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Pico-Tesla TMS Therapy on Multiple Sclerosis

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Abstract

Background: Magnetoencephalography (MEG) is a well-established noninvasive method for investigating human brain activity.
Objectives: The present study aimed at identifying any change in the brain state after pico- Tesla Transcranial Magnetic Stimulation (pT-TMS) on patients with multiple sclerosis (MS).
Methods: A whole-head 122 - channel MEG system in a magnetically shielded room with low magnetic noise was used. The study population comprised of 2 male and 8 female volunteers with MS, with a mean age of 41.3 $\pm$ 9.5 years. External magnetic field of pT-TMS was applied on the above patients with proper field characteristics (magnetic field amplitude: 1 - 7.5 pT, frequency: the alpha rhythm of the patient 8 - 13 Hz), obtained prior to the application of pT-TMS.
Results: A significant effect was observed with an increase of frequencies in the range of 2 - 7 Hz among the participants. The results were statistically significant in 7 out of 10 patients (70%).
Conclusions: The pT-TMS has the prospective to be a significant noninvasive secure and effective means in managing MS symptoms.

Keywords: MEG, Multiple Slerosis, pT-TMS, Brain Frequencies

1. Background

We tried to manage the symptoms of MS patients applying pico-Tesla transcranial magnetic stimulation (pT-TMS). After pT-TMS, an increase in the frequencies of the participants' brain activity in the range of 2 - 7 Hz was noted. Most of the MS patients reported a benefit from the pT-TMS treatment.

Transcranial magnetic stimulation (TMS) is a noninvasive and well-tolerated method without any direct contact with the underlying skin and has been used to investigate a variety of clinical conditions (1). TMS have been applied in the study of a variety of neurological diseases including MS (2). Magnetoencephalography (MEG) is a well-established noninvasive method for investigating human brain activity with whole head neurophysiological measurements. MEG measures weak magnetic fields generated at the scalp surface by the underlying electrical activity in the brain and it is very important for diagnostic purposes.

Anninos and Tsagas (3), using a pico- Tesla (pT) TMS electronic device, 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 participant (4-16). The pT-TMS electronic device is a modified helmet containing up to 122 coils arranged in 5 array groups to cover the main 5 brain regions (frontal, vertex, right and left temporal, and occipital regions). 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 to resemble the firing activity of neurons in the brain.

The present study aimed at identifying any change in the brain state after pT-TMS application on MS patients.

2. Methods

Biomagnetic measurements were performed using a whole-head 122-channel SQUID gradiometer device (Neuromag-122, Neuromag Ltd. Helsinki, Finland) in an electromagnetically shielding room. The spontaneous MEG recordings were taken with a sampling frequency rate of 256 Hz, with associated Nyquist frequency of 128 Hz. The MEG signal was filtered with cutoff frequencies at 0.3 and 40 Hz. The participants were 10 volunteers (2 males and 8 females) with the mean age of 41.3 $\pm$ 9.5 years. Informed consent was obtained from all participants. The research committee of the Democritus University of Thrace approved the research (code: 80347). All patients were referred to our Lab by practicing neurologists. They were asked not to take their medication for 24 hours during their participation in the study. In this study, we did not include healthy participants as controls because this research was published by Troebinger et al. (17), with our pico-Tesla electronic device (3) to determine an effect of pT-TMS in healthy participants. The time taken for

each recording was 2 minutes to ensure alertness for each participant. A software program was developed in our laboratory to detect the amplitude of the primary dominant frequency of the power spectra of the MEG recordings obtained from each migraine patient and channel after the application of Fast Fourier Transform (FFT).

3. Results

Table 1 displays the brain regions and the corresponding channels in each brain region. Table 2 demonstrates the symptoms in each of the 10 MS patients before and after the application of the pT-TMS as evaluated by clinicians through interviews. Table 3 shows the maximum effect before pT-TMS (1st day in our lab) and after pT-TMS (2nd day in our lab) for each of the 10 MS patients. P is for the patient number, RT for the right temporal brain region, LT for the left temporal brain region, RP for the right parietal region, LP for the left parietal region, F for the frontal region, V for the vertex region, and O for the occipital brain region. Table 4 demonstrates the statistical analysis of the results using t test, being statistically significant in 7 out of 10 patients (70%). Figure 1A displays the 122-channel MEG system, Figure 1B exhibits the pT-TMS electronic device, whereas Figure 1C shows a MEG record obtained from Patient 1 from whom the primary dominant frequency was 3.2 Hz.

Table 1. This Shows Shows the Brain Regions and the Corresponding Channels in Each Brain Region

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

4. Discussion

In the present study, we did not include healthy controls because this was investigated by Troebinger et al. (17), who used an experimental design with our pT-TMS electronic device (3).

The time frame of our clinical investigations was as follows:

1st day: MEG measurements in our lab. Interview by clinicians (Table 2).

2nd day: Application of pT-TMS. MEG measurements in our lab. Interview by clinicians (Table 2).

10th day: MEG recordings and evaluation by the same clinicians. Most of the the patients reported a progressive deterioration of their pretreatment status.

The examination with the MEG in the 2nd day in our lab and after pT-TMS shows that most of the highly abnormal frequencies in the 2-7Hz frequency band were absent. All the MS patients were evaluated clinically and once again in the 10th day with the MEG. Most of the patients reported that they progressively deteriorated to their pretreatment status. To ascertain if the responses elicited in our lab were reproducible, the patients were advised to apply the pT-TMS treatment nightly at home at 11 PM with the electronic device mentioned before. Then, all the MS patients were evaluated again after a month and they all reported to have benefited from this treatment.

The mechanisms by which the application of the pT-TMS attenuated the MS syndrome are unknown. However, one possible explanation is that these magnetic fields have been shown to influence the activity of the pineal gland (PG), which regulates the endogenous opioid functions (18) and the dopaminergic modulator (19), GABA (20, 21).

In conclusion, this method of pT-TMS has some prospective to be an important noninvasive, secure and efficacious modality in managing MS. However, additional investigations are necessary with more participants to evaluate its possible beneficial contribution to manage MS symptoms.

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Footnotes

Conflict of Interest: The authors have declared that no conflicts of interest exist.

Table 3. It Is Shown the Maximum Effect Before (BS) and After Real (AS) Stimulations for Each of the 10 Multiple Sclerosis Patients

P	RT BS	RT AS	LT BS	LT AS	RP BS	RP AS	LP BS	LP AS	F BS	F AS	V BS	V AS	O BS	O AS
1	2.75	5.63	1.75	5.63	2.50	4.88	2.63	5.75	1.13	5.50	2.63	3.38	0.63	5.75
2	0.94	0.59	2.00	0.97	2.09	0.88	2.0	1.5	4.03	3.75	1.63	3.00	-0.03	0.47
3	2.41	2.72	2.34	3.72	4.81	5.25	1.88	4.53	3.63	4.97	5.47	5.25	2.88	3.53
4	2.84	5.34	4.56	5.60	3.13	4.78	4.91	3.75	4.21	3.03	5.1	3.38	2.47	3.53
5	3.81	4.34	3.78	5.41	3.81	4.34	2.16	5.41	3.94	2.1	2.1	3.94	3.25	5.31
6	5.1	5.13	5.13	3.25	4.75	5.00	5.13	3.25	3.56	3.44	5.13	2.81	5.56	3.00
7	4.84	5.31	3.47	4.91	4.84	5.31	3.94	5.63	2.63	5.13	4.84	5.31	3.28	4.88
8	2.69	3.63	3.1	3.56	2.1	4.13	3.31	4.50	4.75	2.75	3.31	3.63	4.75	5.19
9	1.94	4.81	0.56	4.00	4.56	4.81	4.19	4.00	2.88	2.88	4.56	4.81	5.31	4.88
10	3.91	5.19	1.69	4.66	2.34	5.19	2.88	4.81	3.53	4.21	1.69	5.19	4.81	5.22

Abbreviations: F, frontal region; LP, left parietal region; LT, left temporal brain region; O, occipital brain region; P, patient number; RP, right parietal region; RT, right temporal brain region; V, vertex region.

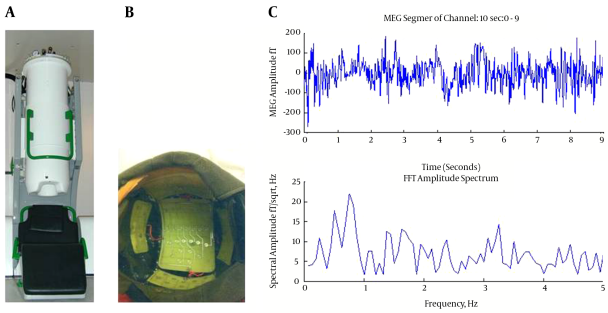

Figure 1. A, The 122-Channel MEG System; B, the pT-TMS Electronic Device; C, a MEG Record of 9 seconds Obtained from Patient 1 from Which in B, after FFT Analysis the Primary Dominant Frequency is 3.2 Hz

Table 4. Statistical Analysis of the Results (T-Test)[a,b]

Patient	BS	AS	P Value
1	2.003 ± 0.85	5.22 ± 0.86	0.0001
2	1.81 ± 1.24	1.98 ± 1.28	0.75
3	3.33 ± 1.36	4.3 ± 1.00	0.05
4	4.17 ± 0.99	4.20 ± 1.02	0.58
5	3.26 ± 0.8	4.41 ± 1.2	0.05
6	3.7 ± 0.95	4.87 ± 0.65	0.019
7	3.98 ± 0.9	5.21 ± 0.26	0.0043
8	3.43 ± 0.9	3.92 ± 0.8	0.33
9	3.38 ± 1.7	4.4 ± 0.75	0.05
10	2.96 ± 1.17	4.93 ± 0.39	0.001

[a] Values are expressed as mean ± SD.
[b] The results were statistical significant in 7 out of 10 patients (70%).

Authors' Contribution: Study concept and design: Photios Anninos; acquisition of data: Photios Anninos; analysis and interpretation of data: Athanasia Kotini, Adam Adamopoulos; drafting of the manuscript: Photios Anninos; critical revision of the manuscript for important intellectual content: Nicolaos Tsagas; statistical analysis: Athanasia Kotini; administrative, technical, and material support: Adam Adamopoulos; study supervision: Photios Anninos.

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Table 2. The Symptoms of the 10 MS Patients Evaluated by Interview by Clinicians According to Expanded Disability Status Scale (EDSS), Before pT-TMS (1st Day in Our Lab) and After pT-TMS (2nd Day in Our Lab)

Patients	Sex	Symptoms Before pT-TMS	Symptoms After pT-TMS
1	F	Pyramidal Functions: 1. Abnormal signs without disability.	Pyramidal functions: 0. normal
		Cerebellar Functions: 3. Limb ataxia	Cerebellar functions: 0. normal
		Brain Stem Functions: 5. Inability to shallow or to speak	Brain stem functions: 0. normal
		Sensory Functions: 3. Moderate decrease in touch	Sensory functions: 0. normal
		Bowel and Bladder Functions:1. Mild urinary hesitancy	Bowel and bladder functions: 0. normal
		Visual Functions: 3.moderate decrease in fields	Visual functions: 0.normal
		Cerebral Functions: Mild decrease in mentation	Cerebral functions: 0.normal
2	F	Pyramidal Functions: 1. Abnormal signs without disability.	Cerebellar functions: 3. moderated
		Cerebellar Functions: 1. Abnormal signs without disability	Brain stem functions: 5. inability to speak
		Brain Stem Functions: 5. Inability to speak	Sensory functions: 3. moderate decrease of pain
		Sensory Functions: 3. Moderate decrease in pain	Bowel and bladder functions: 1. mild urinary hesitancy
		Bowel and Bladder Functions: 1. Mild urinary hesitancy	Visual functions: 0. Normal
		Visual Functions: 0. Normal	Cerebral functions: 1. mood alteration only
		Cerebral Functions: 1. Mood alteration only	Pyramidal functions: 1. abnormal
3	M	Pyramidal Functions: 2. Minimal disability	Pyramidal functions: 0. normal
		Cerebellar Functions: 2. Mild ataxia	Cerebellar Functions: 0. Normal
		Brain stem functions: 5. inability to speak	Brain stem functions: 0. normal
		Sensory Functions: 3.Moderate decrease in position	Sensory functions: 0. normal
		Bowel and bladder functions: 1. mild urinary hesitancy	Bowel and bladder functions: 0. normal
		Visual Functions: 0. Normal	Visual functions: 0. normal
		Cerebral Functions: 2. Mild decrease in mentation	Cerebral functions: 0. normal
4	F	Pyramidal Functions: 2. Minimal disability.	Pyramidal functions: 2. minimal disability
		Cerebellar functions: 2. mild ataxia	Cerebellar functions: 2. mild ataxia
		Brain Stem Functions: 5. Inability to swallow	Brain stem functions: 5. inability to shallow
		Sensory Functions: 3. Moderate decrease in pain	Sensory functions: 0. normal
		Bowel and bladder functions: 1. mild urinary hesitancy	Bowel and bladder functions: 0. normal
		Visual functions: 0. normal	Visual functions: 0. normal

		Cerebral Functions: 1. mood alteration only	Cerebral functions: 0. normal
5	F	Pyramidal functions: 2. minimal disability.	Pyramidal functions: 0. normal
		Cerebellar Functions: 2. Mild ataxia	Cerebellar functions: 0. normal
		Brain stem functions: 5. inability to swallow	Brain stem functions: 0. normal
		Sensory functions: 3. moderate decrease in touch	Sensory functions: 0. normal
		Bowel and bladder functions: mild urinary hesitancy	Bowel and bladder functions: 0. normal
		Visual functions: 0. normal	Visual functions: 0. normal
		Cerebral functions: 1. mood alteration only	Cerebral functions: 0. normal
6	F	Pyramidal functions: 1. abnormal signs without disability.	Pyramidal functions: 0. normal
		Cerebellar functions: 1. abnormal signs without disability	Cerebellar functions: 0. normal
		Brain stem functions: 5. inability to swallow	Brain stem functions: 0. normal
		Sensory Functions: 3. Moderate decrease in position	Sensory functions: 0. normal
		Bowel and bladder functions: mild urinary retention	Bowel and bladder functions: 0. normal
		Visual functions: 0. normal	Visual functions: 0. normal
		Cerebral functions: 2. mild decrease in mentation	Cerebral functions: 0. normal
7	F	Pyramidal functions: 2. minimal disability.	Pyramidal functions: 0.normal
		Cerebellar functions 2. mild ataxia	Cerebellar functions: 0. normal
		Brain Stem Functions: 5. Inability to speak	Brain stem functions: 0. normal
		Sensory functions: 3. moderate decrease in position	Sensory functions: 0. normal
		Bowel and bladder functions: 2. mild urinary retention	Bowel and bladder functions: 0. normal
		Visual functions: 0. normal	Visual functions: 0. normal
		Cerebral functions: 2. mild decrease in mentation	Cerebral functions: 0. normal
8	M	Pyramidal functions: 3. mild paraparesis	Pyramidal functions: 3. mild paraparesis
		Cerebellar functions: 1. abnormal signs without disability	Cerebellar functions: 1. abnormal signs
		Brain stem functions: 5. inability to speak	Brain stem functions: 5. inability to speak
		Sensory Functions: 3. Moderate decrease in position	Sensory functions: 0. normal
		Bowel and bladder functions: 3. mild urinary hesitancy	hesitancy bowel and bladder functions: 3. mild urinary
		Visual functions: 0. normal	Visual functions: 0. normal
		Cerebral functions: 1. mood alteration only	Cerebral functions: 1. mood alteration only

9	F	Pyramidal functions: 1. abnormal signs without disability.	Pyramidal functions: 0. normal
		Cerebellar functions: 1. abnormal signs without disability	Cerebellar functions: 0. normal
		Brain stem functions: 5. inability to speak	Brain stem functions: 0. normal
		Sensory Functions: 3.Moderate decrease in touch	Sensory functions: 0. normal
		Bowel and Bladder Functions: 8. Mild urinary urgency	Bowel and bladder functions: 0. normal
		Visual Functions: 0. Normal	Visual functions: 0. normal
		Cerebral functions: 1. mood alteration only	Cerebral functions: 0. normal
10	F	Pyramidal functions: 2. minimal disability.	Pyramidal functions: 0. normal
		Cerebellar Functions: 2. Mild ataxia	Cerebellar functions: 0. normal
		Brain stem functions: 2. moderate nystagmus	Brain stem functions: 0. normal
		Sensory functions: 1. figure writing decrease only	Sensory functions: 0. normal
		Bowel and bladder functions: 9. mild urinary urgency	Bowel and bladder functions: 0. normal
		Visual functions: 0. normal	Visual functions: 0. normal
		Cerebral functions: 1. mood alteration only	Cerebral functions: 0. normal

Abbreviations: F, female; M, male.