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Effect of Repetitive Transcranial Magnetic Stimulation (RTMS) on EEG Changes, Sleep, Physical Activity and Psychological States of Migraine: A Randomised Controlled Trial (Magnet-EM)

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Abstract

Migraine is one of the leading causes of morbidity in the world and the cause of health care visits (Seidel et al 2017). Progression of the disease usually leads to unfavourable outcomes including medication overused and tendency towards psychiatric comorbidities. Moving towards preventive medicine, this study measured the effect of rTMS on migraine as secondary prevention. In this article, per protocol analysis was used. It is a double-blinded randomised, controlled trial Sixty-four migraine subjects were included in the analysis, randomized into placebo group and treatment group. Maximum Intensity of pulse is decided by muscle twitching when single pulse RTMS is delivered. 20 Hz RTMS is delivered on dorsolateral prefrontal cortex (dLPFC) with 80% of maximum intensity in 2000 pulse of 25 seconds interval for twenty minutes each session. EEG, PSQI, GPAQ and DASS-21 questionnaires and headache diary were delivered to the participants pre- and post-RTMS. The study found a statistically significant difference in the proportion of photic driving response pre- and post-rTMS, $p = .005$, $\eta p^2 = .336$) in the rTMS group vs. placebo. Sleep, anxiety, physical activity and stress scores in the rTMS group vs placebo has no significant changes but there was a statistically significant reduction in the depression score ($X^2 = 9.60$, p= 0.022). To conclude, rTMS on dLPFC may offer beneficial effects to reduce depressive symptoms in migraine. Although this is an early finding, the current rTMS study protocol could be used by clinician as an early adjunctive treatment for migraine patient with comorbid depression.

Keywords: Dorsolateral Prefrontal Cortex, Migraine, Repetitive Transcranial Magnetic Stimulation, Sleep Quality, Emotional States

Introduction

The leading age-standardized disability-adjusted life-years (DALYs) in neurological disorders is migraine with 704.7 cases per 100 000 (S Bazargan-Hejazi et al. 2020). Burden of migraine include interictal phase symptoms and presence of comorbidities (Gupta J et al. 2022). Comorbidities might co-exist with migraine include psychiatric disorders (depression, anxiety, schizophrenia, stress), cardiovascular diseases (stroke, hypertension) epilepsy, vertigo and asthma. 'Limbically augmented pain syndrome' is a term used to describe chronicity in recurrent pain leads to recurrent arousal, thus maladaptive brain response which impairs adequate adjustment (Rome HP Jr et al. 2000).

While transcranial magnetic stimulation (TMS) is used to alter the hyperexcitability states of migraine brain. Targetting dorsolateral prefrontal cortex (dLPFC) area of brain for the treatment of affective disorders has been approved by Food and Drug Administration (FDA). However, in migraine, only open-labeled and pilot study are available. The repetitive stimulation was given in this study for the purpose of prophylaxis treatment to sustain headache-free phase in episodic migraine in long-term or completely remove the attacks.
This study aimed to reduce the symptoms of comorbid conditions in migraine patients including low sleep quality, physical inactivity, depression, anxiety and stress. Thus, mental health parameters, sleep quality and physical activity domains are analyzed in this study.

Methods

This study is part of the main clinical trial; MAGNET-EM; a double-blinded randomised, controlled trial which included seventy-six participants randomised into treatment arm and sham. However only sixty-four subjects completed the treatment. Full protocol of the clinical trial was published and registered at clinicaltrial.gov. The study was conducted in compliance with the clinicaltrial.gov protocol and JKEUPM standard operating procedures. This study analyses the secondary health outcomes; on difference of electroencephalography (EEG), sleep, physical activity, sleep as well as mental health. The measures used for each outcome were observed EEG changes, GPAQ, PSQI, DASS-21 questionnaires were given to the participants pre- and post-RTMS respectively.
Subject was required to undergo EEG and answer questionnaires before the procedures and three months after the final treatment day. Subject was instructed to seat on a comfortable position and had to remain immobile until the end of the treatment to maintain the same distance between brain and stimulators. Then, the abductor pollicis brevis muscle was taped with electrodes to search for motor threshold. Stimulation at motor area was delivered to observe muscles movement thus motor threshold is confirmed. Once the motor threshold was determined, 80% from it was calculated and recorded as the power for stimulation. Magstim 200 stimulators through a Bistim module (Magstim Co., Dyfed, UK) was used in this study. RTMS was then delivered as per protocol. Each session of r-TMS consisted of 2000 pulses. The pulses were delivered in 40 trains, each train duration was 5 seconds consisting of 50 pulses at 20 Hz with intertrain interval of 25 seconds.
After three consecutive days, subjects had to come on the consecutive week for another two sessions. Thus, total of five days of treatment had to be completed. The subject was requested to come after three months for another sets of questionnaires and EEG procedure. In this study, DASS-21 was used to measure negative emotions which were depression, anxiety and stress.

Findings and Argument

Wilcoxon Rank test has computed to examine physical activity pre- and post-treatment. Per protocol (PP) analysis was used. Per protocol analysis only include subjects who completed the study protocol. Drop-outs were left out from PP analysis and will not be discussed in this article. Per protocol analysis may has better precision describing the result of treatment in clinical setting. The findings demonstrated in table 1.1 and 1.2 showed that there was no significant different in physical activity score between pre- and post-treatment in rTMS group for per protocol (PP) analysis (Z = -1.177, p=0.239). Wilcoxon Rank test has also computed to examine sleep quality pre- and post-treatment. The findings demonstrated in table 1.1 and 1.2 showed that in per protocol analysis (PP), there was no significant difference in Pittsburgh Sleep Quality (PSQI) score pre-and post-treatment in both placebo and RTMS groups. On the contrary, there was a significant difference in depression score post-RTMS, Z=2.239, *P= 0.025* with median of 8.0 pre-RTMS and reduced to 6.0 post-RTMS for RTMS group while no significant changes in placebo group with P=0.334.

Depression is twice more common in migraine than healthy population (Silberstein et al. 1995). Reducing depressive symptoms may increase quality of life of migraine patients and reduce burden of disease(B. Lee Peterlin et al. 2014). This study showed that rTMS may reduce depression symptoms perceived by migraine patients. This study showed that rTMS may reduce depression symptoms perceived by migraine patients. This study cannot evict the possibility that rTMS targeting prefrontal region may reduce perceived depressive symptoms. However, this study used self-reported questionnaires in which the symptoms were based on participants' own perception.

Table 1
Per Protocol (PP) Analysis for Placebo

Variables Pair	Median Pre	Negative Ranks Post	Mean	Positive Ranks Sum	Mean	Sum	Z	P value
PA Post - PA Pre	597.50	600.00	5.5	16.5	6.19	49.5	-1.468^b	0.142
SQ Post - SQ Pre	6	5	13.97	251.50	15.45	154.50	-1.113^b	0.266
DS Post – DS Pre	6	4	12.38	198.00	14.11	127.00	$-.966^b$	0.334
AS Post – AS Pre	6	6	13.34	127.00	14.95	164.50	$-.595^b$	0.552
SS Post – SS Pre	6	7	14.25	228.00	15.84	396.00	$-.228^b$	0.820

Table 2
Per Protocol (PP) Analysis for RTMS Group

Varia bles Pair	M edian P re	ost	Negative Ranks ean	M um	S ean	Positive Ranks M um	S value	Z value	P
PA Post - PA Pre	1 40	(00		6 4	2 .75	6 4	5 1.177^b	- .239	0
SQ Post - SQ Pre	6	!	3.97	1 51.50	2 5.45	1 54.50	1 1.113^b	- .266	0
DS Post – DS Pre	8	(	4.82	1 81.50	2 2.06	1 6.50	9 2.239^b	- .025*	0
AS Post – AS Pre	8	(	3.16	1 10.50	2 5.23	1 67.50	1 $.530^b$	- .569	0
SS Post – SS Pre	8	(	3.19	1 11.00	2 3.19	1 11.00	2 $.903^b$	- .366	0

*Significant p-value<0.05, PA=physical activity, SQ=sleep Quality, DS=Depression score, AS=Anxiety Score, SS=Stress score, Post=Post-treatment, Pre=Pre-treatment.

Sixty-four subjects took part in the intervention study designed for migraine prophylaxis. An exact McNemar's test determined that there was statistically significant difference in the proportion of the PDR pre and post intervention, p=0.005. Figure 1.0 showed the histogram representing result of PDR analysis. Recent study also reported there is significant difference in PDR for migraine without aura (MWOA) as compared to migraine with aura (MWA) when photic stimulation is delivered interictally at frequency 5, 8, 15 and 20 Hz. The stimulation is stronger in MWOA (Tomohiko Shiina et al. 2019).

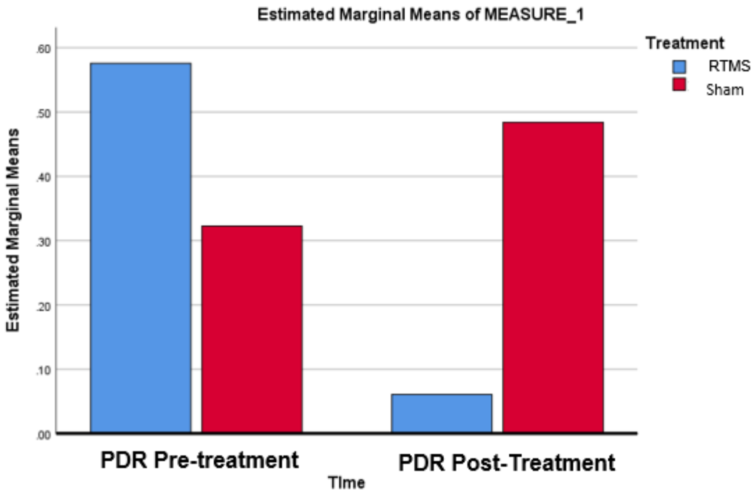

Figure 1. Per protocol (PP) analysis for PDR
*PDR= Photic driving response

Conclusions

In conclusion, the rTMS may have some beneficial effects on improving secondary health outcomes such as the photic driving response and depressive symptoms in patient with episodic migraine. The current study protocol assessed the effectiveness of rTMS on neurophysiological, clinical aspects and emotional states of migraine. However, it did not yield positive outcomes for anxiety, stress and physical activity. The notable finding for EEG application in episodic migraine to measure photic driving response and significant reduction in depressive symptoms may serve as a basis for adjunctive treatment of episodic migraine with comorbid depression while, future research with the help of advanced current knowledge in machine learning and other types of brain imaging for instance functional MRI.

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References

Gupta J., Gaurkar S. S. (2022) Migraine: An Underestimated Neurological Condition Affecting Billions. Cureus. Aug 24;14(8):e28347. doi: 10.7759/cureus.28347. PMID: 36168353; PMCID: PMC9506374.

Rome HP J. R, Rome J. D. Limbically augmented pain syndrome (LAPS): kindling, corticolimbic sensitization, and the convergence of affective and sensory symptoms in chronic pain disorders. Pain Med. 2000 Mar;1(1):7-23. doi: 10.1046/j.1526-4637.2000.99105.x. PMID: 15101960.

Seidel, S., Beisteiner R., Manecke, M. (2017 Feb 9). Psychiatric comorbidities and photophobia in patients with migraine. J Headache Pain. 2017 Dec;18(1):18. doi: 10.1186/s10194-017-0718-1. Epub Erratum in: J Headache Pain. 2017 Dec;18(1):33. PMID: 28185159; PMCID: PMC5307401.

Safiri S., Kolahi, A. A., Noori, M. Nejadghaderi, S. A., Karamzad N., Bragazzi N. L., Sullman M. J. M., Abdollahi, M., Collins, G. S., Kaufman, J. S., Grieger, J. A. (2019). Burden of anemia and its underlying causes in 204 countries and territories, 1990-2019: results from the Global Burden of Disease Study J Hematol Oncol. 2021 Nov 4;14(1):185. doi: 10.1186/s13045-021-01202-2. PMID: 34736513; PMCID: PMC8567696.

Silberstein, S. D., LIPTON, R. B., BRESLAU, N. Migraine: association with personality characteristics and psychopathology. Cephalalgia: An International Journal of Headache, [s. l.], v. 15, n. 5, p. 358–369, 1995.

Shiinaa, T., Takashimaa, R. R. D. (2018) Pascual-Marqui et al Evaluation of Electroencephalogram Using Exact Low- Resolution Electromagnetic Tomography During Photic Driving Response in Patients with Migraine. *Neuropsychobiology* DOI: 10.1159/000489715