STUDY OF MEP RESPONSE OF TRANSCRANIAL MAGNETIC STIMULATION IN MULTIPLE MUSCLES ON HEALTHY SUBJECTS

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Dedicate to my beloved family, lecturers, friends and silat family for their endless support and encouragement throughout my years as a student

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ABSTRACT

Transcranial Magnetic Stimulation (TMS) is a device that is used to stimulate the brain for diagnostic or therapeutic purpose. It is usually used in post stroke treatment, depression treatment and pain control. Myriad research was done on the Muscle Evoked Potential (MEP) of the muscles when the TMS had been applied to the motor cortex of the brain. Most studies that involve single muscle are only either on the hand or leg. There are also studies involve multiple muscles for different goals and different targeted muscles. This study will focus on obtaining the optimum motor threshold that are out from the TMS to the motor cortex in order to obtain the MEP amplitude of the targeted muscles. The signals of the EMG of the APB, FCR and ADM were recorded using Bioradio analysed in Matlab by filter algorithm consists of High Pass filter and Notch filter. From the project, the MEP of the selected muscle were obtained with APB muscles with 0.12 mV, FCR is 0.11 mV and for muscle of ADM is 0.12 mV. The APB and ADM that have high MEP shows that it is easily stimulated by the TMS compare to FCR. The Motor Threshold that was obtained through this project is enough to make the targeted muscles responses of 64% from the full power of the TMS. This Motor Threshold can be used as the benchmark for other research on the minimum level of power needed by TMS. This minimum level power given to the subject is needed to study the reponse of three muscles involved.

ABSTRAK

Transcranial Magnetic Stimulation (TMS) adalah sebuah peranti yang digunakan untuk merangsang otak sama ada untuk tujuan diagnosis atau terapi. Kebiasaanya ia digunakan untuk rawatan penyakit seperti rawatan selepas strok, depresi, mengawal kesakitan dan lain-lain. Ramai penyelidik telah melakukan kajian mengenai MEP pada otot apabila TMS dirangsang pada kawalan motor dibahagian otak. Kebanyakkannya hanya melibatkan penglibatan satu otot sama ada dibahagian tangan atau kaki. Terdapat juga kajian yang melibatkan penggunaan beberapa jenis otot tetapi mempunyai tujuan yang berbeza dan jenis ototnya yang digunakan juga berbeza. Kajian ini akan menfokuskan untuk mendapatkan nilai optima ambang motor yang diberikan oleh TMS kepada bahagian motor untuk mendapatkan amplitud MEP pada APB, FCR dan ADM. Bacaan EMG daripada otot uang dipilih akan direkod mengunakan Bioradio dan akan dianalisis lebih lanjut di dalam Matlab mengunakan algorithma penapis yang digunakan untuk menyah isyarat 50 Hz dan menyekat isyarat berfrekuensi rendah. Melalui kajian ini. MEP daripada otot uang dipilih telah diperoleh dengan ABP sebanyak 0.12mV, FCR sebanyak 0.11 mV dan otot ADM sebanyak 0.12 mV. ABP dan ADM mempunyai MEP yang tinggi menunjukkan ianya mudah untuk dirangsang oleh TMS berbanding FCR. Ambang motor yang diperolehi dari kajian ini yang sesuai unuk membuat otot yang disasarkan memberi respon adalah 64% daripada kuasa penuh TMS. Ambang motor ini boleh digunakan sebagai panduan kepada penyelidik lain mengenai para minimum tenaga yang diperlukan TMS untuk memberikan respon kepada ketiga-tiga otot dalam kajian ini.

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LIST OF ABBREVIATIONS

ABR	-	Auditory Brain Response
ADM	-	Abductor Digiti Minimi
AEP	-	Auditory Evoked Potential
AER	-	Auditory Evoked Response
APB	-	Abductor Pollicis Brevis
EDC	-	Extensor Digitorum Communis
EEG	-	Electroencephalography
EP	-	Evoked Potential
EPB	-	Extensor Pollicis Brevis
ERP	-	Evoked Related Potential
FCR	-	Flexor Carpi Radialis
FCU	-	Flexor Carpi Ulnaris
FDI	-	First Dorsal Interosseous
FDS	-	Flexor Digitorum Superficialis
FES	-	Functional Electrical Stimulator
MCS	-	Motor Cortex Stimulation
MEP	-	Motor Evoked Potential
MFC	-	Medial Frontal Cortex
MT	-	Motor Threshold
RMT	-	Resting Motor Threshold
rTMS	-	Repetitive Transcranial Magnetic Stimulation
SCI	-	Spinal Cord Injury
TA	-	Tibialis Anterior

TMS	-	Transcranial Magnetic Stimulation
VER	-	Visual Evoked Response
WBV	-	Whole Body Vibration

CHAPTER 1

INTRODUCTION

This project was done to study MEP response due to TMS in multiple muscles. This chapter includes the background, problem statement, objective and scope of this project.

1.1 Thesis Layout

This thesis consists of 5 chapters, starting from chapter 1 giving the background of this project, problem statement, objectives and scopes of the project. Inside chapter 2, literature review on the previous research that had been done before will be covered. Chapter 3 will elaborate on the material and experimental procedure that used in this project. Next, chapter 4 that will elaborate and discuss more on the results obtains from the experiment. Finally, the conclusions of this project were stated inside chapter 5.

1.2 Background

Nervous system functions to give out commands to other organs for certain tasks. Nervous system consists of two parts which are central nervous system (CNS) and peripheral nervous system (PNS). Brain and spinal cords are in the CNS while PNS are the small nerves coming out from the CNS to the entire of the body. Brain is the main organ in our body and all the commands give out to the entire body come from it. The body will receive this information; send it to the brain to process and then being sent back to other part of the body to responds to the stimulus. Sometimes an obstruction occurs in the pathway from the receptor to the brain or from the brain to the motor. Researcher discovered these diseases after trying several methods and equipment that are suitable for several kind of diagnosis such as neurodegenerative, nerve injury and others. In order to understand more about the brain, first we need to understand the part of brain itself and it functions.

Transcranial Magnetic Stimulation (TMS) is a technique that is being used to stimulate certain parts of the brain [1]. It is being used noninvasively to stimulate the brain by generating a brief and high intensity of magnetic field to the part of the brain and see the effect of it reaction to the other parts of the body. The magnetic field being generated by passing brief current into the magnetic coil and the magnetic field will start to be generated from this process. The idea of TMS has been started based on Michael Faraday's principle where each current that passed through a wire will generate a magnetic field on it surrounding. If there is another wire near the first wire that having electric current inside it, the magnetic field produce from the first wire will induces another electric current to flow in the second wire [2]. Based on this principle, researchers are applying this concept in the research involving TMS as there are similarities on the characteristics of the part itself. The coil of the TMS act as the first wire and the human brain will function as the second wire in which it induced by the TMS coil for research purpose or treatment. The electrical energy given by the TMS to induce the motor cortex is called Motor Threshold (MT) and it is varies across individuals. The intensity of TMS given is relative to the MT. Study done by [3] observed in a depressed cohort

that the MT increases as the distance from coil to cortex increase. Study on resting motor threshold (MT) were done by [4] stated that the MT were defined as the intensity of the stimulation in which the Motor Evoked Potential (MEP) are recorded with the surface Electromyography (EMG) is about 50% out of 11–20 consecutive trial.

There is another device commonly used by the researcher to detect brain activity which is Electroencephalogram (EEG). EEG is used to diagnose epilepsy. In addition, it also used to diagnose sleep disorders, coma, encephalopathy, brain death, and diagnosis of tumours, stroke and other focal brain disorders. Derivatives of the EEG technique include evoked potentials (EP), which involves averaging the EEG activity time-locked to show the present of a stimulus in visual, somatosensory, or auditory. Event-related potentials (ERP) refer to averaged EEG responses that are time-locked to more complexes processing of stimuli. EP commonly occurs in response to a physical stimulus in which the physical stimuli are converted to patterns of energy which are received by the senses and they are corresponded to the sensory receptors to convert this energy into nerve impulse to the brain [5]. The nerve impulses interpreted in the cerebral cortex as sensations in which these sensations been evoked by delivering auditory stimuli such as click stimuli or tone burst stimuli.

Visual evoked potential is an electrical signal trigger from the brain during a visual presented to the subject. It can be used to detect ocular diseases in patients who are visually impaired [5]. The responses can be used to detect eye diseases like glaucoma, diabetic retinopathy, multiple sclerosis, loss of peripheral (side) vision, macular degeneration and colour blindness. Additionally, there is Auditory Evoked Potential (AEP) which is an electrical signal produce from the brain while an auditory stimulus is given to the subject. The signal consists of reproducible positive or negative peaks, latency, amplitude and behavioural correlation [5]. The amplitude produced is much smaller compared to the EEG signals. This signal can be separated as either transient or steady-state. The AEP signal is triggered while perceiving

audio stimuli with slow rate to avoid overlapping of the immediate stimuli response and the corresponding evoked potentials are known as transient AEP.

EEG and TMS can detect the functions of the brain. However, for EEG, it is not capable of inducing any magnetic field in the brain in order to see the body reaction. EEG can detect the nerve of the body and whether it can function normally or not but is only suitable for certain conditions, such as Auditory Evoked Response (AER) and Visual Evoked Response (VER). TMS on the other hand, can be used to detect the functionality of the nerve between the brain and the other motor sensory. Therefore, we use TMS to generate some electrical impulse from the brain to see the condition of the nerve from the brain to the target muscle by measuring the EMG of the target muscle.

While AER is used for checking the nerve connection between brain and ear and VER is used for checking the nerve connection between the brain and eyes, MEP is used to check the nerve condition between the brain and the muscles which use the same principle as AER and VER where all of them were evoked by certain stimulus. The AER is used to study the auditory performance by using sound as stimulus, VER for the study of visual performance by giving visual stimulus while MEP is used to study muscle performance by stimulating the brain to evoke the resting muscles or by moving the muscles voluntarily. The study involving muscles performance will use MEP data instead of AER and VER. Most of the study involving motor function will use MEP of the targeted muscles for evaluation of certain disease. From a clinical perspective, the uses of MEP are as a tool for diagnosis and evaluation of multiple sclerosis and as a prognostic indicator after stroke motor recovery [6]. The MEP amplitude also been choose for muscle evaluation because its amplitude can be used to infer the structural integrity of corticospinal tracts of the subjects [7].

Many studies have been done using TMS on the performance of single and multiples muscles. Study on single muscle such as APB have been done on stroke

patients [8] and healthy subjects [3]. Others single muscles that been study including EDC from [9], ADM from [10] and FDI [11]. The MEP should be obtained from multiple muscles compared to single muscles because the MEP of each muscle obtained from different experiments are different due to delay in response time [12]. Many researches involve multiple muscles either on the upper limb or lower limb. The recent studies are focusing more on the upper limb compared to the lower limb. Researcher from [13] and [14] do their study on multiple muscle involving swallowing muscle.

Meanwhile, researchers from [15] and [12] do their study on the upper limb muscles such as APB, FDI, FCR and ADM but for different purposes of study. Researchers from [15] study focusing on the upper limb to find the motor mapping on the brain using the MEP results while researcher from [12] do their study focusing on the MEP latency of the subjects using MEP value. The differences of this study from [12] and [15] are this study focusing on obtaining the range of MEP amplitude at minimum Motor Threshold. More study on multiple muscle done by [16] on extensor pollicis brevis (EPB) to evaluate the corticospinal excitability of both hemispheres of the brain during the reaction times. Other study involving extensor spine muscles and multiple muscles of the abdominal were done by [17], [18] respectively.

This project will focus more on the MEP amplitude of the muscles of upper limb which are APB, FCR and ADM at the minimum TMS power to identify the range of MEP amplitude that healthy subjects have at minimum Motor Threshold. The purpose of choosing APB, FCR and ADM instead of lower limb or other muscles in the body are because the distal muscle are easier to evoke a response from compared to proximal muscles due to the larger cortical representation [19] and lower activation thresholds [20] present on this area. The muscle of FCR, ADM and APB also contract independently compare to another muscle near this area [21].

1.3 Problem Statement

The existing method of using TMS is to measure the effective of the treatment towards the subjects who have nerve dysfunction. The study done is focused on investigating the activity of multiple muscles of healthy subject induced by the TMS simultaneously already done but less focusing on the MEP amplitude of the subjects. The different MEP amplitude might occur between each targeted muscle due to different latency [12]. There are some researcher do their study on the same interest but on different targeted muscles. Researcher might have difficulties comparing the healthy subject with subject that have diseases due to less study focusing on the MEP amplitude itself. Research done mostly focus on finding the motor mapping using MEP amplitude and some researcher do their study on MEP latency. Therefore this study is done to study the activity of the motor function of the healthy subject when TMS is induced to act as fundamental for other researchers.

1.4 Objectives

The aims of this project are as follows:

1. To study the optimum level of the Motor Threshold for healthy subjects when double TMS applied.
2. To employ EMG measurement algorithm that can detect the Motor Threshold from EMG signal.
3. To differentiate the Motor Evoked Potential response of abductor pollicis brevis, flexor carpi radialis and abductor digiti minimi..

1.5 Scope

This study involves 20 healthy adults as recommended by [15] with age range between 20 to 28 years old. It consists of both males and females. The muscles involved in this study are flexor carpi radialis, abductor digiti minimi and abductor pollicis brevis. TMS with C-B60 Coil (figure 8 coils) was used in this study because it deliver high power compare to single coil TMS and the EMG was taken with bipolar electrode configuration.

The TMS will be applied on the motor cortex area at the brain while the EMG electrode will be placed at the FCR, ADM, and ABP. This experiment will be done three times at the same day the subject undergoes the experiment to find the consistency of the data obtained. This experiment was conducted at the Neural Engineering Lab at Faculty of Bioscience and Medical Engineering, University Teknologi Malaysia, Skudai.

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