

EEG Changes due to Low-Frequency Electrical Stimulation to the BL62 and KI6 of Elderly Women

Sanghun Lee¹, Kwang-Ho Choi¹, Seong Jin Cho¹,
Sun-Mi Choi¹, Kwon Eui Hong², Yeon-Hee Ryu¹

¹Acupuncture, Moxibustion & Meridian Research Group, Korea Institute of Oriental Medicine,
²Department of Acupuncture and Moxibustion, Daejeon University

노년 여성의 신맥 · 조해 저주파 자극이 뇌파에 미치는 영향

이상훈¹ · 최광호¹ · 조성진¹ · 최선미¹ · 홍권의² · 류연희¹

¹한국한의학연구원 의료연구본부 침구경락연구그룹, ²대전대학교 침구의학교실

Objectives : This study aimed to investigate the general effects of low-frequency electrical stimulation of the ankle joint acupuncture points(BL62 and KI6) on the brain waves of elderly women as a pilot study to figure out the possibility of candidate non-invasive and non-chemical stimulation method for the enhancing the brain function. **Methods :** A randomized, controlled, double-blinded clinical trial was performed in 31 healthy women(mean age, 54.5 years) within a treatment duration of 12 sessions. In the experimental group, low-frequency electrical stimulation was applied using the maximum range of the individual insensible strength(mean current, 0.04 μ A). The control group received sham stimulation. The background electroencephalographic activity was measured before and after the 12 sessions. **Results :** After 12 sessions of stimulation, the relative power of the alpha wave increased(32 of 32 channels: significant difference in 11 channels, $p < 0.05$); the theta(30 of 32 channels: significant difference in 10 channels, $p < 0.05$), beta(31 of 32 channels), and gamma(30 of 32 channels: significant difference in 7 channels, $p < 0.05$) powers were also decreased compared with the sham group. **Conclusions :** Electrical stimulation on the ankle joint acupuncture points(BL62 and KI6) seemed to stabilize the elderly women brain by inducing the alpha power and reducing beta, theta, and gamma powers. These results provide insight into the action mechanism of the stimulation and can assist the future development of a non-invasive and non-chemical treatment technique for stressor related cognitive problems.

Key words : randomized controlled trial, brainwaves, electrical stimulation, background EEG, BL62, KI6

Introduction

With significant increases in life expectancy rates, the prevalence of cognitive impairment has emerged as one of

the most serious health threats¹⁾. Because of the such social importance, Cabeza merged the fields of neuroscience and cognitive psychology of aging into "Cognitive Neuroscience of Aging"²⁾. In addition, the recent social phenomenon of the

Received May 27, 2013, Revised June 13, 2013, Accepted June 14, 2013

Corresponding author: **Yeon-Hee Ryu**

Acupuncture, Moxibustion & Meridian Research Group, Korea Institute of Oriental Medicine, 1672 Yuseong dae-ro, Yuseong-gu, Daejeon 305-811, Korea
Tel: +82-42-868-9484, Fax: +82-42-863-9464, E-mail: yhyu@kiom.re.kr

This study was supported by grants from the Development of Footwear for Brain Activity Revitalization by IT Fusion Technology and Acupuncture Stimulation(G11070) and the Korea Institute of Oriental Medicine for the Development of Acupuncture and Moxibustion Health Technology(K13011).

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rapid increase in stress can also raise the prevalence of cognitive impairment. Many researchers who studied stress-induced cognitive impairment have concluded that social and emotional stress can accelerate cognitive decline^{3,4}. Particularly in the case of the elderly people, the sleep-wake cycle becomes considerably disrupted with aging, and the poor sleep quality can lead to medical or psychiatric diseases(e.g., chronic pain, dementia, and depression)⁵ and age-related cognitive decline⁶. With a focus on these observations, challenging studies about improving cognitive function by improving the quality of sleep have been conducted in these days^{7,8}.

Acupuncture is a traditional medicine used worldwide, especially in East Asia. Acupuncture point is a special spot on the meridian, the stimulation of which produces a unique effect on the subject. A number of researchers have made attempts to improve the brain function by stimulating acupuncture points, and the studies have been conducted with fMRI⁹, EEG¹⁰, blind-spot mapping¹¹, etc. Recently, Jason showed that acupuncture can reduce anxiety and improve the working memory also¹². Traditional records state that concurrent stimulation of 2 acupuncture points-BL62 and KI6, which are located on the ankle joint, is used to primarily treat sleep disorders and secondarily treat psychiatric disorders¹³. Interestingly, the recent study result for relationship with cognition and sleep is very similar with the statement of traditional record of acupuncture points-BL62 and KI6. We focused on this record. Therefore, considering recent research results and the traditional records, we tried to investigate the effect of low-frequency electrical stimulation, and figure out the possibility of candidate

non-invasive and non-chemical stimulation method for the enhancing the brain function in this study.

Materials and Methods

1. Study design

This study was a double-blinded, randomized-controlled, parallel trial conducted in a clinical research center in South Korea from March to June 2011; Korea Institute of Oriental Medicine(Daejeon University Hospital). The institutional review board approved the research protocol before study onset. Participants were recruited through advertisements in local newspapers and posters. A written consent form was obtained from all participants.

1) Participants: Thirty-one healthy women were recruited. The inclusion criteria were as follows: female gender, age: 50~60 years, normal health status, and could sit for >1 h without discomfort. The exclusion criteria were as follows: history of surgery under general anesthesia within 1 year; having metal implants; being under medication; skin disease or hypersensitivity; psychiatric disorders or other brain-associated diseases; and head, neck, and facial problems or other conditions that could affect the electroencephalography(EEG) measurement.

2) Intervention and blinding: Self-adhesive electrode pads(Tens electrode-4848, Bioprotech, Korea) were cut into small size(20×20 mm) and used for low-frequency electrical stimulation of the acupuncture points, BL62 and KI6(Fig. 1)¹⁴. Alternating current stimulation with a frequency of 2 Hz was conducted by low frequency electrical stimulator(PG-306,

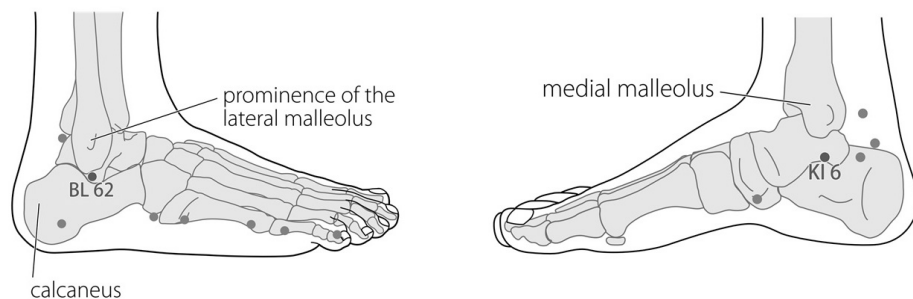


Fig. 1. Stimulation of the acupuncture points.

BL62 is the 62nd acupoint of the bladder meridian, and KI6 is the 6th acupoint of the kidney meridian. These acupoints are used together to treat sleep disorders, and each acupoints are used to treat mental disorders also(The standard acupuncture points are selected by the WHO/WPRO standard acupuncture point).

Suzuki, Japan). At the first session, all participants were tested for the measuring the minimum stimulation amplitude they could feel. According to this measurmnet, intervention amplitude was decide to 1 unit below the measured amplitude.

Two sets of electrical codes were arranged before the study. One set was normal(20 set), and the other(10 set) was disconnected. Their appearance was same, and no indications were allowed. The subjects were recruited consecutively, and the electrical code set was selected in a random way for each subject. At the end of the first session, identification numbers were given to the subjects and electrical codes for matching. After all participant had completed the total session, the matched electrical code was unsealed to keep the double blinding.

3) Procedure details: The experimental procedure comprised 14 sessions as follows: The firstday-Background EEG measurement, the second day-first low-frequency electrical stimulation(in this session, the subjects were randomly divided into the real and sham groups), Second to the 13th day-low-frequency electrical stimulation, 14th day-Back-ground EEG measurement. Stimulation is carried out 3 times a week and the interval of each session was guided more than 1 day. Total session is carried in at least 6 weeks.

4) Measurement: To measure the brain status, the Back ground EEG is used. Before and after the 12 stimulation sessions, Background EEG was measured for 5 min in an independent shield room by using QEEG32(Laxtha Inc., Korea). Data were acquired using a 32 monopolar electrode, a 256-Hz sampling rate, and a 0.5~50 Hz band-path filter, and saved into a computer through a 12-bit AD conversion and analyzed using a dedicated analysis software(TeleScan CD-TS-2.2, Laxtha, korea). The electrodes were attached according to the international 10~20 system(Fig. 2).

2. Data analysis

To determine the differences between the real and sham groups, the EEG changes of the relative power in alpha, beta, theta, gamma wave were examined by analysis of covariance (ANCOVA, model: difference=stim+baseline). To calibrate individual differences and normalize, relative power was

used. The related power was calculated by the equation: Absolute power of target brain wave/Absolute power of Total Brain wave). Each analysis was conducted using the SAS package(SAS version 9.1; SAS Institute Inc., Cary, NC) at a 95% significance level. The overall blindness index of the study was tested using the Fisher's exact test.

Results

1. Recruitment and allocation

Initially, 31 subjects were assessed online for eligibility, and no subject was excluded in the screening. During the progress of the stimulation sessions, 1 subject was discontinued appealing fatigue, and recruited again(Fig. 3). Therefore, there were 20 total subjects in the real group and 11 subjects in the sham group. The data of 1 subject in the real group was excluded from analysis as an outlier.

The baseline characteristics did not show any important differences between the 2 groups(Table 1).

2. Background EEG analyze

Background EEG was analyzed for further study. The

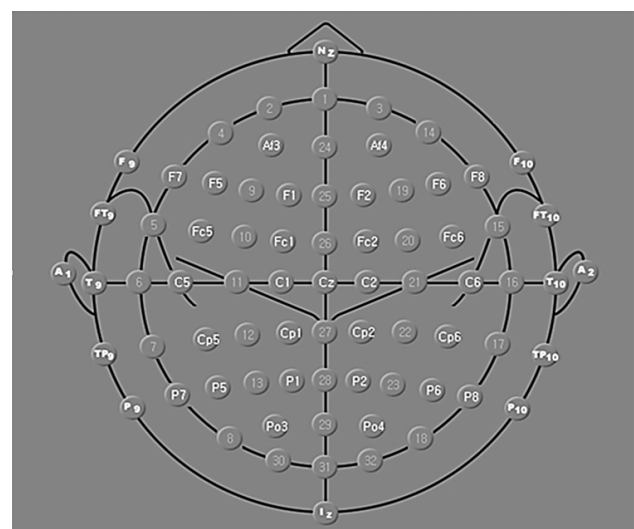


Fig. 2. Positions of the 32 Electrodes.
The 32 positions (numbered; in yellow) were used in this study according to the international 10~20 system.

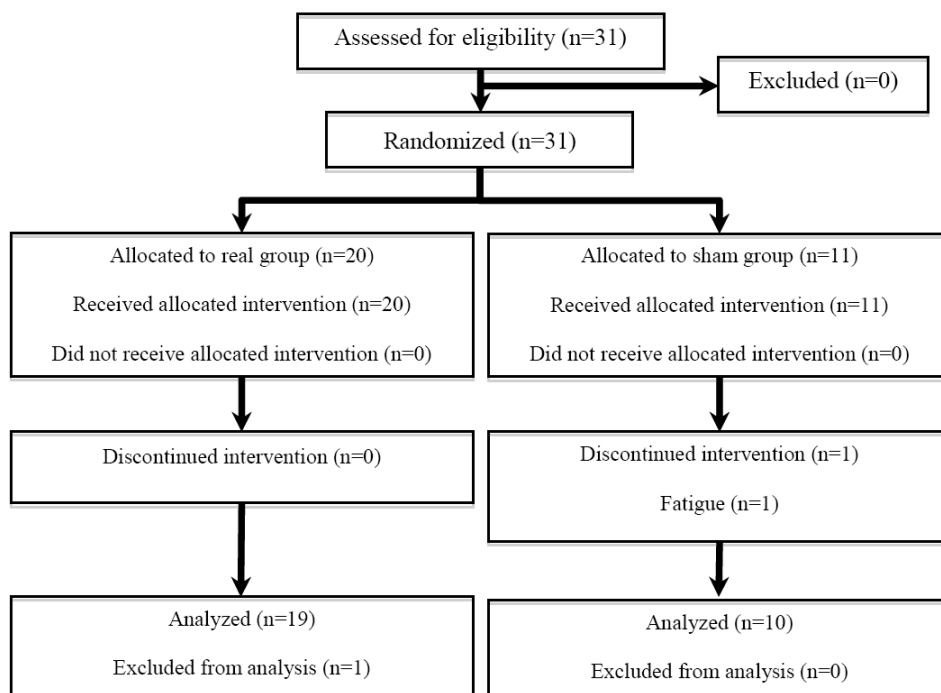


Fig. 3. Study flow chart.

Table 1. Characteristics of Subjects

Group	Real(n=19)	Sham(n=10)
Age(SD)	54.47(0.61)	50.94(3.45)
Minimum sensible current(SD)	0.04(0.003) μ A	0.04(0.004) μ A

differences in relative theta, alpha, beta, and gamma powers before and after stimulation were compared between the 2 groups.

1) **Relative alpha wave power:** The relative alpha power was increased in the real group at all channels, while that in the sham group showed a decrease in 26 of 32 channels. Eleven of 32 channels on the area around parietal lobe(F3, C3, CP3, P3, Cp4, P4, Fz, Fcz, Cpz, Pz, and Poz) showed significant increases between the 2 groups(Fig. 5).

2) **Relative beta wave power:** The relative beta power was decreased in the real group at all channels, while the sham group showed a decrease in 11 of 32 channels; however, no channel showed a significant difference between the 2 groups(Fig. 6).

3) **Relative gamma wave power:** The relative gamma power was decreased in the real group at 30 of 32 channels, while that in the sham group showed an increase in 19 of

32 channels. Seven of 32 channels including parietal lobe and frontal lobe(Fp2, F3, Fc3, Afz, Fz, Fcz, and Cpz) showed a significant decrease between the 2 groups(Fig. 7).

4) **Relative theta wave power:** The relative theta power was decreased in the real group at 26 of 32 channels, while the sham group showed an increase in 30 of 32 channels. Ten of 32 channels including parietal lobe, occipital lobe and right temporal lobe(Po5, Cp3, P3, Ft8, T8, Tp8, Po6, P4, Fcz, and Poz) showed a significant decrease compared with the sham group(Fig. 4).

3. Blind index

To check blindness of this study, all participants were asked to guess their group at the end of study. There was no significant difference in the answers, and blindness was successfully maintained throughout the study(Table 2).

4. Adverse events

A single case of fatigue was reported in the sham group. One patient claimed that the electrical stimulation did not benefit her in any way, and she voluntarily discontinued the treatment. No unusual symptoms were found during clinical examination.

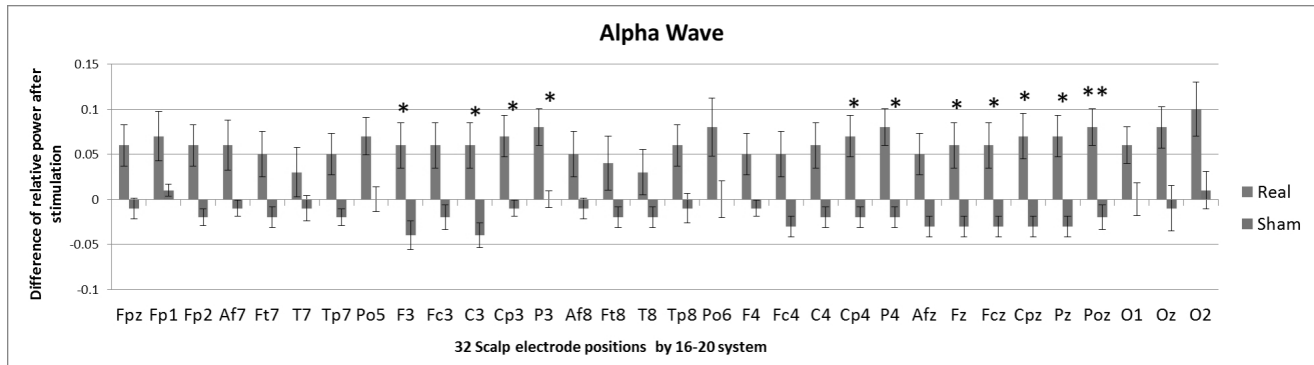


Fig. 4. Differences of the relative alpha power before and after stimulation in real and sham groups. All channels showed an increase in the relative alpha power after real stimulation, whereas 26 of 32 channels showed a decrease in the relative alpha power after sham stimulation. Eleven of 32 channels on the area around parietal lobe (F3, C3, CP3, P3, Cp4, P4, Fz, Fcz, Cpz, Pz, and Poz) in the real group showed a significant increase compared with those in the sham group.

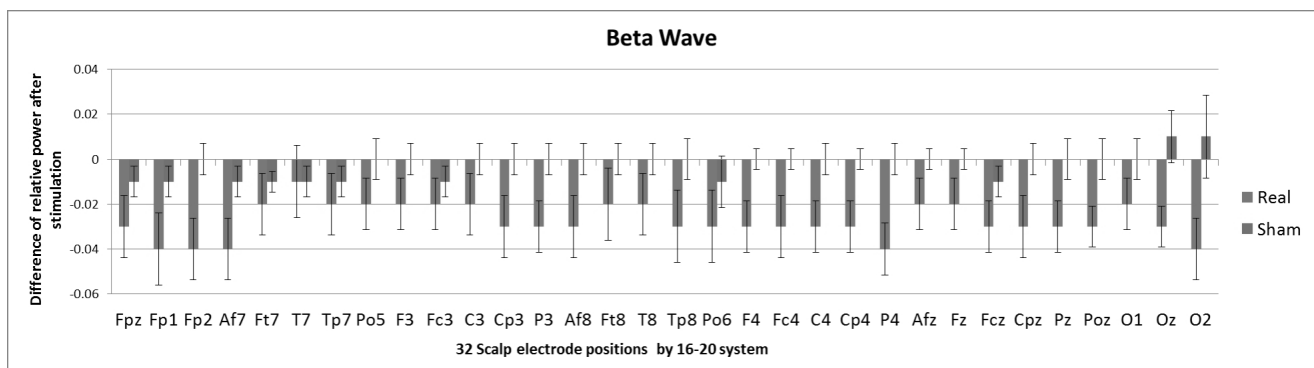


Fig. 5. Differences of the relative beta power before and after stimulation in real and sham groups. All channels showed a decrease in the relative beta power after real stimulation, whereas 11 of 32 channels showed a decrease after sham stimulation. But, no channel showed significant changes between the 2 groups.

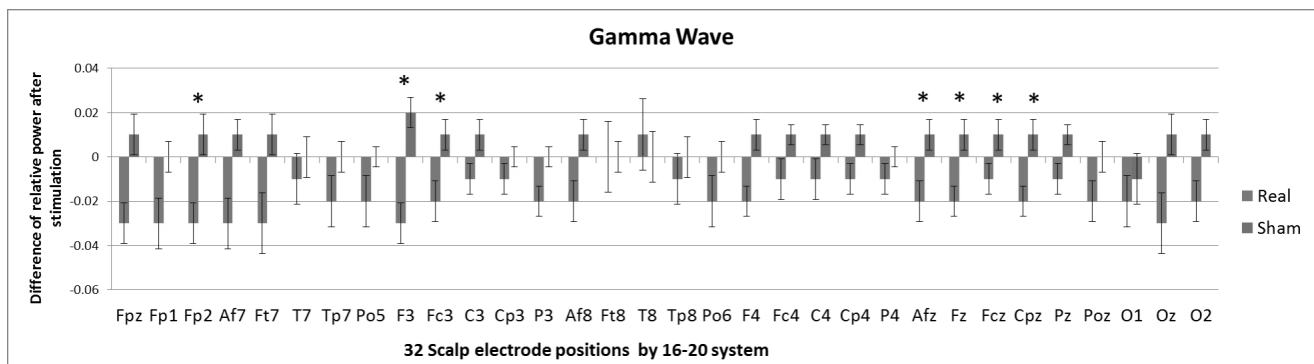


Fig. 6. Differences of the relative gamma power before and after stimulation in real and sham groups. Thirty of 32 channels showed a decrease in the relative gamma power after real stimulation, whereas 19 of 32 channels showed an increase after sham stimulation. Seven of 32 channels including parietal lobe and frontal lobe (Fp2, F3, Fc3, Afz, Fz, Fcz, and Cpz) in the real group showed a significant decrease compared with those in the sham group ($p < 0.05$).

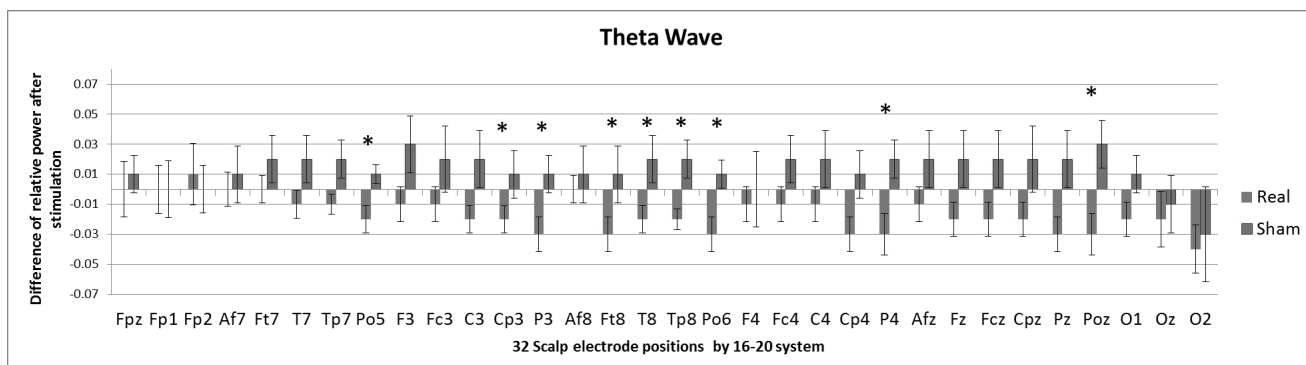


Fig. 7. Differences of the relative theta power before and after stimulation in real and sham groups. Twenty-six of 32 channels showed a decrease in theta power after real stimulation, whereas 27 of 32 channels showed an increase after sham stimulation. In the real group, 10 of 32 channels including parietal lobe, occipital lobe and right temporal lobe (Po5, Cp3, P3, Ft8, T8, Tp8, Po6, P4, Fcz, and Poz) showed significant decreases compared with those in the sham group (* $p < 0.05$).

Table 2. Blind Index

Guess/Group	Real		Sham		Unknown		Total		p value [†]
	n	(%)	n	(%)	n	(%)	n	(%)	
Real	11	(57.89)	4	(21.05)	4	(21.05)	19	(67.86)	0.1231
Sham	4	(44.44)	5	(55.56)	0	(0.00)	9	(32.14)	
Total	15	(53.57)	9	(32.14)	4	(14.29)	28*	(100.00)	

* : 3 missing value, % : row percent, [†] Fisher's exact test.

Discussion

Acupuncture is the most famous traditional medicine in the world. Electroacupuncture was first proposed in 1816 by Louis Berlioz in France, who suggested that electrical stimulation combined with acupuncture could enhance the effectiveness of a treatment. He used low-frequency electrical stimulation on acupuncture needles and attempted to enhance the needling stimulation on the acupuncture point. After 180 years, a Chinese researcher found that a 2-Hz stimulation can increase Met-enkephalin-Arg-Phe levels, while a 100 Hz stimulation increases dynorphin A levels in the cerebrospinal fluid¹⁵.

In 1972, a prototype of The cranial electrotherapy stimulation (CES) was developed by Dr. Margaret Patterson using the electrical stimulation to control the brain activity^{16,17}. U.S Food and Drug Administration approved it for the use of pulsed, low-intensity current on the earlobes or scalp. Many controlled study evidenced that CES is effective for the treatment of insomnia, depression, anxiety, head-

aches, drug withdrawal symptoms etc¹⁸. In 2003, the American company Neurowave Medical Technologies (Chicago, IL) customized a wristband with a low-frequency electrical stimulator targeted to an acupuncture point (PC6) and developed a new health-care product for reducing vomiting (ReliefBand). The case of Relief Band evidenced new possibilities for controlling symptoms without the use of drugs based on the acupuncture technique.

We were inspired by the traditional records that the stimulation of ankle joint acupuncture points-BL62 and KI6 together can treat sleep disorders and psychiatric disorders¹³, and tried to find the effect of low-frequency electrical stimulation by EEG measuring for developing the new method of non-invasive assistive device of brain activity in this research.

Low amplitude stimulation was performed for each subject in 12 sessions. The existing researches about electroacupuncture used a strong stimulation enough to notice and was not double-blinded. We tested the minimum noticeable strength before the stimulation session in each subject and

used the power of one step low; unnoticeable maximum stimulation to keep double-blinding in stimulation session. At the result of unnoticeable stimulation, there were no significant differences in the answers of the subjects from the 2 groups, when asked to guess the presence of real stimulation.

We used Background EEG comparing to find out the general changes in the brainwave before and after the 12 sessions. The alpha wave is in the 8~12 Hz range of brain waves. It is a well-known signal of a compatible state of the brain. In neurofeedback training, increasing the alpha power concomitant with the decrease in the theta power is considered an effective method of increasing cognitive performance¹⁹⁾. There are also many attempts to induce alpha brainwave by auditory²⁰⁾, visual²¹⁾, and composite stimulations²²⁾ for relaxation or improving cognitive ability. Beta and gamma waves are known as indicators of the state of stress or data processing. The decrease of the fast component in Background EEG means that the brain is more slow down and relaxed. However, the slow down of brain activity is not always good, especially for the older population. Because slower brain process speed is regarded as signs of the aging process²³⁾. In this study, despite the reduction in the fast waves(gamma and beta), the theta wave was not increased, but reduced significantly. Therefore, the alpha wave was selectively increased in the slow-wave area. While the real group showed the increase of alpha wave, the sham group showed oppsite result; increasing fast waves(gamma and beta) and decreasing slow waves(alpha and theta). Altogether, These results provide insight of the possibility that the low-frequency electrical stimulation on the acupuncture points at the ankle joint can assist the future development of a non-invasive and non-chemical treatment technique for stress or related cognitive problems.

This study was conducted to find the effects of low-frequency electrical stimulation on the BL62 and KI6 acupuncture points in the brain activity of the aged population and got a result of selective increase in alpha wave area. However, as a pilot study, we only chose women, the reason why they are easier to recruit and control the alcohol-free condition, and normal sleep state, etc.; therefore, the results

are not representative of both elderly men and women. At the other hand, there was only Background EEG analysis, and no study was done with the stress related questionnaires or else. We hope that another study involving the related questionnaires will be conducted in a near future, focusing on its effects on stress reduction and associated brain activities with both gender subject.

Conclusion

Low-frequency electrical stimulation on the acupuncture points(BL62 and KI6) of the ankle joint may stabilize elderly women brain by inducing the alpha wave selectively and reducing beta, theta, and gamma powers. Thus, we suggested this new method using the low frequency electrical stimulation on the acupuncture points as a candidate technique for stress or related cognitive problems.

Acknowledgements

This study was supported by grants from the Development of Footwear for Brain Activity Revitalization by IT Fusion Technology and Acupuncture Stimulation(G11070) and the Korea Institute of Oriental Medicine for the Development of Acupuncture and Moxibustion Health Technology(K13011).

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국문초록

목적: 본 연구는 노년층의 여성에게 신맥(BL62), 조해(KI6)혈에 대한 저주파자극이 뇌파에 어떠한 영향을 미치는지 알아보고 뇌 기능을 개선 하는데 비화학적이고 비침습적인 자극 방법의 후보로써 가능성을 탐구해보고자 실시된 탐색적 연구이다. **방법:** 31명의 건강한 여성 피험자(평균연령, 54.5세)를 대상으로 이중맹검 무작위배정 임상연구가 12세션동안 실시되었다. 시험군에서는 감지할 수 없는 최대의 저주파자극이 실시되었으며(평균전류량, 0.04 μ A), 대조군에서는 거짓자극이 실시되었다. 결과분석을 위해 12세션을 전후로 배경뇌파가 측정되었다. **결과:** 12세션의 자극이 실시된 후 대조군에 비해 실험군의 알파파 상대값은 11채널에서 유의한 증가를 보였으며($p < 0.05$), 감마파의 상대값은 7채널에서, 세타파의 상대값은 10채널에서 유의한 감소를 보였다. **결론:** 발목관절에 있는 신맥(BL62), 조해(KI6)혈에 대한 저주파 자극은 노년의 여성의 뇌에 베타, 세타, 감마파의 감소를 일으키는 반면 알파파를 선택적으로 증가시켜 뇌를 안정시키는 효과가 있는 것으로 보인다. 이러한 결과는 저주파자극이 향후 스트레스와 관련된 인지 문제를 치료하는 비침습적이고 비화학적인 도구로서의 가능성을 제공할 수 있을 것으로 보이며, 그 이전에 대한 추가적 연구가 필요할 것으로 보인다.