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Research Article

Autism Disorder and Pico-Tesla TMS

Photios Anninos[1]*, Athanasios Chatzimichael[2], Adam Adamopoulos[1], Athanasia Kotini[1], and Nicolaos Tsagas[3]

[1]*Department of Medical Physics, Democritus University of Thrace, Greece*
[2]*Department of Paediatrics, Democritus University of Thrace, Greece*
[3]*Department of Electrical Engineering, Democritus University of Thrace, Greece*

***Corresponding author**
Photios A. Anninos, Department of Medical Physics, School of Medicine Democritus University of Thrace, University Campus, Alexandroupoli 68100, Greece, Tel: 302551030392; Fax: 302551030392; Email: pans.photios.anninos@gmail.com

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Abstract

Magnetoencephalographic (MEG) recordings from 8 autistic children, 4 boys and 4 girls, with ages 5-12 years old (mean ± SD: 8.5 ± 2.3) were obtained using a whole-head 122-channel MEG system in a magnetically shielded room. Pico-Tesla transcranial magnetic stimulation (pT-TMS) was applied on the above patients with magnetic field amplitude (1-7.5pT) and frequency the alpha – rhythm of each patient (8-13Hz). A significant improvement was found in 6 out of 8 patients (75%). It was also observed an increase of alpha activity in autistic children at the end of one month after pT-TMS treatment at home. The application of pT-TMS has the potential to be a non invasive, secure and significant modality in the managing of autistic children. Of course, more studies in a larger population are needed before firm conclusions can be drawn.

INTRODUCTION

Transcranial Magnetic stimulation (TMS) is a technique with diagnostic and therapeutic uses in a lot of neurological conditions [1-17]. It is safe, non-invasive and was developed as an alternative to transcranial electrical simulation [18,19].

Anninos et al. [15], using external pico-Tesla Transcranial Magnetic stimulation (pT-TMS), were able to successfully attenuate seizure activity in patients suffered with many neurological disorders such as Epilepsy, Parkinson, Multiple Sclerosis, Alzheimer etc. The application of pT-TMS with intensity 1-7.5pT and frequency the a-rhythm of the patient (8-13Hz), resulted in a rapid attenuation of the MEG activity.

In our study we used our pico Tesla TMS (pT-TMS) electronic device [7], for the therapeutic treatment of children suffering from Autism because the higher level of TMS might have side effects to children. This device is a modified helmet containing up to 122 coils which have 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 each subject. It is designed to create pT-TMS range modulations of magnetic flux in the alpha frequency range (8-13 Hz) of each patient [1-15]. We have used only the a-rhythm because it is the physiological frequency for each subject. The pT-TMS device is calibrated with the a-rhythm frequency of each patient and was configured to generate a square wave so as to resemble with the firing activity of neurons in the brain. We have tested also other frequencies and other forms of oscillations before but we didn't have any effects.

METHODS

Biomagnetic measurements were performed from 8 autistic children (4 boys and 4 girls, with ages ranged from 5-12 years, mean ± SD: 8.5 ± 2.3) using a whole-head 122-channel MEG system (Neuromag-122, Neuromag Ltd. Helsinki, Finland) [1-15,20-23] in an electromagnetically shielded room. These recordings were taken with a sampling frequency rate of 256Hz and associated Nyquist frequency 128Hz. The MEG signals were filtered with cut-off frequencies at 0.3Hz and 40Hz.

This research was approved by the Research Committee of the Democritus University of Thrace by a decision with the project number 80347. All patients were referred to our Laboratory of Medical Physics in Alexandroupoli, Greece, by practicing neurologists. For all patients, informed consent for the methodology and the aim of the study was obtained by their parents prior to the procedure. In our study, we have not included healthy subjects as controls because this research was already published by Troebinger et al. [25], who have used a double-blind experimental design with our pT-TMS electronic device [7], in order to look for an effect on healthy subjects.

All patients were at the same condition (at rest with eyes closed in order to avoid artifacts and to enhance alpha rhythm) during the MEG. All MEG data tracings were visually inspected 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 ensure alertness for each subject.

A software program was developed in our laboratory in order to detect the amplitude of the first primary dominant frequency

of the power spectra of the MEG recordings obtained from each autistic patient and channel before and after the application of Fast Fourier Transform (FFT) in order to see if there are differences which will be evaluated by neurology clinicians.

RESULTS

Table (1) shows the brain regions and the corresponding channels in each brain region. Table (2) shows the symptoms in each of the 8 autistic children evaluated by the same clinicians at the end of one month after daily pT-TMS treatment at home. Furthermore it demonstrates the increase of alpha activity in autistic children at the end of one month. In addition we observed an improvement at 6 out of 8 patients (75%) as is indicated by the neurology clinicians.

Figure (1) shows the pT-TMS electronic device and the frequency output from it which was calibrated to 9Hz. Figure (2) shows the MEG record of 9 sec obtained from an autistic child. We applied FFT on the above MEG by which we get the first primary dominant frequency in the range of (2-7)Hz, which is 2.6 Hz.

DISCUSSION

The time frame of our clinical investigations was as follows:

1st day: MEG measurements in our lab. Application of pT-TMS and MEG recordings afterwards. The MEG spectrum was almost normal in the majority of the patients with absence most of the abnormal frequencies. Interview by clinicians. They confirmed our MEG findings.

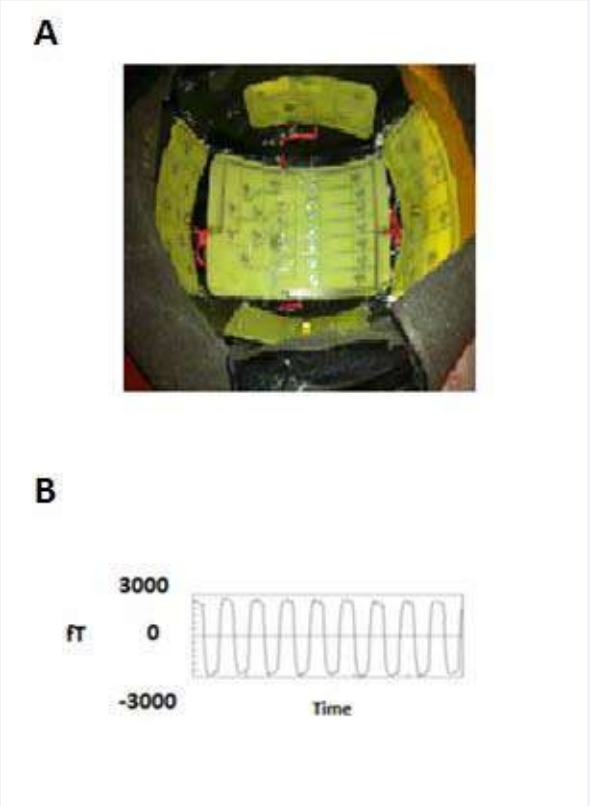

Figure 1 A) The configuration of the stimulation coils within the helmet of the electronic device. B) The frequency output from the electronic device which has calibrated to 9Hz.

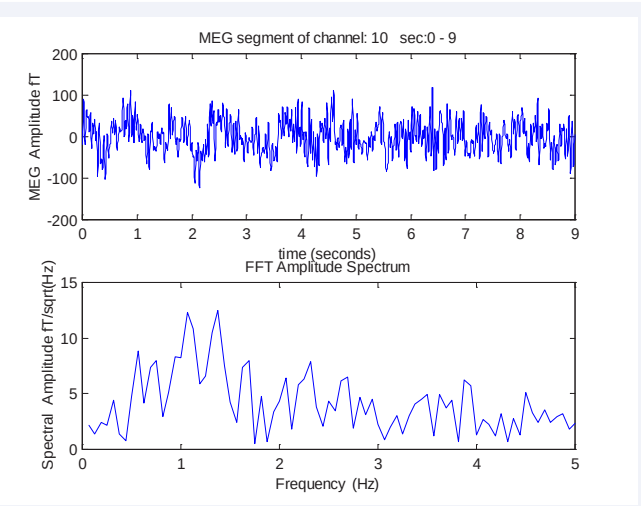

Figure 2 The MEG record of 9 sec obtained from an autistic patient. Application of FFT on the above MEG record we get the first primary dominant frequency in the 2-5Hz which is 2.6 Hz.

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

In order to confirm that the responses to pT-TMS were reproducible we have advised the relatives of all autistic patients to apply the pT-TMS treatment with the electronic device nightly (23:00 pm) at home. The instructions given to their relatives were as follows:

1. Place the helmet of the device on the patient head.

2. Turn the power switch on the electronic box of the device which is calibrated to produce pT-TMS with the characteristics of each autistic patient for 2 min. This is indicated by the green light.

3. When the green light of the electronic box of the device is turned off, turn the power switch off.

4. Remove the helmet from the head of the patient.

5. The relative of each patient should turn off all the lights in the room and the patient should go to bed immediately after treatment.

6. The relatives should store the electronic device in safe and dry place.

After one month of pT-TMS treatment at home all the autistic patients were evaluated again with MEG recordings and interview by the same clinicians and a majority of them had benefit from this treatment as it is shown in Table (2).

The mechanism by which the application of the pT-TMS has some beneficial effects in the autistic patients is unknown. Nevertheless, one potential reason is that these magnetic fields (pT-TMS) have been shown to influence the activity of the pineal gland (PG) which regulates the endogenous opioid functions [25], the dopaminergic modulation [26], and GABA [27]. Two

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

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

Table 2: This table shows the full-text of diagnostic criteria for autism spectrum disorder (ASD) and the related diagnosis of social communication disorder (SCD) as they appear in the 5th edition of Diagnostic and Manual of Mental Disorders (DSM-5) as of May 2013 and have evaluated by interview of the 8 autistics patients by neurology clinicians after one month treatment with pT-TMS at home.

Patient	Age	Sex	Symptoms before pT-TMS	Symptoms after one month with pT-TMS	Alpha before pT-TMS in Hz	Alpha after pT-TMS Hz
1	8	F	Persistent deficits in social communication and social interaction, as is manifested by the deficits in social approach and failure of normal back-and-forth conversation, to reduced sharing of interests, emotions, or affect, to failure to initiate or respond to social interactions. difficulties in sharing imaginative play or in making friends and intellectual disability **Severity Level 1** Deficits in social communication and difficulty initiating social interactions	Normal changes and behavior in this list of disorders	8.8	12
2	8	F	Persistent deficits in social communication and social interaction, as is manifested by the deficits in social approach and failure of normal back-and-forth conversation, to reduced sharing of interests, emotions, or affect, to failure to initiate or respond to social interactions. difficulties in sharing imaginative play or in making friends and intellectual disability **Severity Level 1** Deficits in social communication and difficulty initiating social interactions	Mixed changes in the list of disorders	8.0	12
3	9	F	Persistent deficits in social communication and social interaction, as is manifested by the deficits in social approach and failure of normal back-and-forth conversation, to reduced sharing of interests, emotions, or affect, to failure to initiate or respond to social interactions. difficulties in sharing imaginative play or in making friends and intellectual disability **Severity Level 1** Deficits in social communication and difficulty initiating social interactions	Minor Changes from the list of behaviors	8.4	12
4	11	F	Persistent deficits in social communication and social interaction, as is manifested by the deficits in social approach and failure of normal back-and-forth conversation, to reduced sharing of interests, emotions, or affect, to failure to initiate or respond to social interactions. difficulties in sharing imaginative play or in making friends and intellectual disability **Severity Level 1** Deficits in social communication and difficulty initiating social interactions	Major changes in this list of disorders	8.3	11
5	9	M	Persistent deficits in social communication and social interaction, as is manifested by the deficits in social approach and failure of normal back-and-forth conversation, to reduced sharing of interests, emotions, or affect, to failure to initiate or respond to social interactions. difficulties in sharing imaginative play or in making friends and intellectual disability **Severity Level 1** Deficits in social communication and difficulty initiating social interactions	Normal changes and behavior in the list of disorders	8.9	13

6	5	M	Persistent deficits in social communication and social interaction, as is manifested by the deficits in social approach and failure of normal back-and-forth conversation, to reduced sharing of interests, emotions, or affect, to failure to initiate or respond to social interactions. difficulties in sharing imaginative play or in making friends and intellectual disability **Severity Level 1** Deficits in social communication and difficulty initiating social interactions	Major changes in this list of disorders	8.9	12
7	6	M	Persistent deficits in social communication and social interaction, as is manifested by the deficits in social approach and failure of normal back-and-forth conversation, to reduced sharing of interests, emotions, or affect, to failure to initiate or respond to social interactions. difficulties in sharing imaginative play or in making friends and intellectual disability **Severity Level 1** Deficits in social communication and difficulty initiating social interactions	Major changes in this list of disorders	9.3	13
8	12	M	Persistent deficits in social communication and social interaction, as is manifested by the deficits in social approach and failure of normal back-and-forth conversation, to reduced sharing of interests, emotions, or affect, to failure to initiate or respond to social interactions. difficulties in sharing imaginative play or in making friends and intellectual disability **Severity Level 1** Deficits in social communication and difficulty initiating social interactions	Minor Changes from the list of behaviors	8.6	10

patents demonstrated the role of pineal gland after pT-TMS) [6, 16]. Anninou and Tsagas patent [16], revealed the strengthening of the immune system which is controlled by the PG. Anninos et al., patent [6], demonstrated the decalcification of epiphysis using magnetic fields with characteristics determined by MEG and our pT-TMS electronic device. Nocturnal plasma melatonin levels have been shown to decline progressively during childhood reaching a lowest point at puberty. This gradually decline in melatonin secretion during childhood facilitates the maturation of alpha rhythm. Accordingly, the existence of alpha rhythm could be used as a neurophysiological marker for the activity of the PG and for the disorders associated with missing or delayed maturation of the alpha rhythm such as autism, dyslexia, epilepsy, Parkinson etc, which might be related to disturbances of PG melatonin functions in early life [28].

CONCLUSION

This method of the pT-TMS might be considered as a non invasive secure and efficacious modality in managing the symptoms of autistic children. However, additional investigation with more patients is required in order to estimate the prospective effect of pT-TMS and its essential contribution.

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