

Neural Activation in the Somatosensory Cortex by Electrotactile Stimulation of the Fingers: A Human fMRI Study

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Objective: The aim of this study is to investigate 1) somatotopic arrangement of the second and third fingers in SI area 2) difference of neural activation in the SI area produced by stimulation with different frequencies 3) correlation between the intensity of tactile perception by different stimulus intensity and the level of brain activation measurable by means of fMRI.

Background: Somatosensory cortex can obtain the information of environmental stimuli about "where" (e.g., on the left palm), "what" (e.g., a book or a dog), and "how" (e.g., scrub gently or scrub roughly) to organism. However, compared to visual sense, the neural mechanism underlying the processing of specific electrotactile stimulus is still unknown.

Method: 10 right-handed subjects participated in this study. Non-painful electrotactile stimuli were delivered to two different finger tips of right hand. Functional brain images were collected from 3.0T MRI using the single-shot EPI method. The scanning parameters were as follows: TR and TE were 3000, 35ms, respectively, flip angle 60, FOV 24 x 24cm, matrix size 64 x 64, slice thickness 4mm (no gap). SPM5 was used to analyze the fMRI data.

Results: Significant activations produced by the stimulation were found in the SI, SII, the subcentral gyrus, the precentral gyrus, and the insula. In all participants, statistically significant activation was observed in the contralateral SI area and the bilateral SII areas by the stimulation on the fingers but ipsilaterally dominant. The SI area representing the second finger generally located in the more lateral and inferior side than that of the third finger across all the subjects. But no difference in brain area was found for the stimulation of the fingers by different frequencies. And two typical patterns were observed on the relationship between the perceived psychological intensity and the amount of voxels in the primary sensory cortex during the stimulation.

Conclusion: It was possible to discriminate the representation sites in the SI by electrotactile stimulation of digit2 and digit3. But we could not find the differences of the brain areas according to different stimulation frequencies from 3 to 300Hz.

Application: The results of the study can provide a deeper understanding of somatosensory cortex and offer the information for tactile display for blinds.

Keywords: Electrotactile stimulation, Frequency, Functional magnetic resonance imaging, Somatosensory area

1. Introduction

Tactile sensation is one of the important primary senses acquiring and judging the most basic information on object through dermal sensation. Namely, tactile sensation is a sensory function sensing physical stimulation on skin. The tactile sensation can be divided into pressure sensation, friction sensation and location sensation. A human identifies the surrounding environment and objects by accepting and integrating the sensations, and judges and evaluates the objects through emotional pleasantness and unpleasantness. Since the emotional evaluation on the objects may affect decision making on purchase, etc., it has very important significance in industrial setting. As the importance of tactile sensation emerges recently, attempts to develop technologies to perceive and embody the tactile sensation that can be utilized in robot development and clinical medicine by applying the tactile sensation increase. To develop such a tactile sensation embodying technology, it is essential to examine the mechanism of tactile sensation. Therefore, studies on nerve network and psychophysical function on tactile sensation continue so far. Especially, as brain area activation has been effectively analyzed scientifically since 1990s, and can become visualized, due to the development of brain imaging technology (Ogawa et al., 1992), studies to examine brain mechanism are carried out, according to tactile stimulation location and physical characteristics by using brain imaging technology.

Kurth et al. (1998) proposed electro tactile stimulation on the second and fifth fingers to 20 experiment participants. As a result of individual analysis, it was identified that the activation area of the second finger was located in the more inferior and lateral side, compared to the fifth finger. Boakye et al. (2000) tried to find out the activation pattern of somatosensory area, according to frequency difference using fMRI (functional magnetic resonance imaging). 5.1Hz electrotactile stimulation was presented to five participants, and 50Hz electrotactile stimulation was presented to other five participants. As a result of group analysis, the SI (somatosensory cortex I) and SII (somatosensory cortex II) areas and parietal periculum, insula, frontal cortex, supplementary motor, posterior parietal cortices (BA7, 40) areas were activated. According to the comparison of stimulation frequency difference, there was no difference in the 5.1Hz and 50Hz volumes of cortical activation in the SI and SII areas. Francis et al. (2000) presented 80Hz vibrotactile stimulation to the second and fifth fingers of eight participants, and 30Hz and 80Hz vibrotactile stimulation to the second fingers of four participants. As a result, the SI and SII areas and subcentral gyrus, precentral gyrus, posterior insula, posterior parietal region, posterior cingulate areas were activated. Also, in the SI area, the cortical area of the second finger was located in the more lateral side, compared to the fifth finger. There was no significant difference in the activation area size, according to frequency. Harrington and Hunter (2001) tried to examine the somatosensory cortex differences, according to frequency, namely, the differences of Messner and Pacinian receptor in the brain cortical area. To this end, they presented non-painful stimulation to the three fingers (1, 2 and 3) of seven participants using the vibrotactile buzzer. The 35Hz and 150Hz stimuli were presented to the three fingers for 19.2 seconds, respectively, (five times of repetition). According to SI area analysis result, BA 1, 2 and 3 were activated from three participants out of the seven participants by 35Hz stimulation, and only BA 1 and 2 were activated by 150Hz stimulation. According to SII area analysis result, the activated cortical area after presenting 150Hz stimulation and the cortical area activated after presenting 35Hz were overlapped (Harrington and Hunter, 2001).

As such, although, there were many studies to examine the brain mechanism of stimulated frequencies using fMRI, these preceding studies mostly used only two types of frequency stimuli as the comparison of difference between low and high frequencies. And thus, there was limitation in examining brain activation mechanism. However, this study is expected to investigate influences, according to differently presented stimulation frequencies, as well as the stimulation types and variables that were not applied in the preceding studies, by making a paradigm that can diversely present frequencies ranging from low frequency to high frequency including 10Hz, 30Hz, 50Hz, 150Hz and 300Hz.

Also, this study is to verify the homunculus acquired by electrotactile stimulating patients' brains through the imaging technique. Although, the preceding studies tried to examine tactile cortical area differences responding to each finger, the existing studies tried to identify the differences in areas responding to the second and fifth fingers. This study investigates whether the classification

of brain cortical areas responding to the second and third fingers, namely, the fingers located closely, is possible.

By analyzing the correlation of psychological data and brain cortical responses, this study intends to examine mental-physiological relationship. The studies researching the differences in activation by stimulation frequency at the initial stages mainly focused on SI area. This study also analyzes ROI (region of interest), focusing on SI area, based on the preceding studies. This study checks the response mechanism of brain cortex by tactile stimulation, and examines relations with psychological tactile sensation. Towards this end, this study is to discover functional relationship between these by identifying the dynamic characteristics of external stimuli, resultant psychological perception and relationship between responses of brain cortex using eletrotactile stimulation. In other words, this paper identifies the differences in brain activation areas, according to tactile stimulation presented in different areas. This paper investigates responses on the somatosensory cortex by the frequency of electrotactile stimulation. Lastly, this paper identifies psychological perception and relationship between somatosensory cortical responses.

2. Method

2.1 Subjects

12 undergraduate students at Chungnam National University participated in the experiment. All the participants are female and right-handed students. Their age distribution was from 19 to 25, and they had no huge difficulties in the feeling of tactile stimulation without the history of brain injury or mental disease. The experiment participants were limited to female students in this study, and the reason is that variability related to sensitivity or the status of pain is huge, according to gender. Overall things on the experiment were explained to all the participants, and consent was acquired from them. All experiment procedures conformed to the regulations of the Institutional Review Committee.

2.2 Electrotactile stimuli

This study used low frequency therapeutic apparatus used in everyday life to present electrotactile stimulation. The low frequency therapeutic apparatus used in this study can present various frequencies between 3-300Hz, and physical intensity can be controlled from 1 to 8. This study intends to present equal stimulation intensity, according to all frequencies, since the purpose of this study is to see the differences in brain activation responses, according to stimulation frequency. To find proper stimulation intensity, a preliminary experiment was conducted targeting 30 people. Namely, whether stimulation was felt was measured, when stimulation was presented at physical intensity of 1 to 8, and also whether pain was felt was measured, when stimulation was presented at physical intensity of 1 to 8. As a result, when stimulation with weak physical intensity (intensity 2 and lower) was presented at low frequency (3Hz), all the participants did not perceive the stimulation, and 93.3% of the participants perceived the stimulation, when stimulation with physical intensity 4 was presented. When stimulation (7 and higher) with physical intensity at 300Hz was presented, all the participants felt pain and unpleasantness. When stimulation with physical intensity 4 was presented, 10% of the participants said pain was caused. When stimulation with physical intensity 5 was presented, 56.6% of the participants said pain was caused. Through this preliminary experiment, the physical intensity 4.5 to be used in this experiment was selected as proper physical intensity not causing pain, while the participants can perceive stimulation. This study composed the paradigm to present various frequencies from low to high frequencies including 3Hz, 10Hz, 30Hz, 100Hz and 300Hz to supplement the limitation of existing preceding studies, in which frequency was limited, and to compare the differences of low and high frequencies.

Based on the preceding studies that identified the differences of brain cortex responding to the second and fifth fingers, this study presented stimulation to the second and third fingers, respectively, to find out whether brain cortical area classification responding to the fingers located closely is possible.

2.3 Experimental procedures and stimuli paradigm

The experiment participants was guided to read experiment instructions and be familiar with them, as they had time to adapt to the experiment in the lab, while electrodes were attached to their fingers. To prevent noise occurrence, due to head shaking, an instruction not to move head was provided upon shooting the images. And then, about 10-min of experiment was carried out (three dummy images: nine sec, five 30 sec blocks: five min), after lining anterior commissure and posterior commissure through about 10-min shimmering in the fMRI. After that, about 15-min of T1 image was acquired (Figure 1). The experiment stimulation paradigm consisted of two sessions with boxcar design (second and third fingers) (Figure 2), and each session was comprised of ten blocks. In each block, control stimulation and tactile stimulation (3, 10, 30, 100, 300Hz) were presented alternately for 15 sec. When the experiment was finished in the fMRI, the experiment participants evaluated psychological intensity on the stimulation of five frequencies. The experiment was conducted to each participant under the same condition each time using such a process.

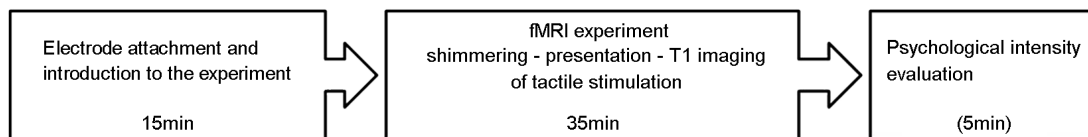


Figure 1. Experimental procedures

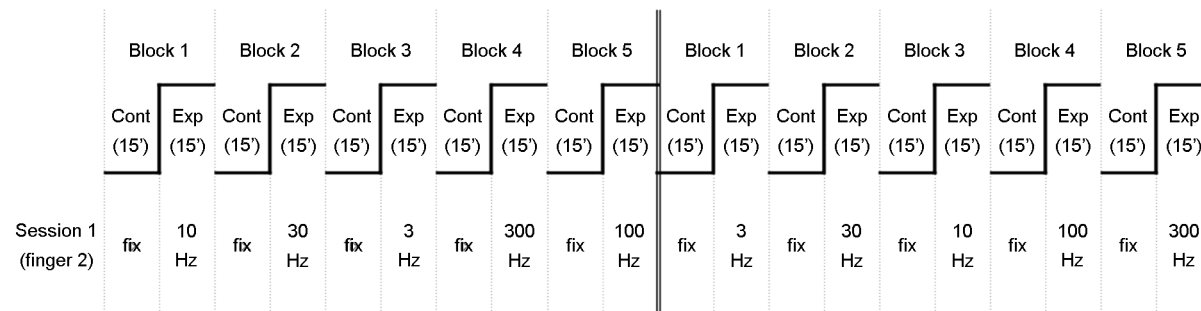


Figure 2. The example of stimuli paradigm

2.4 Psychological data acquisition

After the fMRI experiment was finished, the experiment participants wrote psychological evaluation scale to evaluate how much the electro-tactile stimulation set was strong. To evaluate how much tactile stimulation was felt, the scale consisted of five-scale: hardly felt (one point) to very strongly felt (five points).

2.5 MRI data acquisition and analysis

For MRI data acquisition, ISOL 3.0T Forte installed at the fMRI Center was used. While the participants undertake the task, while feeling the tactile stimulation presented through the electrodes attached to the fingers, the MRI data was acquired using the EPI-BOLD (Echo Planner Imaging Blood Oxygen Level Dependent) technique. Other conditions were as follows:

TR 3000, TE 35msec, slice thickness 4mm no gap, 35 slices, 64×64 Matrix, FOV 24×24cm, flip angle 60°. For each experiment session, 103 total volume images were acquired including three dummy images for 300 sec. Concerning anatomical brain images, T1 emphasis images were collected (TR/TE 3000/35msec, slice thickness 1mm no gap, 256×256 Matrix, FOV 24×24cm, flip angle 60°).

The fMRI data was ultimately analyzed through the following procedures using SPM 99 software (Wellcome Department of Cognitive Neurology, London, UK): slice timing indicating calibration on the image (data) acquisition time, motion-correction for head movement calibration, coregistration to coordinate anatomical images and functional images and normalization to conform individual brain to standard brain (Montreal Neurologic Institute, MNI), and then smoothing stage using 8mm Isotropic Gaussian Kernel. From the pre-processing, two participants' brain MRI data could not be used, due to big head movement. Targeting the data from the remaining ten participants, the activation of nerve network was identified at the stimulation presentation time, when significant activation was bigger than the base condition using subtraction, after finding the statistically significantly activated brain area in each condition through the general linear model. Regarding the area coordinate confirmed in the brain function map, the brain area was checked using Talairach-Tournoux system in the MNI coordinate.

3. Results

3.1 Brain activation by stimulation of fingers

Among the 12 participants, two participants, whose head movement was severe to affect brain image signal, were excluded from brain image analysis. As a result of individual analysis, all the ten participants' contralateral SI area (brodmann area 1, 2 and 3 on the left hemisphere) was activated. Among them, four participants' bilateral SI areas were activated. All the ten participants' bilateral SII areas (SII area of left and right hemispheres, brodmann area 40) were activated. As a result of group analysis, when stimulation was presented to a finger, the contralateral SI area was activated. The activated areas, other than the somatosensory area, were bilateral inferior frontal gyrus, bilateral middle frontal gyrus, right insula and left inferior parietal lobule (Figure 3).

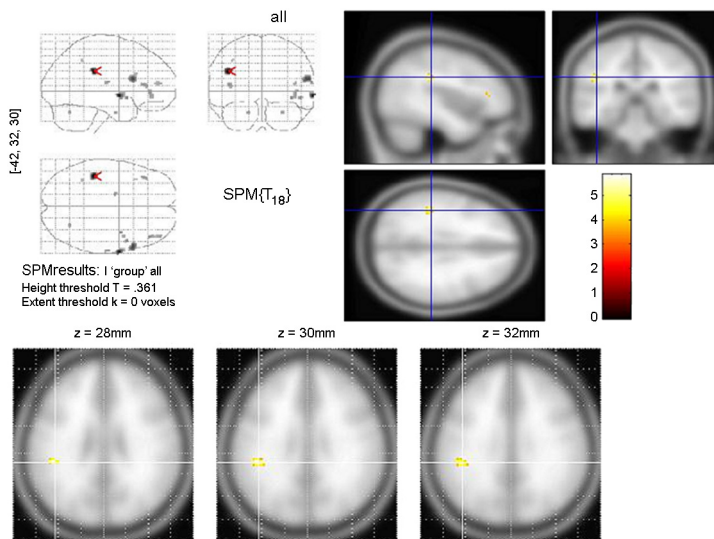


Figure 3. Brain activation by group analysis

3.2 Brain activation with different frequencies

This study designated left SI area as the region of interest (ROI), and location differences were compared between activation areas, according to frequency. Through the group analysis result, Table 1 summarizes the voxel coordinates with the biggest Z score, and the Z scores among the activated SI areas ($p < .001$, uncorrected).

Table 1. Montreal Neurological Institute (MNI) coordinates of cortical areas activated by stimuli of each frequency

	Talairach coordinate			Z-score
	X mm	Y mm	Z mm	
3	-40	-32	30	4.3
10	-48	-22	34	4.5
30	-32	-42	56	3.93
100	-50	-34	44	5.89
300	-56	-32	52	4.5

The following figure shows SI area that is activated in the contrast condition of each stimulation presentation and base state (Figure 4). As a result of group analysis, there was difference in voxel location having the biggest Z score within the activated area, according to frequency; however, there were many parts, where activation cluster was overlapped overall.

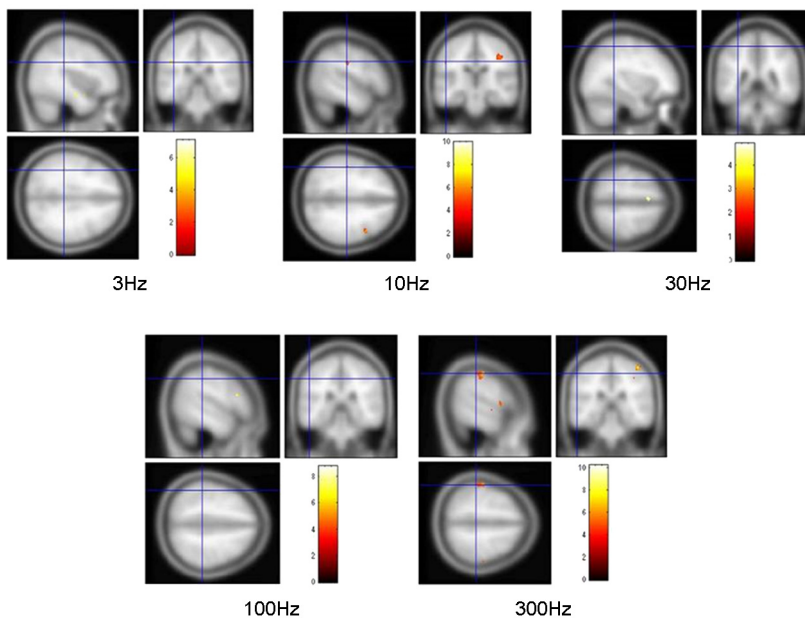


Figure 4. Brain activations with different frequencies (3Hz, 10Hz, 30Hz, 100Hz, 300Hz)

3.3 Brain activation area by stimulation of two different fingers

From all the ten participants, the locations of brain area responding to the second and third fingers were differently demonstrated, respectively (Table 2). The following figure shows activation within the SI area of a participant (Figure 5). From seven out of the ten participants, the somatosensory cortex area representing the second finger was located in the more lateral and inferior side than the somatosensory cortex area representing the third finger.

Table 2. Montreal Neurological Institute (MNI) coordinates of different finger representation

Participant	Second finger			Third finger		
	X mm	Y mm	Z mm	X mm	Y mm	Z mm
1	-55.3	-35.5	52.8	-19.4	-31.7	53.6
2	-63.6	-27.9	45.5	-53.7	-27.9	47.2
3	-43.1	-31.7	52.8	-40.0	-30.1	58.2
4	-18.7	-53.4	56.7	-49.9	-52.9	50.6
5	-37.7	-21.4	55.1	-65.9	-33.6	43.7
6	-49.9	-13.4	49	-49.2	-15.7	56.7
7	-47.6	-36.7	48.3	-35.4	-51.9	53.6
8	-31.7	-39.4	50.0	-35.5	-45.0	51.9
9	-58.3	-23.7	46.0	-37.7	-31.7	45.2
10	-56.8	-23.7	47.4	-45.3	-26.3	49.0

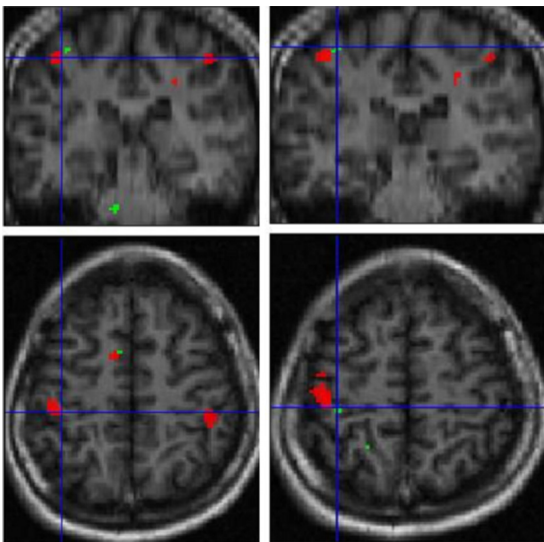


Figure 5. The example of brain activation by stimulation of two different fingers (Red: second finger, Green: third finger)

3.4 Voxel size by stimulation of different frequencies

To check the brain area size activated according to different frequencies, this study calculated the number of statistically significantly activated voxels within the SI area. Figure 6 shows the response pattern on the number of voxels activated, according to frequency by individual. As the frequency increased, the response pattern of the number of activated voxels was not demonstrated in a consistent form, and differences between individuals were huge.

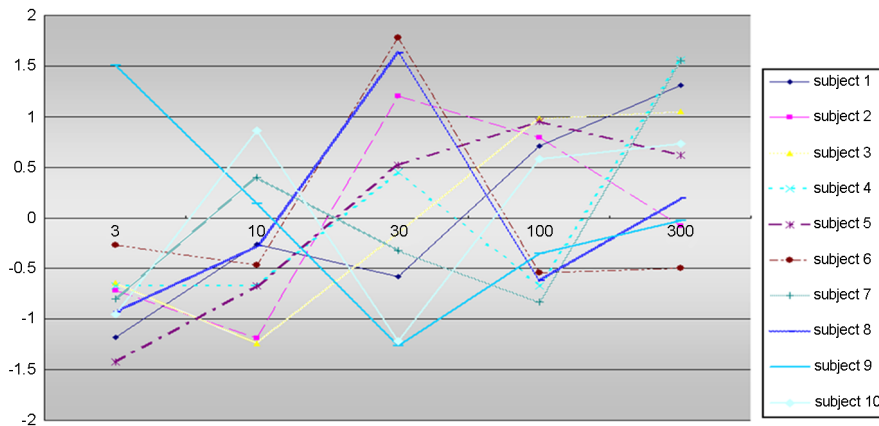


Figure 6. Activation pattern in the SI area by different frequencies by individuals (x axis: frequency, y axis: number of activated voxels)

3.5 The relationship between the perceived intensity and brain activation

Each individual's psychological evaluation intensity by frequency and the response pattern of activated voxels took similar forms (Figure 7). Typical two pattern relationship was observed between the perceived psychological intensity and the number of activated voxels in SI, while stimulation was presented (Figure 7). Very interestingly, as the perceived intensity on the stimulation

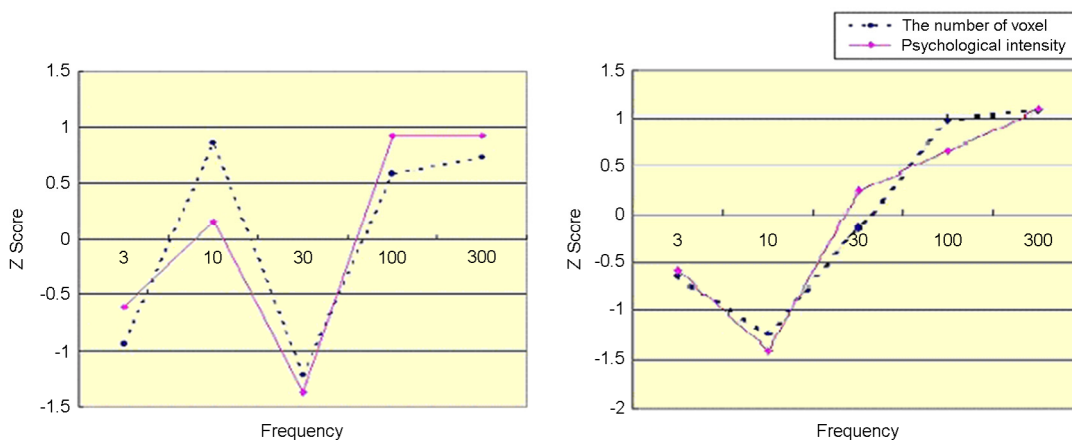


Figure 7. Two typical patterns for the relationship between the perceived intensity and brain activation (x axis represents stimulation frequencies, exponentially described)

was stronger, the activation of SI area increased, irrelevant of pattern, and a strong positive correlation was confirmed ($t = 2.58$, $p < 0.05$, $r = 0.71$).

4. Conclusion

The group analysis result is consistent with other imaging study results that electrotactile stimulation activates the contralateral SI area and bilateral SII areas (Boakye et al., 2000; Francis et al., 2000; Kurth et al., 1988). The activated areas other than the somatosensory area are Bilateral Inferior Frontal Gyrus, Bilateral Middle Frontal Gyrus, Right Insula and Left Inferior Parietal Lobule, which are almost consistent with the recent preceding study result using the neuroimaging technique (Burton et al., 1993; Disbrow et al., 2000; Gelnar et al., 1998; Ledburg et al., 1995; Polonara et al., 1999; Reed et al., 1998; Ruben et al., 2001). As a result of group analysis on the differences in brain's activated locations, according to frequency, by designating SI area as ROI area, there were many overlapped parts in the activated cluster, and location differences were not consistent, according to individual. This is partially consistent with the research result of Boakye et al. (2000), and the frequency size and activated location are predicted to have no relevance.

The result in this study demonstrates the somatosensory cortical area representing to the second finger is located in the more lateral and inferior side than the somatosensory cortical area representing the third finger. This finding is consistent with the homunculus made by electrotactile stimulating the brain of brain tumor patients, and also is similar to the study result of Francis et al. (2000) that examined the location differences of brain cortical area responding to the second and fifth fingers through fMRI.

To find out brain cortex activation, when different frequencies were presented, the brain response demonstrated according to change in stimulation's physical intensity was measured, while the participants received stimulation passively. The activation response pattern, according to frequency presented to each individual, did not show consistent result and individual differences were huge.

Assuming that individual's perceived psychological factors hugely affect the activation of somatosensory cortical area, rather than by stimulation's physical characteristics, this study verified the response patterns of psychological evaluation intensity and the number of activated voxels. As a result, similar psychological pattern and brain activation pattern within each participant were exhibited, although, psychological response pattern or the response pattern of central nervous system was not consistent between each experiment participant. This implies that brain activation is more related with individual's perceived psychological cognitive factors than stimulation's physical characteristics.

The limitation of this study is that the number of experiment participants was so small. Although, the location classification of somatosensory area representing the second and third fingers was possible, according to the study result, there was a difficulty in generalizing the result acquired from the ten participants. In the further study, it is necessary to generalize the study result by increasing the number of cases. Consistent central nervous system response pattern was not shown by each individual, and there was big difference in the number of activated voxels within one individual. The reason seems that signal and noise were not discerned well, due to unstable state of the fMRI equipment used in this study. For this reason, it is necessary to ensure stability in generalizing response pattern by identifying the consistency of central nervous system response, according to physical and psychological intensities demonstrated within each individual in the further study. In addition, the preceding studies of Francis et al. (2000) and Harrington & Hunter (2001) developed electrotactile stimulation devices and used them, however, this study used low frequency therapeutic apparatus and different stimuli were presented according to frequency, instead of using an electrotactile stimulation device as shown in the preceding studies, since the electrotactile stimulation device could not be used in this study. Consequently, the physical characteristics-force (N) and presented area size (cm²) of the presented tactile stimulation were not

controlled. For further study, after the experiment in this study, the development of an electrotactile stimulation device as shown in the preceding studies seems to be necessary.

Despite such a limitation, this study examined the brain cortical activation mechanism according to the presented location and size of tactile stimulation, and identified that the brain activation response of tactile stimulation is correlated with psychological and cognitive factors, rather than the presented physical size. The basic study on the examination of brain nerve network of tactile sensation is expected to be used in the tactile perception, embodiment and artificial neuroinformatics technology fields.

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