

MEG Study of Pico-Tesla Transcranial Magnetic Stimulation on Patients with Depression

Photios Anninos^{1*}, Adam Adamopoulos¹, Athanasia Kotini¹ and Nicolaos Tsagas²

¹Laboratory of Medical Physics, Department of Medicine, School of Health Sciences, Democritus University of Thrace, University Campus, Alexandroupoli, Greece

²Department of Electrical Engineering, Polytechnic School, Democritus University of Thrace, Xanthi, Greece

***Corresponding Author:** Emeritus Professor Photios Anninos, Laboratory of Medical Physics, Department of Medicine, School of Health Sciences, Democritus University of Thrace, University Campus, Alexandroupoli, Greece.

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Abstract

We used a whole-head 122 channel MEG system to patients with depression. Ten patients with depression (3 male, 7 female) ranging from 25 - 40 years of age were participated in the study. Pico-Tesla transcranial magnetic stimulation (pT-TMS) was applied to the patients with magnetic field amplitude (1 - 7.5pT) and frequency (8 - 13Hz). An important effect was observed with an increase of frequencies in the range of 2-7 Hz across the subjects followed by a considerable mood improvement and normalization of the MEG. The greater part of the patients reported assistance from the pT-TMS treatment. This technique of the pT-TMS has the prospective to be a significant non-invasive, safe and important means in the managing of patients with depression.

Keywords: MEG; pT-TMS; Depression

Introduction

Trancranial Magnetic Stimulation (TMS) was used as an extra alternative means for treatments for patients suffering from depression, reflecting the limited therapeutic advances with conventional antidepressants and the appearance of protected and efficient neurostimulation therapies. The use of TMS is for the reason that it is a non-invasive technique to stimulate the human brain. TMS was introduced as a neurophysiological technique, when Barker., *et al.* [1] developed a machine that permitted non-invasive stimulation of the cerebral cortex. Since its introduction, TMS has been used to assess the motor system, to study the function of several cerebral regions, and for the pathophysiology of several neuropsychiatric illnesses. In addition, Anninos and Tsagas [2] suggested that pico Tesla TMS (pT-TMS) with an electronic device might have therapeutic potential by increased the abnormal (2 - 7 Hz) frequencies of the brain activity towards frequencies of less than or equal to those frequencies of the alpha frequency range (8 - 13 Hz) of each patient [3-14]. One possible electrophysiological clarification for the efficacy of pT-TMS has been provided by the proposed "Neural Net Model" [8] which suggests that magnetic stimulation causes a temporally modulated neuronal inhibition in areas exhibiting abnormal activity in the frequency range of 2 - 7 Hz. This suggestion is in concordance with data presented by other researchers [15-17].

The aim of this study is to identify any change in the MEG brain activity in agreement with our predictions that the pT-TMS should enhance the 2 - 7 Hz band frequencies towards frequencies \leq 8 - 13 Hz for every depression patient.

Methods

MEG measurements were performed using a whole-head 122-channel MEG system (Neuromag-122, Neuromag Ltd. Helsinki, Finland) in an electromagnetically shielding room. The sampling frequency rate was 256Hz and the associated Nyquist frequency 128 Hz. The MEG signal was filtered with cut-off frequencies at 0.3 and 40 Hz. The participants were 3 male and 7 female volunteers in 25 - 40 years of age. Informed consent for the methodology and aim of the study was obtained from all of them prior to the process. The research was

approved by the Research Committee of the Democritus University of Thrace (code number 80347). All patients were referred to our Laboratory of Medical Physics in Alexandroupoli, Greece, by practicing neurologists. They were off medication for 24 hours during their participation in the study. In our research, we haven't included healthy subjects as controls because this study was formerly done and published by Troebinger, *et al.* [14] in which we have used a double-blind experimental design with our pico-Tesla TMS electronic device [2] in order to look for an effect of pT-TMS in healthy subjects.

All MEG data tracings were visually inspected carefully off-line for movement artifacts and periods contaminated with movement artifacts were cut off. The time taken for each recording was 2 min in order to make sure alertness for each subject.

The pT-TMS electronic device

The pT-TMS electronic device is a modified helmet containing up to 122 coils which are arranged in five array groups, so as to cover the main 7 brain regions (frontal, vertex, right and left temporal, right and left parietal, and occipital regions) of the subject. It is designed to create pT-TMS range modulations of magnetic flux in the alpha frequency range (8 – 13 Hz) of each patient. The pT-TMS device was configured for each individual to generate a square wave (so as to resemble the firing activity of neurons in the brain). Anninos, *et al.* [7] modulated magnetic field at the individual's mean peak alpha frequency - generated in the subject's occipital lobe. A schematic of the alpha wave generated by the electronic device can be seen in Anninos, *et al* [12].

Spectral estimates

A software program was developed in our laboratory in order to detect the amplitude of the primary dominant frequency of the power spectra of the MEG recordings obtained from every depression patient and channel after the application of Fast Fourier Transform (FFT) (Figure 1). Then it was interesting to look (alpha for calibration of the electronic device) and (2 – 7 Hz, 8 – 13 Hz and 14 – 24 Hz for the analysis) and as it was stated above at the principal dominant frequency of the power spectra of the MEG recordings obtained from each patient and channel after the application of the FFT. In Figure 1 the actual signal length for analysis is 2 min and the FFT was applied only to 9 secs, and in order to explain the primary dominant frequency it was necessary to use the Matlab program to magnify the spectrum. Thus, in the spectrum is not seen the whole frequency range which is 0 - 7 Hz, but only see the range 0 - 5 Hz due to the magnification.

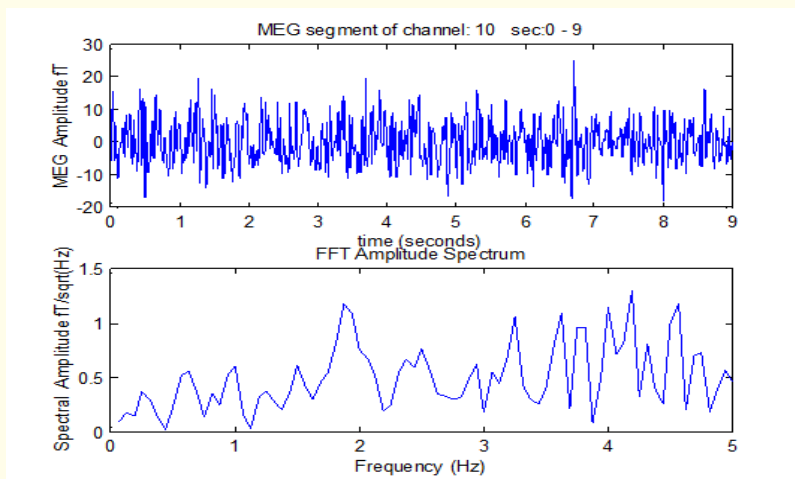


Figure 1: A) An MEG record of 9 sec obtained from a patient B) the application of FFT on the MEG record in which we can see that the first primary dominant frequency is 2.5 Hz.

Results

Table 1 shows the brain regions and the corresponding channels in each brain region. Table 2 shows the symptoms in each of the patients evaluated by clinicians one month after daily pT-TMS treatment at home.

Brain Regions	Channels
Right Temporal	1-14 ,111-120
Left Temporal	43-50,55-62,67-74
Right Parietal	5-6,11-16,97-100,109,110 ,115-122
Left Parietal	47-52,59-64,71-74,79,80,87-90
Frontal	17-42
Occipital	75-86,91-96, 101-110
Vertex	13-16,49-54,61-66,73,74,89,90,99,100, 117-122

Table 1: This table shows the brain regions and the corresponding channels in each brain region.

Patient	Sex	Symptoms before pT-TMS	Symptoms after pT-TMS
1	F	1.Depressed mood, Score 3 2.Feelings of Guilt, Score 3 3.Suicide, Score 1 4.Insomnia early, Score 1 5.Insomnia middle, Score 1 6.Insomnia Late, Score 2 7.Work and Activities, Score 2 8.Retardation, Score 1 9. Agitation, Score 2 10.Anxiety(psychological), Score 2 11. Anxiety(somatic), Score 1 12.Somatic symptoms (gastrointestinal), Score 1 13.Somatic symptoms general, Score 1 14. Genital symptoms, Score 1 15.Hypochondriasis, Score 3 16.Loss of Weight, Score 1 17. Insight, Score 1	1.Absent, Score 0 2.Absent, Score 0 3.Absent, Score 0 4. Insomnia early, Score 0 5.Insomnia middle, Score 0 6.Insomnia Late, Score 0 7.Work and Activities, Score 0 8.Retardation, Score 0 9.Agitation, Score 1 10.Anxiety (psychological), Score 0 11. Anxiety (somatic), Score 1 12. Somatic symptoms (gastrointestinal), Score 0 13.Somatic symptoms general, Score 0 14. Genital symptoms, Score 1 15.Hypochondriasis, Score 0 16.Loss of Weight, Score 0 17. Insight, Score 0
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3	F	<ol style="list-style-type: none"> 1. Depressed mood, Score 1 2. Feelings of Guilt, Score 1 3. Suicide, Score 0 4. Insomnia early, Score 1 5. Insomnia middle, Score 1 6. Insomnia Late, Score 1 7. Work and Activities, Score 1 8. Retardation, Score 1 9. Agitation, Score 2 10. Anxiety (psychological), Score 1 11. Anxiety (somatic), Score 1 12. Somatic symptoms (gastrointestinal), Score 1 13. Somatic symptoms general, Score 1 14. Genital symptoms, Score 1 15. Hypochondriasis, Score 2 16. Loss of Weight, Score 1 17. Insight, Score 1 	<ol style="list-style-type: none"> 1. Absent, Score 0 2. Absent, Score 0 3. Absent, Score 0 4. Insomnia early, Score 0 5. Insomnia middle, Score 0 6. Insomnia Late, Score 0 7. Work and Activities, Score 0 8. Retardation, Score 1 9. Agitation, Score 0 10. Anxiety (psychological), Score 1 11. Anxiety (somatic), Score 1 12. Somatic symptoms (gastrointestinal), Score 0 13. Somatic symptoms general, Score 0 14. Genital symptoms, Score 0 15. Hypochondriasis, Score 0 16. Loss of Weight, Score 0 17. Insight, Score 0
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8	M	<ol style="list-style-type: none"> 1. Depressed mood, Score 1 2. Feelings of Guilt, Score 1 3. Suicide, Score 1 4. Insomnia early, Score 1 5. Insomnia middle, Score 1 6. Insomnia Late, Score 2 7. Work and Activities, Score 1 8. Retardation, Score 1 9. Agitation, Score 3 10. Anxiety (psychological), Score 2 11. Anxiety (somatic), Score 1 12. Somatic symptoms (gastrointestinal), Score 1 13. Somatic symptoms general, Score 1 14. Genital symptoms, Score 1 15. Hypochondriasis, Score 2 16. Loss of Weight, Score 1 17. Insight, Score 1 	<ol style="list-style-type: none"> 1. Depressed mood, Score 0 2. Feelings of Guilt, Score 0 3. Suicide, Score 0 4. Insomnia early, Score 0 5. Insomnia middle, Score 0 6. Insomnia Late, Score 0 7. Work and Activities, Score 0 8. Retardation, Score 0 9. Agitation, Score 0 10. Anxiety (psychological), Score 0 11. Anxiety (somatic), Score 1 12. Somatic symptoms (gastrointestinal), Score 0 13. Somatic symptoms general, Score 0 14. Genital symptoms, Score 1 15. Hypochondriasis, Score 0 16. Loss of Weight, Score 0 17. Insight, Score 0

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Table 2: This table shows the symptoms for the Hamilton Rating Scale for the 10 depression patients before and after pT-TMS as were evaluated by interview by clinicians one month after daily pT-TMS treatment at home (F: female; M: male).

The time frame of our clinical investigations were as follows:

1st day: MEG measurements in our lab.

2nd day: Application of real pT-TMS and MEG recordings afterwards. The patients' MEG spectrum was almost like normal in the greater part of them with nonexistence most of the abnormal frequencies.

3rd day: Interview by clinicians after pT-TMS. They confirmed our findings of our MEG recordings.

10th day: MEG recordings and evaluation by clinicians.

Discussion

We have attempted to influence the depression patients with the pT-TMS electronic device [2]. The coils of the device were constructed to emit back to the brain magnetic fields of appropriate intensities and frequencies to those emitted prior to the application of pT-TMS. This resulted to decrease of the maximal magnetic power emitted from these areas and an attenuation of the depression disorder activity.

It is known that magnetic fields modify the activity of the pineal gland, which has been shown to control dopaminergic, and endogenous opioid functions [18]. On a cellular level, the consequences of magnetic fields on depression activity may be related to alterations in properties and stability of biological membranes and their transport characteristics including their intra- and extra cellular distributions and flux of calcium ions [17]. Chervyakov, *et al.* [19] in a review article analyzed the potential mechanisms underlying the therapeutic effects of TMS. They concluded that the total therapeutic effects of repetitive TMS may be determined by their total impact on a number of processes in the brain, including long-term potentiation, long-term depression, changes in cerebral blood flow, the activity of certain enzymes, interactions between cortical and subcortical structures, and gene expression.

In this study was set out to reproduce the effects of the increased abnormal dominant frequencies of 2 - 7 Hz band due to the effect of the pT-TMS in patients with depression. The following day's examination (2nd, 3rd day) with the MEG showed that their spectrum was almost like normal with absent most of the high abnormal frequencies in the 2 - 7 Hz frequency band. All depression patients were evaluated clinically and with the MEG a week after the first application of the pT-TMS in our lab (10th day). Most of the patients reported a progressive worsening to their pretreatment status. To conclude if the responses elicited in our lab were reproducible, it was advised the patients to apply the pT-TMS treatment every night (23.00 pm) at home. After one month, nightly application of pT-TMS at home, all depression patients were assessed again and the majority of them reported to have benefit from this treatment (Table 2).

This method of the pT-TMS has potential effects to be a significant non-invasive secure and effectual modality in the managing of depression patients. Nevertheless, further research with more patients are required in order to evaluate its potential important contribution for managing the symptoms of depression patients.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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