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Research Article

Frequency Analysis from the Effect of Pico Tesla-Transcranial Magnetic Stimulation in Migraine Patients Using Magnetoencephalography

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Abstract

The purpose of this research is to identify any change in the frequencies of 2 - 7 Hz in the brain state of migraine patients after pico-Tesla transcranial magnetic stimulation (pT-TMS). It is a noninvasive technique for treating neurological disorders. We used magneto encephalographic (MEG) recordings of 10 Migraine patients with a whole-head 122 - channel MEG system in a magnetically shielded room of low magnetic noise. The subjects were 3 male and 7 female migraine volunteers between 45 - 67 years of age. Afterwards external pT-TMS was applied to the above patients. A software program was developed in our lab in order to detect the primary dominant frequency of the power spectra of the MEG obtained from every patient and channel before and after the application of pT-TMS. We found that 7 out of 10 patients (70%) had increased their 2 - 7 Hz frequencies after the application of pT-TMS. We concluded that frequency analysis is a promising means for the assessment of migraine disorders.

Keywords: *MEG; FFT; pT-TMS; Migraine*

Introduction

Magnetoencephalography (MEG) and frequency analysis are valuable tools for the evaluation of brain function. Rosen., *et al*. [1] studied the effects of eyes-open and closed resting paradigm and alcohol challenge on the spatial profile of spontaneous MEG and EEG oscillations using fast Fourier transform (FFT). Sueda., *et al.* [2] assessed the effectiveness of surgery for epilepsy, by analyzing rhythmic fast activity before and after surgery using time-frequency analysis and MEG. Millman., *et al.* [3] investigated the mechanisms involved in the perception of perceptually salient frequency modulation using auditory steady-state responses measured with MEG. They used FFT of each MEG channel to obtain the phase and magnitude of the auditory steady-state responses in sensor-space. Puligheddu., *et al*. [4] investigated the potential relevance of distribution and age variation of spontaneous theta activity (4 - 8 Hz) in normal subjects using MEG. The pre-processed data were transformed into the frequency domain by FFT. Mouri., *et al.* [5] used MEG responses to odor (amyl-acetate) and non-odor stimuli for 1 second in healthy volunteers and evaluated by FFT.

Transcranial brain stimulation (TMS) method has experimental, diagnostic, and therapeutic potential. The pico Tesla-TMS electronic tool invented by Anninos and Tsagas 1995 [6], 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 every patient. The pT-TMS device was configured for each individual to produce a square wave (so as to resemble the firing activity of neurons in the brain) [7-17].

Aim of the Study

The aim of this study is to discover any modification in the brain state of migraine patients with the use of the pT-TMS and FFT.

Materials and Methods

In our lab, we used a whole-head 122 channel MEG (Neuromag-122,Neuromag Ltd, Helsinki, Finland) in a magnetically shielded room. The subjects were 3 male and 7 female volunteers between 45 - 67 years of age.

Data Acquisition

The MEG recordings were filtered with cut off frequencies at 0.3 Hz and 40 Hz. The MEG sampling frequency was 256 Hz and the associated Nyquist frequency was 128 Hz, which was well above of the constituent frequency components of interest in our MEG recordings, thus avoiding aliasing artifacts.

The study protocol was approved by the Research Committee of our Democritus University of Thrace. Funding for this work was provided by our collaboration of General Secretariat of Research and Technology, GR and the ERGO AEBE,INC,GR under research program (Grant Number: 80623).

Data analysis

Our lab developed a software program in order to detect the amplitude of the primary dominant frequency of the power spectra of the MEG obtained from every patient and channel after the application of FFT. Then, we looked for the alpha frequency (8 - 13 Hz) for calibration of the electronic device and the (2 - 7 Hz) frequencies for the analysis to obtain the primary dominant frequencies and the power spectra of the MEG [18-23].

We used the FFT algorithm to obtain the maps of the power spectra of the MEG data. Different colors in the maps represent different dominant frequencies. The numbers in the maps squares represent the 122 MEG channels in every parts of the brain area according to table 1.

Every patient was scanned in two sessions. The first session consisted of 2-minute resting state MEG scan and the data were used to establish the subject's alpha frequency (8 - 13 Hz) for calibration of the pT-TMS electronic device. In the second session the pT-TMS electronic device was set to real stimulation. Then, 2 minutes of pre-stimulus baseline MEG data were recorded. Next, 2-minutes of real pT-TMS stimulation were administered with the patient sitting just outside the scanner room. Following these 2-minutes of stimulation, an additional 2-minutes of resting state MEG was acquired to patients.

Results and Discussion

Table 1 exhibits the brain regions and the corresponding channels in each brain region. Table 2, shows the true effect of pT-TMS. In this table the BS and AS represent the effect prior and after pT-TMS for each of the 10 migraine patients in each of the 7 brain regions as we have included in table 1. Table 3 shows the statistical analysis for the migraine patients using unpaired t-test. The results were statistically significant at 7 out of 10 patients (70%). Table 4 shows the symptoms before and after pT-TMS. We observe that 3 out of 10 patients haven't got improvement (no 6,7,8) according to the statistical analysis of table 3. Especially 2 out of 7 female patients (28%) and 1 out of 3 male patients (33%) haven't got improvement.

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.*

P	RT BS(F)	RT AS(F)	LT BS(F)	LT AS(F)	RP BS(F)	RP AS(F)	LP BS(F)	LP AS(F)	F BS(F)	F AS(F)	O BS(F)	O AS(F)	V BS(F)	V AS(F)	Figures
1	3	7	4	7	3	7	5	7	5	4	3	5	5	7	Figure 1(A,B)
2	6	7	3	7	4	7	3	7	6	7	3	7	4	7	Figure 2(A,B)
3	3	7	4	5	7	7	2	6	3	5	5	7	2	7	Figure 3(A,B)
4	6	7	7	7	6	7	7	7	6	7	7	7	6	7	Figure 4(A,B)
5	5	4	4	4	6	4	4	4	5	4	6	5	5	4	Figure 5(A,B)
6	6	7	7	4	7	7	7	4	4	6	6	7	7	7	Figure 6(A,B)
7	5	7	6	7	5	7	6	7	6	4	7	7	6	7	Figure 7(A,B)
8	7	7	7	7	7	7	6	7	3	7	6	7	6	7	Figure 8(A,B)
9	4	7	6	7	6	7	6	7	6	5	6	7	6	7	Figure 9(A,B)
10	3	4	3	7	3	5	3	7	3	3	3	5	3	7	Figure 10(A,B)

Table 2: *This Table is shown the maximum frequency between the first MEG recording before stimulation and the MEG recording after the real stimulation for each of the 10 migraine patients .In this table the first column P is the patient number, in the other columns the RT is the right temporal brain region, the LT the left temporal region, the RP the right parietal region, the LP the left parietal region, the F the Frontal region, the V the Vertex region and the O the Occipital brain region. (BS and AS are for before and after stimulation). The last column is shown the figures for the maps of the spatial distribution for the first dominant frequencies before and after pT-TMS for each of the 10 migraine patient.*

Patients	Mean f(BS) ± SD	Mean f(AS) ± SD	P Values t-test
1	4.00 ± 1.00	6.29 ± 1.25	**0.0027**
2	4.14 ± 1.35	7.00 ± 0.00	**0.0001**
3	3.71 ± 1.80	6.29 ± 0.95	**0.0059**
4	3.71 ± 1.80	6.50 ± 0.55	**0.0040**
5	5.00 ± 0.82	4.14 ± 0.38	**0.0269**
6	6.29 ± 1.11	6.00 ± 1.41	0.6818
7	5.86 ± 0.69	6.57 ± 1.13	0.1800
8	6.00 ± 1.41	6.71 ± 0.76	0.2614
9	5.71 ± 0.76	6.71 ± 0.76	**0.0292**
10	3.00 ± 00	5.43 ± 1.62	**0.0019**

Table 3: *This Table is shown the statistical analysis for the 10 migraine patients in table 2. The results are statistical significant at the level of 0.05 (marked bold).*

Patients	Gender	Symptoms before pT-TMS	Symptoms after pT-TMS
1	Female	She had attack of headaches	Improved
2	Female	She had moderate or severe headaches	Improved
3	Male	He had headaches any time of the day	Improved
4	Female	She had headaches and feeling sick	Improved
5	Male	She had headaches and feeling sick	Improved
6	Female	She had headaches any time of the day	Not improved
7	Male	He had headaches in the morning	Not improved
8	Female	She had severe some time headaches	Not improved
9	Female	She had headaches several a week	Improved
10	Female	She had headaches and feeling for vomiting	Improved

Table 4: *This table is shows the symptoms before and after pT-TMS.*

Figures 1-10 represent the maps of the application of FFT on MEG data before and after pT-TMS for each patient. The numbers in the maps in each square give each of the 122 channels of the MEG system according to table 1. Different colors represent different primary dominant frequencies (red = 2 Hz, orange = 3 Hz, yellow = 4 Hz, green = 5 Hz, blue ≥ 6 Hz).

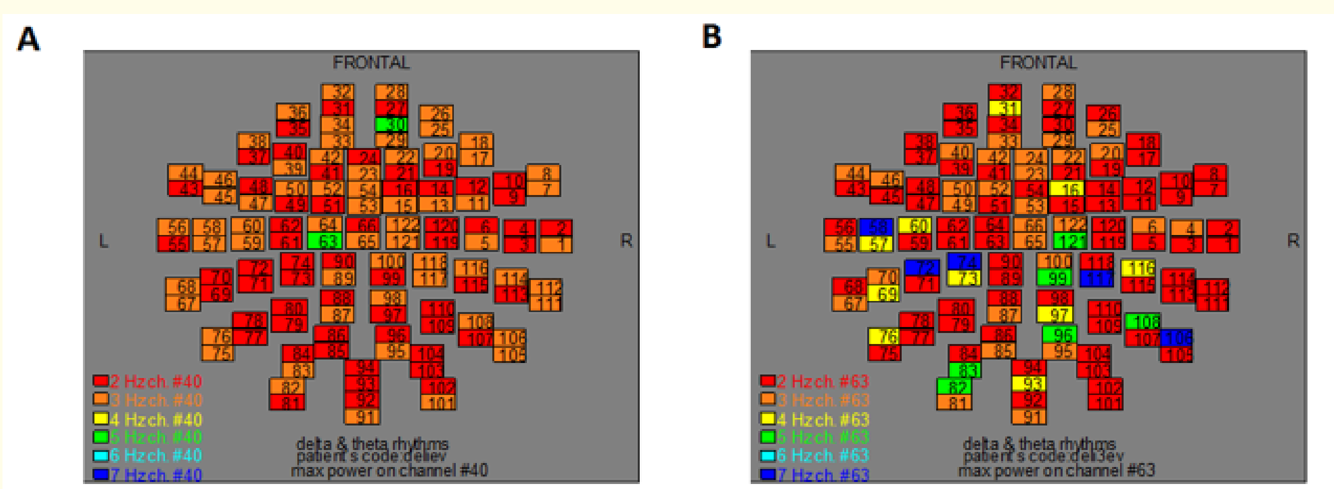

Figure 1: *The map of the power spectra of patient 1 A) before pT-TMS and B) after pT-TMS..*

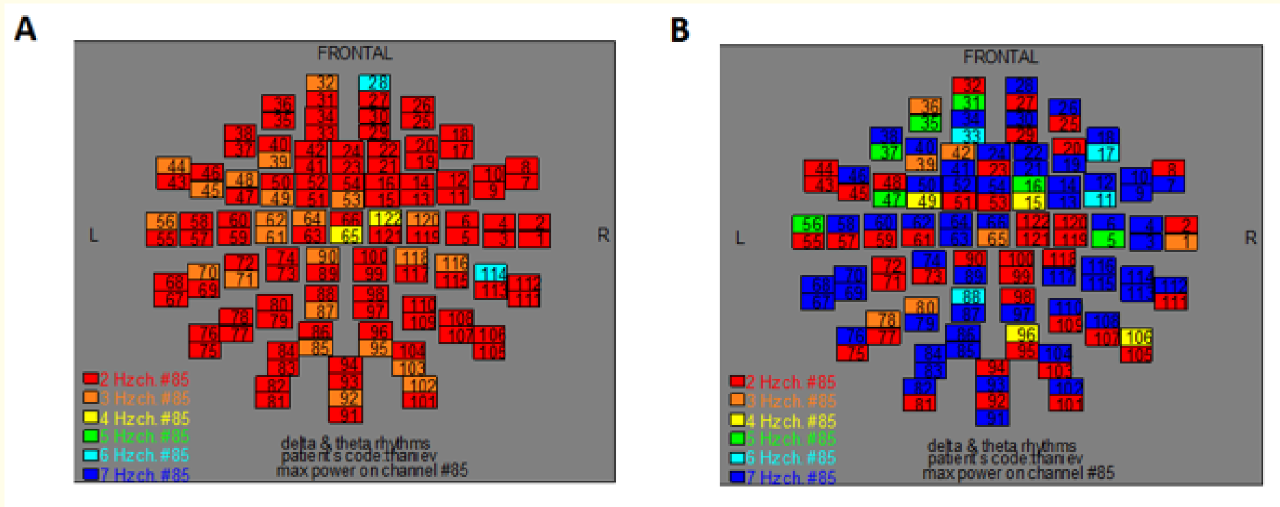

Figure 2: *The map of the power spectra of patient 2 A) before pT-TMS and B) after pT-TMS.*

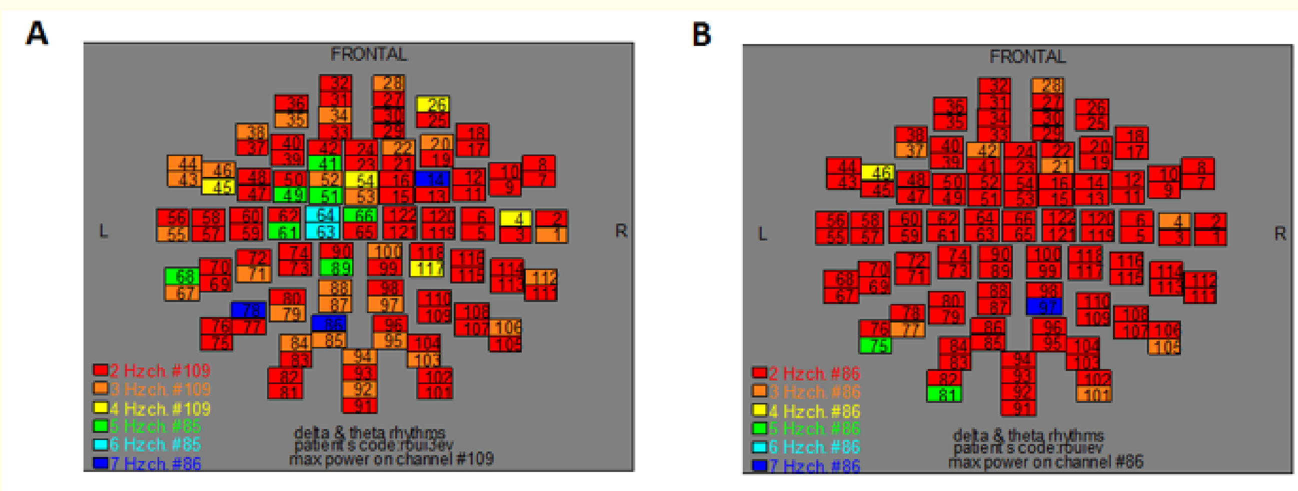

Figure 3: *The map of the power spectra of patient 3 B) before pT-TMS and A) after pT-TMS.*

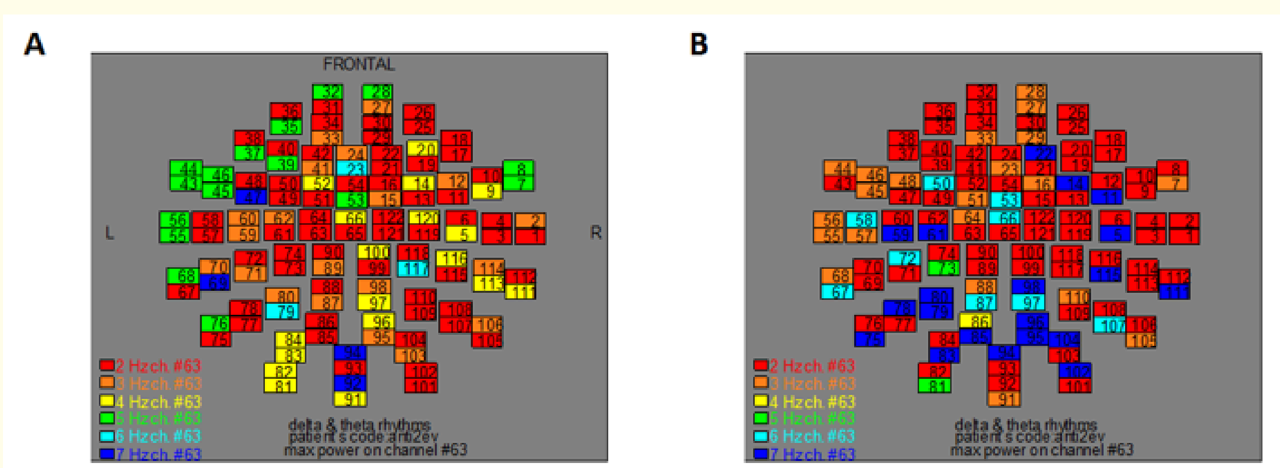

Figure 4: *The map of the power spectra of patient 4 A) before pT-TMS and B) after pT-TMS.*

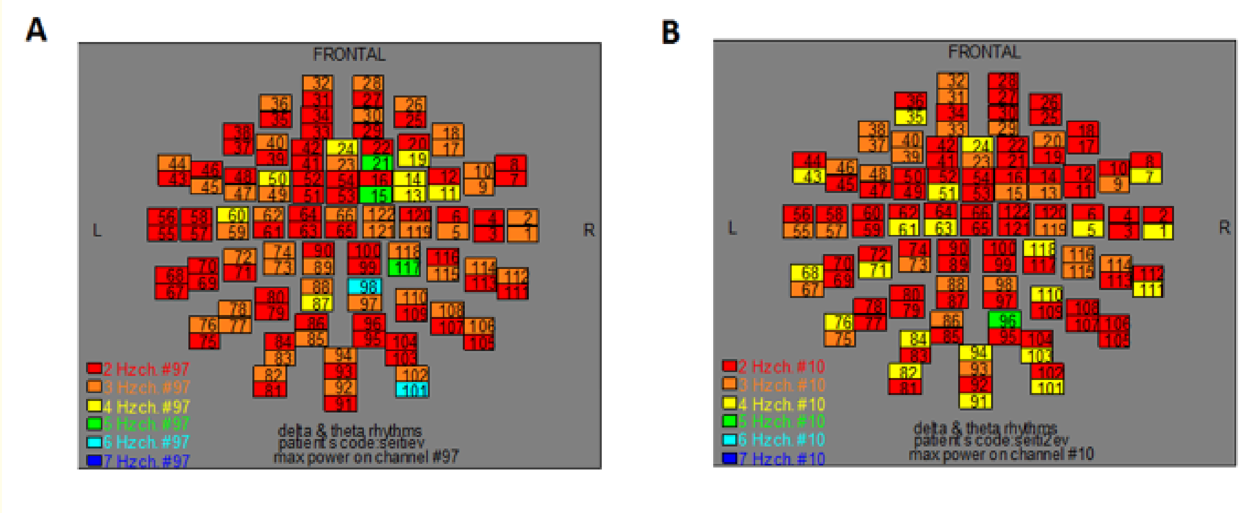

Figure 5: *The map of the power spectra of patient 5 A) before pT-TMS and B) after pT-TMS.*

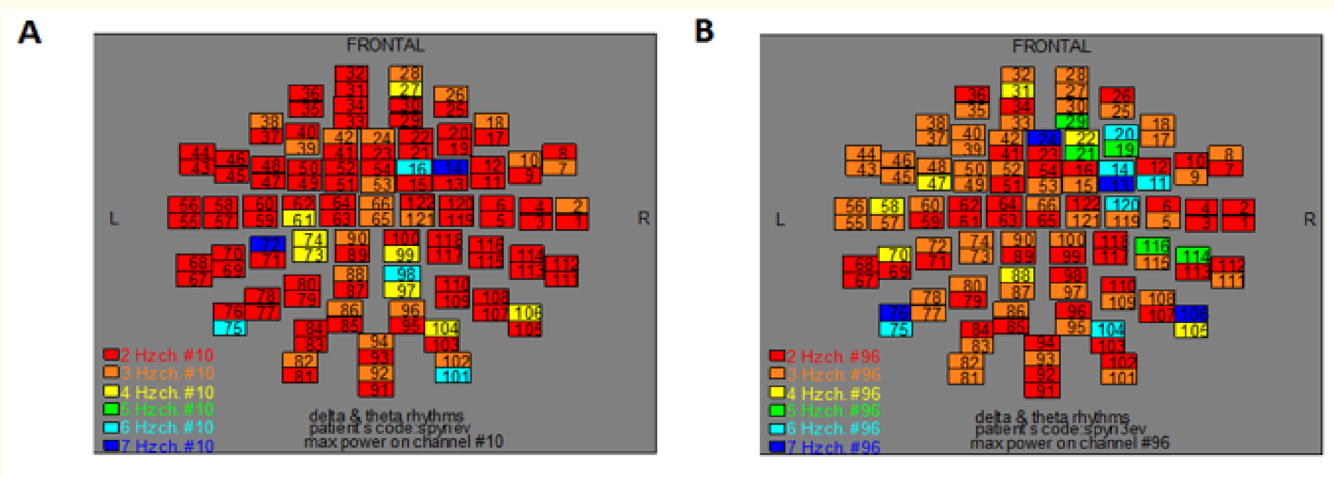

Figure 6: *The map of the power spectra of patient 6 A) before pT-TMS and B) after pT-TMS.*

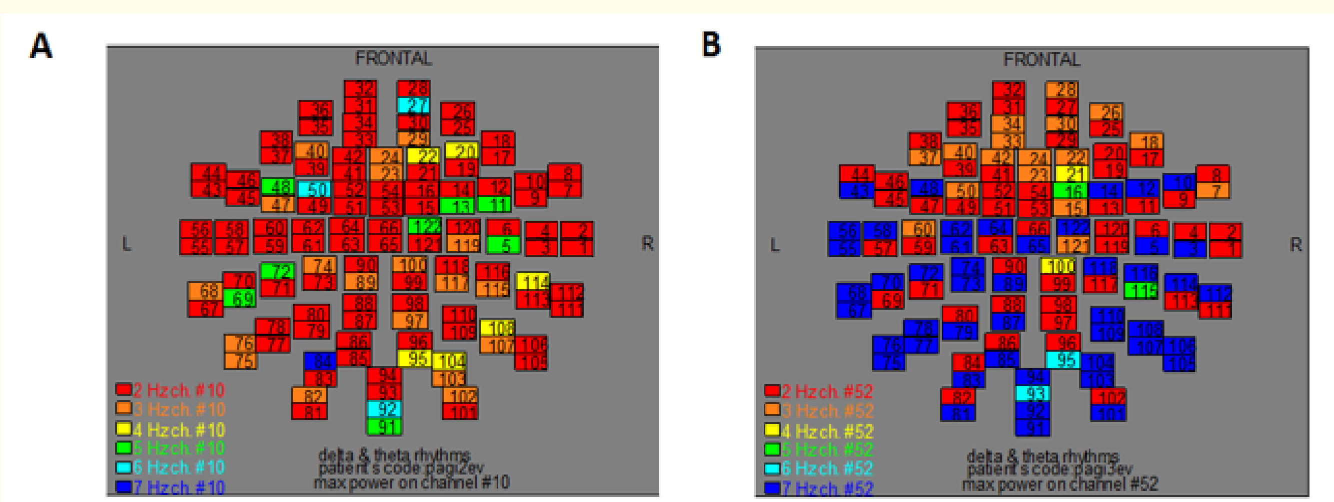

Figure 7: *The map of the power spectra of patient 7 A) before pT-TMS and B) after pT-TMS.*

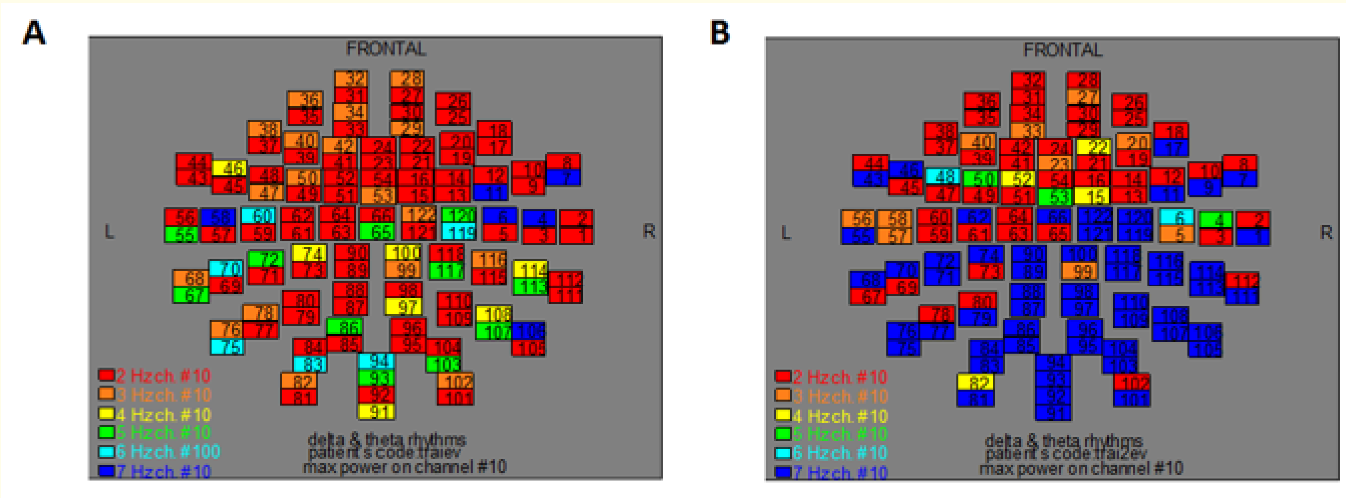

Figure 8: *The map of the power spectra of patient 8 A) before pT-TMS and B) after pT-TMS.*

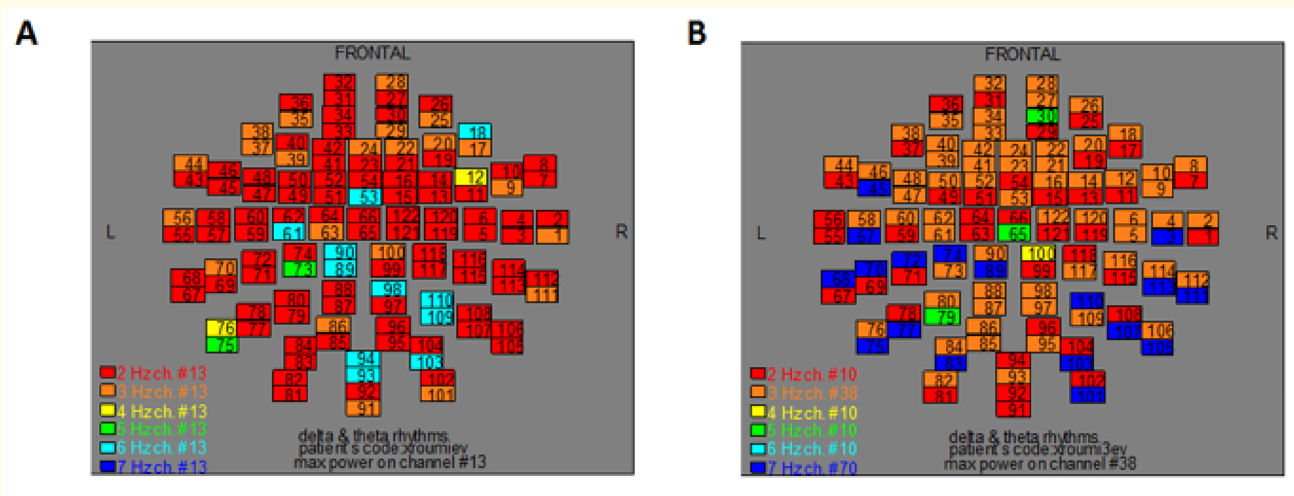

Figure 9: *The map of the power spectra of patient 9 A) before pT-TMS and B) after pT-TMS.*

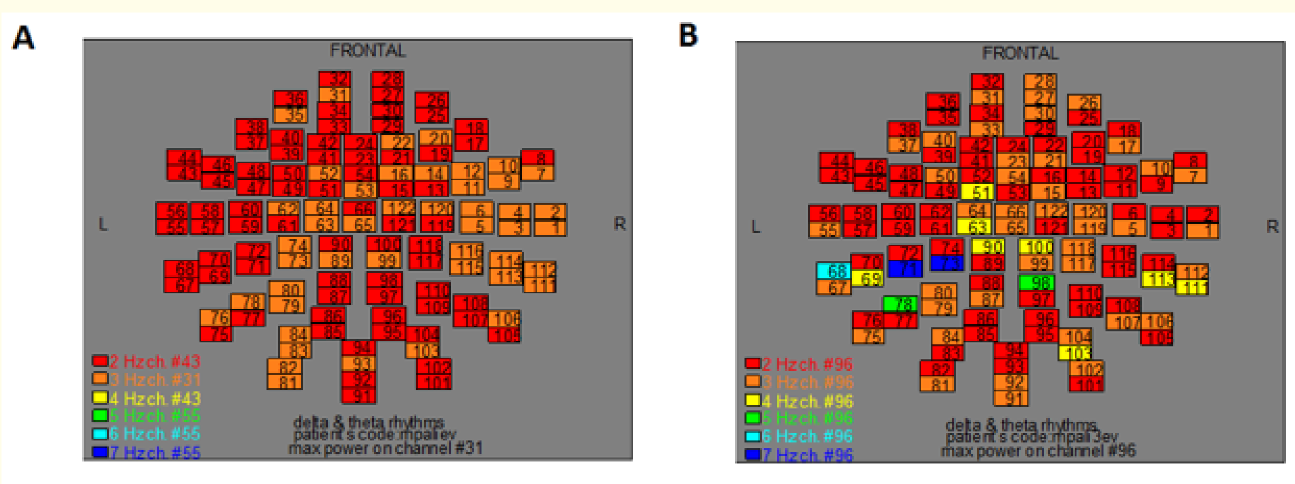

Figure 10: *The map of the power spectra of patient 10 A) before pT-TMS and B) after pT-TMS.*

The mechanisms by which the application of the pT-TMS attenuated the migraine patient's syndrome are unknown. Nevertheless one potential reason is that these magnetic fields have been shown to influence the action of the pineal gland which regulates the endogenous opioid functions [24] and the dopaminergic modulator [25], GABA [26]. Furthermore, on the cellular level, magnetic fields have been shown to influence the properties and constancy of biological membranes and their transport characteristics including the intra and extracellular distributions and fluctuation of calcium ions [27].

Conclusion

Therefore, it is possible to conclude that this technique of pT-TMS has some prospective to be a significant non-invasive secure modality in managing migraine patients. Nevertheless, additional investigations with more migraine patients are needed before firm conclusions can be drawn.

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