TIPTEKNO'18
TIP TEKNOLOJİLERİ KONGRESİ
8-10 Kasım 2018 / Gazi Magosa / KKTC

Analysis of EEG Signals to Extract the Effects of Transcranial Magnetic Stimulation on Depression

Ibrahim KOVAN and Mazlum UNAY
Biomedical Engineering
Izmir Katip Çelebi University
Izmir, Turkey
ibrahim_kovan@gmail.com, mazlum.unay@ikc.edu.tr

Ozlem KARABIBER CURA and Aydin AKAN
Biomedical Engineering
Izmir Katip Çelebi University
Izmir, Turkey
ozlem.karabiber@ikc.edu.tr, aydin.akan@ikc.edu.tr

***Abstract* – In the treatment of mental disorders, stimulation of the electrical activity of the brain by Transcranial Magnetic Stimulation has become an increasingly non-invasive treatment method. Mental disorders such as migraine, dementia, bipolar disorder, schizophrenia, stroke, Amyotrophic Lateral Sclerosis, Multiple Sclerosis, Epilepsy, Unconsciousness, tinnitus, depression, anxiety disorders, obsessive-compulsive disorders can be treated by magnetic stimulation of brain. In this study, changes in EEG signals recorded from patients with depression caused by TMS treatment are analyzed using signal processing techniques. The frequency analysis is performed by Fourier transform for each EEG channel of each patient before and after TMS treatment. Here, changes in EEG data of depressed patients with TMS treatment are analyzed using signal processing techniques in MATLAB®. The frequency analyses are obtained from Fourier Transform for each EEG channel of patients before TMS and after TMS treatment. Then these frequency values are compared for each patient. Also the respective IMF (intrinsic mode function) values of each channel are analyzed using the MEMD (Multivariate Empirical Mode Decomposition) algorithm. In this way, the alpha rhythm of EEG datas are detected and the changes in the alpha rhythm of each channel before and after treatment were analyzed.**

Keywords — Transcranial Magnetic Stimulation, Depression, EEG, Fourier Transform, MEMD, IMF

I. INTRODUCTION

Mental disorders affect life of the human negatively. According to World Health Organization, there are 500 million people worldwide with mental disorder. According to the report of Turkey Health Interview Survey, depression is the most common disease with an incidence of 11% among individuals aged 15 years and older. Nowadays, antidepressant drugs are used in the treatment of depression. According to Republic of Turkey Ministry of Health, rate of antidepressant use increase 25.6% in Turkey between years of 2011 and 2016.

A transcranial magnetic stimulation device was developed in 1985, which aims to increase neuronal activity by magnetic stimulation as an alternative method of antidepressant use. Transcranial magnetic stimulation is a non-invasive method for stimulating the brain using electromagnetic induction. In transcranial magnetic stimulation, a strong current is released quickly through a coil of a certain shape that is placed against the scalp [1]. From Faraday's electromagnetic induction principle, the generated magnetic field pulse penetrates the skull without attenuation and induces a current flow in the underlying superficial neuronal tissue as the charged particles in the tissue will experience a force induced by the incident time-varying magnetic field according to Faraday's law of induction [2]. A large transient magnetic field induces an electric field in the weakly conductive brain tissue sufficient to active neurons by depolarization. Locally, the currents induced in the cortical surface can directly excite or inhibit electrical neuronal activation by depolarizing or polarizing cell membranes. TMS has been approved by the US Food and Drug Administration in 2008 for the treatment of illness-resistant unipolar depression patients who failed the pharmacological trials, and, since then, it has been used successfully for the treatment of depression in clinical practice, with response and remission rates of 53.4% and 31.5%. Experiments have shown that magnetic stimulation applied with drugs such as quetiapine and paroxetine is more effective than single use. On the other hand, theoretically, it is known that transcranial magnetic stimulation will cause epilepsy as a side effect because it affects electrical activity in the brain. However, no such findings have been found in experimental studies on rats or in treated patients yet. It is also anticipated that epilepsy can be treated in the same way as it affects electrical activity between neurons. Depending on the patient's condition, the response to Transcranial Magnetic Stimulation will also vary and treatment should be administered at the physician's control.

Depression is a mental disorder in which alpha rhythm becomes dominant. Functional neuroimaging studies in depression usually indicate a decrease in left prefrontal cortex activity. In high-frequency TMS treatment, it is aimed to increase the activation of the left dorsolateral prefrontal cortex

978-1-5386-6852-8/18/$31.00 ©2018 IEEE

region. Depression can be determined by analyzing the EEG values of the patient as well as psychiatry. It is known that with the stabilization of the alpha waves, the patient is relieved of the depressive mood. In this study, 3 depression patients' EEG values before stimulated and after stimulated with TMS are analyzed by using MATLAB®. The efficacy of TMS is investigated on depressed patients and compare EEG signals by analyze Fourier transforms and time axis of the EEG signals (between before TMS and after treat TMS is the same patient) of the patients. The oscillations of the signal for each channel were analyzed using the MEMD algorithm.

II. TRANSCRANIAL MAGNETIC STIMULATION

A. Technical Information

TMS uses electromagnetic induction to generate an electric current across the scalp and skull without physical contact [3]. A plastic-enclosed coil of wire is held next to the skull and when activated, produces a magnetic field oriented orthogonally to the plane of the coil. The magnetic field passes unimpeded through the skin and skull, inducing an oppositely directed current in the brain that activates nearby nerve cells in much the same way as currents applied directly to the cortical surface [4]. Figure 3 shows a typically stimulation circuit in which low voltage ac is transformed to a higher voltage and then rectified. This higher voltage dc charges a capacitor which is fired via a thyristor switch into the stimulation core [5].

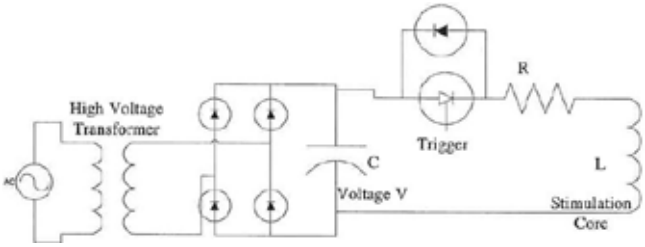

Figure 1. Typical stimulation circuit [6]

B. Adverse Effects

Although TMS is generally regarded as safe, there are still several potential side effects associated with this technique. These side effects are more common in high frequency rTMS. The most obvious and dangerous side effect of RTMS, the provocation and experience of epileptic seizures, suggest that current equipment is strong enough to produce them [7].

Different studies indicate a very small likelihood of structural brain damage, even at dangerous TMS concentrations and long treatment durations [8]. More research is needed to see if there are possible side effects in the long run, but for the time being there is no indication that this is the case.

C. TMS Protocols

Multiple TMS protocols have been developed that demonstrate certain advantages for different applications of this technique. The effects of TMS can be divided into three types depending on the protocol used for stimulation.

Single Pulse TMS: The single-pulse TMS protocol is used to depolarize neocortex neurons to evacuate an action potential. To warn neurons only once, a single burst of current is released into the excitation coil. If stimulating neurons are involved in motor cortex, muscle activity called motor evoked potential (MEP) is produced. MEP densities vary depending on the power of the stimulating electric field [9].

Paired Pulse TMS: In paired-pulsed TMS, two different current pulses are sent through the coil, each with different densities and different time intervals (1-20 millisecond), also known as interim distance (ISI). This technique can be used to examine the dynamic aspects of neuro- activity. For example, inhibitory and facilitating interactions in the cortex can be examined by combining a subthreshold stimulation stimulus with a subthreshold threshold stimulus at different short inter-stimulus intervals along the same TMS coil [10].

Repetitive TMS (rTMS): The first two protocols were used a few decades ago. However, due to improvements in the development of magnetic stimulation devices, rTMS has become possible and is now the most common technique [11]. The rTMS consists of the stimulus pulses (1-20 pulses per second), all of the same intensity. rTMS may produce long-term effects that are not limited only to the stimulation period. Many of these effects are related to the excitability of the treated areas and are largely dependent on the frequency and intensity of the stimulus. However, the exact mechanisms behind these effects are still unclear. Existing TMS devices can produce two different excitation waveforms that are either monophasic or biphasic of the induced current. Studies showing biphasic pulses with single-pulse TMS are more effective for stimulation in terms of being more powerful than monophasic waveforms [12].

III. DATA ANALYSIS AND RESULTS

The EEG data of each of the 3 patients were classified as before applying TMS and after applying TMS. Then each data was plotted to compare the graphs on time domain and frequency domain for each channel. The signal energies of the channels were found and the energy of the signals before and after treatment with the help of excel were compared. With the MEMD algorithm, 18 oscillations were detected for the first patient, 17 for the second patient, and 18 for the third patient. In order to be able to demonstrate the effectiveness of the treatment and to better detect the change in alpha waves, the oscillations (IMFS) of each channel of each patient before and after magnetic stimulation were examined. Since the cases where the alpha wave is dominant are depression, the first 5 IMF that alpha wave will be found were studied in 12 channels and the energies of these images were found. The table was compiled using Excel and compared.

A. Fourier Transform Analysis

Fourier Transform examines the signal in frequency domain to investigate periodic events such as oscillation and vibration movements in the signal. In this way, it is possible to determine the frequency band within the signal.

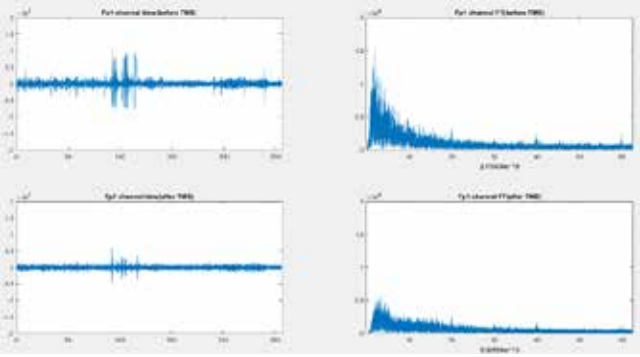

Figure 2. Before and after the application of TMS therapy, the signals of the Fp1 channel of the EEG data of the third patient. The top left-Fp1 channel time domain before TMS therapy, bottom left-Fp1 channel time domain after TMS therapy; top right-Fp1 channel frequency domain before TMS therapy, bottom right-Fp1 channel of frequency domain after TMS therapy

As a result of magnetic stimulation, there is a visible decrease in the magnitude of the patient's frequency axis.

The energy of some channel was examined before and after treatment and is shown in the graphs below.

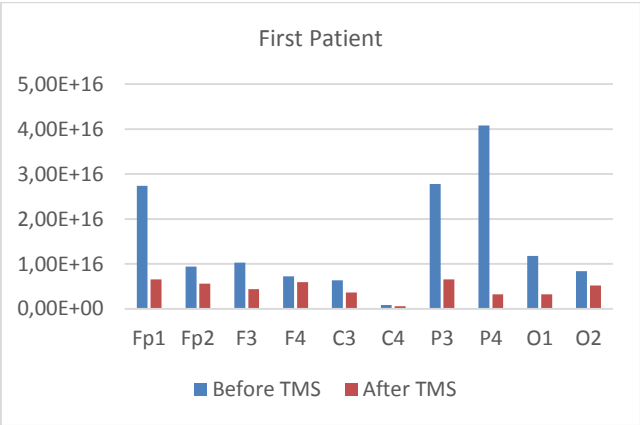

Figure 3. Comparison of signal energies before TMS treatment and after TMS treatment in some channels

When all channels of all of our patients were examined, there was a noticeable decrease in signal energy.

Table 1: Most affected channel after TMS treatment and change ratio of this channel

Patients	Most affected channel	Change ratio
First Patient	P4	92.01%
Second Patient	P3	83.02%
Third Patient	Fp1	47.24%

B. Alpha rhythm detect with MEMD Algorithm

With the MEMD algorithm, the oscillations of the signals are detected. In order to better analyze how alpha waves (8 Hz-18 Hz) are affected from the treatment, the MEMD algorithm was also run in MATLAB® and the necessary algorithm was developed to apply the patients to the EEG data. The first 5 IMF values were found because alpha waves could be distributed in 1.IMF-2.IMF; 2.IMF-3.IMF; 3.IMF-4.IMF; 4.IMF-5.IMF ranges. Figure 4 also shows the first 5 IMF charts of some channels before TMS and after TMS.

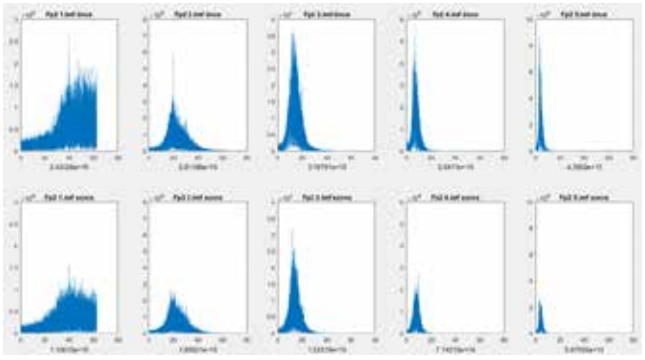

Figure 4. First 5 IMF in Fp2 channel of second patient (top-before TMS treatment; bottom after TMS treatment)

IMF ANALYSIS

The total energy of IMFs is calculated for each channel before TMS and after TMS. The energy of the signals of each channel was calculated and charted with the help of excel to see the change.

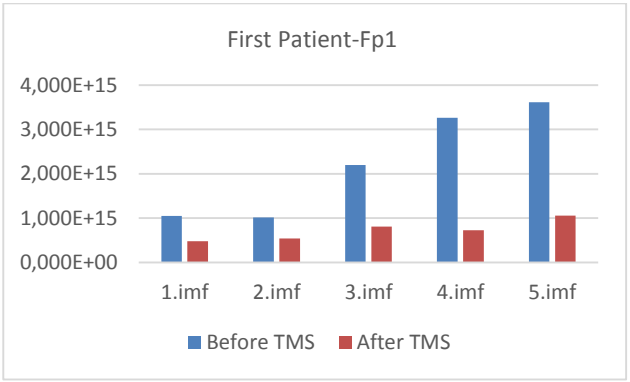

Figure 5. The signal energies of first 5 IMF in Fp1 channel of first patient (top-before TMS treatment; bottom after TMS treatment)

Table 2: Most affected IMF, channel after TMS treatment and change ratio of these channel for each patient

Patients	Most affected channel-IMF	Change ratio
First Patient	Fp1 – 4.imf	77.63%
Second Patient	Fp2 – 5.imf	86.26%
Third Patient	Fp1 – 5.imf	68.87%

IV. DISCUSSION

This study examined the effect of TMS therapy on depression patients on EEG signals of patients. The changes in alpha waves, which are dominant in EEG data of depressed patients, are analyzed as before TMS treatment and after TMS treatment in MATLAB®. As a result, we can say that there is a visible decrease in the magnitude of the frequency axis of all patients after treatment. In order to investigate the depression, which is the dominant state of alpha waves, the IMF graphs were extracted with the MEMD algorithm. First 5 IMF of each channel of each patient that alpha waves exist are examined and selected the most appropriate. Table 2 shows that the highest decrease ratio of IMF that found in alpha waves. We can also see from other graphs that TMS therapy suppresses alpha waves. Further studies may also be tested with the drug treatment for depression.In addition, work should be done on mice in different regions of the brain.It should be compared with the drugs used in today's treatment. At the same time, the alpha wave level of the depressed patients is determined and the standard is established for each level to be applied to the Magnetic Stimulus Level.This can greatly increase the ability of physicians to diagnose correctly.There is no doubt that various studies to be done will also be a source to follow the long term effect of Magnetic Stimulus of brain.

Since Transcranial Magnetic Stimulus is applied to certain areas of the brain, it is very important to study the human brain for its discovery and its use in the diagnostic phase. This study experimentally investigated the effect of stimulation of the relevant parts of the brain (left prefrontal cortex related to depression) by magnetic stimulation non-invasively. Magnetic stimulation of the brain and stimulating neurons gives hope to humanity for other cannot treated mental disorders.

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