjects was then added by 25% of the minimum, which resulted in 12 people. This was done to reduce the possibility of sample drop-out. Furthermore, subject recruitment was carried out step by step. The first step resulted in 40 subjects who met criteria number 1,3,4,5,6. For the second step, 13 subjects met the HKND criteria and then became the subject of the intervention. The research was conducted during the Covid-19 pandemic. This caused dropouts in some subjects who could not continue the intervention. At the beginning of the study, there were 10 subjects whose EEG we managed to record. Unfortunately, some subjects were not able to participate further due to potential risks for the elderly that could occur during the pandemic condition. In the final, the subject who was able to fully participate in the whole study was 7 people.

There are four male subjects and six female subjects. Seven out of ten subjects contracted type II Diabetes Mellitus. Five out of ten subjects contracted hypercholesterolemia disease, and three out of ten subjects contracted hypertension. All subjects underwent several examinations before the intervention as follows, MoCA-Ina psychometric examination, blood sampling, and recording of EEG signals. However, out of ten subjects, three withdrew from the research subject in the middle of the intervention.

Table 1. Subject characteristics

	n	%
Age (Mean ± SD)	68,1 ± 2,92	
60-70	7	70%
71-75	3	30%
Gender		
Male	4	40%
Female	6	60%
Comorbid		
DM	7	70%
Hypercholesterolemia	5	50%
HT	3	30%

2.1. EEG Dataset

EEG signal recording was carried out twice, namely before and after the walking intervention. EEG recording using the Neurospectrum 64 Neurosoft device with number of channels 47 channels, sensitivity 0.01 - 10.000.000 μV/mm, and sampling rate 2000 Hz. Recording was done in the morning until noon with the duration of recording on each subject for 20 minutes with a time division of 10 minutes at the beginning of the eyes open and 10 minutes at the end of the eyes closed. The international standard 10-20 is applied to 16 electrodes during recording. Channels records are FP1, F3, C3, P3, O1, F7, T3, T5, FP2, F4, C4, P4, O2, F8, T4, and T6 (Figure 2). Digital EEG has a sampling frequency of 500 Hz and data is stored in the European Data Format (EDF).

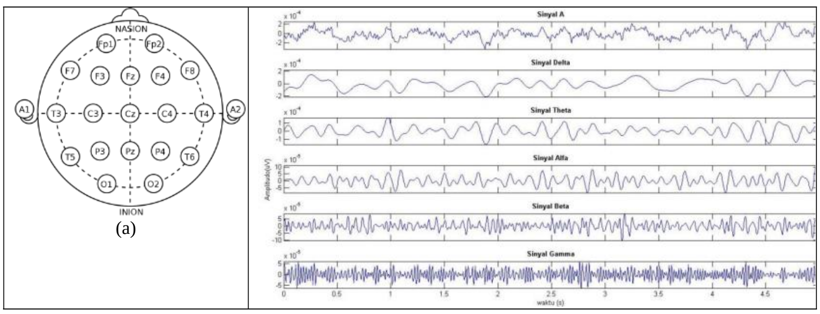

Figure 2. (a) Channel records of EEG, (b) frequency band of EEG Signal

2.2. Quantitative Electroencephalography Analysis

After the digital EEG data is obtained, then the process is carried out to obtain the QEEG value and then analyze it (Figure 3). The first step is to pre-process the data. Data were selected in the first 3 minutes for eyes open and the last 3 minutes for eyes closed. Furthermore, signal filtering is performed at a frequency of 0.1 - 49 Hz and separation at each frequency. Each frequency is in the form of delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30Hz), and gamma (30-49 Hz). We calculate the absolute and relative power from each peak of the frequency band. The signal at each frequency is calculated for its power spectral density value using the Welch method with segmentation every 2 seconds and 75% overlap. Quantitative EEG in this study calculates the absolute power and relative power value for each frequency band.

The absolute power and relative power values in the delta frequency band before and after the intervention will be calculated on average for all channels and compared with the values before and after the intervention.

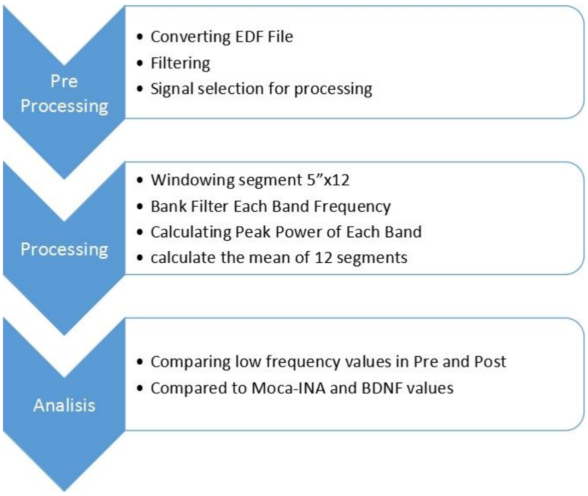

Figure 3. Processing EEG to QEEG

3. RESULTS AND DISCUSSION

3.1. QEEG analysis

QEEG processing is carried out using MATLAB 2017 software. This QEEG calculation is adopted from research conducted by Cynthia and Sofiah [11,12] by using absolute and relative power calculations. Power is calculated based on the highest power value in each frequency band, namely delta, theta, alpha, beta, and gamma frequencies. The calculation is done when the subject's eyes are open and closed. Power absolute was power spectral of Welch method with 2-second windowing and 50% overlap. [11,12] The Welch method can be used to calculate the average power of a signal by isolating the data into parts to be calculated. This method is popular for calculating long signal power. Using this method on EEG signals, each signal segment is divided into sequential Hamming window sub-segments with adjustable overlap, then each sub-segment is then calculated to its power spectrum and averaged.[13]

$$P_f(c, s) = \max(\text{peak}(P_k(c, s, f)))$$

$P_f(c, s)$ was maximum peak of signal power in every band frequency, $P_k(c, s, f)$was the peak of every band frequency in every 2-second windowing. $r_{xx}[n]$ is the autocorrelation function, and N is the length of the data. The power relative is expressed from the sum of power one of frequency divided by the sum power of all frequencies.

$$P_{rel} = \frac{P_x}{P_{tot}}$$

With P_{rel} as Power relative, P_x is the total of power in all channels in one of the frequencies, and P_{tot} is the total amount of powers in all frequencies.

Table 2 shows that on average, people with MCI had high power at the delta and theta frequencies before the intervention. This is in line with research conducted by Hadiyoso, et al [6]. In addition to the high value of delta, the MCI subjects before the activity of walking the beta wave look quite low. The power values in theta and beta can be used as early detection of MCI. [14] This is caused by the loss of cortico-cortical connectivity.

Table 2 shows that the power value when the eyes are open at the delta frequency decrease from 167.44 to 104.48. In addition to the delta frequency, alpha frequency increase from 4.21 to 4.32. This shows that walking activity can increase alpha signals and decrease delta signals. These parameters indicates that walking activity can stimulate an increase in neuroplasticity activity in the brain [15].

In addition to the absolute power parameter, we also get the relative power for each frequency band. From Table 2, it is found that the absolute power value at the delta and theta frequencies before the intervention was quite high, while the alpha and beta frequencies were low. This is also in line with research conducted by Hadiyoso, et al [6]. After the intervention of walking 4000 steps per day, the relative power values for the delta and theta frequencies decreased, while the alpha and beta increased.

Table 2. Data presented as mean of power absolute and power relative of pre and post intervention. Eyes are open during the recording.

Eyes Open				
Test Variables	Power Absolute		Power Relative	
	Pre Treatment (Mean)	Post 3 months Treatment (Mean)	Pre Treatment (Mean)	Post 3 months Treatment (Mean)
Delta (0.5-4 Hz)	167.44	104.48	0.75	0.69
Theta (4-8 Hz)	7.00	6.17	0.12	0.09
Alfa (8-13 Hz)	4.21	4.32	0.08	0.10
Beta (13-30 Hz)	2.16	2.49	0.05	0.06
Gamma (30-49 Hz)	1.16	0.83	0.03	0.02

Table 3 shows the absolute power value of the EEG when the eyes are closed. In contrast to table 2, in table 3 the power in the theta and beta waves looks low before the intervention. Values in the low beta and theta frequency bands are sufficient for early detection of MCI. Table 3 shows the power value when the eyes are closed as the theta frequencies increase. The power value at the theta frequency increased from 5.54 to 6.88. It is the same as when the eyes are open. After the intervention, the values of theta and beta seemed to increase significantly.

In addition to absolute power, the relative power value can also be seen in table 3. The relative power value in the beta frequency band before the intervention is lower than after the intervention. This shows that there is an increase in cognitive function in the subject. However, in this closed-eye recording, the value of relative power and absolute power in the delta theta frequency before the intervention was higher than after the intervention. This could be due to differences in the condition of the subject at the time of EEG recording after the intervention, such as the subject being sleepy when recording with his eyes closed.

Table 3. Data presented as mean of power absolute pre and post intervention. Eyes are closed during the recording.

Eyes Close				
	Power Absolute		Power Relative	
Test Variables	Pre Treatment (Mean)	Post 3 months Treatment (Mean)	Pre Treatment (Mean)	Post 3 months Treatment (Mean)
Delta (0.5-4 Hz)	36.99	64.99	0.67	0.71
Theta (4-8 Hz)	5.54	6.88	0.12	0.12
Alfa (8-13 Hz)	6.87	4.94	0.15	0.10
Beta (13-30 Hz)	2.42	2.81	0.05	0.06
Gamma (30-49 Hz)	1.09	0.67	0.01	0.01

From Table 3, we will focus more on the Alpha and Beta frequency bands. Figure 4 and 5 are graphs of absolute power (4) and relative power (5) when the eyes are closed in the temporal area. The temporal area includes the T3, T4, T5, and T6 EEG channels. The T3 and T5 channels represent the left temporal area, while T4 and T6 are the right temporal area. From Figure 4, it can be seen that almost all channels had a significant increase. However, there was a decrease in the T5 channel. This anomaly can be caused by brain activity during sleep. During the EEG recording, the eyes of subjects were closed which can lead them to become sleepy. From this graph, it is confirmed that the activity in the temporal area mostly elevated after the intervention.

In Figure 5, the relative power of the alpha frequency band from each channel also increased quite significantly. However, the increase in the beta frequency band is still not visible. This is because the amount of power from the beta frequency compared to the overall frequency band is still very small.

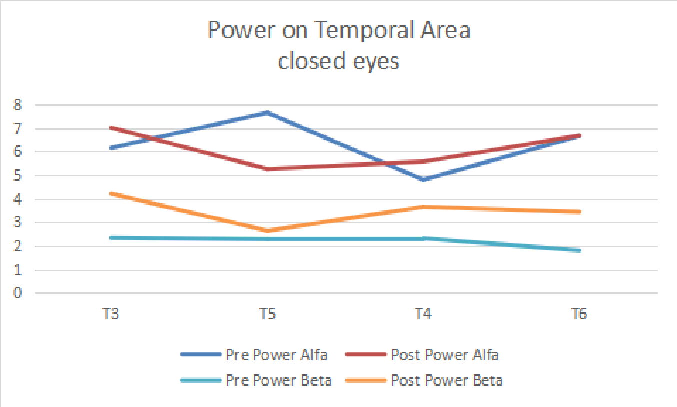

Figure 4a. Power Spectral on Temporal Area Closed Eyes

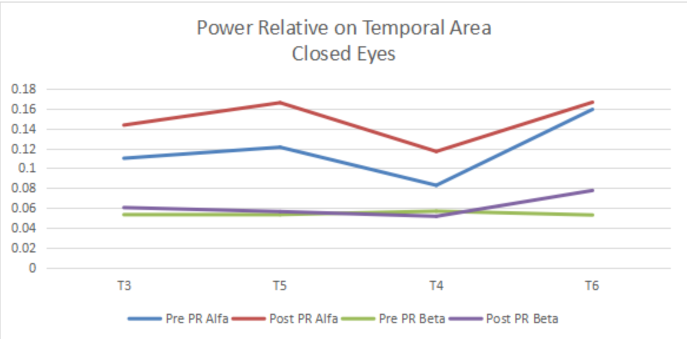

Figure 5. Power Relative on Temporal Area Closed Eyes

Figures 6 and 7 are graphs of Absolute power (6) and relative power (7) in the Temporal area when the eyes are open. Figures 6 and 7 also show quite significant results. The alpha absolute power in each channel in the temporal area increased. The same thing happened to Relative Power.

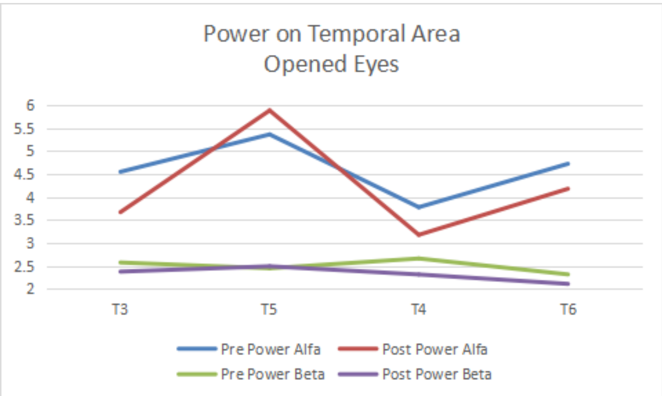

Figure 6. Power Spectral on Temporal Area Opened Eyes

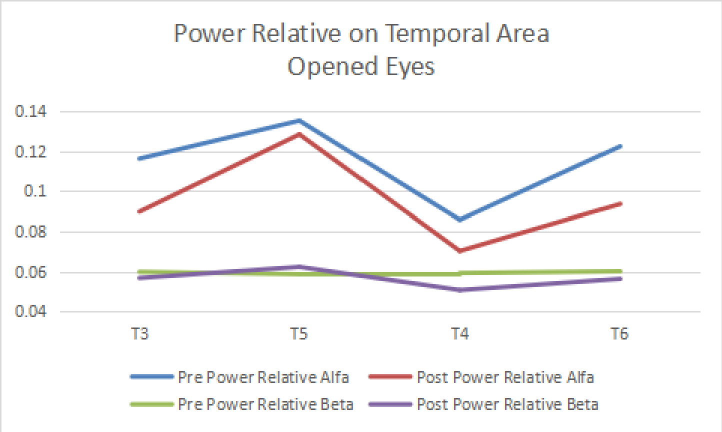

Figure 7. Power Relative on Temporal Area Opened Eyes

Figures 8 and 9 are graphs of absolute power (8) and relative power (9) when the eyes are closed in the frontal area. Channels F3, F7, F4, and F8 are EEG channels located in the Frontal area. In the graph, it can be seen that the absolute power and frequency power on all channels has increased. The increase occurred in the alpha and beta band frequencies. However, there is one channel that has decreased in relative power. This may be due to the subject being drowsy at the time of the EEG recording with his eyes closed.

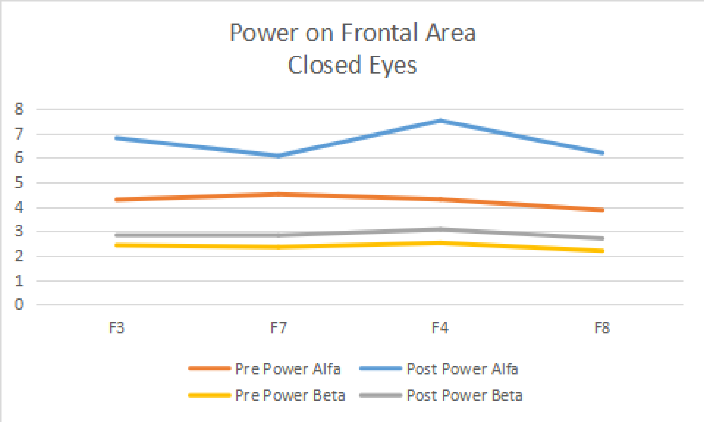

Figure 8. Power Spectral on Frontal Area Closed Eyes

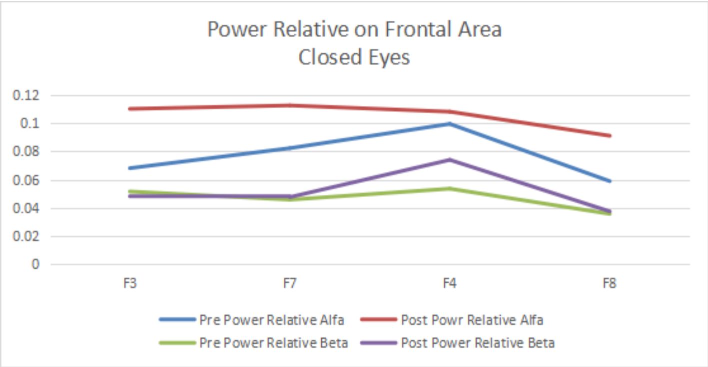

Figure 9. Power Relative on Frontal Area Closed Eyes

Figures 10 and 11 are graphs of absolute power (10) and relative power (11) when the eyes are open in the frontal area. Figure 10 also shows a significant increase in power. However, the increase of relative power only occurs in the F4 channel. This could happen because when the eyes are open, the subject's focus shifts to the occipital area. Therefore, this will make other brain areas experience a significant decrease in power.

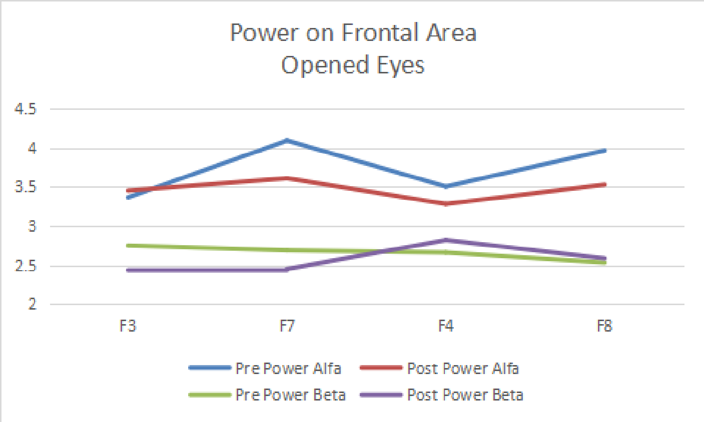

Figure 10. Power spectral on Frontal Area with opened Eyes

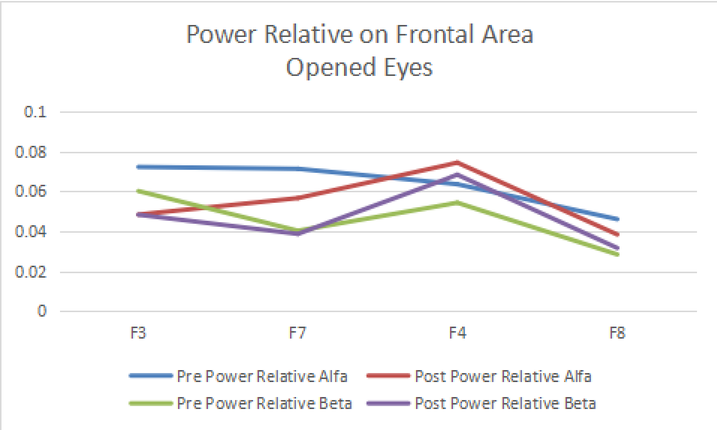

Figure 11. Power Relative on frontal Area with opened Eyes.

The temporal and frontal areas are the main focus of this study. The temporal area is an area of executive function. Patients with MCI experience decreased executive/visuospatial function. This can be seen from the MOCA Ina value on executive/visuospatial functions in table 4.

Table 4. Table of average results of the MOCA-Ina examination and the visuospatial aspect.

Assessment	Pre Treatment	Post Treatment (3 months)
Moca-Ina	26 ± 3.162	27.29 ± 1.496
Visospasial/fungsi eksekutif	3.9 ± 0.815	4.72 ± 0.488

Table 4 shows the average results of the overall MOCA-Ina examination and the visuospatial aspect. The overall MOCA-Ina value increased significantly, from 26 to 27.29. This is in line with the QEEG results with an increase in power at the alpha and beta frequencies.

The results obtained from the absolute and relative power values showed an increase in the number of neurons in the brain significantly and was a long-term effect. The absolute and relative power values in this EEG signal indicate that the brain has increased plasticity after the subject has been walking regularly every day for 3 months. This is caused by an increase in neurotransmitters in the brain than before doing measured walking activities [17]. In addition to the visuospatial aspect/executive function, the area that has an increased value of function was the memory area. This can be seen from the overall value of MOCA-Ina and the value of its executive function. In previous studies, it was stated that acute exercise can improve memory power in people with MCI. [18]. In our research, it is proven that the longer the exercise is done, the better improvement of executive function and memory in the brain could occur.

The value of absolute power and relative power of QEEG on channels T3, T4, and T6 increased significantly. These channels are located in the temporal area, which is the area of memory function. The recording of EEG both with eyes open or closed significantly increased the three channels. Previous studies have suggested that some areas of the frontal, parietal and temporal lobes can be stimulated noninvasively to improve neural networks and memory [19,20]. Previous studies stated that memory is also a part of visuospatial/executive function. This is due to the wordy transfer of information between the central executive system and visuospatial sketches in the background network is necessary for efficient working memory function.[21]

The absolute and relative power values of QEEG on visuospatial/executive functions have increased significantly. This can be seen in the F3, F7, F4, and F8 channels, which increased with each EEG recording. From Figure 8-11, we can conclude that the F4 channel has been improving consistently. Previous studies found that MCI sufferers experienced a decrease in executive function. The functional magnetic resonance imaging (fMRI) showed that the areas that experienced decreased executive function were in the prefrontal area, [22] as our study found the decreased executive function was also in the frontal area. After the intervention of walking for 3 months, the power value in the frontal area increased. This has also been supported by the results of previous studies, which stated that acute exercise can improve executive function in MCI people. [19] However, some studies also mention that executive function can also be seen in the temporal area. [23,24] This is because each function in the brain will still be related to other, so it cannot be separated in one area only.

Our research found candidates novelty as biomarkers of executive function and memory in MCI are located in the F4, T3, T4, and T6 channels. It corresponds to the frontal area for executive function and the temporal area for memory.

Assessment using this EEG is a fairly subjective and safe assessment because the EEG recording is done without injuring the subject. Another study reported that exercise can regulate the proliferation of nerve cells, increase blood flow to the brain, increase blood permeability of the brain layer, and increase the number of temporary neurons [25].

4. CONCLUSION

The activity of walking 4000 steps every day for 3 months can increase neuroplasticity in the elderly with mild cognitive impairment. This can be proven by the brain signals measured using QEEG parameters to be better at the theta and beta frequencies which describe the improvement in cognitive function and the increase in neurotransmitters in the brain. It found on biomarker of executive function and memory in MCI are located in the F4, T3, T4, and T6 channels. Our study indicated that walking activities can improve cognitive function in the elderly, especially elderly in Indonesia. Suggestions for further studies are to research pre-elderly age to see neuroplasticity.

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