Brain responses to high frequencies (270 Hz-480 Hz) changes due to vibratory stimulation of human fingertips: An fMRI study

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Abstract. This fMRI study investigated the effects of vibratory stimulation on somatosensory areas during high-frequencies stimulation using a piezoelectric finger stimulation system during an fMRI scan. Twelve healthy right-handed subjects were stimulated at 270 Hz-480 Hz and the fMRI dataset was analysed to generate the activated regions due to the high-frequencies stimulation. The activated regions were identified and thresholded at Puncorrected<0.001 for multiple comparisons. The average effect of frequencies revealed significant activation in the left thalamus, right inferior parietal gyrus, right medial frontal gyrus, and right precuneus whereas the main effect of frequencies revealed significant activation in the left thalamus. The positive effect of frequencies displayed significant activation in the left pallidum, right amygdala, right superior temporal gyrus, right medial temporal gyrus. The vibratory stimulation at a frequency of 330 Hz and 360 Hz (330 Hz<360 Hz) revealed a significant difference in the left thalamus. Findings indicated the role of the secondary somatosensory areas processing and transporting sensory information to perform the perceptual and cognitive function.

1. Introduction

Recent fMRI studies using vibratory stimulation have been able to differentiate somatotopic mapping of index fingertips by applying low-frequencies stimulation [1]. However, limited studies were done to examine the effect of high-frequencies stimulation on somatosensory area. In this study, cortical responses of somatosensory areas were investigated using piezoelectric finger stimulation system on twelve subjects at 3 tesla. Previous fMRI vibratory studies reported significant activation was elicited within the SII area, yielding a reproducible result for brain mapping studies [1]. Thus, an adequate understanding on the effect of high-frequencies stimulation on the somatosensory areas are needed.

In this study, we aim to localise the activated brain region due to the vibratory stimulation in hope to understand the underlying mechanism of high-frequencies stimulation towards the somatosensory area, in return apply the knowledge to the future neurophysiological and somatosensory studies [2].

2. Materials and methods

Twelve healthy right-handed subjects (n=12, 7 males and 5 females, age 20 ± 10 years, mean = 24.75, SD = 4.97) were recruited in this study. The subjects were briefed to ensure the subjects understood all
the procedures of the study and have written informed consent as a proof of agreement before the fMRI scan was performed. Handedness was determined by the Edinburgh Handedness Inventory [1]. The procedures were performed in accordance to the approval by the Human Research Ethics Committee (HREC) (USM/JEPeM/17070349).

2.1. Experimental paradigm
The MRI compatible piezoelectric stimulation system device (Ben Krasnow, Redwood City, CA) was attached to subjects together with an eye mask and earpiece as described previously [1]. The stimulation frequencies vary from 270 Hz, 300 Hz, 330 Hz, 360 Hz, 390 Hz, 420 Hz, 450 Hz and 480 Hz. A block design paradigm (refer to figure 1) was developed using E-Prime software [1].

2.2. MR image acquisition
Neuroimaging data were acquired using a 3-T MRI scanner (Achieva, Philips, Netherlands) equipped with a standard 32-channel SENSE head coil. For each subject, the T1-weighted, high-resolution structural images were acquired for anatomical localization. The images then processed by overlaying the images to get better visualization as described elsewhere [1].

2.3. Data analysis
The preprocessing steps were corrected and spatially smoothed [1]. Random effect analyses of one-way analysis of variance (ANOVA) was applied for a within-subject analysis. Frequency as a factor was used at $P_{\text{uncorrected}} < 0.001$ for multiple comparisons. Activated regions were identified with SPM Wake Forest University (WFU) PickAtlas toolbox.

3. Results and Discussion
One-way ANOVA analysis revealed that there were significant average effects of frequencies during subject-specific responses in the left thalamus, right inferior parietal gyrus, right medial frontal gyrus and right precuneus at different range of high frequencies stimulation due to the perceptual categorisation due to the frequency selectivity characteristics of the brain. It was suggested that these activations reflected the significant role of high frequencies in the secondary somatosensory areas. The main effect of frequencies was shown in the left thalamus indicated significant effects in contrast to interest. Subsequently, the positive effect of frequencies at $P_{\text{uncorrected}} < 0.001$ were found in the left pallidum, right amygdala, right superior temporal gyrus and right medial temporal gyrus, meanwhile at a frequency of 330 Hz<360 Hz, significant activation in the left thalamus were found. A summary of the areas of activation, coordinates, and Z-score at a significant level were tabulated in the table 1 and displayed in the figure 2.

Table 1. Summary of the areas of the activation, coordinates, and Z-score at $P_{\text{uncorrected}} < 0.001$ for multiple comparisons

| Areas of activation                      | $^a$NOV | Coordinates (mm) | Z-score |
|------------------------------------------|---------|-----------------|---------|
| **Average effect of frequencies**        |         | x   | y | z   |       |
| Left thalamus                            | 302     | -11 | -18 | 18 | 6.71  |
| Right inferior parietal gyrus            | 157     | 41  | -52 | 46 | 5.29  |
This study aims to examine the effect of high-frequencies vibratory stimulation on the somatotopic organisation of the somatosensory areas. The results indicated signification activations in the left thalamus, right inferior parietal gyrus (rIPG), right medial frontal gyrus (rMFG), right precuneus, left pallidum, right amygdala, right superior and medial temporal gyrus.

The average effect of frequencies reported significant activation in the left thalamus, rIPG, rMFG and right precuneus. The activation in the left thalamus reportedly due to the sensory information relayed to the SI area and distributed to perform perceptual and cognitive functions [3], in accordance with hierarchical order of human somatosensory network [4]. The high frequencies stimulation activated the SII regions [5] thus, evoked significant activation in the rIPG. Commonly linked with parietal region, activation of rIPG signified its role in processing of sensory information [6]. Similarly, activation in the rMFG was suggested due to processing of sensory and tactile information [7]. The significant activation in the right precuneus was suggested due to frequency and discrimination in localisation during vibratory stimulation [7,9] while detecting incongruency in visuo-tactile stimulus [10].

The positive effect of high frequencies exposed significant activation in the left pallidum. It was suggested that the activation was due to the region residing in the basal ganglia i.e. suppression of the region often associated with frequency discrimination [9], thus improved the cognition and motor control by developing goal-directed actions [11]. Significant activation in the right amygdala was suggested due to the location of amygdala i.e. caused startling responses during electrical stimulation [12]. The amygdala is a prominent structure in learning and maintaining the sensory stimuli i.e. activation of the amygdala was suggested in encoding cognitive information, thus contributed in localisation of cognitive processes [12]. In the temporal cortices of right superior and right medial, interference of these regions with tactile stimulus during vibratory stimulation was due to the region’s pathway in the cerebral cortex [9]. Meanwhile, activation in the left thalamus for comparison of 330 Hz and 360 Hz was suggested due to the period of stimulation; high-resolution acquisition was known to produce a robust activation in the sensory thalamus with cluster of activations were observed approximately 80-90% within 18-24 minutes of the measurement [3]. Thus, it is proposed that the longer the period of stimulation, the higher the signal changes in the SII region [1].

*NOV=number of voxels

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**Table 1.** Brain activation of the average effect of frequencies, the main effect of frequencies and positive effect of frequencies at Puncorrected<0.001

| Brain Region                  | X  | Y  | Z  | Zcl. | Zpeak | puncorrected |
|-------------------------------|----|----|----|------|--------|--------------|
| Right medial frontal gyrus    | 207| 33 | 28 | 50   | 4.79   |              |
| Right precuneus               | 206| 11 | -66| 38   | 4.34   |              |
| Left thalamus                 | 148| -11| -18| 18   | 5.49   |              |
| Left pallidum                 | 73 | -24| -6 | -2   | 4.98   |              |
| Right amygdala                | 22 | 29 | -3 | -22  | 5.39   |              |
| Right superior temporal gyrus | 23 | 57 | 1  | -10  | 3.84   |              |
| Right medial temporal gyrus   | 33 | 54 | 4  | -26  | 4.06   |              |
| Left thalamus                 | 24 | -15| -22| -2   | 3.99   |              |

**Figure 2.** Brain activation of the average effect of frequencies, the main effect of frequencies and positive effect of frequencies at Puncorrected<0.001
4. Conclusion
The present study explored the cortical responses of the somatosensory areas during vibratory stimulation of high frequencies. It was demonstrated that high frequencies predominantly activated the secondary somatosensory areas and its neighbouring regions. For future studies, our findings suggested implementing connectivity analysis integrating low and high frequencies during vibratory stimulation, so it is permissible for this study to be used as a reference for intervention studies.

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