Effects of Scalp Acupuncture Versus Upper and Lower Limb Acupuncture on Signal Activation of Blood Oxygen Level Dependent (BOLD) fMRI of the Brain and Somatosensory Cortex

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Abstract

Objective: The objective of this article is to investigate brain activity of scalp acupuncture (SA) as compared to upper and lower limb acupuncture (ULLA) using functional magnetic resonance imaging (fMRI).
Subjects and methods: Ten (10) healthy right-handed female volunteers aged 20–35 were divided into 2 groups: a SA group and an ULLA group. The SA group had needles inserted at the left Sishencong (HN1), GB18, GB9, TH20, and the ULLA group at the right LI1, LI10, LV3, ST36 for 20 minutes, respectively. Both groups had tactile stimulation in the order of the right LI1, LI10, LV3, ST36 before and after acupuncture for a block of 21 seconds repeated 3 times. The blood oxygen level dependent (BOLD) fMRI was used to observe the brain and somatosensory cortex signal activation.
Results: We compared the signal activation before and after acupuncture needling, and the images showed signal activation after removing the acupuncture needles and the contralateral somatosensory association cortex, the postcentral gyrus, and the parietal lobe were more activated in the SA group. The right occipital lobe, the lingual gyrus, the visual association cortex, the right parahippocampal gyrus, the limbic lobe, the hippocampus, the left anterior lobe, the culmen, and the cerebellum were activated in the ULLA group.
Conclusions: We concluded that there were different signal activations of BOLD fMRI before and after SA versus ULLA, which can be thought to be caused by the sensitivity of acupoints and the different sensory receptors to acupuncture needling.

Introduction

Most meridians run either from scalp to extremities or in the reverse direction, enabling treatment of diseases through acupuncture of upper and lower limbs.1 On the other hand, scalp acupuncture (SA) has combined the concept of the cerebral cortex and its function with the principles of acupuncture, allowing treatment of diseases through needling of points on the scalp. In SA, the Stimulation Area corresponds with the cerebral cortex functions. It includes the Motor Area, Sensory Area, Language Area, Balance Area, and the Reproduction Area.2 Many parts of the cerebral cortex connect to these areas and play an important role in exchanging data between them. SA is used and has been reported to be clinically effective based on the principle that neurons in the cerebral cortex do not function directly on their own, but link to each other either temporarily or permanently to maintain connection.3–6 However, there is a need for fundamental research on SA and for a method to verify how the cerebral cortex functions; for this, functional magnetic resonance imaging (fMRI) is widely used.
Recently, fMRI has been used to image areas of the brain activated by visual, motor, and sensory stimuli and to visualize cognitive functions such as language and memory (functional brain mapping).7–19 Thus, early diagnosis and treatment of certain diseases through observation of brain...
functions prior to the structural change occurs has become possible.\textsuperscript{20-25} fMRI is also being utilized to verify the mechanisms and the efficacy of acupuncture. There have been several studies to observe which part of the brain is activated when a specific acupoint is stimulated,\textsuperscript{26-28} or after multiple acupoints were stimulated,\textsuperscript{29,30} and to see whether different methods of needling have different brain activations.\textsuperscript{31,32} These studies used acupuncture to a limited extent on the upper and lower limbs to see the effects of acupuncture on the brain.

However, this study observed the activation and deactivation of the brain and investigated which part of the brain performs specific functions of the high cerebral cortex when tactile stimulation was done on upper and lower limbs using fMRI. Furthermore, we observed the duration of the effects of acupuncture and compared blood oxygen level dependent (BOLD) fMRI signal activations before and after acupuncture in the SA and the upper and lower limb acupuncture (ULLA) groups.

Materials and Methods

Subjects

Ten (10) healthy right-handed female volunteers aged 20–35 were recruited and consented to the study. None of the participants were menstruating or pregnant. Volunteer candidates suffering from neurological, mental, or internal problems; drug abuse; alcohol abuse; or those with a history of cardiovascular or cerebrovascular diseases and on medications that could affect cerebral blood flow were excluded. Caffeinated drinks such as coffee were restricted on the day of the examination.

Materials

For acupuncture, disposable, stainless steel 0.25 mm × 40 mm (diameter × length) needles made by Dong-bang Acupuncture & Moxibustion Company were used.

Methods

The 10 subjects were randomized into 2 groups: a SA group and an ULLA group. After 30 minutes of rest, cotton tips were used to stimulate the members of both groups 3 times on the right upper and lower limbs (LI1, LI10, LV3, ST36) and the first fMRI was administered. After 5 minutes of rest, the SA group was stimulated at the left Sishencong (HT1) and the first fMRI was performed. After multiple comparison using NONE p-value below 0.001 was considered significantly different.

Image acquisition

Preparations. A subject was positioned supine, with the head in the standard head coil to adapt to the surroundings after 30 minutes of rest. The head was fixed by a sponge and during fMRI shooting the subject was not supposed to move or open her eyes. The fMRI room was lit darkly and there was no sound other than the sounds from the fMRI machine. All images were acquired by a well-trained professional operator at East-West Neo Medical Center, Kyunghee University.

fMRI imaging. 3.0 Tesla MRI (Philips, Acheiva, Best, The Netherlands) was used. To maximize the effect of BOLD, gradient-echo technique was used. With the echo planar imaging technique, matrix size 64 × 64, field of view (FOV) 230 × 148 × 230-mm T2-weighted images (echo time [TE] = 30 ms, repetition time [TR] = 3000 ms, flip angle = 90°) were acquired. There were 30 slices, 5-mm width, the gap between slices was 0 mm, the size of voxel was 3.43 × 3.43 × 5 mm, and there were 42 volume images.

Anatomical MR acquisition. Additional 3D-T1-weighted images (TE = 5 ms, TR = 9.335 ms, flip angle = 8°, FOV = 240 × 240 × 185 mm, 120 slices, slice width 1.0 mm) were obtained to see the anatomical structure.

Data analyses

SPM 2 (Wellcome Department of Cognitive Neurology, London, UK) was used for data analyses.

Motion correction. Motion of the head was calculated by rotation and translation on X, Y, and Z coordinates and realigned automatically using 3D motion correction.

Spatial normalization. fMRI images and anatomical MR images have different resolutions, so there needs to be a procedure to compound on the common coordinates. First, anatomical images were standardized using standard anatomical space\textsuperscript{33} devised by Talairach and Tournoux. Anatomical images before normalization and fMRI images went through coregistration, and anatomical images were normalized in the same fashion as the anatomical images.\textsuperscript{34}

Spatial smoothing. Gaussian filter was used to smooth the checkered 64 × 64 plane resolution and 5 mm in width data. The full width at half maximum was set to 9 × 9 × 12 mm for multi-analysis.

Statistical analysis. 1. Individual statistical analysis.

Each normalized image was processed by general linear model (GLM) taking hemodynamic response into consideration. Among the GLM-processed BOLD signal, we chose significantly activated areas to analyze.

We obtained a contrast map for activated areas of each experimental group. Through multiple comparison using NONE p-value below 0.001 was considered significantly different.

2. Group statistical analysis

To compare the BOLD fMRI signal activation before and after acupuncture, we used a contrast map of individual patient and went through an analysis of variance test.
1. Study design

10 Healthy, right-handed female volunteers aged 20–35 were randomized; scalp acupuncture (SA) Group: 5 upper and lower limb acupuncture (ULLA) Group: 5

↓

30-minute rest

↓

BOLD-based functional MRI, fMRI Tactile stimulation each point for 21 seconds repeated 3 times (R-S-R-S-R-S) 126 seconds, all 4 points (at LI1, LI10, LV3, ST36 about 9 minutes)

↓

After 5-minute rest, the SA group and the ULLA group had 4 acupoints stimulated, respectively. 20-minute needle retention, de qi, 30-sec de qi before pulling out the needles

SA: sishencong (HN1) GB18, GB9, TH20 (left side)
ULLA: LI1, LI10, LV3, ST36 (right side)

↓

BOLD-based functional MRI, fMRI Tactile stimulation each point for 21 seconds repeated 3 times (R-S-R-S-R-S) 126 seconds, all 4 points (at LI1, LI10, LV3, ST36 about 9 minutes)

↓

Analysis of fMRI before and after acupuncture

SA: sishencong (HN1) GB18, GB9, TH20 (left side)
ULLA: LI1, LI10, LV3, ST36 (right side)

R: Rest, S: stimulation

2. Procedure of tactile stimulation

DS | S1 | S2 | S3
---|----|----|----
12s 0s | 21s | 42s |
63s | 84s |
105s | 126s |

Dummy scan was carried out during 12 seconds before the experiment. After 21 seconds of rest, tactile stimulation with cotton tips at the acupoints was performed for 21 seconds. This procedure (Rest-S1-Rest-S2-Rest-S3) was repeated 3 times (in the order of LI1, LI10, LV3, ST36).

DS: dummy scan, R: rest, S: stimulation

P-value less than 0.001–0.05 was considered significantly different.

Results

Change of BOLD fMRI signal activation after tactile stimulation (total 10 volunteers)

LI1. Tactile stimulation at the right LI1 activated the left parietal lobe, the postcentral gyrus, the primary somatosensory cortex (BA 1, 2, 3), and the primary motor cortex (BA 4) ($p = 0.001$) (Fig. 1).

LI10. Tactile stimulation at the right LI10 activated the right frontal lobe, inferior frontal gyrus, the middle frontal gyrus (BA 9, 44, 45, $p = 0.005$) and the left sublobar, the claustrum, the frontal lobe, and the subgyral insula (BA 13, 45, 47, $p = 0.01$) (Fig. 1).

LV3. Tactile stimulation at the right LV3 activated the left parietal lobe, the inferior parietal lobule, the postcentral gyrus, BA 2, 40 (primary somatosensory cortex, supramarginal gyrus part of Wernicke’s area, $p = 0.001$) (Fig. 1).

ST36. Tactile stimulation at the right ST36 activated the left frontal lobe, the superior frontal, the middle frontal inferior frontal gyrus, the subgyral (BA 8, 9, 10, 46), the interhemispheric, the right cerebellum, the posterior lobe, the pyramis, the tuber, the uvula, the inferior semilunar lobule, the parietal lobe, the inferior parietal lobule, the sublobar, the
Change of BOLD fMRI signal activation before and after acupuncture in the ULLA group (group statistical analysis, 5 subjects)

There was more signal activations before acupuncture in the left and right sublobar, the thalamus, the right frontal lobe, the left inferior semilunar lobule and after acupuncture the left and right occipital lobe, the lingual gyrus, the visual association cortex (BA 18, 19), the right parahippocampal gyrus, the limbic lobe, the hippocampus, the left anterior lobe, the culmen, and the cerebellum (Table 2).

Comparison between BOLD fMRI signal activation of the SA group versus upper and lower limb group (Group statistical analysis)

In the ULLA group, there was more activation on the left side of the brain such as the left frontal lobe, the precentral gyrus, the postcentral gyrus, the subcentral area, the parietal lobe, and the right parietal cortex before acupuncture and both sides of the occipital lobe, the lingual gyrus, the visual association cortex, and the right parahippocampal gyrus, the hippocampus, the limbic lobe, the left anterior lobe, the culmen, and the cerebellum became more activated.

Discussion

With the instrumental development of MRI and its new imaging techniques in the 1990s, it has become possible for us to get functional information of the brain such as diffusion, perfusion, MR spectroscopy, and functional brain mapping as well as anatomical information. Images by fMRI, which is capable of mapping brain functions, show a close correlation with those obtained by positron emission tomography, and are excellent in spatial resolution and do not require any radioisotope or contrast media with its repeated use, so fMRI is being widely used. Healthy subjects have been part of the studies that visualize images of activated brain areas invoked by visual, motor, and sensory stimulation. Recently, cognitive functions such as language and memory functions are also being visualized by fMRI. Clinically in brain tumor removal operations, fMRI is used to decide which part of the tumor should be operated and to predict functional damages after the surgery. It is also used to locate language dominance in patients with epilepsy, to evaluate recovery from strokes, and to explain reorganization of the brain.

In the field of Korean traditional medicine, fMRI is mainly used to investigate the mechanisms of acupuncture and to verify its effect. There have been several studies to observe which part of the brain is activated after a specific acupoint is needled, or after multiple acupoints were needled, and to see whether different methods of needling have different brain activations. However, there has been no study so far involving scalp acupuncture with fMRI because of technical problems. A previous study was done to see whether the fMRI images were still valid after 30 minutes of acupuncture, and was designed to investigate brain activity after acupuncture needles were pulled out. Thus, we designed this study accordingly to compare before and after acupuncture needling when sensory tactile stimulation was done throughout the session.

This fMRI study proves the theory that tactile stimulation is received bilaterally in the brain but shows contralateral dominance. Also, tactile stimulation is consistent with high cerebral cortex functions and the specific acupoint ST36 showed diverse activations in the frontal lobe, the parietal lobe, the cerebellum, the posterior lobe, as well as the inter-hemispheric.

In a preliminary study where they used electroacupuncture, manipulation time varied at the same frequency in each subject to make sure de qi was achieved. After SA on the left side, we could observe that the right parietal lobe, the postcentral gyrus, and the somatosensory association cortex were activated (Table 1). It mostly accords with the areas activated by tactile stimulation, but the fact that the right parts of the brain were more activated by acupuncture needling shows that acupuncture stimulates the contralateral side of the brain compared to tactile stimulation. We could infer that tactile stimulation sets off the left sides of the brain activations and SA stimulates contralateral parts of the brain.

In the upper (LI1, LI10) and lower (LV3, ST36) limb acupuncture group, we could see both sides of sublobes, the thalamus, right frontal lobe, and left inferior semilunar lobe activated before acupuncture and both sides of the occipital lobe, the lingual gyrus, the visual association cortex, and the right parahippocampal gyrus, the hippocampus, the limbic lobe, the left anterior lobe, the culmen, and the cerebellum activated (Table 2). To sum up, after ULLA activations in the left sublobe, the thalamus, and the frontal lobe disappeared and the bilateral occipital lobe, the lingual gyrus, the visual association cortex and the right parahippocampal gyrus, the hippocampus, the limbic lobe, the left anterior lobe, the culmen, and the cerebellum became more activated. It indicates that after pulling out the needles, the activations of the brain remain as in the SA group but in the ULLA group it showed more signal activations in various regions than the SA group or in case of tactile stimulation. Among the 4 acupoints, ST36 showed the signal activations in the occipital lobe, the visual association cortex, and the cerebellum, suggesting that ST36 has the strongest effect. On the other hand, the right parahippocampal gyrus, the hippocampus, and the limbic lobe were only activated because the left sides were offset, showing dominance only on the right sides. This is possibly explained as follows. Acupuncture at ST36 sends signals to the multiple levels at the occipital lobe, the lingual gyrus, the visual association cortex, and the right parahippocampal gyrus, the hippocampus, the limbic lobe, the left anterior lobe, the culmen, and the cerebellum.
In comparing the SA and the ULLA groups, it may be concluded that the ULLA group had more activated areas doubled with tactile stimulation at the same acupoints, whereas in the SA group the effect of the left acupoints on the scalp and that of the right lower limb acupoints counterbalances each other, or further research is needed to see whether SA chiefly activated contralateral parts of the brain.

The sensory system of our body perceives and controls the organs against surroundings consciously and unconsciously. The sensory system consists of the exteroceptive sensation, the interoceptive sensation, and the proprioception sense. The exteroceptive sensation perceives stimuli or change from surroundings such as pain, temperature, position, and touch. Thus, stimuli such as acupuncture and tactile stimulation are perceived through receptors, which change mechanical, chemical, and optical energy into electronic signals and the generated action potential is transmitted to the central nervous system via the special sensory route. Various outer

**FIG. 1.** Brain areas with significantly increased cortical and brain activation during sensory tactile stimulation. HT, height threshold; ET, extent threshold; BA, Brodmann area.
stimuli are perceived by respective sensory receptors or sensory end organs and via peripheral nerves reaching the central nervous system, the dorsal root ganglia, the spinal cord, the brain stem, the thalamus, and the cortex.

Tactile stimulation on the upper and lower limb synapses at the nucleus cuneatus and nucleus gracilis of the medulla, respectively. Then the secondary afferents cross on the other side of the brain via the internal arcuate fiber and synapse in the thalamus (ventroposterolateral [VPL] nucleus) via the medial lemniscus, which ascends all the way through the brainstem to the primary somatosensory cortex through the posterior limb of the internal capsule.

SA travels through the trigeminothalamic pathway on the fifth cranial nerve, and its first sensory neuron is in the spinal gray matter of the spinal cord and has a fast conduction speed through wide-diameter fibers. Information from the peripheral sensory end organs and via peripheral nerves reaching the central nervous system is transmitted through the afferent fibers (corticospinal fibers) of the spinal cord through the Aβ fiber. One segment upward synapses at the second neuron in the dorsal horn, goes through the ventral white commissure, ascends to the thalamus (VPL nucleus) through the contralateral white matter. When the SA group and the upper and lower limb group were compared, the latter was shown to follow this route because the left frontal lobe, the precentral gyrus, the postcentral gyrus, the subcentral area, the parietal lobe and the right parietal lobe, the postcentral gyrus, and the primary somatosensory cortex including insula were activated (Table 1).

When we compared results between before and after acupuncture, the ULLA group showed activations in the cerebellum, the occipital lobe, the visual association cortex, the limbic lobe, the hippocampus, and the posterior lobe (Table 2). This can be explained by the following two theories: that the subject could have moved her eyes or acupuncture has something to do with the spinocerebellar tract. The unconscious proprioception is conveyed through the dorsal and ventral spinocerebellar tract to the cerebellum and engages in the unconscious control of posture and movement. This comes from the neuron in the intermediate gray matter of the spinal cord and has a fast conduction speed through wide-diameter fibers. Information from the lower limb is transmitted to both sides of the cerebellum. The dorsal spinocerebellar tract and the cuneocerebellar tract deliver the proprioception and the exteroceptive signal generated in the muscle to the cerebellum and control the feedback of fine motor control through the cortical and the subcortical motor nucleus. Therefore, we could observe both sides of the cerebellum activations after acupuncture needling, and further research is required.

### Table 1. Brain Areas with Significantly Increased Signal Activation During Sensory Stimulation Before and After Scalp Acupuncture

<table>
<thead>
<tr>
<th>Brain regions included in cluster</th>
<th>Side</th>
<th>BA</th>
<th>Coordinates x y z</th>
<th>Peak Z-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parietal lobe, postcentral gyrus</td>
<td>Right</td>
<td>30, -52, 70</td>
<td>3.30</td>
<td></td>
</tr>
<tr>
<td>Parietal lobe, postcentral gyrus</td>
<td>Right</td>
<td>26, -52, 72</td>
<td>3.39</td>
<td></td>
</tr>
<tr>
<td>Parietal lobe, superior parietal lobe</td>
<td>Right</td>
<td>34, -24, 62</td>
<td>3.90</td>
<td></td>
</tr>
</tbody>
</table>

Height threshold: \( p = 0.001 \) uncorrected. BA, Brodmann area.

### Table 2. Brain Areas with Significantly Increased Signal Activation During Sensory Stimulation After Upper and Lower Limb Acupuncture (Height Threshold: \( p = 0.001 \) Uncorrected)

<table>
<thead>
<tr>
<th>Brain regions included in cluster</th>
<th>Side</th>
<th>BA</th>
<th>Coordinates x y z</th>
<th>Peak Z-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sublobar, thalamus</td>
<td>Left</td>
<td>-2, -24, 8</td>
<td>3.53</td>
<td></td>
</tr>
<tr>
<td>Cerebellum, posterior lobe, inferior semilunar lobule</td>
<td>Left</td>
<td>-20, -84, -40</td>
<td>3.51</td>
<td></td>
</tr>
<tr>
<td>Sublobar, thalamus</td>
<td>Right</td>
<td>4, 0, 6</td>
<td>3.11</td>
<td></td>
</tr>
<tr>
<td>Fronto lobe, inferior frontal gyrus,</td>
<td>Right</td>
<td>45</td>
<td>46, 24, 14</td>
<td>3.11</td>
</tr>
<tr>
<td>Occipital lobe, lingual gyrus,</td>
<td>Right</td>
<td>18</td>
<td>32, -74, -6</td>
<td>3.45</td>
</tr>
<tr>
<td>Occipital lobe, middle occipital gyrus,</td>
<td>Right</td>
<td>19</td>
<td>40, -78, 4</td>
<td>3.20</td>
</tr>
<tr>
<td>Limbic lobe, parahippocampal gyrus, hippocampus</td>
<td>Right</td>
<td>22, -42, 6</td>
<td>3.17</td>
<td></td>
</tr>
<tr>
<td>Occipital lobe, lingual gyrus</td>
<td>Left</td>
<td>-22, -76, -2</td>
<td>3.50</td>
<td></td>
</tr>
<tr>
<td>Cerebellum, anterior lobe, culmen</td>
<td>Left</td>
<td>-16, -38, -12</td>
<td>3.22</td>
<td></td>
</tr>
</tbody>
</table>

Pre, before upper and lower limb acupuncture (ULLA); post, after ULLA; BA, Brodmann area.
Table 3. Brain Areas with Significantly Increased Cortical Activation During Sensory Stimulation After Scalp Acupuncture Versus Upper and Lower Limb Acupuncture (Height Threshold: \( p = 0.0001 \) Uncorrected)

<table>
<thead>
<tr>
<th>Brain regions included in cluster</th>
<th>Side</th>
<th>BA</th>
<th>Coordinates ( x \ y \ z )</th>
<th>Peak Z-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper and lower limb &gt; scalp</td>
<td>Left</td>
<td>43</td>
<td>(-48, -6, 12)</td>
<td>4.29</td>
</tr>
<tr>
<td>Frontal lobe, precentral gyrus</td>
<td>Left</td>
<td>43</td>
<td>(-48, 10, 18)</td>
<td>3.54</td>
</tr>
<tr>
<td>Parietal lobe, postcentral gyrus</td>
<td>Left</td>
<td>13</td>
<td>(-42, 0, 8)</td>
<td>3.30</td>
</tr>
<tr>
<td>Insula</td>
<td>Right</td>
<td>2</td>
<td>(48, -24, 36)</td>
<td>3.43</td>
</tr>
<tr>
<td>Parietal lobe, postcentral gyrus</td>
<td>Right</td>
<td>3, 4</td>
<td>(38, -24, 60)</td>
<td>3.69</td>
</tr>
<tr>
<td>Scalp &gt; upper and lower limb acupuncture</td>
<td>Right</td>
<td>3, 4</td>
<td>(34, -24, 62)</td>
<td>3.56</td>
</tr>
<tr>
<td>Frontal lobe, precentral gyrus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parietal lobe, postcentral gyrus</td>
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<td>Parietal lobe, postcentral gyrus</td>
<td></td>
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</tr>
</tbody>
</table>

BA, Brodman area.

Conclusions

In conclusion, when the 4 acupoints were tactile stimulated, it was received bilaterally in the brain but showed dominance in the contralateral side of the brain. It is consistent with the functions of high cerebral cortex. On tactile stimulation at ST36, various locations such as the frontal lobe, the parietal lobe, the posterior lobe, and the cerebellum as well as the inter-hemispheric showed activations. In the SA group it showed more activation after acupuncture to prove the stimulation remains even after pulling out the needles. The left SA activated the right side of the brain. The left SA activated the right side of the brain, which can be explained as signifying that the left side of the brain activation could have been offset by tactile stimulation or that acupuncture activated the brain contralaterally. It also showed brain activations after the needles were pulled out in the ULLA group, and the typical contralateral activations were different from those with tactile stimulation.

This study is different from the previous study, which focused on the parts of the brain activated after a specific acupoint was needle24–29,41 in that it had tactile stimulation at the 4 acupoints before and after SA and ULLA, respectively, and observed the effects of acupuncture after pulling out the needles and the difference of brain signal activations between the two groups. Thus, we excluded the data of each acupoint’s brain activity in this article.

On a final note, the LI1 acupoint showed contralateral and bilateral activations, particularly in the limbic lobe, and the anterior cingulate to show that LI1 may have aroused emotional stimulation caused by strong pain. In the upper and lower limb group, LI10 and LV3 did not show signal activation after the needles were pulled out in the limbic lobe, and the anterior cingulate where it controls fear and instinct,40,42 thus showing a need for further research on a specific acupoint involving in the pain control mechanisms by suppressing the pain stimulus ascending to the brain through the descending analgesia circuit.

Acknowledgments

We would like to thank Ja-Young Gwak and Yun-Kyung Park for their time and efforts spent on this study. This research was supported by the Kyunghee University Research Fund in 2007 (KHU-20070622).

Disclosure Statement

All of the authors declare that no competing financial interests exist.

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