

**THE USE OF MAGNETOENCEPHALOGRAPHIC BRAINWAVES IN
DETECTING NEUROCOGNITIVE IMPAIRMENTS IN TRAUMATIC BRAIN
INJURY**

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**Dissertation submitted in Partial Fulfillment of the requirement for the
Degree of Master of Surgery (Neurosurgery)**



**SCHOOL OF MEDICAL SCIENCES
UNIVERSITI SAINS MALAYSIA
2018**

**THESIS PRODUCED ACCORDING TO
NEW USM MANUSCRIPT FORMAT**

Acknowledgements:

- *Professor Zamzuri Idris for his constant guidance and mentorship. His priceless advice and encouragement provided the fuel for the inspiration, and motivation for this study.*
- *Professor Jafri Malin for sharing his experience and view how to progress this study.*
- *Mr Johari for his advice and encouragement of this study*
- *Dr Faruque Reza for his knowledge and guidance in interpretation of the MEG analysis*
- *Puan Wan Azlen Wan Muhamad for her assistance in performing the neuropsychological assessments which were often difficult and time consuming.*
- *Cik Amalina who also assisted in the neuropsychological assessments.*
- *Hazim and his team in the MEG room who helped facilitate the MEG scans for the patients*
- *This study was (ref : USM/JEPeM/271.3(11)) approved by Human Research Ethics Committee USM, School of Medical Sciences, Kubang Kerian, Kelantan, Malaysia.*

Authors note: This manuscript was prepared for submission to Neurological Research Taylor & Francis and follows the format for that journal.

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LIST OF ABBREVIATIONS

<i>Abbreviation</i>	<i>Description</i>
<i>EEG</i>	<i>Electroencephalography</i>
<i>GCS</i>	<i>Glasgow Coma Scale</i>
<i>MEG</i>	<i>Magnetoencephalography</i>
<i>TBI</i>	<i>Traumatic Brain Injury</i>

ABSTRAK

Latar belakang :Perubahan pada sambungan saraf- saraf otak selepas kemalangan dapat diselidik dalam peringkat awal dengan bantuan MEG (magnetoencephalography) . Hipotesis kajian ini membandingkan masalah neuropsikologi yang dialami pesakit selepas kemalangan .Oleh itu, kami mengkaji potensi pengimejan MEG (magnetoencephalography) dan hubungannya dengan penilaian neuropsikologi.

Metodologi :Kami mengkaji dua belas pesakit yang mengalami kemalangan jalan raya dengan GCS (glasgow coma scale) 9 ke 13 dalam masa 24 jam. Pesakit terbahagi kepada 2 kumpulan iaitu ‘mild head injury’ (GCS; 13) dan kumpulan ‘moderate head injury’ (GCS 9-12). Neuropsikologi dijalankan sebelum MEG dilakukan keatas pesakit tersebut. MEG digunakan untuk mengesan frekuensi alfa, beta, gama dan delta.

Keputusan : Frekuensi beta didapati rendah, theta/beta didapati tinggi seperti yang direkodkan oleh MEG dalam kumpulan ‘moderate head injury’ berbanding dengan kumpulan ‘mild head injury’ ,dimana neuropsikologi tidak dapat mengesan perbezaannya .

Kesimpulan : Analisa yang dilakukan mendapati bahawa terdapat perubahan yang ketara untuk pesakit yang dalam kumpulan ‘moderate head injury’ . Oleh demikian, penggunaan MEG untuk menilai dan mengkaji

saraf-saraf ini mungkin dapat membantu dalam ramalan awal kerosakan saraf saraf otak dan diharap dapat membantu meningkatkan mutu ingatan dan tumpuan pesakit di masa hadapan .

Abstract:

Objectives: The purpose of this study was to investigate the potential of magnetoencephalography (MEG) as a tool for early detection of brainwave disruption in traumatic brain injury (TBI) patients and compare the MEG results to neuropsychological assessments.

Methods: Our study consisted of 12 TBI patients aged 14–26 who had a Glasgow Coma Scale (GCS) of 9–13 in the first 24 hours after a motor vehicle accident. According to the severity of their GCS score, and regardless of the type of brain injury, patients were then distributed into two groups, moderate TBI (GCS score 9–12) or mild TBI (GCS score of 13). Neuropsychological tests were given to patients before the MEG recording. MEG was used to measure the power of the different frequency bands delta, theta, alpha, beta, and gamma.

Results: The power of the beta frequency band was reduced and the theta/beta ratio was significantly increased in the moderate TBI group compared to the mild TBI group. Neuropsychological assessments results tended to support this finding but did not reach significance.

Discussion: The MEG results suggest that moderate TBI patients have greater processing and attention deficits than mild TBI patients. We concluded that MEG plays an important role in objectively detecting brain wave changes after TBI, which has implications for the prediction of cognitive sequelae after TBI.

Keywords: Magnetoencephalography, neuropsychology tests, spectral analysis, traumatic brain injury, brainwaves

1. INTRODUCTION & LITERATURE REVIEW

Trauma cases contributed to 11.65% of visits to emergency departments at Malaysia Ministry of health general hospitals, of which about 80% involved head injury. Traumatic brain injury (TBI) may lead to a wide range of short- or long-term issues affecting cognitive and motor functions, sensation, and emotion (1, 2). TBI can cause brain connectivity disruption in widely disparate brain regions which may not necessarily correspond to the locations of focal lesions as shown using conventional neuroanatomical imaging such as Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) (1). Another limitation of conventional neuroanatomical imaging is its inability to show functional abnormalities in patients with TBI (3, 4). We therefore sought to use brainwave data obtained via magnetoencephalography (MEG) as a tool to diagnose functional disturbances. There are few studies regarding the use of quantitative brainwave or electroencephalography (EEG), using spectral power analyses, for TBI (3,4). We chose to conduct spectral analysis using MEG, which is a non-invasive imaging technique that directly measures neuronal current brain activity in grey matter, with high temporal resolution (< 1 ms) and a spatial localization accuracy of 2–3 mm at the cortical level (5). Electrical conductivity differences between the brain, cerebrospinal fluid skull, and scalp interfere with the scalp EEG view of the brain's electrical activity but have minimal impact on MEG (6). A few studies have examined changes in the spectral power bands of TBI patients and have found that TBI patients have more prominent low-frequency amplitude waves, such as delta and theta bands (7, 8) and these injured neuronal tissues who generate the multifocal low-frequency neuronal magnetic signal that can be localized directly using MEG instead of EEG. These changes are linked to cognitive and affective sequelae. Pioneering studies by Lewine et al(8) showed that MEG

slow waves were 65% sensitive in detecting symptomatic concussions, whereas EEG was only 20–25% sensitive, and MRI was only 20% sensitive in detecting lesions in patients with mild or moderate TBI. In 2002, MEG achieved recognition as reimbursable clinical procedure by the American Medical Association, including recording and analysis of spontaneous brain magnetic activity for epileptic foci and of evoked magnetic fields (e.g. sensory, motor, language, visual cortex, etc.) under Current Procedure Terminology (CPT) (9).

We used the Glasgow Coma Scale (GCS) to indicate the severity of TBI among our sample subjects. GCS is a clinical tool designed to measure cognitive impairment. GCS scores of 3 to 8 are indicative of severe TBI, scores of 9 to 12 indicate moderate TBI, and scores of 13 to 15 indicate mild TBI. We then evaluated cognitive impairment in mild and moderate TBI patients using neuropsychological assessments, which are specialized task-oriented evaluations of human brain-behaviour relationships that incorporate patient history, presentation, and clinical findings. MEG data for all patients was then recorded.

Spectral analysis subdivides MEG results into several bands—the delta, theta, alpha, beta, and gamma bands. We hypothesized that all bands could be affected by TBI, with consequences for cognitive impairment. The hippocampus is especially prone to injury in TBI, which will subsequently reduce hippocampal Theta activity, causing persistent learning and memory deficits. The hippocampus plays a vital role in a variety of memory tasks and is normally dominated by theta bands, which synchronize activity across distal brain regions for cognitive processing (10, 11). A pathological increase in theta bands is also seen in patients with Alzheimer's disease (12) which is characterized by a loss of cholinergic functions that is believed to be an important contributor to cognitive deficits. Cholinergic neuronal loss is

found in several areas of the limbic system, such as the medial septal nucleus, which have major projections to the hippocampus (13). Thus, cholinergic dysfunction after TBI may also contribute to learning, memory and attention deficits (14). Alpha band power reduction is related to post-traumatic stress disorder symptoms (15). Alpha rhythms also play roles in perceptual learning (16, 17), and attention is one of the key factors that can determine perceptual learning outcomes. The alpha band is also responsible for the synchronization of working memory (18). The functional role of the beta band, which originates in the sensorimotor cortex, is related to action-related language processing (19) Hirata et al (20) reported that increased beta from MEG signals from the inferior frontal gyrus and middle frontal gyrus during a word-reading test without phonation. A decrease in beta power is also seen in attention deficit disorder(21). The amygdala is a subcortical area involved in emotional processing and regulation. Numerous studies have shown that gamma band oscillations are observed in the amygdala during emotional memory and processing (22, 23). Gamma oscillation is also seen in the hippocampus (24) and in several areas of the neocortex (25), as well as in the thalamus (26). It is also thought to have a role in cognitive execution (27). Abnormal slow/delta-waves are not specific as it can also been found in neurological/psychiatric disorders such as epilepsy, brain tumors, Alzheimer's disease, and other organic brain disease. Other external factors such as neuroleptic, sedative,and hypnotic medications, as well as sleep deprivation may also contribute to increase slow waves. However , Huang and colleagues study shown injured neurons due to TBI, causing deafferentation from axonal injury to the associated white matter fiber tracts, which detected by diffusion tensor imaging as reduced fractional anisotropy(28). However, delta band

activity also increases, mainly in the frontal lobes, during tasks such as mental calculations and semantic tasks (29).

We hypothesized that the combination of MEG data with neuropsychological assessments in the detection of potential neurological and cognitive deficits would yield clinically relevant data that would not be easily acquired via routine bedside neurological examination. Our results include analysis of patient MEG findings in relation to neuropsychological scores for memory, attention and language.

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2. Objective

2.1 General Objective

The main purpose of this study is to examine neural network properties at separate time-points during recovery from traumatic brain injury (TBI) during and after the acute phase

2.2 Specific Objective

- 1) Sensitivity of MEG and neuropsychological on these 2 groups of traumatic brain injury – Mild and Moderate TBI group
- 2) Comparison of the eyes closed and eyes open results recorded in MEG .
- 3) Relevance of the spectral analysis (alpha,beta,gamma,delta,theta) in TBI

3.0 Thesis approval



Jawatankuasa Etika Penyelidikan Manusia USM (JEPeM)
Human Research Ethics Committee USM (HREC)

15th July 2015

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JEPeM Code : USM/JEPeM/[271.3(11)]

Protocol Title : Investigating Functional Connectivity in Memory and Attention after Moderate Traumatic Brain Injury.

Dear Mr.,

We wish to inform you that your study protocol has been reviewed and is hereby granted approval for implementation by the Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia (JEPeM-USM). Your study has been assigned study protocol code **USM/JEPeM/[271.3(11)]**, which should be used for all communication to the JEPeM-USM related to this study. This ethical clearance is valid from July 2015 until June 2016.

The following documents have been approved for use in the study.

1. Research Proposal

In addition to the abovementioned documents, the following technical document was included in the review on which this approval was based:

1. Participant Information Sheet and Consent Form (English version)
2. Participant Information Sheet and Consent Form (Malay version)
3. Data Collection Form

Attached document is the list of members of JEPeM-USM present during the full board meeting reviewing your protocol.

While the study is in progress, we request you to submit to us the following documents:

1. Application for renewal of ethical approval 60 days before the expiration date of this approval through submission of **JEPeM-USM FORM 3(B) 2014: Continuing Review Application Form**. Subsequently this need to be done yearly as long as the research goes on.
2. Any changes in the protocol, especially those that may adversely affect the safety of the participants during the conduct of the trial including changes in personnel, must be submitted or reported using **JEPeM-USM FORM 3(A) 2014: Study Protocol Amendment Submission Form**.
3. Revisions in the informed consent form using the **JEPeM-USM FORM 3(A) 2014: Study Protocol Amendment Submission Form**.
4. Reports of adverse events including from other study sites (national, international) using the **JEPeM-USM FORM 3(G) 2014: Adverse Events Report**.
5. Notice of early termination of the study and reasons for such using **JEPeM-USM FORM 3(E) 2014**.
6. Any event which may have ethical significance.
7. Any information which is needed by the JEPeM-USM to do ongoing review.
8. Notice of time of completion of the study using **JEPeM-USM FORM 3(C) 2014: Final Report Form**.

Please note that forms may be downloaded from the JEPeM-USM website: www.jepem.kk.usm.my

Jawatankuasa Etika Penyelidikan (Manusia), JEPeM-USM is in compliance with the Declaration of Helsinki, International Conference on Harmonization (ICH) Guidelines, Good Clinical Practice (GCP) Standards, Council for International Organizations of Medical Sciences (CIOMS) Guidelines, World Health Organization (WHO) Standards and Operational Guidance for Ethics Review of Health-Related Research and Surveying and Evaluating Ethical Review Practices, EC/IRB Standard Operating Procedures (SOPs), and Local Regulations and Standards in Ethical Review.

Thank you.

"ENSURING A SUSTAINABLE TOMORROW"

Very truly yours,



PROF. DR. HANS AMIN VAN ROSTENBERGHE

Chairperson

Jawatankuasa Etika Penyelidikan (Manusia) JEPeM

Universiti Sains Malaysia

Title: The Use of Magnetoencephalographic Brainwaves in Detecting Neurocognitive Impairments in Traumatic Brain Injury

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4.2 Abstract:

Objectives: The purpose of this study was to investigate the potential of magnetoencephalography (MEG) as a tool for early detection of brainwave disruption in traumatic brain injury (TBI) patients and compare the MEG results to neuropsychological assessments.

Methods: Our study consisted of 12 TBI patients aged 14–26 who had a Glasgow Coma Scale (GCS) of 9–13 in the first 24 hours after a motor vehicle accident. According to the severity of their GCS score, and regardless of the type of brain injury, patients were then distributed into two groups, moderate TBI (GCS score 9–12) or mild TBI (GCS score of 13). Neuropsychological tests were given to patients before the MEG recording. MEG was used to measure the power of the different frequency bands delta, theta, alpha, beta, and gamma.

Results: The power of the beta frequency band was reduced and the theta/beta ratio was significantly increased in the moderate TBI group compared to the mild TBI group. Neuropsychological assessments results tended to support this finding but did not reach significance.

Discussion: The MEG results suggest that moderate TBI patients have greater processing and attention deficits than mild TBI patients. We concluded that MEG plays an important role in objectively detecting brain wave changes after TBI, which has implications for the prediction of cognitive sequelae after TBI.

Keywords: Magnetoencephalography, neuropsychology tests, spectral analysis, traumatic brain injury, brainwaves

4.3 Introduction:

Trauma cases contributed to 11.65% of visits to emergency departments at Malaysia Ministry of health general hospitals, of which about 80% involved head injury. Traumatic brain injury (TBI) may lead to a wide range of short- or long-term issues affecting cognitive and motor functions, sensation, and emotion (1, 2). TBI can cause brain connectivity disruption in widely disparate brain regions which may not necessarily correspond to the locations of focal lesions as shown using conventional neuroanatomical imaging such as Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) (1). Another limitation of conventional neuroanatomical imaging is its inability to show functional abnormalities in patients with TBI(3, 4). We therefore sought to use brainwave data obtained via magnetoencephalography (MEG) as a tool to diagnose functional disturbances. There are few studies regarding the use of quantitative brainwave or electroencephalography (EEG), using spectral power analyses, for TBI (3,4). We chose to conduct spectral analysis using MEG, which is a non-invasive imaging technique that directly measures neuronal current brain activity in grey matter, with high temporal resolution (< 1 ms) and a spatial localization accuracy of 2–3 mm at the cortical level (5). Electrical conductivity differences between the brain, cerebrospinal fluid skull, and scalp interfere with the scalp EEG view of the brain's electrical activity but have minimal impact on MEG (6). A few studies have examined changes in the spectral power bands of TBI patients and have found that TBI patients have more prominent low-frequency amplitude waves, such as delta and theta bands (7, 8) and these injured neuronal tissues who generate the multifocal low-frequency neuronal magnetic signal that can be localized directly using MEG instead of EEG. These changes are linked to cognitive and affective sequelae. Pioneering studies by Lewine et al(8) showed that MEG slow

waves were 65% sensitive in detecting symptomatic concussions, whereas EEG was only 20–25% sensitive, and MRI was only 20% sensitive in detecting lesions in patients with mild or moderate TBI. In 2002, MEG achieved recognition as reimbursable clinical procedure by the American Medical Association, including recording and analysis of spontaneous brain magnetic activity for epileptic foci and of evoked magnetic fields (e.g. sensory, motor, language, visual cortex, etc.) under Current Procedure Terminology (CPT) (9).

We used the Glasgow Coma Scale (GCS) to indicate the severity of TBI among our sample subjects. GCS is a clinical tool designed to measure cognitive impairment. GCS scores of 3 to 8 are indicative of severe TBI, scores of 9 to 12 indicate moderate TBI, and scores of 13 to 15 indicate mild TBI. We then evaluated cognitive impairment in mild and moderate TBI patients using neuropsychological assessments, which are specialized task-oriented evaluations of human brain-behaviour relationships that incorporate patient history, presentation, and clinical findings. MEG data for all patients was then recorded.

Spectral analysis subdivides MEG results into several bands—the delta, theta, alpha, beta, and gamma bands. We hypothesized that all bands could be affected by TBI, with consequences for cognitive impairment. The hippocampus is especially prone to injury in TBI, which will subsequently reduce hippocampal Theta activity, causing persistent learning and memory deficits. The hippocampus plays a vital role in a variety of memory tasks and is normally dominated by theta bands, which synchronize activity across distal brain regions for cognitive processing (10, 11). A pathological increase in theta bands is also seen in patients with Alzheimer's disease (12) which is characterized by a loss of cholinergic functions that is believed to be an important contributor to cognitive deficits. Cholinergic neuronal loss is found in several areas of the limbic system, such as the medial septal nucleus, which have

major projections to the hippocampus (13). Thus, cholinergic dysfunction after TBI may also contribute to learning, memory and attention deficits (14). Alpha band power reduction is related to post-traumatic stress disorder symptoms (15). Alpha rhythms also play roles in perceptual learning (16, 17), and attention is one of the key factors that can determine perceptual learning outcomes. The alpha band is also responsible for the synchronization of working memory (18). The functional role of the beta band, which originates in the sensorimotor cortex, is related to action-related language processing (19) Hirata et al(20) reported that increased beta from MEG signals from the inferior frontal gyrus and middle frontal gyrus during a word-reading test without phonation. A decrease in beta power is also seen in attention deficit disorder (21). The amygdala is a subcortical area involved in emotional processing and regulation. Numerous studies have shown that gamma band oscillations are observed in the amygdala during emotional memory and processing (22, 23). Gamma oscillation is also seen in the hippocampus (24) and in several areas of the neocortex (25), as well as in the thalamus (26). It is also thought to have a role in cognitive execution (27). Abnormal slow/delta-waves are not specific as it can also been found in neurological/psychiatric disorders such as epilepsy, brain tumors, Alzheimer's disease, and other organic brain disease. Other external factors such as neuroleptic, sedative, and hypnotic medications, as well as sleep deprivation may also contribute to increase slow waves. However, Huang and colleagues study shown injured neurons due to TBI, causing deafferentation from axonal injury to the associated white matter fiber tracts, which detected by diffusion tensor imaging as reduced fractional anisotropy(28). However, delta band activity also increases, mainly in the frontal lobes, during tasks such as mental calculations and semantic tasks (29).

We hypothesized that the combination of MEG data with neuropsychological assessments in the detection of potential neurological and cognitive deficits would yield clinically relevant data that would not be easily acquired via routine bedside neurological examination. Our results include analysis of patient MEG findings in relation to neuropsychological scores for memory, attention and language.

4.4 METHODOLOGY

Materials and methods

4.41 The subjects

This prospective study was approved by Universiti Sains Malaysia Kubang Kerian Human Ethical Committee (ref. HUSM/11/020/Jld.6). The study consisted patients of Malaysian population aged of 14–30 years old who received a GCS score of 9–13, were recruited from the emergency department of Hospital Universiti Sains Malaysia during the first 24 hours after injury. Inclusion criteria were: between 14 and 30 years of age; causes of head injury were clear (e.g. sustaining a force to the head); Glasgow Coma Scale from 9-13 (within 24 h of injury); Modified Marshall I-V on basis of CT scan findings, Every participant was able to tolerate enclosed space for MEG; Malay or English speaking, to comply with instructions to complete tasks during MEG and able to give informed consent . Exclusion criteria included ferrous metal inside the body or items that might interfere with MEG data acquisition; presence of implanted medical devices; seizures or other neurological disorders, or active substance abuse; certain ongoing medications (anticonvulsants, benzodiazepines, and/or GABA antagonists) known to directly or significantly influence electroencephalographic (EEG) findings.

4.42 Neuropsychological assessments

All participants underwent cognitive-behavioural testing including the Wechsler Abbreviated Scale of Intelligence (WASI), Wechsler Memory Scales 1 (WMS1, Immediate), Wechsler Memory Scales 2 (WMS2, Delayed), Wechsler Memory Scales 3 (WMS3, Total), Benton Visual Retention Scale (BVRT), Rey Auditory Verbal Learning Test 1 (RAVLT1, Immediate Recall), Rey Auditory Verbal Learning Test 2 (RAVLT2,

Delayed Recall), and Comprehensive Trail Making Test (CTMT). These assessments were carried out by a trained research associates .The results were scored, double scored, and reviewed by a licensed neuropsychologist to maintain reliability. All evaluations were administered in a single session in a quiet room, within 1 week of the MEG .

4.43 Sample groups

On the basis of clinical admission measures, the patients were placed into two different groups. Criteria for assignment to the Mild head injury group were GCS 13, post traumatic amnesia (PTA) less than 1 hour, and loss of consciousness LOC less than 20 minutes. Criteria for the Moderate head injury group were GCS 9-12, PTA 1hour to 6days and LOC 1 hour to 24 hours. The sample size of this study calculated based on the previous study by Huang et al(1) published in Brain injury journal of Taylor &Francis in 2017. The calculated sample size for this study using software GPower 3.1.7 , tests - Means: Difference between two dependent means (matched pairs),analysis:A priori: Compute required sample size ,Input:Tail(s)=One,Effect size dz =0.95, α err prob=0.05, Power (1- β err prob)=0.90.Output: Noncentrality parameter $\delta=3.1507936$, Critical t=1.8124611, Df=10, Total sample size=11, Actual power=0.9002194

4.44 MEG recordings

Our MEG recordings were performed in a magnetically shielded room using a whole-head

Electa Neuromag 306 channel MEG system (Helsinki, Finland) in the Laboratory for MEG, Department of Neurosciences, Universiti Sains Malaysia. Prior to recording, four small coils were applied to the left and right side of each patient's forehead: to the left and right mastoid processes, for head position indicator and head digitization points on the nasion, and at left and right preauricular positions. The sampling rate was 1,000 Hz. Spontaneous MEG recording was conducted for 30 minutes for each TBI patients in two resting conditions, eyes closed and eyes open. A 1-minute sample of artefact- and noise-free magnetometer data was selected for the analysis of the total power in the delta (0.5–4 Hz), theta (4–7 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–50 Hz) bands using Fast Fourier Transform (fft-size-1024, fft-step 512, hanning type window). MEG brainwaves detection and localization is usually manually performed by MEG analysts. In our study, MEG data were recorded from TBI patients, who were all within 1 months of injury.

4.45 Statistical methods

Band power from the MEG spontaneous data was compared between the two groups of TBI patients using non-parametric Man-Whitney U tests (SPSS version 22.0 for Windows) for each condition (eyes close and eyes open) from 15 brain regions (left anterior temporal, left posterior temporal, left frontal, left central, left parietal, midline fronto-polar, midline frontal, midline central, midline parietal, mid occipito-polar, right frontal, right central, right parietal, right anterior temporal, and right posterior temporal) . The significance level was set at $p < 0.05$.

4.5.Results

Twelve TBI patients with GCS scores ranging from 9 to 13 were recruited into our study: one patient each with a GCS score of 9, 10, and 12; three patients with a GCS score of 11; and six patients with a GCS score of 13. Their mean age was 18.4 (with a standard deviation of 4.1). There were three females and nine males, with a mixture of intracranial pathologies detected on neuroanatomical CT imaging. Demographic data is illustrated in Table 1. Resting state MEG data were recorded.

4.51 Neuropsychological test outcomes

The two groups were compared in terms of age, mean GCS score, and neuropsychological test results. The two group, showed statistically significant difference happened in the power band spectral analysis ($p = 0.002$). Neuropsychological tests for memory, attention, and language failed to show statistically significant differences between the two groups. Table 2 illustrates those detailed parameters.

4.52 MEG spectral analysis during two resting state conditions

4.52 (a) Eyes-closed condition

Regarding spontaneous MEG power spectral analysis during the eyes-closed condition, there were no significant differences found in the delta, theta, alpha, and gamma frequency bands between the two groups of TBI patients in any of the 15 brain regions we examined. However, there was lower beta power in the midline and right parietal regions (Table 3), a higher theta/beta ratio in left anterior temporal and left central regions (Table 4), and a higher alpha/beta ratio in the left and right central brain regions (Table 5) in moderate TBI

group compare to mild TBI group.

4.52(b) Eye open condition

During eyes-open condition, there were again no significant differences found in delta, theta, alpha, beta, and gamma frequency bands between the two groups. Although the difference in beta power between the two groups was significantly lower in the eyes-closed condition, this was not true for the eyes-open condition. Similarly, there was no significant difference in alpha/beta ratio between the two groups during the eyes-closed condition. However, similar to the results in the eyes-open condition, during the eyes-closed condition a higher theta/beta ratio was observed in the left and right central brain regions of patients in the moderate TBI group as compared to those in the mild TBI group (Table 6). Table 7 summarises our MEG results.

4.6 Discussion

4.61 TBI

TBI causes damage to the white matter tracts of the brain via diffuse axonal injury or focal brain damage, resulting in contusion and intracranial haemorrhage. These kinds of injury result in neuronal degeneration and disrupted connectivity within and between brain areas, which leads to a loss or reduction of cognitive function (31)

4.62 Functions of the different bands

Spectral analysis subdivides MEG results into several bands—the delta, theta, alpha, beta, and gamma bands. We hypothesized that all bands could be affected by TBI, with consequences for cognitive impairment. Ishihara et al (32) was the first who reported frontal

midline theta rhythm that appears over medial frontal areas in the EEG of normal subjects when performing a broad range of cognitive tasks demanding mental concentration. Mild and moderate TBI in this study, due to midline and temporal polar zones are affected (33) facing distortion of theta/beta signal is detected mainly through a task of voluntary orienting of attention. The result of Theta/beta ratio decrease in mild head injury may signify the recovery of the cerebral function (34) or it can also mean the increase theta/beta ratio in moderate TBI group suffered more obvious attention deficit comparing to the mild TBI group. Egnér and Grunzelier (35) summarized that enhanced beta power may increase activation in a noradrenergic vigilance and alertness network. The parietal and mid-central are linked to visual and cognitive aspects of visuo-motor transformation (36). In our study lower beta power is seen in midline and right parietal region which meant patient lack of attentiveness to proceed and execute a task. Higher alpha/beta ratio in left and right central brain region is seen in our study. This is supported by previous study (37) which showed abnormal induced and evoked alpha activity due to poor working memory capacity.

4.63 Comparison of the eyes closed and eyes open results

The power of the brainwave bands change from childhood through adulthood. Up until the sixth decade of life, low-frequency bands such as delta and theta bands decrease over time, while high-frequency bands (particularly the beta band) increase significantly (38, 39). Our study therefore selected patients in the age group 14–30 to avoid age-related confounding variables. Resting-state MEG recordings are a crucial tool for studying intrinsic brain activity. MEG acts as a complementary tool to fMRI for analyses of cortical communication patterns as well as analysis of the fundamental differences in connectivity between healthy

and diseased populations (40, 41). When a patient is relaxed with closed eyes, their brainwave activity is usually characterized by the posteriorly dominant alpha rhythm. Recent studies have established the existence of α -oscillations, which exert inhibitory effects on irrelevant or interfering processing and can thus improve behavioural performance (42, 43). This supports our result that the eyes-close condition gave more reliable information than eyes-open condition.

4.64 Sensitivity of neuropsychological test versus MEG

Neuropsychological tests, which are used after TBI to assess various aspects of behaviour (e.g., social functioning, cognitive abilities, and psychiatric symptoms), typically show that some significant behavioural impairment will be prolonged (44, 45). However, in our study, neuropsychological assessments were not able to detect significant differences between mild and moderate TBI patients even when MEG recordings showed significant changes in the frequency band activity of the two groups. This can be explained by the fact that MEG is an objective measurement while neuropsychology tests are subjective assessments.

4.7 Conclusions

MEG may aid in the prognostication by analysing the power of patients' brainwave frequency bands. Patients with neurocognitive limitations should be given greater attention and provided with proper rehabilitation. However, the findings of our study need to be replicated with a larger sample in order to make clinical recommendations.

4.8 Limitation and Future Recommendation