

Original Research

MEG recordings of patients with cerebral palsy before and after the application of pico-Tesla weak magnetic fields

Photios Anninos^{1,*}, Athanasia Kotini¹, Adam Adamopoulos¹ and Nicolaos Tsagas²¹Laboratory of Medical Physics, Medical School, Democritus University of Thrace, University Campus, Alexandroupoli 68100, Greece²Department of Electrical Engineer, Polytechnic School, Democritus University of Thrace, Alexandroupoli 68100, Greece*Correspondence: anninos@med.duth.gr (Photios Anninos)

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MEG data for five cerebral palsy patients were taken using a whole-head 122-channel MEG system. An experiment was designed to identify the possible effect of external pico-Tesla weak magnetic fields. The subjects were five male volunteers 17-46 years of age. External stimulation, field amplitude 1-7.5 pico-Tesla, was applied to each subject at their alpha-rhythm frequency. Fast Fourier transforms were applied to the data of all MEG channels and the rhythms of the patients were evaluated before and after pico-Tesla transcranial magnetic stimulation. The application of pico-Tesla weak magnetic fields showed the brains of the cerebral palsy patients had an enhance of the frequencies of (2-7 Hz) for each patient. This was followed by an improvement and normalization of their MEG. The results had a statistical significance in four out of five subjects (80%) and suggested the stimulation provided a positive contribution to the management of the symptoms of cerebral palsy patients.

Keywords

MEG; cerebral palsy; pT-TMS; Fourier transform; alpha frequency

1. Introduction

The technique of transcranial magnetic stimulation (TMS) of the brain provides promising results in neurologic and psychiatric disorders due to its investigational, diagnostic, and therapeutic prospective (Hameed et al., 2017). Anninos and Tsagas (1995) invented an electronic device that emits pico-Tesla (pT) TMS ($1 \text{ pT} = 10^{-12} \text{ Tesla}$) and increases the frequencies of (2-7 Hz) toward the alpha frequency (8-13 Hz) of each patient (Anninos et al., 2016a,b,c, 2008, 2007, 2003, 2000, 1986). One probable electrophysiological explanation for the effectiveness of pT-TMS has been provided by the "Neural Net Model" (Anninos et al., 1986). This model suggests that magnetic stimulation induces a temporally modulated neuronal inhibition in regions that exhibit abnormal activity in the frequency range of 2-7 Hz. This hypothesis is agreement with information reported by other researchers (John, 1967).

This paper aims to identify any change in the brain state of

cerebral palsy (CP) patients with the use of a pT helmet electronic device (Hameed et al., 2017). Only Pihko et al (2014) have previously investigated and reported the reactivity of sensorimotor oscillations in children with hemiplegic CP to the use of magnetoencephalography (MEG) and TMS. Their results were in agreement with extensive alterations found in information processing in the sensorimotor system.

2. Methods

2.1 Data Acquisition

MEG recordings were filtered with cut off frequencies at 0.3 Hz and 40 Hz. The MEG sampling frequency was 256 Hz. The research protocol were approved by the Research Committee of our University.

A whole-head 122 channel MEG (Neuromag-122, Neuromag Ltd, Helsinki, Finland) was employed for recording in a magnetically shielded room. The study group was five male CP subjects in the age 17-46 years.

2.2. Data analysis

We developed a software program to detect the amplitude of the primary dominant frequency of the power spectra of the MEG obtained from every CP subject and channel after the appliance of fast Fourier transform (FFT). The alpha frequency (8-13 Hz) was employed for calibration of the electronic device and the frequencies 2-7 Hz were used in the analysis of the power spectra of the MEG records obtained from each CP patient and channel after the analysis by FFT.

The FFT algorithm was employed to obtain maps of the power spectra of the MEG data. Different map colors represented different dominant frequencies. The numbers in the map squares represent the 122 MEG channels studied in all areas of the brain according to Table. 1.

Each CP subject was scanned in two sessions. The first one consisted of a two minute resting state MEG scan and was used to establish the subject's alpha frequency (8-13 Hz) for calibration of the pT-TMS device. In the second one the pT-TMS electronic device was set to real stimulation and two minutes of pre-stimulus baseline MEG data were recorded. Next, two minutes of real pT-

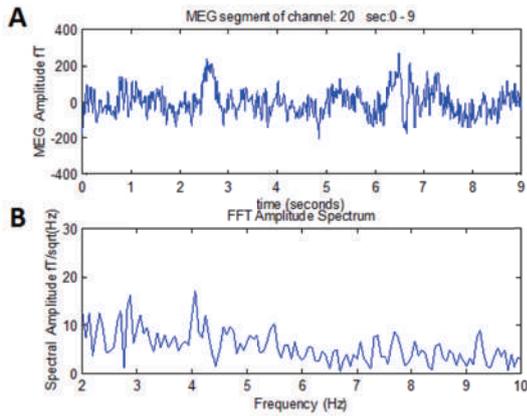


Figure 1. A) Nine second MEG record obtained from a CP patient. B) The application of FFT to the MEG record gives the primary dominant frequency as 2.8 Hz.

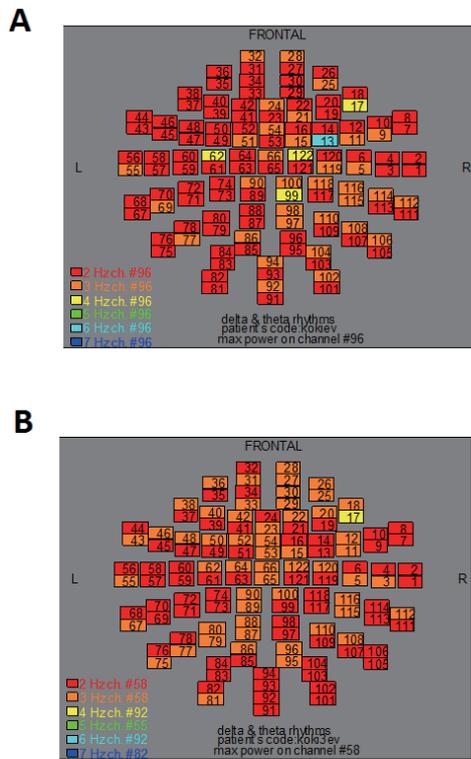


Figure 2. Power spectra map for subject one. A) Before pT-TMS, and B) After pT-TMS.

TMS stimulation were administered with the patient sitting comfortably just outside the scanner room. Following this stimulation, a further two minutes of resting state MEG was acquired from the subjects.

2.3. The pT-TMS electronic device

The pT-TMS electronic device is a modified helmet containing up to 122 coils arranged in five groups of arrays to cover the frontal, vertex, right and left temporal, right and left parietal, and occipital

Table 1. Brain regions and their corresponding channels

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

regions (Table 1). The device is designed to create pT-TMS range modulations of magnetic flux in the alpha frequency range (8-13 Hz) and it was configured to generate a square wave stimulus for each individual (Anninos et al., 2016a,b,c, 2008, 2007, 2003, 2000, 1986, 1970).

3. Results

Fig. 1A shows a MEG record of nine seconds duration obtained from a CP subject. The x-axis gives the time whereas the y-axis gives MEG amplitude in femtoTesla (fT, 10^{-15} Tesla). The actual signal length for analysis is two minutes but the FFT was applied to only nine seconds because this temporal duration was sufficient to identify the primary dominant frequency within the target 2-7

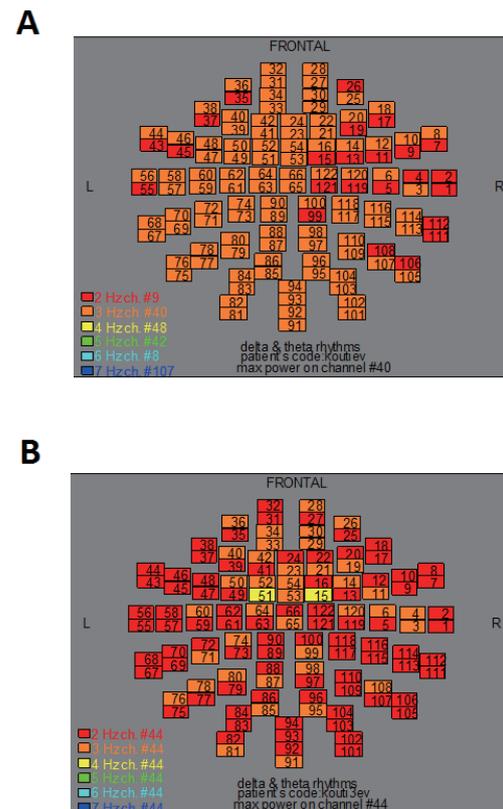


Figure 3. Power spectra map for subject two. A) Before pT-TMS, and B) After pT-TMS.

Table 2. Frequency before (BS) and after (AS) pT-TMS for each CP subject. (P: subject number, RT: right temporal, LT: left temporal, RP: right parietal, LP: left parietal, F: frontal, V: vertex, O: occipital)

P	RT(f)	RT(f)	LT(f)	LT(f)	RP(f)	RP(f)	LP(f)	LP(f)	F(f)	F(f)	O(f)	O(f)	V(f)	V(f)
	BS	AS	BS	AS	BS	AS	BS	AS	BS	AS	BS	AS	BS	AS
1	6	3	4	3	4	3	4	3	4	4	3	2	6	3
2	3	3	3	3	3	4	3	4	3	3	3	3	3	4
3	3	5	3	7	5	6	3	7	3	6	4	7	5	6
4	3	7	4	7	3	7	4	7	3	7	4	7	4	4
5	3	7	3	7	3	7	3	7	4	6	3	7	3	7

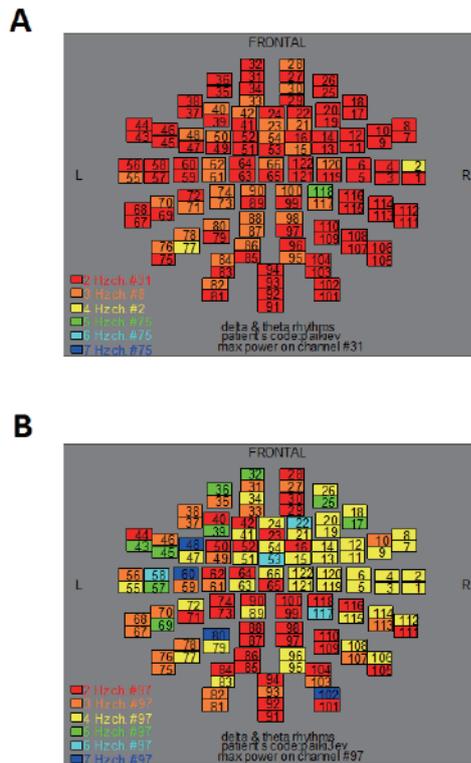


Figure 4. Power spectra for subject three. A) Before pT-TMS, and B) After pT-TMS.

Hz frequency range. The application of FFT to the MEG record that gives that the primary dominant frequency as 2.8 Hz, is shown in Fig. 1B.

Fig. 2-Fig. 6 gives the maps of the application of FFT to MEG data before and after the pT-TMS stimulus applied to each patient. The numbers in the maps correspond to the 122 channels of the MEG system according to Table. 1. Different colors represent different frequencies (red = 2 Hz, orange = 3 Hz, yellow = 4 Hz, green = 5 Hz, blue \geq 6 Hz).

Fig. 2A and Fig. 2B: Map of the primary dominant frequencies over the scalp for subject one. Fig. 2A: one channel 6 Hz and 4 channels 4 Hz (blue and yellow, respectively), remainder are 2 Hz and 3 Hz (red and orange, respectively). Fig. 2B: Following pT-TMS stimulation, one channel 4 Hz (yellow), remainder 2 Hz and 3 Hz (red and orange, respectively).

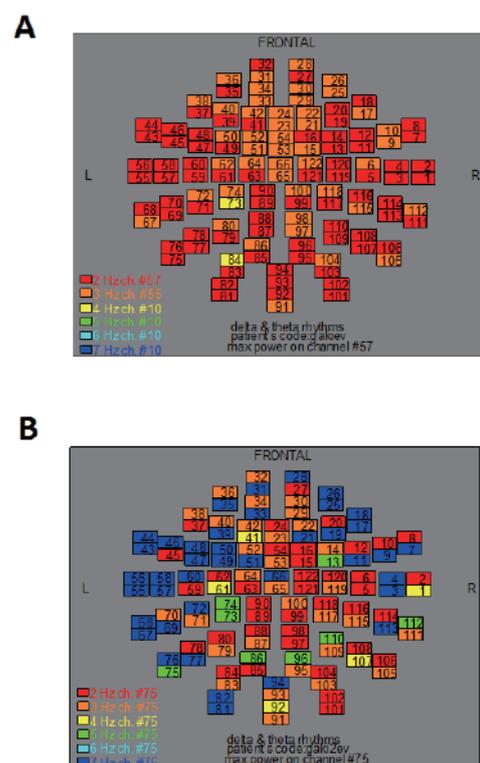


Figure 5. Power spectra map for subject four. A) Before pT-TMS, and B) After pT-TMS.

Fig. 3A and Fig. 3B: Map of the primary dominant frequencies over the scalp for subject two. Fig. 3A: All channels 2 Hz and 3 Hz (red and orange respectively). Fig. 3B: Following pT-TMS stimulation, two channels 4 Hz, remainder 2 Hz (yellow and orange respectively).

Fig. 4A and Fig. 4B: Map of the primary dominant frequencies over the scalp for subject three. Fig. 4A: One channel 5 Hz and two channels 4 Hz (green and yellow, respectively), remainder 4 Hz and 3 Hz (red and orange, respectively). Fig. 4B: After pT-TMS stimulation 2-7 Hz channels indicated in different colors.

Fig. 5A and Fig. 5B: Map of the primary dominant frequencies over the scalp for subject four. Fig. 5A: Two channels 4 Hz (yellow), remainder 2 Hz and 3 Hz, (red and orange, respectively). Fig. 5B: After pT-TMS stimulation 2-7 Hz channels indicated in different colors.

Fig. 6A and Fig. 6B: Map of the primary dominant frequencies over the scalp for patient five. Fig. 6A: One channel 4 Hz (yellow), remainder are 2 Hz and 3 Hz (red and orange, respectively). Fig. 6B: After pT-TMS stimulation 2-7 Hz channels indicated in different colors.

Table 3. Statistical analysis of the five subjects (see Table. 2). $p < 0.05$ (bold)

Patients	Mean f(BS) \pm SD	Mean f(AS) \pm SD	p values t-test
1	4.43 \pm 1.13	3.00 \pm 0.58	0.0117
2	3.00 \pm 0.0	3.43 \pm 0.53	0.0554
3	3.71 \pm 0.95	6.33 \pm 0.82	0.0003
4	3.57 \pm 0.53	6.57 \pm 1.13	0.0001
5	3.14 \pm 0.38	6.86 \pm 0.38	0.0001

In this study, preliminary effects of pT-TMS stimulation of CP subjects included increased amplitudes across the 2-7 Hz range and a substantial improvement and normalization of their MEG as shown in Table. 2 and Table. 3, which show that in four out of five patients. This result was statistically significant at the 0.05 level (80%). Table. 1 shows the corresponding channels for each brain region. Table. 2 shows the true effect of the pT-TMS. In this table BS and AS represent the effect before and after stimulation,

respectively, for each of the five CP subjects in each of the seven brain regions indicated in Table. 1. Table. 3 shows the statistical analysis for the five CP subjects using an unpaired t -test. The results were statistically significant for four out of five subjects (80%). The mechanisms by which the pT-TMS stimulus resolved the abnormal frequencies observed in the subjects are unknown. One possible explanation is that the application of magnetic fields has been shown to influence the activity of the pineal gland which regulates endogenous opioid functions (Lissoni et al., 1986) and dopaminergic modulation (Brandbury et al., 1985).

4. Conclusion

The treatment of CP patients with pT-TMS has the potential to be an significant non-invasive, secure, and efficacious modality. Although the results were positive with only a small number of patients, it encourages more studies using this method so as to evaluate its beneficial contribution to the management of the symptoms of CP patients.

Acknowledgement

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Conflict of Interest

The authors declare that they have no conflict of interest.

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References

Anninos, P., Adamopoulos, A., Kotini, A., Tsagas, N. (2016a) Combined MEG and pT-TMS study in parkinson's disease. *Journal of Integrative Neuroscience* **15**, 145-162.

Anninos, P., Adamopoulos, A., Kotini, A., Tsagas, N. (2016b) MEG evaluation of pico-tesla external TMS on multiple sclerosis patients. *Multiple Sclerosis Related Disorders*. **8**, 45-53.

Anninos, P., Chatzimichael, A., Adamopoulos, A., Kotini, A., Tsagas, N. (2016c) A combined study of MEG and pico-tesla TMS on children with autism disorder. *Journal of Integrative Neuroscience* **15**, 497-513.

Anninos, P., Adamopoulos, A., Kotini, A., Tsagas, N., Tamiolakis, D., Prassopoulos, P. (2007) MEG evaluation of parkinson's diseased patients after external magnetic stimulation. *Acta Neurologica Belgica* **107**, 5-10.

Anninos, P., Kotini, A., Anninou, N., Adamopoulos, A., Papastergiou, A., Tsagas, N. (2008) MEG recordings of patients with CNS disorders before and after external magnetic stimulation. *Journal of Integrative Neuroscience* **7**, 17-27.

Anninos, P., Kotini, A., Adamopoulos, A., Tsagas, N. (2003) Magnetic stimulation can modulate seizures in epileptic patients. *Brain Topography* **16**, 57-64.

Anninos, P. A., Adamopoulos, A. V., Kotini, A., Tsagas, N. (2000) Nonlinear analysis of brain activity in magnetic influenced parkinson patients. *Brain Topography* **13**, 135-144.

Anninos, P. A. and Tsagas, N. (1995) *Electronic apparatus for treating epileptic individuals*. USA patent NO. 5453072.

Anninos, P. A., Tsagas, N. and Adamopoulos, A. (1986) A brain model theory for epilepsy and the mechanism for treatment with

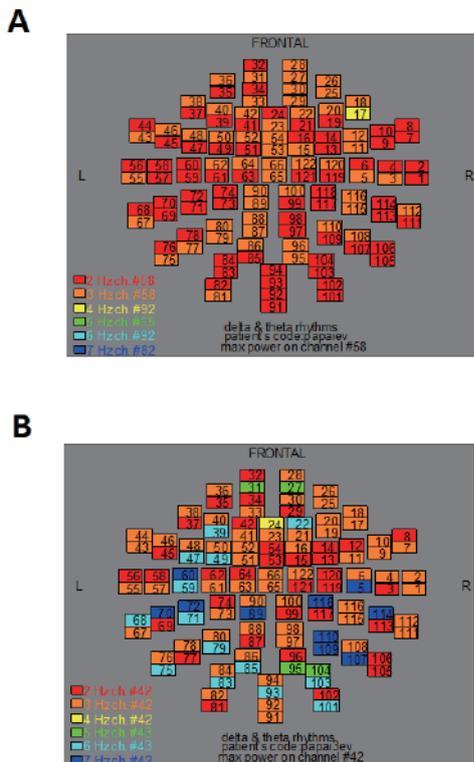


Figure 6. Power spectra map for patient five. A) Before pT-TMS, and B) After pT-TMS.

- experimental verification using SQUID measurements. In, Cotterill R.M. (ed). *Models of Brain Function* (pp. 405-421). New York: Cambridge University Press.
- Anninos, P. A., Beck, B., Csermely, T. J., Harth, E. and Pertile, G. (1970) Dynamics of neural structures. *Journal of Theoretical Biology* **26**, 121-148.
- Brandbury, A. J., Kelly, M. E. and Smith, J. A. (1985) Melatonin action in the mid-brain can regulate dopamine function both behaviorally and biochemically. In, Brown, G. M. and Wainwright, S. D. (eds). *The Pineal Gland, Endocrine Aspects* (pp. 327-332). Oxford: Pergamon Press.
- Hameed, M. Q., Dhamne, S. C., Gersner, R., Kaye, H. L., Oberman, L. M., Pascual-Leone, A. and Rotenberg, A. (2017) Transcranial magnetic and direct current stimulation in children. *Current Neurology and Neuroscience Reports* **17**, 11-15.
- John, E. R. (1967) *Mechanisms of Memory in Representational Systems*. New York: Academic Press.
- Lissoni, P., Esposti, D., Esposti, G., Mauri, R., Resentini, M., Morabito, F., Fumagalli, P., Santagostino, A., Delitala, G. and Fraschini, F. (1986) A clinical study on the relationship between the pineal gland and the opioid system. *Journal of Neural Transmission* **65**, 63-73.
- Pihko, E., Nevalainen, P., Vaalto, S., Laaksonen, K., Mäenpää, H., Valanne, L. and Lauronen, L. (2014) Reactivity of sensorimotor oscillations is altered in children with hemiplegic cerebral palsy: a magnetoencephalographic study. *Human Brain Mapping* **35**, 4105-4117.