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To cite this article: FAS Seri *et al* 2019 *J. Phys.: Conf. Ser.* **1248** 012029

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Brain responses to frequency changes due to vibratory stimulation of human fingertips: An fMRI study

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Abstract. Vibratory (e.g., piezoelectric) devices can stimulate cortical responses from the somatosensory area during functional magnetic resonance imaging. Twelve healthy, right-handed subjects (7 males and 5 females) were scanned with a 3.0 T magnetic resonance imaging scanner and stimulated at 30–240 Hz using a piezoelectric vibrator attached to the subjects' index fingers. The functional images were analysed to determine the brain activation region by performing random effects analyses at the group level. One-way analysis of variance was used to measure changes in frequency on brain activity. The activated regions were identified with WFU PickAtlas software, and the images were thresholded at $P_{uncorrected} < 0.001$ for multiple comparisons. The average effect of frequency revealed significant activations in the right insula and right middle frontal gyrus; the corresponding region in the somatosensory area may act as a top-down control signal to improve sensory targets. Results revealed significant differences between frequencies; 90 Hz > 120 Hz activated right inferior parietal gyrus, 120 Hz > 150 Hz activated right cerebellum, and 60 Hz > 90 Hz activated right supramarginal gyrus and bilateral inferior frontal gyrus pars triangularis. Findings indicated the role of secondary somatosensory areas and the cerebellum in performing higher-order functions and discriminating various frequencies during vibratory stimulation. Increasing the patient sample size and testing higher frequencies in future experiments will contribute to furthering brain mapping of somatosensory areas.

1. Introduction

Functional magnetic resonance imaging (fMRI) is widely used for brain function and localization studies [2,4,18]. In this study, stimulus-evoked fMRI was applied to observe the changes of somatosensory responses on the cortical level. To produce a robust somatotopic map of the brain, localizing accurately the somatosensory region is needed by examining the brain signal at a different level of vibratory frequency [1]. In this study, the electrical device called piezoelectric finger stimulation system was used to produce a vibratory stimulus to measure the cortical responses of somatosensory area. Previous fMRI studies reported brain activation within SI and SII region elicited by vibratory stimulation [2-3] known to yield reproducible results for brain mapping studies [2,3,4,12].

There are limited number of studies that precisely discuss the effect of frequencies on the somatosensory region to create a comprehensive model of somatotopic mapping of fingers [1-3,19]. Thus, an adequate understanding on the effect of vibratory stimulation on the brain cortex is needed.



In this study, we aim to measure the activated brain responses due to vibratory stimulation of frequencies. Thus, the output from this study will increase our understanding and can be applied to clinical settings (e.g. preoperative planning and optimization of neurorehabilitation strategies) and provide fundamental knowledge for future somatosensory studies.

2. Material and method

2.1. Subject

Twelve healthy right-handed subjects ($n=12$, 7 males and 5 females, age 20 ± 10 years, mean = 24.75, SD = 4.97) with no neurological or psychiatric diseases were scanned with 3.0 T MRI scanner (Achieva, Philips, Netherlands) equipped with a 32-channel SENSE head coil. The experimental procedures were conducted in accordance with the principles of the Declaration of Helsinki [15] and approval of the protocol was obtained from the ethics committee of the Human Research Ethics Committee of USM (HREC) (USM/JEPeM/17070349). All participants were right-handed as measured by Edinburgh Handedness Inventory [14].

2.2. Experimental paradigm

The vibratory stimulus was delivered using an MRI compatible piezoelectric finger stimulation system device (Ben Krasnow, Redwood City, CA). The piezoelectric actuators were attached to the left and right index fingertips of the subject, and the vibration was produced through the transmission of an alternating current. The stimulation frequencies were from 30 Hz, 60 Hz, 90 Hz, 120 Hz, 150 Hz, 180 Hz, 210 Hz and 240 Hz. An fMRI experiment was performed using a block design paradigm (see Figure 1) developed in E-Prime System to synchronise the timing with the MRI scanner. The block design consists of 16 active blocks and 16 rest blocks per run; per run total time was 330 seconds, and the cycle were repeated for six times. Each stimulation blocks were arranged in pseudorandom order. Each of the participants were asked to use an eye mask [6] to reduce visual artefacts in the MRI room [13]. The subject's head was immobilized using foam paddings to minimize movement artefacts [4].

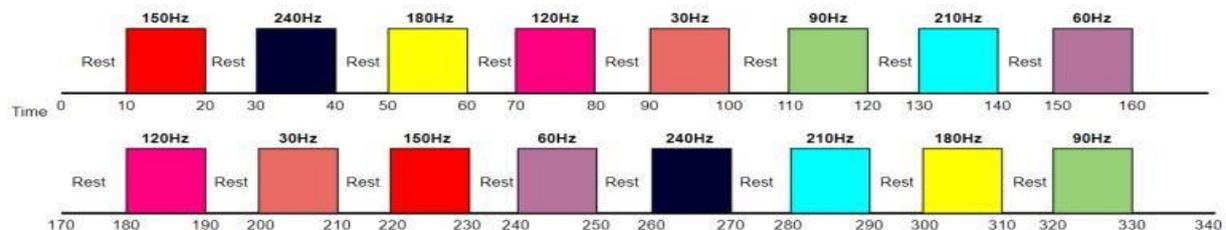


Figure 1. One cycle of block paradigm for somatosensory task.

2.3. MR image acquisition

For each subject, a T1-weighted, high resolution structural image (TR/TE/slice/FOV=9.7ms/4.6ms/1.2mm/250mm x 250mm) was obtained for anatomical localization. An echo-planar imaging (EPI) sequence with the following parameter (TR/TE/slice/flip angle/FOV=3000ms/33ms/4mm slices/80°/230mm).

2.4. Data analysis

Image analysis was performed using the MATLAB R2015a (Mathworks Inc., Natick, MA, USA) and the Statistical Parametric Mapping 12 (Wellcome Department of Imaging Neurosciences, Institute of Neurology, University College of London, UK) software packages. The data analysis involved the following pre-processing steps: 1) slice-timing, 2) realignment, 3) normalization, and 4) smoothing (full-width half maximum of 6 mm) [7]. Random effects analyses of one-way analysis of variance (ANOVA) were performed within-subject factor of frequency at $P_{uncorrected} < 0.001$ for multiple comparisons.

The activated brain regions were identified with Wake Forest University (WFU) PickAtlas software [24].

3. Results

The one-way ANOVA was used to determine the significant changes of the brain activation between different frequency level. One-way ANOVA revealed there was no significant main effect of frequencies in any activated brain region. However, there are significant result in average effect and the positive effect of frequencies. **Table 1** shows a summary of the areas of the activation, coordinates, and Z-score at a significant level.

3.1. Average effect of frequencies

The average effect of frequencies indicates the variability of frequencies in the subject specific responses. In this study, a significant average effect of frequencies is shown in the right insula and the right middle frontal gyrus. **Figure 2** shows the brain activation of the average effect of frequencies.

3.2. Positive effect of frequencies

A positive effect of frequencies indicates a strong effect of frequency at a region as compared to other frequencies [10]. Positive effect of frequency shows significant brain activation (Puncorrected<0.001) for 1) 90 Hz>120 Hz – activated the right inferior parietal gyrus (rIPG), 2) 120 Hz>150 Hz – activated the right cerebellum, 3) 60 Hz<90 Hz – activated the right supramarginal gyrus (rSMG) and bilateral inferior frontal gyrus (IFG), 4) 90 Hz<120 Hz – activated the right inferior parietal gyrus (rIPG) and **Figure 3** shows the activated brain areas of positive effect of frequency.

Table 1. Summary of the areas of the activation, coordinates, and Z-score at Puncorrected<0.001 for multiple comparisons.

	Areas of activation	NOV	Coordinates (mm)			Z-score
			x	y	z	
AEOF	Right insula	631	33	-22	14	7.57
	Right middle frontal	341	38	-4	62	4.95
EOF 90 Hz>120 Hz	Right inferior parietal gyrus	42	50	-39	50	3.79
EOF 120 Hz>150 Hz	Right cerebellum	24	11	-54	-18	3.90
EOF 60 Hz<90 Hz	Right supramarginal gyrus	22	48	-40	42	3.83
	Bilateral inferior frontal (pars triangularis)	56	41	31	10	4.16

Abbreviations: AEOF=average effect of frequencies, EOF=effect of frequencies, NOV=number of voxels.

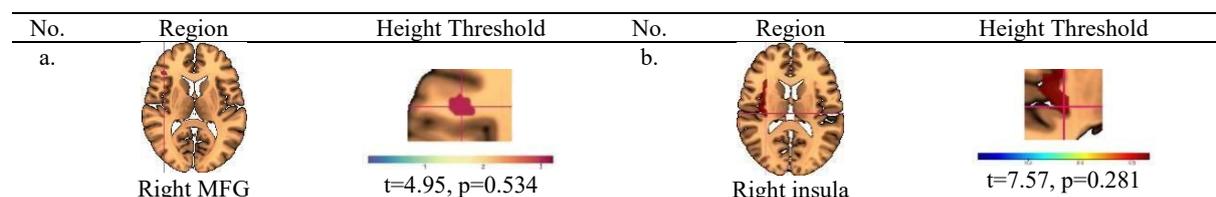


Figure 2. The average effect of frequencies at Puncorrected<0.001 for multiple comparisons.

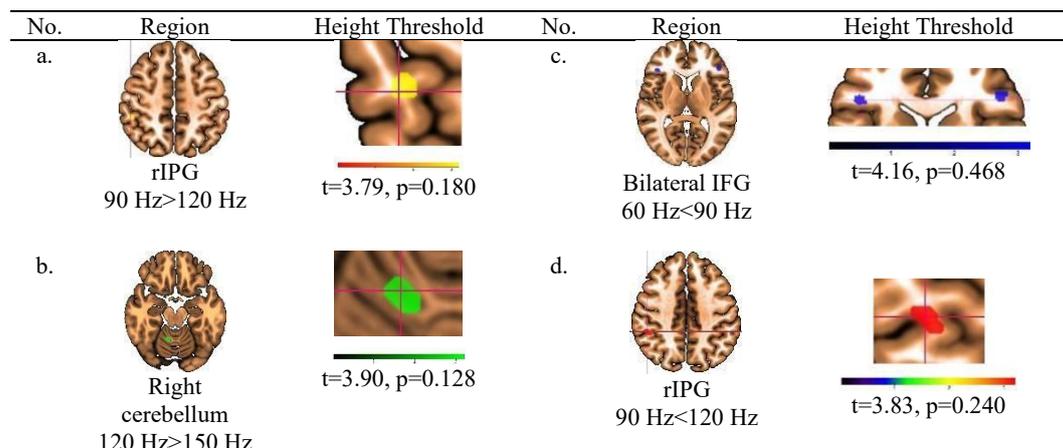


Figure 3. Brain activation of the positive effect of frequency at $P_{uncorrected} < 0.001$ for multiple comparisons.

4. Discussion

This study aims to examine the activated brain region and its cortical responses due to the vibratory stimulation of frequencies. Vibratory stimulation of the bilateral index fingertips shows significant signal changes [3] in the right insula and rMFG, rIPG, right cerebellum, rSMG and rIFG pars triangularis. These activated regions are consistent in previous studies; includes the somatosensory areas such as SI and SII region [2,10,17,23], parietal cortex [2], insula [10,17-18], frontal gyrus [21-22], cerebellum hemisphere [13] and supramarginal gyrus [18].

Vibratory stimulation activates the right insula and rMFG. The activation in the right insula (at Brodmann area 13) is similar with the findings by Gelnar, Krauss, Szeverenyi, & Apkarian [5]; vibratory stimulation of lip, hand and foot activated the parietal operculum (located in insula cortex). The parietal operculum and insula cortex are assumed as SII region [17]. Subsequently, pain studies by Schnitzler et al. [17] suggested that insula is related to somatosensory modalities based on the physiological work on the thalamic and cortical connectivity. Temporal analysis suggested robust activation of insula is associated with vibratory frequency discrimination; insula being a multimodal area that integrate information from distinct brain region [19]. Significant activation in the rMFG during vibratory stimulation is similar in the study by Wei et al. [22] using a frequency of 1 Hz. It is suggested that in the somatosensory domain, the MFG provides a top-down control signal that improves sensory targets [24]. Brain activity in frontal region is known to represent the frequency information by encoding quantitative information in a supramodal manner using non-human primate electrophysiology and human EEG studies [16]. Significant activation in the rIPG (at Brodmann area 40) was observed at the frequency of 90 Hz in contrast to 120 Hz. The activation of rIPG is due to the functionality of mechanoreceptor Pacinian [1,4]. High frequency activates more Pacinian than Meissner as Pacinian corpuscles possess low field density and wide receptive field [1]. High frequency predominantly activates SII compared to SI region [2,4,8]. Therefore, Pacinian is known to poorly localized the SI area compared to SII area [4]. The activation of parietal cortex shows its involvement as the third major subdivision of somatosensory cortex in vibratory stimulation [15]. This result corroborated with Tommerdahl et al. [20] when frequency of 25 Hz was compared with 200 Hz, using near-infrared optical imaging to study the temporal dynamics of cortical responses. A contrast of 120 Hz compared to 150 Hz yields significant activation in the right cerebellum (at the anterior lobe of the cerebellum). Similar pattern of activation in the right cerebellum also reported by Noohibezanjani et al. [13] with eyes closed during vestibular stimulation. The activation is suggested due to vibratory frequency discrimination [19].

The comparison of 90 Hz and 60 Hz activates rSMG and IFG pars triangularis. The activation of rSMG is consistent with the finding by Choi et al. [1]; human sensitivity increased with vibratory, as frequency increase above 100 Hz. The comparison of 128 Hz and 32 Hz in the study by Jacobs et al. [7]

shown the same pattern (rSMG activated at lower vibratory threshold). Choi et al. [1] suggested that a significant activation of rSMG is due to the structure of Pacinian mechanoreceptor possessing a low field density with wide receptive field. Moreover, Kim et al. [9] suggested that activation of rSMG was due to the region being an information carrier for frequency-dependent. Previous studies reported that activation of high frequency resulted in rSMG, also known as SII region [2,17]. The SII region was found to function as an area that handles vibratory frequency discrimination [2]. In this study, the activation of rSMG indicates frequency discrimination at high frequency.

Meanwhile, the comparison between 90 Hz and 60 Hz shows significant activation in bilateral IFG pars triangularis. Trulsson et al. [21] reported that the activation of IFG yields the strongest response at 100 Hz as compared to frequencies below 50 Hz. Similar findings reported by Choi et al. [1] in the study of 300 Hz as compared to 30 Hz. Deuchert et al. [3] found that the greater brain response in the bilateral IFG is suggested due to human sensitivity increased with the increasing frequencies of vibratory stimulation. Thus, it is proposed that the higher the level of frequencies, the higher the signal changes in the IFG.

5. Conclusion

Bilateral stimulation of index fingertips evokes cortical responses in the somatosensory areas, primarily the SII region in the insula. High frequencies of vibratory stimulation predominantly activate SII region meanwhile low frequencies activate the SI region. As for future studies, it is recommended to increase the sample size to produce a reliable somatotopic map due to vibratory stimulation. Additionally, application of lower frequencies altogether with high frequencies should be applied to localize the somatosensory areas accurately so that it is permissible for this study to be used as a reference for intervention studies (e.g. rehabilitation in neurological disorders) in the future.

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Acknowledgement

This research was supported by the Universiti Sains Malaysia Short Term Grant: 304/PPSP/6315090, and Society For Neuroscience (SFN) Kelantan Chapter. The authors would like to thank the radiographers, En. Khew Kuan Kooi, Pn. Che Munirah Che Abdullah, Pn. Siti Afidah Hamat and Pn. Wan Nazryrah Abdul Halim from the Department of Radiology, Hospital Universiti Sains Malaysia, and Science Officers, En. Hazim Omar and Pn. Alwani Liyana Ahmad from the Department of Neurosciences, School of Medical Sciences, Universiti Sains Malaysia.