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Research Article

MEG and Pico-Tesla TMS in Patients with Instability

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Abstract

We used a whole-head 122 - channel MEG system in a magnetically shielded room of low magnetic noise for our magnetoencephalographic (MEG) recordings. Ten instability patients were included in the study, 9 male and one female between 15 - 27 years of age (mean = 19.1 ± 4.4). External pico Tesla transcranial magnetic stimulation (pT-TMS) was applied on the above patients with magnetic field amplitude: 1 - 7.5 pT, frequency: the alpha-rhythm of the patient 8 - 13Hz.

There was an increase in the 2 - 7Hz frequencies range toward the patients' alpha rhythm which was statistically significant at 6 out of 10 patients (60%). The pT-TMS has the potential to be an essential non-invasive secure and effective modality in managing of idiopathic instability patients.

Keywords: *MEG; Instability; pT-TMS; Brain Frequencies*

Introduction

Magnetoencephalography (MEG) is a promising mode to assess the brain processes. MEG is a non-invasive method and records the neuromagnetic field outside the head. It provides better source localization than EEG [1-3]. Transcranial Magnetic Stimulation (TMS) is a non-invasive technique to stimulate the human brain. TMS was introduced as a neurophysiological technique, when Barker., *et al*. [4] 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 the pathophysiology of several neuropsychiatric illnesses.

Anninos and Tsagas [5] invented an electronic device that increased the abnormal (2 - 7Hz) frequencies of the brain activity towards frequencies of less than or equal to those frequencies of the alpha frequency range (8 - 13Hz) of each individual subject [6-17]. One possible electrophysiological explanation for the efficacy of pico-Tesla (pT) - TMS has been provided by a "Neural Net Model" [12] which suggests that magnetic stimulation causes a temporally modulated neuronal inhibition in regions exhibiting abnormal activity in the frequency range of 2 - 7Hz [6-17].

The scope of this study is to identify any change in the abnormal (2 - 7Hz) frequencies in the brain with instability patients with the use of the pT helmet electronic device.

Patients and Methods

Biomagnetic measurements were performed using a whole-head 122-channel MEG gradiometer device (Neuromag-122, Neuromag Ltd. Helsinki, Finland). Recordings were taken in an electromagnetically shielding room in order to avoid extraneous electromagnetic noise. The spontaneous MEG recordings were taken with a sampling frequency rate of 256Hz and the associated Nyquist frequency was

128Hz, which was well above the constituent frequency components of interest in our MEG recordings, avoiding artifacts. The MEG signal was filtered with cut-off frequencies at 0.3 and 40Hz. The subjects were 9 male and 1 female volunteers between 15 - 27 years of age (mean = 19.1 ± 4.4). Informed consent was obtained from all individual participants included in the study. 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 study we didn't include healthy subjects as controls because this research has been published by Troebinger., *et al.* [18], in which we have used a double-blind experimental design with our pico Tesla electronic device [5] in order to look for an effect of pT-TMS in healthy subjects.

The time taken for each recording was 2 minutes in order to ensure alertness for each subject. Each patient was scanned in two separate sessions.

The first session (session 1) consisted of a 2-minutes resting of pre-stimulus baseline state MEG scan. These data were subsequently used to establish the subject's alpha frequency in the range of (8 - 13Hz), for calibration of the pT-TMS electronic device. The second session (session 2), had the following protocol:

At all times the pT-TMS electronic device which was connected to the helmet was set to real stimulation and 2 minutes of real pT-TMS stimulation were administered with the subject sitting comfortably just outside the scanner room. Following these 2 minutes of stimulation, a further 2 minutes of resting state MEG data were acquired.

The pT-TMS electronic device (Figure 1A, 1B)

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 - 13Hz) 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).

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 each instability patient and channel after the application of Fast Fourier Transform (FFT). Figure 1C is an example for the primary dominant frequency in the 2 - 7Hz band from a MEG record of 9 seconds obtained from an instability patient. After power Fourier Statistical analysis we get that the primary dominant frequency is 2.3Hz.

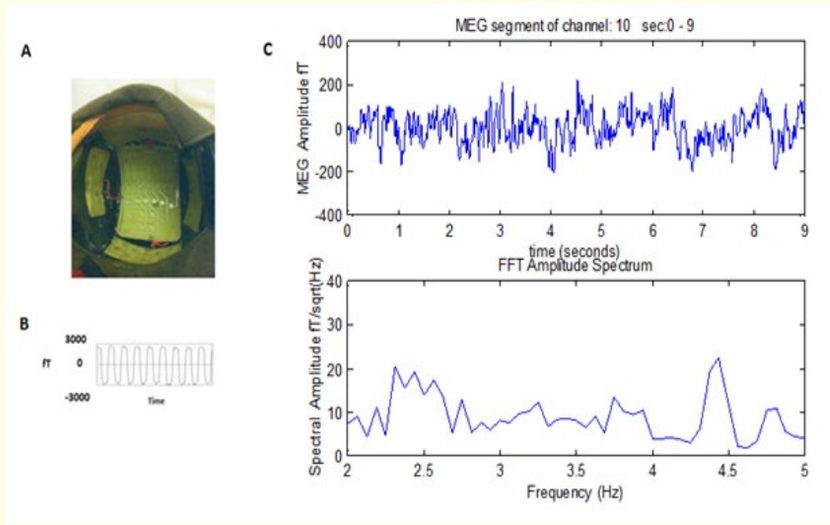

Figure 1: *A) The pico-Tesla electronic device. B) The output of the device. C) This is an example for the primary dominant frequency in the 2-7Hz band from a MEG record of 9secs obtained from an instability patient and after power Fourier Statistical analysis we get that the primary dominant frequency is 2.3Hz.*

Results

Table 1 shows the brain regions and the corresponding channels in each brain region. Table 2 shows the symptoms in each of the 10 instability patients before and after the application of the pT-TMS. Table 3 represents the maximum frequency between the first MEG recordings and the MEG recordings after the real stimulation for each of the 7 brain regions for the 10 instability patients. Table 4 represents the statistical analysis for the 10 patients of table 3. The results were statistically significant at the level of 0.05. We observed from our results that 6 out of 10 patients were statistically significant (60%).

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.*

Patients	Age	Sex	Symptoms before pT-TMS	Symptoms after pT-TMS
1	16	M	Ankle	Normal
2	18	M	Shoulder	Normal
3	15	M	Big toe	No
4	18	M	Knee and Ankle	Normal
5	24	F	Neck and shoulder	Normal
6	16	M	Spine	No
7	27	M	Big toe	Normal
8	16	M	Ankle	No
9	25	M	Knee and Ankle	No
10	16	M	Shoulder	Normal

Table 2: *The symptoms of 10 instability patients before and after pT-TMS as were evaluated by interview by clinicians (F: Female; M: Male)*

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	4.00	5.44	1.72	5.56	4.00	5.16	1.72	5.56	1.94	5.60	1.72	5.56	4.47	5.34
2	2.38	5.06	2.31	4.69	4.44	5.06	2.00	4.69	1.94	1.81	2.38	4.69	4.44	3.50
3	1.19	3.94	3.44	3.94	3.19	3.88	3.06	4.94	4.44	2.69	3.44	4.94	4.13	3.94
4	4.00	5.91	1.19	4.84	3.13	5.53	3.16	4.91	3.06	5.72	4.50	5.06	2.63	5.88
5	3.94	0.97	2.59	1.03	3.94	0.81	0.84	1.03	1.38	2.59	3.94	0.97	2.69	0.97
6	2.84	4.28	1.06	1.34	2.84	4.28	1.22	2.53	1.91	1.38	1.22	2.59	3.81	4.72
7	0.31	5.34	4.00	5.31	2.81	4.50	3.72	3.22	1.00	3.88	3.72	4.50	1.84	5.34
8	1.90	5.00	3.06	1.19	4.01	4.44	2.60	4.53	2.03	2.63	2.6	4.50	4.09	2.60
9	3.2	2.6	3.2	3.4	4	5.1	4.2	5	4.4	5.41	4.2	5	4.2	5
10	0.88	4.81	0.91	1.91	0.81	5.38	0.84	5.50	0.50	3.10	0.81	5.50	5.40	5.34

Table 3: *This table is shown the maximum frequencies (Hz) between the first MEG recording (Run1) and the MEG recording after the real stimulation (Run2) for each of the 10 instability patients. In this Table the first column P is the patient number, in the other columns the RT is for the right temporal brain region, the LT is for left temporal brain region, the RP is for the right parietal brain region, the LP is for the left parietal brain, the F is for the frontal brain region, the V is for the vertex brain region and the O is for the occipital brain region.*

Patients	BS (Mean ± SD)	AS (Mean ± SD)	t-test (P values)
1	5.46 ± 0.16	2.79 ± 1.28	**0.0001**
2	4.22 ± 1.18	2.84 ± 1.11	**0.0442**
3	4.04 ± 0.76	3.27 ± 1.04	0.1394
4	5.41 ± 0.47	3.09 ± 1.05	**0.0002**
5	1.19 ± 0.62	2.76 ± 1.28	**0.0131**
6	3.027 ± 1.42	2.13 ± 1.06	0.2031
7	4.59 ± 0.82	2.49 ± 1.46	**0.0061**
8	3.56 ± 1.42	2.91 ± 0.89	0.3274
9	4.69 ± 1.03	3.92 ± 0.50	0.1097
10	4.51 ± 1.43	1.45 ± 1.75	**0.0038**

Table 4: *Statistical analysis for the 10 instability patients in table 3. The results are statistical significant at the level of 0.05 (marked bold).*

Discussion

In this study we set out to replicate the effects of the increased abnormal dominant frequencies of 2 - 7 Hz band due to the effect of the pT stimulation (6-17) in a group of 10 instability patients. We tried to do our MEG measurements so as to have the highest possible precision as stated before.

In this study we haven't included healthy control subjects because as we have stated before, Troebinger., *et al.* [18] used a double-blind experimental design to look for an effect of our pT-TMS electronic device [5] in healthy subjects using MEG to measure resting state brain activity. After unblinding, we found no significant effect of an increase in the frequency range (2 - 7Hz) across the subject group. This was due to the fact that from the 14 healthy subjects that were involved in the above study only 8 were characterized with abnormal frequencies (2 - 7 Hz) and had the effect of pT-TMS. In our studies we thought it would be interesting to look for more substantial effects in different brain regions of the instability patients, as explained in table 3.

Examination of the instability patients in the following day with the MEG shows that their spectrum was almost like normal with most of the high abnormal frequencies in the 2 - 7Hz frequency band being absent. All the instability patients were evaluated clinically and with the MEG once again after one week after the first application of the pT-TMS in our laboratory. 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 nightly at (23.00 pm) the pT-TMS treatment at home with the electronic device mentioned before in the methods. After this all the instability patients were evaluated again and most of them reported to have benefited from this treatment. The mechanisms by which the application of the pT-TMS attenuated the instability patients are unknown. However one possible explanation is that these magnetic fields have been shown to influence the activity of the pineal gland which regulates the endogenous opioid functions [19] and the dopaminergic modulator [20], GABA [21].

Conclusion

Therefore, it is possible to conclude that this method of the pT-TMS has some potential to be an significant non-invasive, safe and effectual modality in managing the instability patients. Nevertheless, further investigations with more subjects are necessary in order to evaluate the possible beneficial contribution of pT-TMS for managing the symptoms of instability patients.

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SQUID (Superconducting Quantum Interference Device), in order to develop an expert system for automatic acquisition, analysis, evaluation and exploitation of MEG signals that are emitted from different organs of the human body" (Grant Number: 80623).

Conflict of Interest

The authors have declared that no conflicts of interest exist.

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