31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Somatosensory-evoked Potentials and Cortical Activities Evoked by Magnetic Stimulation on Acupoint in Human

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Abstract—**Two acupuncture manipulations are clinically used: manual manipulation and electrical acupuncture. There is little published on the EEG changes during magnetic stimulation on an acupuncture site. In this study, EEG data in response to magnetic stimulation on HeGu (LI 4) acupoint were measured to determine whether magnetic acupoint stimulation might modulate ongoing EEG or not. Eighteen healthy volunteers (13 male, 5 female) 20 to 35 years old were chosen in this experiment, with consent obtained before the study. The highest evoked potential was recorded in FCZ electrode, at about 140-170ms (P150) after acupoint stimulation, but not mock point stimulation. Comparison of the somatosensory-evoked potentials in response to acupoint stimulation and mock point stimulation showed that P150 was specific to acupoint stimulation. With regard to the location of P150 in the human brain, we suggest that magnetic stimulation on HeGu acupoint would affect specific brain areas compared with the mock point. The difference in the anatomical structure of acupoint and non-acupoint may explain the specific acupoint-brain correlation, and P150 may be a characteristic activation in response to acupoint afferent.**

I. Introduction

Acupuncture has been considered a healing art in traditional Chinese medicine and has received an increasing interest by the public. The World Health Organization recommends the use of acupuncture treatment for 43 diseases, particularly for chronic pain. Since acupuncture was proposed by NIH consensus as a therapeutic intervention of complementary medicine, acupuncture efficacy has become more accepted in the Western world [1]. Now, acupuncture has spread to over 160 countries and regions besides China.

Whether acupuncture analgesia has a physiological basis or other psychological effects has long been a focus of argument [2]. Consequently, increasing attention has been paid to exploring the physiological and biochemical mechanisms underlying acupuncture analgesia, particularly the brain mechanism. In the past decades, possible mechanisms for pain relief by acupuncture have been extensively studied in animal experiments, but the underlying mechanisms of acupuncture analgesia in human remain largely unknown [3].

Two acupuncture manipulations are clinically used: manual manipulation (MA) and electrical acupuncture (EA) [4]. In MA, the acupuncture needle is inserted into the acupoint and twisted up and down by hand. In EA, stimulation current is delivered to acupoints via the needles connected to an electrical stimulator. The complicate manipulations of both MA and EA handicap the popularization of acupuncture. In this study, magnetic stimulator was introduced for its convenience and high repeatability of stimulus control. For our magnetic stimulator, an electromagnetic coil was use to placed on the skin over the acupoint, through which a brief current is passed. The rapidly changing magnetic field induces an electric current in the underlying nervous tissue [5].

Recently, a variety of imaging techniques (fMRI, SPECT, PET) have been used to look at the whole mechanism behind pain processing [6, 7]. These imaging studies are limited to observe any interaction between pain inputs and acupuncture afferents as well as the modulation of pain with acupuncture during acupuncture analgesia. In this study, Multi-channels EEG was used to investigate cortical responses to magnetic stimulation, which has an advantage over imaging modalities in that it can provide temporal information on the activity in addition to its location.

The aim of the present study was to examine (a) whether magnetic stimulation at a traditional acupoint site modulates ongoing EEG compared with a mock point, (b) whether specific cortical areas are affected by the topographic examination analysis, and (c) whether any EEG changes are only present during stimulation or lasted to the post stage.

II. Method

A. Subjects

Eighteen healthy right-handed volunteers (13 male, 5 female) 20 to 35 years old were chosen, with consent obtained before the study. No subject had a history of psychiatric or neurological disorders. The subjects were

Manuscript received June 20, 2009. This work was supported by the Natural Science Foundation of CHINA under Grant No.50877023 and the Natural Science Foundation of Hebei Province, CHINA under Grant No.E2008000053 and No.E2009000049.

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excluded from the study if they had any serious skin problems or using medication.

B. Selection of Stimulation Points

The stimulated acupoint was selected following the acupuncture map and the International Standard Nomenclature of Acupuncture. The traditional site of HeGu (LI 4) acupoint of this study lies at the first inter-interosseous muscle. In contrast, the locus of the selected mock point is overlaying the fourth interosseous muscle with few neural fibers in the dorsal hand, as shown in Fig. 1.

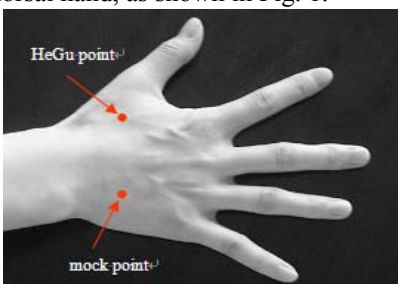

Fig. 1. The position of HeGu point and mock point

C. Experimental Protocol

The trials were carried out in a quiet and air-conditioned room maintained at around $22^{\circ}c$, 8:00 to 11:00 at night. The subjects sat in a comfortable chair with eyes closed and ears plugged earplugs. Each subject attended two experimental sessions (acupoint stimulation and mock point stimulation) separated by one week [8]. The selected acupoint stimulation was LI 4 (HeGu point), lying at the first inter-interosseous muscle of the right hand. The mock point was at the area overlaying the fourth interosseous muscle. The frequency of stimulation was 1Hz, the intensity of stimulation was 80% of the maximal (2.2 T). The duration of each trail was one minute with a frequency of 1Hz for each 50-second stimulus and 10-second rest. Each subject was stimulated 300 times. EEG data were recorded by using a 64-channel Quikcaps (NeuroScan ESI-128 system). Across the sessions, three study stages consisted of 3 min baseline EEG, 6 min stimulation EEG and 10 min post-stimulation EEG. At the stimulation stage, two study conditions were designated as acupoint stimulation and control point stimulation with fixed frequency and intensity.

D. EEG Recording

EEG recordings were made by using a 64-channel Quikcaps (NeuroScan ESI-128 system) from 64 scalp positions evenly positioned over both hemispheres according to the 10-20 system. The electrodes were filled with conductive paste. Each electrode had an active area of $4 \times 5mm^2$, and they were attached to the skin of the head. Electrode impedance was kept below $5\,\mathrm{k}\Omega$. The reference electrode and ground electrode were placed according the Neuroscan4.3 user's manual. The vertical EOG and horizontal EOG were recorded to reduce the ocular artifacts. EEG was recorded with eyes closed and ear plugged earplugs in three stages: before stimulation (Baseline 3 min), during stimulation (Stimulation, 6 min), after stimulation (Post, 10 min).

E. Date Analysis and statistical analysis

Data from two subjects were excluded in our further analysis due to being serious interfered. EEG data were filtered with 0.5-40 Hz band pass filter off-line and were subjected to epoching (from 100ms before to 511 ms after the stimulus), linear-detread, artifact rejection, and averaging. The artifact rejection methods consist of exclusion in epoch with large amplitude (over $\pm 50\,\mu$v), DC bias, blinks, and slow eye movement coincident with EOG.

The amplitudes and latencies of the somatosensory evoked potentials (SEPs) were determined. Considering the differences of the individual subject, the SEPs extracted from at least eight subjects (close to half of the subjects in the experiment) would be recognized as the result of magnetic stimulation. The corresponding sources of the SEPs were localized on the anatomy by using multimodal neuroimaging software CURRY 5.0. The goodness of fit (GOF) indicated the percentage of data that can be explained by the model. GOF values larger than 90% were considered to indicate a good model [9, 10].

Averaging within group is the most frequently used technique in group analysis. However, it may ignore some important information such as inter-subject variability. Hence in this study, the wavelet entropy of each stage was calculated to quantify precisely time dynamics of order/disorder states of the EEG signals and detect the brain regions activated or de-activated for every subject.

Wavelet transform is particularly effective for representing various aspects of signals, such as trends, discontinuities, and repeated patterns, where other signal processing approaches fail or are not as effective. It is especially powerful for non-stationary signal analysis [11]. The wavelet transform provides for optimal time resolution for each frequency and can accordingly extract in a reliable way superimposed event-related oscillation from different frequencies. Entropy is a thermodynamic quantity describing the amount of disorder in the system. From information theory perspective, the concept of entropy is generalized as the amount of information stored in a more general probability distribution. In this study, a method based on the time-frequency decomposition by the wavelet transform, named wavelet entropy (WE), were adopted to quantify precisely time dynamics of order/disorder states in short-duration signals such as the SEPs [12].

The wavelet entropy at resolution level j for the time window k is given by

$$E_j = \sum_k \left| C_j(k) \right|^2 \tag{1}$$

Where $C_j(k)$ represents the wavelet coefficients at a resolution level j included in the time interval k. then the total wavelet energy will be:

$$E_{tot} = \sum_j C_j(k) = \sum_j \sum_k \left| C_j(k) \right|^2 \quad (2)$$

Then the relative wavelet energy is defined as:

$$p_j = \frac{E_j}{E_{tot}} \quad (3)$$

Where p_j represents wavelet energy distribution at a resolution level j. the wavelet entropy is given by:

$$S_{WT} = -\sum_j p_j \log p_j \quad (4)$$

Statistical comparisons were performed on the wavelet entropy of Baseline and Stimulation (acupoint stimulation and mock point, respectively), Baseline and Post respectively by Paired-Samples T-test (P<0.05).

III. Result

The grand mean wave forms of somatosensory-evoked potentials across sixteen subjects elicited by magnetic stimulation were observed remarkably at F3, F1, FZ, F2, F4, FC3, FC1, FCZ, FC2, FC4 electrodes. The highest potential was recorded in FCZ electrode, at about 140-170ms (P150) after acupoint stimulation, but not mock point stimulation, as shown in Fig. 2. Somatosensory-evoked potentials both at left electrodes position and right electrodes position were observed, but amplitudes of late component P150 were larger at left electrodes.

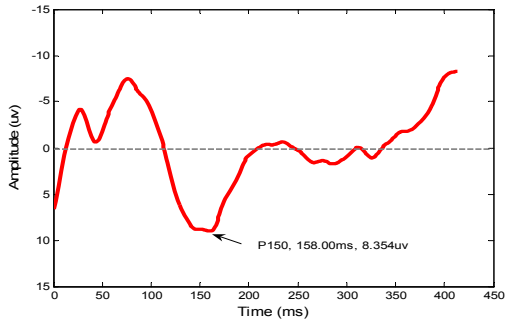

Fig. 2. The late component P150 of one subject

TABLE I
THE LATENCY AND AMPLITUDE OF P150 AT LEECTRODE FCZ

Subject	Latency(ms)	Amplitude(μ v)
1	153.00	2.915
2	148.00	5.301
3	154.00	5.082
4	149.00	2.872
5	148.00	4.076
6	158.00	8.354
7	156.00	7.865
8	154.00	4.810
9	157.00	4.830
10	157.00	4.627
11	146.00	1.714
12	145.00	3.837
13	155.00	6.387
14	147.00	5.942
15	158.00	6.014
16	151.00	4.830

Comparison of the somatosensory-evoked potentials in response to acupoint stimulation (red solid line) and mock point stimulation (blue dash line) at electrode FCZ was shown in Fig. 3. This result showed that P150 was specific to acupoint stimulation.

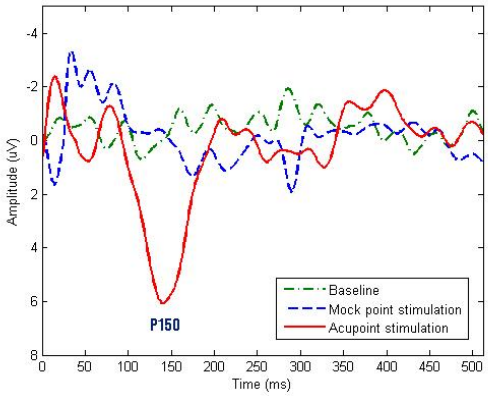

Fig. 3. Comparison of the somatosensory-evoked potentials in responses to acupoint stimulation (red solid line) and mock point stimulation (blue dash line) at electrode FCZ. t=0 is the time of stimulation.

The results of wavelet entropy of subjects and statistical effects are presented in Table I. The main results indicated: (a) the significant differences between baseline and acupoint stimulation (P=0.007<0.05); (b) no significant differences between baseline and mock point stimulation (P=0.679>0.05) or between baseline and post acupoint stimulation (P=0.196>0.05).

TABLE II
THE WAVELET ENTROPY OF SUBJECTS AT ELECTRODE FCZ AND T-TEST

Subject	Baseline	AC	MC	Post
1	2.5412	2.5513	2.4947	2.5831
2	2.5844	2.4485	2.5731	2.5847
3	2.5937	2.5814	2.5616	2.5413
4	2.5074	2.5499	2.4393	2.5743
5	2.5782	2.5333	2.5850	2.5928
6	2.5513	2.1443	2.4888	2.5826
7	2.5739	2.3616	2.5657	2.5937
8	2.5867	2.5641	2.5558	2.5684
9	2.4950	2.3120	2.5739	2.5387
10	2.5421	2.5261	2.5913	2.5701
11	2.5608	2.5778	2.5788	2.4932
12	2.5318	2.5113	2.5597	2.5754
13	2.5849	2.4317	2.6314	2.5796
14	2.5806	2.5190	2.8742	2.5936
15	2.5654	2.4308	2.5438	2.5837
16	2.5834	2.4932	2.4936	2.5957
P Value		**0.007**	**0.679**	**0.196**

AC= Acupoint Stimulation; MC=Mock Point Stimulation; Post= Post Acupoint Stimulation. Significant level: P<0.05.

The corresponding sources of the SEPs were localized on the anatomy by using multimodal neuroimaging software CURRY 5.0. The acupoint-specfic P150 were located to the contralateral anterior cingulated cortex, explain by a single dipole fitted around 150ms, as shown in Fig. 4.

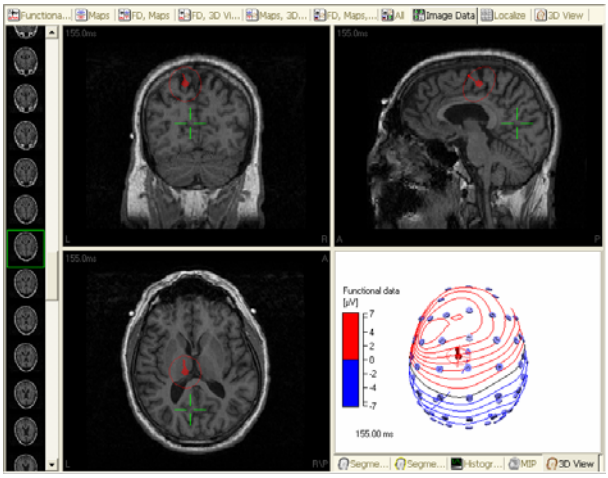

Fig. 4. Schematic projection of the location of single equivalent dipole of P150 fitted around 150 ms after acupoint stimulation.

IV. Discussion

This study revealed the temporal processing of magnetic acupoint stimulation in details and to compare the temporal behavior of cortical activations between acupoint and mock point stimulations. The data showed that the temporal behavior of cortical responses were different in P150, which specific to acupoint stimulations. P150 located in anterior cingulated cortex (ACC). The features of ACC in brain functions, including pain, are reviewed in the contemporary PET/fMRI neuroimaging researches. The ACC has been associated with task difficulty, attention, cognitive operation, attention disorders. Previous studies show that the ACC is also modulated by analgesics and acupuncture analgesia and presumably involved in the affective and cognitive dimension of pain. Our study was consistent with others.

The results of wavelet entropy of subjects and statistical effects showed that there were significant differences between baseline and acupoint stimulation, and no significant differences between baseline and mock point stimulation or between baseline and post acupoint stimulation. The mean wavelet entropy of acupoint stimulation is lower than baseline at F3, F1, FZ, F2, F4, FC3, FC1, FCZ, FC2, FC4 electrode. From these results, we indicated that the cortex regions of these electrodes covered had experienced a transition from a disorder state to an order state. The de-activation of medial prefrontal cortex, anterior cingulate cortex, amygdale, hippocampus, parahippocampus, precuneus, posterior cingulate and retrosplenial cortex has been reported during manual acupuncture and electroacupuncture. On the other hand, some previous studies reported that HeGu stimulation induces activation in midbrain, hypothalamus, insular, anterior cingulated, and cerebellum [13]. Our study was consistent with the former.

The traditional site of HeGu acupoint of this study lies at the first inter-interosseous muscle. The anatomical studies show that there are a large amount of nerve endings and muscle spindles in LI4 (HeGu point), whereas only superficial and deep radial nerves, and less amounts of nerve endings in non-acupoint. Thus, the observed EEG effect in this study could be due to the differences in nerve conduction and excitability between the traditional HeGu acupoint and the selected mock point. Stimulation of the HeGu point has been reported to inhibit a peripheral finger flexion reflex, sympathetic outflow, modulation of some esthetic afferents in the primary somatosensory area of the brain [14].

Neurophysiologic studies indicate that there are abundant nerve endings and muscle spindles distributed in acupoint. We suggest that magnetic stimulation on HeGu acupoint would affect specific brain areas compared with the mock point. The difference in the anatomical structure of acupoint and mock point may explain the specific acupoint-brain correlation, and P150 may be a characteristic activation in response to acupoint afferent.

References

[1] NIH Consensus Conference, "Acupuncture," *J. Am. Med. Assoc*, 280 (1998), pp. 1518-1524.

[2] P. Rosted, P. A. Griffiths, P. Bacon, N. Gravill, "Is there an effect of acupuncture on the resting EEG," *Complementary therapies in medicine*, 9 (2001), pp. 77-81.

[3] W. Q. Jin, Z. F. Zhou, J. S Han, "Electroacupuncture and morphine analgesia potentiality by bestatin and thiorphan administered to the nucleus accubens of the rabbit," *Brain Res*, 380 (1986), pp. 317-324.

[4] zhi-qi Zhao, "neural mechanism underlying acupuncture analgesia," *Progress in Neurobiology*, 85 (2008), pp. 355-375.

[5] C. Bonato, C. Miniussi, P. M. Rossini. "Transcranial magnetic stimulartion and cortical evoked potentials: A TMS/EEG co-registration stud," *Clinical Neurophysiology*, 117 (2006), pp. 1699-1707.

[6] J. L. Fang, T. Krings, J. Weidemann, "Functional MRI in healthy subjects during acupuncture: different effects of needle rotation in real and false acupoints," *Neuropathology*, 46 (2004), pp. 359–362.

[7] M. T. Wu, J. M. Sheen, K. H. Chuang, "Neuronal specificity of acupuncture response: an fMRI study with electroacupuncture," *NeuroImage*, 16 (2002), pp. 1028–1037.

[8] Abdrew C.N. chen, Feng-Jun Liu, Le Wang and Lars Arebdt-Nielsen, "Mode and site of acupuncture modulation in the human brain: 3D (124-ch) EEG power spectrum mapping and source imaging," *NeuroImage*, 29 (2006), pp. 1080-1091.

[9] W. T. Zhang, Z. Jin, G. H. Cui, "Relations between brain network activation and analgesic effect induced by low vs. high frequency electrical acupoint stimulation in different subjects: a functional magnetic resonance imaging study," *BrainRes*, 982 (2003), pp. 168–178.

[10] Yan Zeng, Xun-chang Liang, Jia-pei Dai, Yun Wang, Zhong-le Yang, Man Li, Guang-ying Huang, Jing Shi, "Electroacupuncture modulates cortical activities evoked by noxious somatosensory stimulations in human," *Brain Research*, 1097 (2006), pp. 90-100.

[11] Juliana Yordanova, "Wavelet entropy analysis of event-related potentials indicates modality-independent theta dominance," *Journal of Neuroscience Methods*, 117 (2002), pp. 99-109.

[12] David Papo, Jean-Paul Caverni, Abdel Douri, Ilana Podlipsky, Pierre-Marie Baudonniere, "Time-Varying Spectral entropy differentiates between positive and negative feed back-related EEG activity in a hypothesis testing paradigm," *International Journal of Psychophysiology*, 66, pp. 183-195, 2007.

[13] D. M. Barch, T. S. Braver, E. Akbudak, T. Conturo, J. Ollinger, A. Snyder, "Anterior cingulate cortex and response conflict: effects of response modality and processing domain," *Cerebral Cortex*, 11 (9), pp. 837–848, 2001.

[14] G. Biella, M. L. Sotgiu, G. Pellegata, E. Paulesu, I. Castiglioni, F. Fazio, "Acupuncture produces central activations in pain regions," *NeuroImage*, 14 (1), pp. 60–66, 2001.