Research on Brain Induced Effect by Extremely Low Frequency Pulsed Magnetic Stimulation

Xiang Gao, Xiaolu Wang, Fang Chen, Hongzhi Qi, *IEEE Member,* Xuemin Wang, Dong Ming, *IEEE Member*, Peng Zhou*, *IEEE Member*

Abstract**—In order to evaluate the influence of extremely low frequency pulsed magnetic fields (ELF PMF) on human brain, we conducted the magnetic stimulation experiments (1 Hz, 10 mT, 20 min), and analyzed the changes of spontaneous EEG activity from 10 subjects. Compared with sham exposure group, the EEG power of theta band (3.5-7.5 Hz) and lower-alpha band (7.5-10 Hz) from the stimulation group increased significantly after magnetic stimulation. By analyzing the latency period and amplitude of P300 in auditory oddball task, we found that the latency period extended and the amplitude decreased. We suggested that these results might be explained via event-related synchronization induced by magnetic stimulation.**

I. Introduction

Magnetic stimulation has become a research focus because it's safe, effective, non-invasive, cheap, and it can conduct deep stimulation. Some researchers have applied the magnetic stimulation into the clinical treatment and got some exciting results.

Boris Pasche et al. found that the stimulation of low-frequency pulse magnetic field modulated by radio frequency decrease sleep latency and increase total sleep time [1]. Marcello Massimini et al. used the transcranial magnetic stimulation with each pulse at 1 Hz to evoke high-amplitude slow wave which leaded to a deepening of sleep [2]. R Huber et al. found that exposure to 30-minute extremely magnetic field (900 MHz; spatial peak specific absorption rate 1 W/kg) during the waking period preceding sleep affected human sleep electroencephalogram (EEG) [3]. However, few researchers studied the influence of extremely low frequency pulsed magnetic fields (ELF PMF, stimulus frequency under 100 Hz and magnetic field intensity was under 100mT) to brain.

Wang Mingshi presented a time-varying ELF PMF (changing from 13 Hz to 1 Hz), which could be used to improve sleep quality [4]. However, whether a low consistent frequency stimulation would induce the change of EEG better? If so, it would be very promising in sleep quality improving and adjuvant therapy of insomnia.

Thus, in this paper, we proposed a constant ELF PMF exposure experiment and analyzed the spontaneous EEG and auditory evoked P300 potential of participants both in the real stimulation group and the sham group.

II. Methods

A. Subjects and EEG recording

10 male subjects (age 23-27) participated in the experiment. They were students of Tianjin University, all of which were right-handed, healthy and reported with no history of mental illnesses or attention deficit disorders. In the experiment, we stimulated the occipital region of the subjects with a specially designed magnetic coil [5].The stimulation frequency was 1 Hz; the energy intensity was 10 mT and the distance between axis and the center was 2 cm. The EEG acquisition equipment and the signal analysis system were manufactured by NeuroScan Company. The scalp potential of each channel was amplified separately, band-pass filtered (0.05-70 Hz), and digitized with a sample rate of 1000 Hz.

B. Procedure

Experimental diagram is shown in Fig. 1. Firstly, an 8-minute spontaneous EEG and a 7-minute auditory Oddball task [6] were recorded to acquire the original status of subjects before stimulation. After that, a 20-minute ELF PMF or a sham single-blind experiment proceeded. At last, the spontaneous EEG and P300 evoked potential were recorded again to acquire the final status of subjects after stimulation.

Every subject participated in two sessions, one consisted of a real exposure and the other a sham one, which were blind to subjects. There was one week interval between two sessions, and the real/sham order was randomly. The experiment was conducted in a shielded room, and the subjects were required to be relaxed with their eyes closed and wore a headphone. During the auditory Oddball task, the sound lasted 50 ms with an interval of 1000 ms. This process repeated 400 times. The subjects were required to press the key immediately when hearing an infrequent high-pitched target tone (2000 Hz, with a probability of 20%) which was randomly embedded in a

Research supported by National Natural Science Foundation of China (No.51377120,51007063,31271062,81222021,61172008,81171423), Natural Science Foundation of Tianjin(No.13JCQNJC13900), National Key Technology R&D Program of the Ministry of Science and Technology of China (No. 2012BAI34B02) and Program for New Century Excellent Talents in University of the Ministry of Education of China (No. NCET-10-0618)

First author: Xiang Gao is with School of Precision Instrument and Optoelectronics Engineering, Tianjin University, Tianjin 300072, China.(e-mail: euler990@hotmail.com）

Corresponding author: Peng Zhou (phone: 919-904-6463, e-mail:zpzpa@vip.sina.com) is with School of Precision Instrument and Optoelectronics Engineering, Tianjin University, and Tianjin Key Laboratory of Biomedical Detection Technology and Instrumentation, Tianjin 300072, China.

Xiaolu Wang, Fang Chen, Hongzhi Qi, Xuemin Wang, Dong Ming are all with School of Precision Instrument and Optoelectronics Engineering, Tianjin University, Tianjin 300072, China.

train of frequent low-pitched non-target tones (1000 Hz, with a probability of 80%). Fig. 2 shows the stimulus sequence.

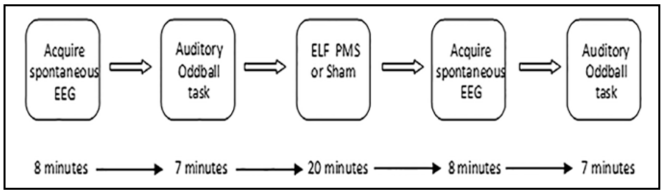

Figure 1. The experiment procedure

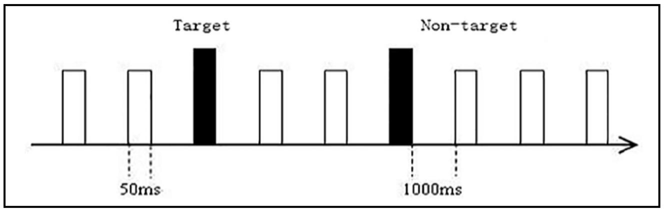

Figure 2. The stimulus sequence.

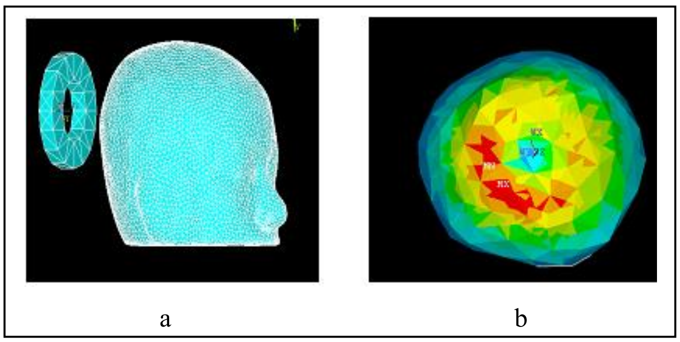

Figure 3. a is the stimulation model. b is the distribution of the stimulation-induced electric field intensity.

C. *Extremely low frequency magnetic stimulation model*

Fig. 3a shows the stimulation FEM model [5, 7] used in this experiment. The magnetic coil was placed about 2 cm above the occipital skull. Fig. 3b shows the distribution of the stimulation-induced electric field intensity in human brain. Red and blue represented the largest and smallest intensity respectively. It is clear that the induced electric field strength was large within the coil projection area on the skull and decreased slightly in the lateral and medial regions.

III. Data Analysis

Firstly, the EEG data were preprocessed by removing the ocular artifact, possible interference from head and muscle movements and 50 Hz power frequency interference. Then, compared with the sham group, we analyzed the EEG data with following methods.

A. *desynchronization and synchronization induced by Magnetic stimulation*

On the basis of the definition of event-related desynchronization and synchronization (ERD/ERS) [8-10], we proposed the concept of event-related desynchronization / synchronization induced by magnetic stimulation (MSI-ERD/ERS). Under the effect of ELF PMF, the brain activity would be inhibited and the low-frequency signal in EEG, especially the power of theta (3.5-7.5 Hz) and alpha band (7.5-12.5 Hz), would increase. This is called magnetic stimulation induced event-related synchronization (MSI-ERS). On the contrary, the phenomenon that the power of high-frequency signal in EEG especially beta band (12.5-30 Hz) decreased, which is called magnetic stimulation induced desynchronization (MSI-ERD). The quantified formula is defined as:

$$\text{MSI-ERD (MSI-ERS)} = (A - R)/R \times 100\% . \qquad (1)$$

Where A stands for the power of the target band in the experimental period, and R is the power of the target band in the reference period. When the calculated value of (1) is negative, it indicates reduction of energy in the specified target band, and this is MSI-ERD: -100 indicates the energy disappeared completely; 0 indicates the energy remains unchanged, that is, no MSI-ERD/MSI-RES. When the value is positive, it indicates that the energy increased, which means MSI-ERS happened, and the higher the value, the more obvious the MSI-RES.

B. *Sample Entropy*

As a nonlinear measurement of signal complexity, Sample Entroy (SE) is the modification of approximate entropy (ApEn) [11]. Unlike ApEn, SE demonstrates advantages such as data length independence and trouble-free implementation. The definition of SE is given in (2). SE applies to both deterministic signal and stochastic signal, which is very useful for analyzing EEG, a combination of deterministic and stochastic components. In EEG analysis, SE is used to measure the complexity of the changes in brain electrical activity. The more complex the EEG sequence, the more active the brain.

$$\mathrm{SE}(m, r, N) = \lim_{N \to \infty} \{-\log |B_{(r)}^{m+1} / B_{(r)}^{m}|\}. \qquad (2)$$

Where, given embedding dimension m, tolerance r and number of data points N, $B_{(r)}^{m}$ is the estimated probability that two sequences match for m points, and $B_{(r)}^{m+1}$ is the estimated probability that the sequences match for m+1 points. In this study, SE was calculated using $m = 2$ and $r = 20\%$.

IV. Result

Firstly, we analyzed the initial state before real and sham stimulations. No significant differences were showed in the spontaneous EEG by using the above methods (all Ps > 0.05). Also, the waveform and behavior results of P300 did not change clearly (all Ps > 0.1). Thus, we would compare EEG data of post-stimulation next.

A. *EEG power spectral analysis before and after stimulation*

After data preprocessing procedure, we analyzed the average power spectrum of EEG signal. Compared with the sham group, the average MSI-ERD/ERS values on each electrode of 10 participants were shown by brain topographic map [12]. Maximum ERD and maximum ERS were coded in blue and red respectively. In Fig. 4, the typical MSI-ERD/ERS pattern could be observed after stimulation.

In theta band and lower-alpha band (7.5-10 Hz), the scalp topographies are mostly red and yellow, which indicate that the MSI-ERS was more intensive over the central brain and occipital area. After Bonferroni correction (0.05/2 = 0.025) examining, the theta band increased significantly in frontal cortical and parietal cortical areas (Fz and Cz) (Fz: $p < 0.002$, $df = 9$, $t = -4.62$; Cz: $p < 0.001$, $df = 9$, $t = -2.92$); as well as the lower-alpha band in frontal and occipital cortical area (Fz, F4 and O2) (Fz: $p < 0.004$, $df = 9$, $t = -3.88$; F4: $p < 0.004$, $df = 9$, $t = -3.86$; O2: $p < 0.008$, $df = 9$, $t = -3.41$).

For the upper-alpha (10 – 12.5 Hz) band and beta band, there was no significant change after magnetic stimulation (all Ps>0.05).

B. SE analysis

In Fig. 5, it shows the histogram of the average SE values on all electrodes of 10 subjects. After Bonferroni correction examining, no significant change was showed (O1 ($p < 0.046$, $df = 9$, $t = -2.31$), T3 ($P = 0.035$, $df = 9$, $t = 2.49$)).

C. Auditory P300 analysis

Auditory P300 evoked potentials were obtained from each participant by averaging the segmented data for targets after data preprocessing. Fig. 6 shows the P300 waveforms on Fz, Cz and Pz electrodes under real or sham exposure. After Bonferroni correction examining, the post-stimulus P300 latent period was noticeably prolonged during target processing (Fz: $P < 0.010$, $df = 9$, $t = -3.27$; Cz: $P < 0.015$, $df = 9$, $t = -3.00$; Pz: $P < 0.024$, $df = 9$, $t = -2.71$). And the post-stimulus P300 amplitude obviously decreased (Fz: $P < 0.025$, $df = 9$, $t = 2.68$; Cz: $P < 0.024$, $df = 9$, $t = 2.72$; Pz: $P < 0.021$, $df = 9$, $t = 2.80$).

D. Behavioral Results

As a behavioral characteristics feature, mean reaction time is always used to evaluate drowsiness. The reaction time of P300 is shown in Table 1. There was an extremely significant difference between the two groups (P<0.01). The mean reaction time of the real group (330.39ms) was much longer than that of sham group (308.80ms).

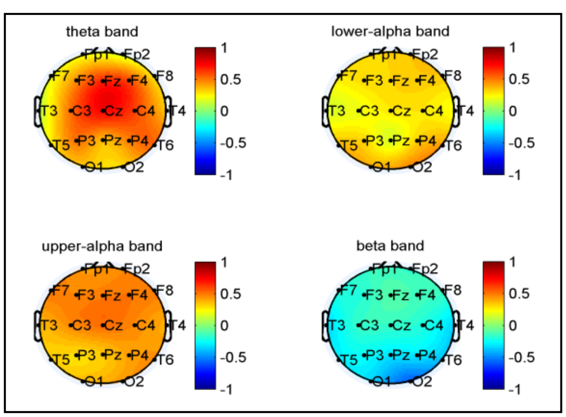

Figure 4. Brain topographic map of MSI-ERD/ERS in different frequencies.

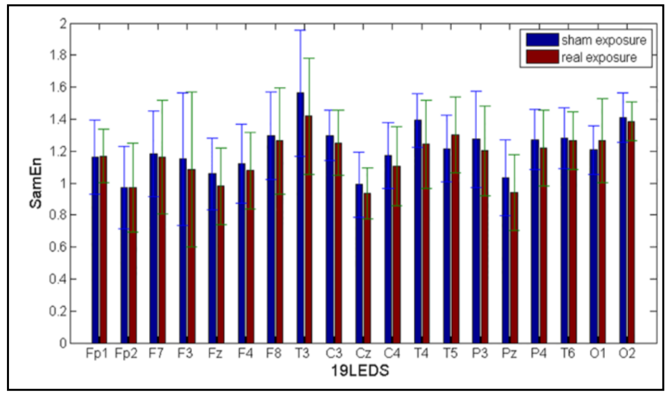

Figure 5. The comparison of Sample Entropy under sham or real exposure.

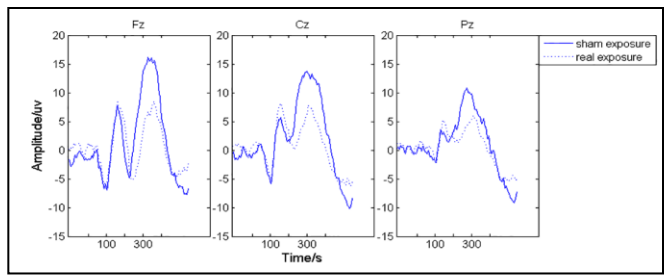

Figure 6. The P300 waves under sham or real exposure

TABLE I. TABLE I. The comparison of average reaction time in auditory oddball experiment before and after the stimulated.

State	Parameter			
	Mean reaction time	***Standard deviation***	***T***	***P***
Sham exposure	308.80	6.76	-3.279	0.002
Real exposure	330.39	5.61		

V. Discussion

In this study, the participants were exposed in 1 Hz, 10 mT ELF PMF or sham one for 20 minutes. Compared to the control condition, the results showed significant MSI-ERS effect, especially in Fz, Cz, F4 and O2 electrodes. In P300 experiment, the latency was longer and the amplitude was lower in real exposure than the sham one. Meanwhile, the reaction time was prolonged. However, no significant SE change was shown.

MSI-ERS, the increase of EEG power in lower-frequency of theta and alpha activity probably reflects a decrease in cortical activation [13, 14], which usually occurred under decreased arousal levels [15-17]. Therefore, the power of alpha and theta frequency band provides an adequate index of the subjects' drowsiness.

P300 is related to information processing of the brain. The latency and amplitude of which are proved to be the objective evaluation indicators of cognition. The amplitude indicates the amount of psychological and mental resources; the length of the latency period represents the reaction time of subjects to stimuli [18-21]. Therefore, the longer latency and the lower amplitude in real exposure indicate that the efforts devoted by participants on psychology and mentality were reduced after ELF PMF.

Behavioral analysis could be more intuitive to reflect the changes in psychological and thinking activities. Prolonged reaction time was observed in the event-related task after real stimulation. In line with the conclusion obtained from the P300 analysis, the inhibiting effect of brain induced by the ELF PMF had great impact on subjects, which was demonstrated by the longer reaction time of participants.

In the experiment, the stimulation energy of ELF PMF was 10mT, which was not sufficient to trigger nerve cells to generate action potentials. Based on cellular transmembrane signal conduction theory [12, 22], electromagnetic field could affect the cells through its influence to the signaling systems, and then had further effects on the whole organism. Therefore, we argue that the ELF PMF used in the experiment just works as a trigger or inducement, which might influence some particular links of biological system, and then the cells amplify and integrate the reactions caused by the influence. After a series of biological reactions, it eventually led to the MSI-ERD/ERS. This interpretation agreed with limit cycle theory about the organism intrinsic regularity [23, 24]. So it might give one possible explanation that ELF PMF could lead to a weakening of brain cell excitability, and suppress the brain activities. These inhibiting effects finally result in prolonged reaction time on behavior.

In conclusion, this study demonstrated that the specified frequency magnetic field could induce an increase of low-frequency activity in EEG and suppress the brain states, which could have a potential application on sleep quality improving, and adjuvant therapy of insomnia. Our study also expect to reveal the mechanism of brain induced effect under ELF PMF and to support further clinical application.

ACKNOWLEDGMENT

Peng Zhou and Xiang Gao thank everyone of the laboratory for their hard working and contribution to the project.

REFERENCES

[1] Amato, IIDavid, Alexandre Barbault, and Jean-Pierre Lebet, "Effects of low energy emission therapy in chronic psychophysiological insomnia," Sleep, vol. 19, no. 4, pp. 327-336, May.1996.

[2] Massimini, Marcello, et al. "Triggering sleep slow waves by transcranial magnetic stimulation." Proceedings of the National Academy of Sciences, vol. 104, no. 20, pp. 8496-8501, May. 2007.

[3] Huber, Reto, et al. "Exposure to pulsed high-frequency electromagnetic field during waking affects human sleep EEG," Neuroreport, vol. 11, no. 15, pp. 3321-3325, Oct. 2000.

[4] Jie, Zhang, Wang Xuemin, and Wang Mingshi, "Bioeffect of time-varying magnetic field on sleep disorders," Engineering in Medicine and Biology Society, Vol. 6, Oct 1998, pp 3300 - 3302. [*Dig. 20th Annual International Conference of the IEEE* Hong Kong, 1998]. Wang, X., et al. "Design of multi-channel brain magnetic stimulator and ANSYS simulation," IJBEM, nol. 7, no. 1, pp. 259-262,Mar. 2005.

[5] Doege, Kathrin, et al. "Reduced event - related low frequency EEG activity in schizophrenia during an auditory oddball task," Psychophysiology, vol. 46, no.3, pp. 566-577, May. 2009.

[6] He, WeiZhong, et al. "Study of the Electromagnetic Field of Transcranial Magnetic Stimulation Based on the Real Head Model," Biomedical Engineering and Informatics, Oct. 2009, pp. 1 - 5. [*BMEI'09. 2nd International Conference on. IEEE* Tianjin, 2009].

[7] Cook, Charles M., Alex W. Thomas, and Frank S. Prato, "Resting EEG is affected by exposure to a pulsed ELF magnetic field," Bioelectromagnetics, vol. 25, no.3, pp. 196-203, Jul. 2004.

[8] Nam, Chang S., et al. "Movement imagery-related lateralization of event-related (de) synchronization (ERD/ERS): Motor-imagery duration effects," Clinical Neurophysiology, vol.122, no. 3, pp. 567-577, Mar. 2011.

[9] Visani, E., et al. "Abnormal ERD/ERS but unaffected BOLD response in patients with Unverricht-Lundborg disease during index extension: a simultaneous EEG-fMRI study," Brain topography, vol. 24, no.1, pp. 65-77, Mar. 2011.

[10] Huang, Tina L., and Christine Charyton, "A comprehensive review of the psychological effects of brainwave entrainment," Alternative Therapies in Health & Medicine, vol. 14, no.5, pp.38-50, Sep-Oct 2008.

[11] Rechtschaffen, Allan, and Anthony Kales. "A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects," 1968.

[12] Cook, Ian A., et al. "Assessing the accuracy of topographic EEG mapping for determining local brain function," Electroencephalography and clinical neurophysiology, vol. 107, no.6, pp. 408-414, Jan. 1998.

[13] Laufs, H., et al. "EEG-correlated fMRI of human alpha activity," Neuroimage, vol. 19, no. 4, pp. 1463-1476, Aug. 2003.

[14] Klimesch, Wolfgang, "EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis," Brain research reviews, vol. 29, no. 2, pp. 169-195, Apr. 1999.

[15] Lafrance, C., and M. Dumont, "Diurnal variations in the waking EEG: comparisons with sleep latencies and subjective alertness," Journal of sleep research, vol. 9, no. 3, pp. 243-248, Dec. 2000.

[16] Oken, Barry S., and Martin Salinsky, "Alertness and attention: basic science and electrophysiologic correlates," Journal of Clinical Neurophysiology, vol. 9, no. 4, pp. 480-494, Oct. 1992.

[17] Fusar-Poli, Paolo, et al. "White matter alterations related to P300 abnormalities in individuals at high risk for psychosis: an MRI–EEG study," Journal of psychiatry & neuroscience: JPN, vol. 36, no. 4, pp. 239, Jul. 2011.

[18] Juckel, Georg, et al. "Diagnostic usefulness of cognitive auditory event-related p300 subcomponents in patients with Alzheimers disease?," Journal of Clinical Neurophysiology, vol. 25, no. 3, pp. 147-152, Jun. 2008.

[19] Righi, Stefania, Luciano Mecacci, and Maria Pia Viggiano, "Anxiety, cognitive self-evaluation and performance: ERP correlates," Journal of Anxiety Disorders, vol. 23, no.8, pp. 1132-1138, Dec. 2009.

[20] Polich, John, "Updating P300: an integrative theory of P3a and P3b," Clinical neurophysiology vol.118, no.10, pp. 2128-2148, Apr. 2007.

[21] Liburdy, Robert P, "Cellular studies and interaction mechanisms of extremely low frequency fields," Radio Science, vol. 30, no. 1, pp. 179-203, Jan-Feb 1995.

[22] Sandweiss, Jack, "On the cyclotron resonance model of ion transport." Bioelectromagnetics, vol. 11, no.2, pp. 203-205, Feb. 1990.

[23] Henriksen, E. A., et al. "Interaction-induced shift of the cyclotron resonance of graphene using infrared spectroscopy." Physical review letters, vol. 104, no. 6, pp. 067404, Feb. 2010.