

Artikel Asli/Original Article

Brain Activation Display Functional Asymmetry in Response to Action, Background and Tonal Frequency During a Pitch Memory Processing: An fMRI Study (Pengaktifan Otak Mempamerkan Ketaksimetrian Kefungsian dalam Respond terhadap Aksi, Latar Belakang dan Frekuensi Nada Semasa Pemprosesan Ingatan Kelangsingan: Satu Kajian fMRI)

AHMAD NAZLIM YUSOFF, FARAH NABILA AB RAHMAN, SITI ZAMRATOL-MAI SARAH MUKARI, KHAIRIAH ABDUL HAMID & MAZLYFARINA MOHAMAD

ABSTRACT

In this study, the asymmetry of the main effects of action, background and tonal frequency during a pitch memory processing were investigated by means of brain activation. Eighteen participants (mean age 27.6 years) were presented with low and high frequency tones in quiet and in noise. They listen, discriminate and recognize the target tone against the final tone in a series of four distracting tones. The main effects were studied using the analysis of variance (ANOVA) with action (to wring (rubber bulb) vs. not to wring), background (in quiet vs. in noise) and frequency (low vs. high) as the factors (and levels respectively). The main effect of action is in the right pre-central gyrus (PCG), in conformation with its contralateral behavior. The main effect of background indicated the bilateral primary auditory cortices (PAC) and is right lateralized, attributable to white noise. The main effect of frequency is also observed in PAC but bilaterally equal and attributable to low frequency tones. Despite the argument that the temporo-spectral lateralization dichotomy is not especially rigid as revealed by the main effect of frequency, right lateralization of PAC for the respective main effect of background clearly demonstrates its functional asymmetry suggesting different perceptual functionality of the right and left PAC.

Keywords: ANOVA; Pitch memory; Noise; SPM; Heschl's gyrus; Primary auditory cortex

ABSTRAK

Dalam kajian ini, kesimetrian kesan utama tindakan, latar belakang dan frekuensi nada semasa pemprosesan ingatan kelangsingan diselidiki berdasarkan pengaktifan otak. Lapan belas peserta kajian (purata umur 27.6 tahun) diperdengarkan nada frekuensi rendah dan tinggi dalam senyap dan dalam hingar. Mereka mendengar, membezakan dan mengecam nada sasaran dan nada terakhir dalam satu siri empat nada pengganggu. Kesan utama dikaji menggunakan analisis varians (ANOVA) dengan tindakan (ramas (bebuli getah) mlwn. tidak ramas), latar belakang (senyap mlwn. hingar) dan frekuensi (rendah mlwn. tinggi) masing-masing sebagai faktor (dan aras). Kesan utama tindakan adalah pada girus presentral kanan, dan berpadanan dengan tingkah laku kontralateral. Kesan utama latar belakang adalah pada korteks auditori primer (PAC) bilateral dan bersifat lateral kanan yang disebabkan oleh hingar putih. Kesan utama frekuensi juga diperhatikan pada PAC bilateral yang disebabkan oleh nada frekuensi rendah. Meskipun hujah bahawa dikotomi kelateralan spektrum-masa adalah tidak tegar, sepertimana didedahkan oleh kesan utama frekuensi dalam kajian ini, sifat kelateralan kanan PAC untuk kesan utama latar belakang jelas menunjukkan kefungsiannya yang tidak simetri dan mencadangkan sifat kefungsi tanggapan yang berbeza bagi PAC kanan dan kiri.

Kata kunci: ANOVA; Ingatan kelangsingan; Hingar; SPM; Girus Heschl; Korteks auditori primer

INTRODUCTION

Human primary auditory cortex (A1) which includes Heschl's gyrus (HG), also known as Brodmann area (BA) 41, is located on the posterior two-thirds of the supratemporal plane in both hemisphere (Boatman 2006). Posterior to Heschl's gyrus on the supratemporal plane is plenum temporale (PT) while anterior to it is plenum polare (PP). These three auditory structures (HG, PT and PP) form the auditory core. A1 receives input directly from the medial

geniculate body (MGB) as well as from the contralateral auditory areas, via a central hub known as corpus callosum (Langers et al. 2005). Surrounding the auditory core is a narrow area known as the belt which receives input directly from the auditory core (Galaburda & Pandya 1983). This belt area is also known as BA42. Adjacent to the belt area is the parabelt which extends onto the lateral surface of the posterior superior temporal gyrus (pSTG), which is also known as BA22. Input into the parabelt area comes from the belt as well as from the MGB. The output from

the parabelt area will be transmitted to other areas outside auditory areas in the temporal, parietal and frontal regions (Romanski et al. 1999).

Despite extensive neuroimaging studies conducted to reveal the contribution of the primary auditory cortex (PAC) in auditory processing (Hamid et al. 2012; Langers & van Dijk 2012; Yusoff et al. 2011), its role during the performance of pitch discrimination still remains unclear. For example, when the task is performed with the presence of distracting background noise and when the stimuli are pure tones with different frequency levels (Yusoff et al. 2013). In many circumstances, the results yielded were not uniform and sometimes contradictory. Furthermore, even though it is known that activations in PAC are evoked contralateral to the ear that receives the stimulus, the lateralization of the PAC activations due to different types of stimuli has hardly been studied.

There have been debates on the specialized function of the right and left hemisphere auditory cortex as well as other cortices in processing speech and non-speech stimuli. Previous studies (Gaab et al. 2003) revealed that neither left temporal lesion nor lobectomies would affect one's ability for pitch judgment and melodic discrimination but it was the opposite for the right thus showing that left and right auditory areas possess different auditory perceptual functionality. It has long been known that tonal or spectral content of stimuli such as noise, pure tones and music evoke more responses in the right hemisphere auditory cortex while activation in the left auditory cortex is attributable to temporally complex, rapidly changing sound characteristic of stimuli such as speech and words (Burton et al. 2012; Hwang et al. 2005; Specht & Reul 2003; Tervaniemi & Hugdahl 2003; Zatorre et al. 1992). However, in a study on lateralization of the brain cortices, speech was associated with enhanced activity in the superior temporal cortex of the language-dominant left hemisphere, as well as in the superior and middle temporal cortex of the right hemisphere (Alho et al. 2003), showing a bilateral functional specialization characteristics. On the same ground, the left hemisphere auditory cortex has also been associated to the processing of non-verbal stimuli (Obleser et al. 2008; Zatorre & Gandour 2008) such as pure tones (Gaab et al. 2003).

We undertook the current study to test the presently accepted dichotomy of the primary auditory cortex in a pitch memory experiment conducted in an fMRI environment using different background and tonal frequency. The purpose of this study was to investigate the effects of motor action, background noise and tonal frequency on the asymmetrical processing of the related brain areas. The main effect of action should occur in the primary motor area, contralateral to the hand that was used to respond to the task. It is hypothesized that ignoring the type of action, pitch discrimination in quiet and in noisy conditions evokes similar height and spatial extent of activations. We also hypothesized that similar brain activation pattern will be

evoked in discriminating low and high frequency tones, ignoring the background conditions.

METHODS

PARTICIPANTS

This study was a part of a comprehensive assessment of human cortical activation during the performance of a pitch memory task (Yusoff et al. 2013). Eighteen healthy right and left-handed Malay participants (14 right handed, 4 left handed, 8 females), aged 20 to 40 years old (mean = 27.6 years, standard deviation = 4.4 years), agreed to participate by filling in the informed consent and screening forms. Prior to signing, the participants were given full explanation about the nature and risks to the research, as required by the Institutional Ethics Committee (IEC) (Reference no. NN-197-2010). All participants had no hearing impairment and no history of long time exposure to loud noise. The participants' hearing level for both ears were not greater than 30 dB (HL) in the frequency range of 250-8000 Hz. None of the participants received any musical education or training.

fMRI SCANS AND STIMULI

A sparse temporal sampling functional magnetic resonance imaging (STS-fMRI) was used in this study to avoid the auditory paradigm to be interfered with the scanner sound. There were altogether 218 functional scans in every imaging session. The first two scans were dummies and were automatically discarded by the BOLD imaging protocol to eliminate the magnetic saturation effect. Each functional volume consisted of 35 axial slices that were acquired in 3-s acquisition time (TA) with an inter-scan interval (TR) of 13 s. The STS-fMRI scans were performed using a 3-tesla magnetic resonance imaging (MRI) system (Siemens Magnetom Verio).

The post-stimulus scans were carried out following the delivery of series of pure tones that were generated using Adobe Audition 2.0 software (Adobe Systems Inc., San Jose, CA, USA). The tones were alternatively delivered in a quiet (Q) and in a white background noise (N). Six pure tones of 700 Hz, 1000 Hz, 2000 Hz, 3500 Hz, 4000 Hz and 4500 Hz were used as stimuli. All the pure tone stimuli were recorded and presented at equal amplitudes.

DATA ACQUISITION

Each STS-fMRI session had 36 trials and each trial consisted of six conditions. The six conditions that contained a trial were i) no stimulus in quiet condition (Q) in which the participants were instructed to stay calm, ii) stimulus presented in a quiet background (SQY) in which the participants were supposed to respond (by wringing the rubber bulb using the left hand), iii) stimulus presented in

a quiet background (SQN) in which the participants were not supposed to respond, iv) stimulus presented in a noisy background (SNY) in which the participants were supposed to respond, v) stimulus presented in a noisy background (SNN) in which the participants were not supposed to respond and finally vi) listening only to white noise stimulus (N). The stimulus which was a series of pure tones named as the target tone f_0 and the distracting tones (f_1 , f_2 , f_3 and f_4) were grouped together in either high (3500 Hz, 4000 Hz, 4500 Hz) or low frequency (700 Hz, 1000 Hz, 2000 Hz) category. Any tone may appear twice in a series of distracting tones.

The stimulus was binaurally delivered to the participants via an MRI-compatible headphone connected to a digital audio playback system through an air conducting tube. The intensity level of the stimulus was kept constant at 70 dB sound pressure level (SPL). The white noise, pure tones in quiet background and pure tones in noisy background were satisfactorily received and heard, as claimed by the participants. The duration of the stimulus from the onset of f_0 until the end of f_4 was 6 seconds. The duration of f_0 was 2 seconds while each of the distracting tone lasted 0.8 seconds. The gap between consecutive tones was kept at 0.2 seconds. The participants were instructed to pay attention, recognize, discriminate and match the target tone (f_0) with the last tone (f_4) of the four distracting tones. If the participants noticed that both the f_0 and f_4 were similar, they were required to wring the rubber bulb using his/her left hand and remained calm if otherwise.

SPATIAL PREPROCESSING OF DATA

The fMRI data were analyzed using MATLAB 7.4-R2008a (Mathworks Inc. MA, USA) and Statistical Parametric Mapping (SPM8) (Functional Imaging Laboratory, Wellcome Department of Imaging Neuroscience, Institute of Neurology, University College of London). Functional images from each measurement were realigned using the 6-parameter affine transformation in translational (x, y and z) and rotational (pitch, roll and yaw) directions. The normalization procedure used a 12-parameter affine transformation. The images were then smoothed using an 8-mm full-width-at-half-maximum (FWHM) Gaussian kernel. Low-frequency responses caused by aliased biorhythms, cardiac effects and other oscillatory signal variations were removed using a high-passed filter.

STATISTICAL ANALYSIS

The details regarding model specification for individual and group analyses are given in (Yusoff et al. 2013). In this study, three factors which were motor action, background noise and tonal frequency were used to determine the BOLD signal change over baseline e.g. the height and spatial extent of activation during pitch memory processing. The determinations were accomplished using a two-way

repeated measure ANOVA in a random effect analysis (RFX) framework in the second level analyses. The analyses were divided into i) action vs. background experiment with Action (2 levels: to wring and not to wring) and Background (2 levels: quiet and noisy) as factors (and levels) and ii) frequency vs. background experiment with Frequency (2 levels: low and high) and Background (2 levels: quiet and noisy) as factors (and levels). The main effects were reported at $p < 0.05$ corrected for multiple comparisons.

RESULTS

BRAIN ACTIVATION DUE TO THE MAIN EFFECT OF ACTION

As can be seen in in Figure 1 and Table 1, there is only a single cluster of activation (145 voxels) that survived the height threshold of $\alpha = 0.05$, corrected for multiple comparisons. The activation was fully right lateralized and centered on the right pre-central gyrus (PCG), activating parts of BA6, BA4a and BA1. The activation is contralateral to the left hand that was used by the participants to wring the rubber bulb in responding to the stimuli.

BRAIN ACTIVATION DUE TO THE MAIN EFFECT OF BACKGROUND

The results obtained from ANOVA in search of any activated voxels that survived the height threshold of $\alpha = 0.05$ for the main effect of background are given in Figure 2 and Table 2 for both the action vs. background and frequency vs. background experiments. Similar patterns of activation for the main effect of background were obtained from the two experiments. The background (white noise) had activated the primary auditory cortex (PAC) bilaterally with the maximum intensity voxel centered in the right Heschl's gyrus (HG) and left superior temporal gyrus (STG), from which the right hemisphere area having a greater height and spatial extent of activation as compared to the left. The activations were found to occur specifically in the bilateral TE1.0, TE1.1 and TE1.2. From the brain activation data shown in Table 2, it can be concluded that the main effect of background from the two experiments are strongly right lateralized. The results are consistent with our previous findings using a *t*-test (Yusoff et al. 2013). The asymmetry of activation is also observed in terms of the location of the center of activation in which the point of maximum intensity in the right hemisphere is not the mirror image of the point of maximum intensity in the left hemisphere. The magnitudes of the displacement between the two maximum intensity points for both the action vs. background and frequency vs. background experiments are 7.48 and 10.95 mm respectively.

BRAIN ACTIVATION DUE TO THE MAIN EFFECT OF FREQUENCY

The results for the main effect of frequency for the frequency vs. background experiment are given in Table 3 and Figure 3. At a corrected ($p < 0.05$) significant level, two small clusters of activation of equal size and intensity were found in the right HG and left STG (bilateral TE1.0). This activation of high specificity clearly indicates a symmetrical activation but an asymmetry in the location of the activation center in which the point of maximum

intensity in the right hemisphere is not the mirror image of the point of maximum intensity in the left hemisphere and both are displaced by a distance of 11.49 mm.

INTERACTION

From the ANOVA results, no voxel survived the height threshold of $p < 0.05$ for the interaction, indicating that no significant interaction existed between action and background and between frequency and background.

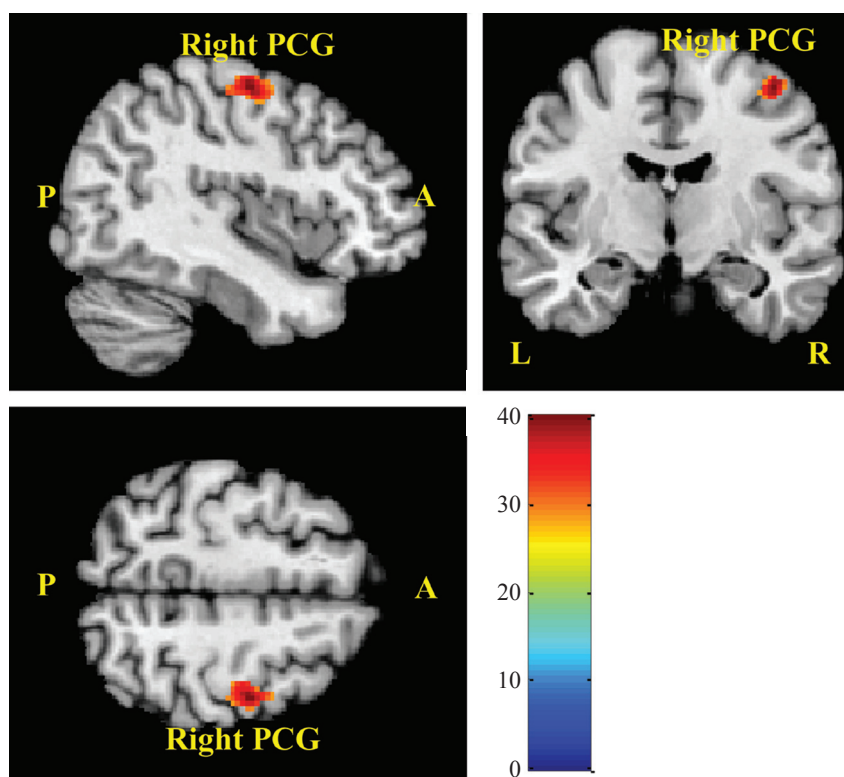
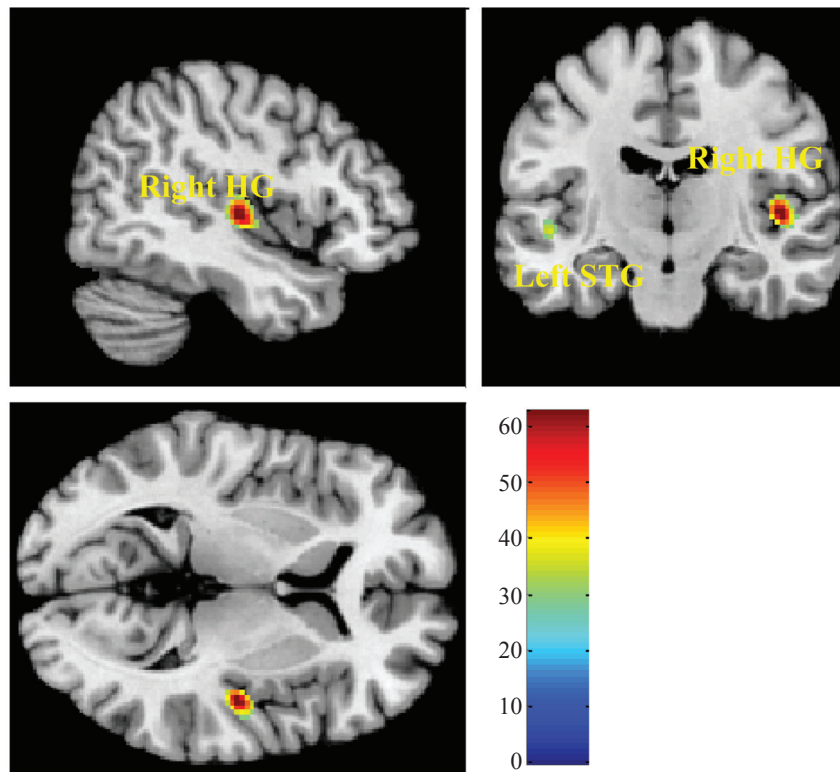


FIGURE 1. Group activation ($p < 0.05$) due to main effect of action in sagittal, coronal and axial views. The activation is fully right lateralized and centered on the right pre-central gyrus. Color codes represent increased F statistics from blue to red. A: anterior, P: posterior, L: left and R: right

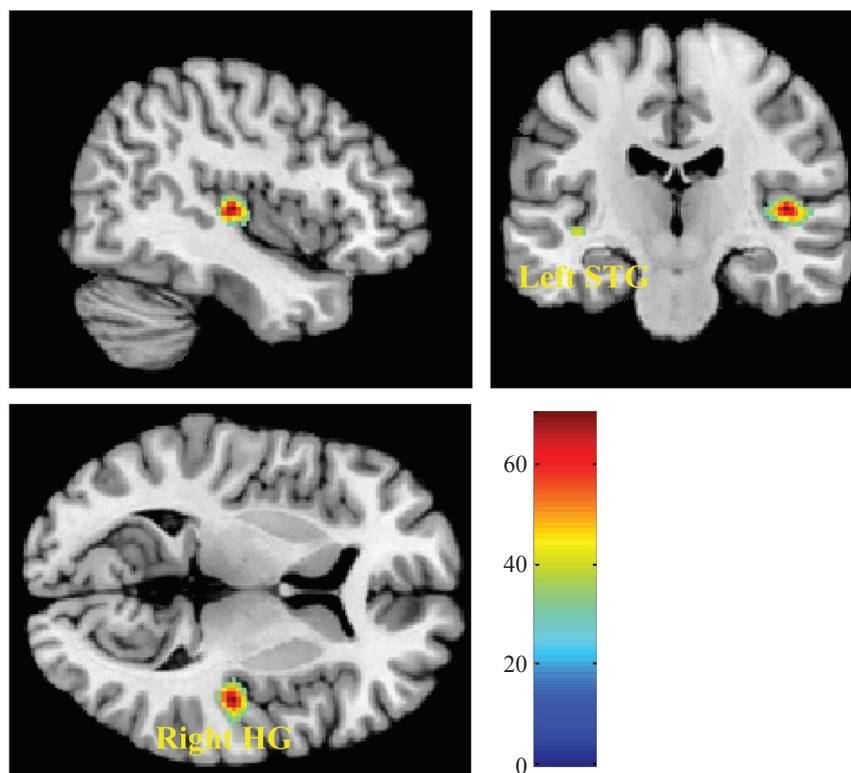
TABLE 1. Brain activation characteristics obtained from ANOVA in the second level analysis showing the main effect of action

No. of activated clusters	Cluster level p -value	No. of activated voxels	Peak level p -value	Peak level F value	MNI coordinates			Activated areas
					x	y	z	
<i>Main effect of action ($p_{corrected} = 0.05$, extent threshold = 0 voxel)</i>								
1	*	145	*	40.14	42	-14	60	Right Pre-central Gyrus BA6 (87.5%), BA4a (8.0%), BA1 (2.8%)

* $p < 0.05$



(a)



(b)

FIGURE 2. Group activation ($p < 0.05$) due to main effect of background in sagittal, coronal and axial views for (a) action vs. background and (b) frequency vs. background experiments. In both cases, the activation is right lateralized and centered on the right Heschl's gyrus. Color codes represent increased F statistics from blue to red.

TABLE 2. Brain activation characteristics obtained from ANOVA in the second level analysis showing the main effect of background

No. of activated clusters	Cluster level <i>p</i> -value	No. of activated voxels	Peak level <i>p</i> -value	Peak level <i>F</i> value	MNI coordinates			Activated areas
					<i>x</i>	<i>y</i>	<i>z</i>	
<i>Main effect of background for action vs. background experiment ($p_{corrected} = 0.05$, extent threshold = 0 voxel)</i>								
2	*	248	*	64.12	46	-20	8	Right Heschl's gyrus TE1.0 (62.7%), TE1.1 (8.7%), OP1 (7.5%), TE1.2 (0.8%)
	*	51	*	38.86	-50	-18	2	Left superior temporal gyrus TE1.0 (63.6%), TE1.2 (1.1%), TE1.1 (0.5%)
<i>Main effect of background for frequency vs. background experiment ($p_{corrected} = 0.05$, extent threshold = 15 voxels)</i>								
2	*	246	*	69.99	44	-24	10	Right Heschl's gyrus/Right superior temporal gyrus TE1.1 (35.3%), TE1.0 (35.2%), OP1 (4.3%), TE1.2 (1.6%)
	*	79	*	41.28	-40	-26	0	Left superior temporal gyrus TE1.0 (29.3%), TE1.1 (5.9%), OP4 (1.9%), TE1.2 (0.3%)

**p* < 0.05

TABLE 3. Brain activation characteristics obtained from ANOVA at corrected (*p* < 0.05) significant level in the second level analysis showing the main effect of frequency

No. of activated clusters	Cluster level <i>p</i> -value	No. of activated voxels	Peak level <i>p</i> -value	Peak level <i>F</i> value	MNI coordinates			Activated areas
					<i>x</i>	<i>y</i>	<i>z</i>	
<i>Main effect of frequency ($p_{corrected} = 0.05$, extent threshold = 0 voxel)</i>								
2	*	5	0.014	33.12	44	-22	10	Right Heschl's gyrus TE1.0 (82.5%), OP1 (17.5%)
	*	5	0.026	31.11	-48	-18	0	Left superior temporal gyrus TE1.0 (67.5%)

**p* < 0.05

DISCUSSION

In our previous study (Yusoff et al. 2013) using a *t*-test, we identified regions of cortical activation in response to action (To wring > Not to wring), background noise (Noisy > Quiet) and frequency (Low > High and High > Low). We found no significant activation for the comparisons “Not to wring” > “To wring” and “Quiet” > “Noisy.” However, the activation obtained from the *t*-test was significant only at uncorrected significant level (*p* < 0.001). In this study, we used ANOVA to investigate the main effects and obtained brain activations that are similar to the results of the *t*-test but at a corrected significant level (*p* < 0.05). It is thus believed that reliable results of brain activation would be produced when the analysis takes into consideration the variance that persists. The findings are reported in the following paragraphs.

Our results demonstrate that the significantly (*p* < 0.05) activated right pre-central gyrus (PCG) for the

main effect of action is mainly due to the action done by the participants to respond to the pitch discrimination task by wringing the rubber bulb using their left hand, regardless of whether the task is done in quiet or in noisy background. The participants' action was limited to the left hand, thereby resulting in an overall higher activation in the right PCG (Bangert et al. 2006). The PCG is well known for its contralaterality behavior (Manan et al. 2015; Yusoff et al. 2013). Contralaterality refers to the way the cortex fibre receives signal predominantly from the contralateral limbs (Bernal & Altman 2001). Results from previous neuroimaging studies on human have reported that PCG is activated during various voluntary hand movements (Ehrsson et al. 2000; Manan et al. 2015; Roland & Zilles 1996; Yusoff et al. 2010). Furthermore, PCG, the supplementary motor area (SMA) and the premotor cortex (PMC) were activated whenever a movement is triggered using the hand (Colebatch et al. 1991; Grefkes et al. 2008).

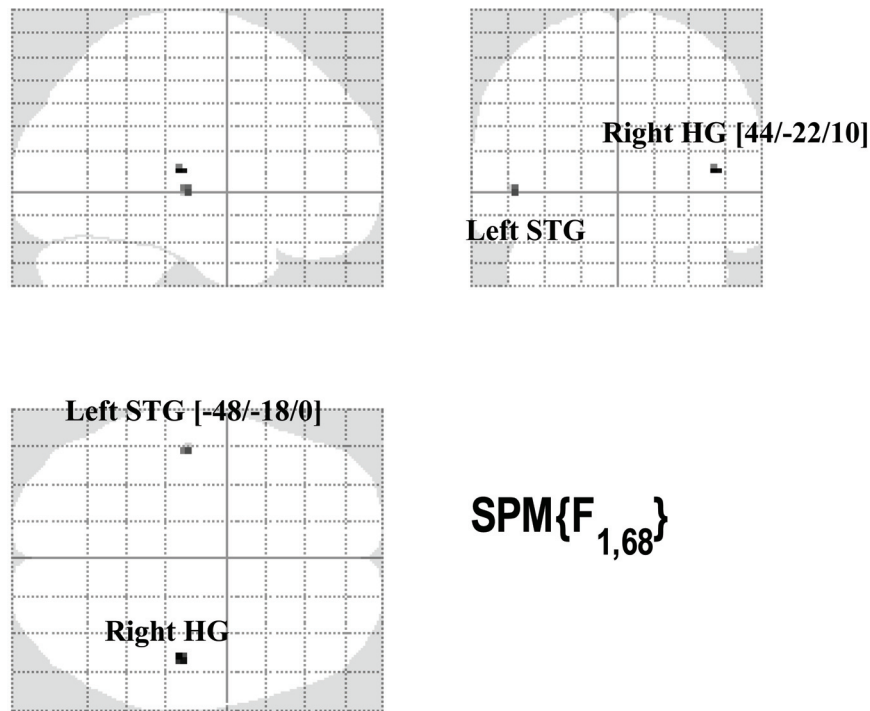


FIGURE 3 Maximum intensity projection for the brain activation due to the main effect of frequency at a corrected level of significance $\alpha = 0.05$

In addition to that, PCG could have also been implicated with its role in absolute pitch (AP) perception (Wengenroth et al. 2014) according to the nature of the present task which involved sensation (listening to the delivered tones), cognition (recognizing and decision making) and action (to wring or not to wring the rubber bulb). Absolute pitch perception refers to the auditory ability to effortlessly identify or recognize a given pitch of any tone without the use of any external reference (Zatorre 2003) such as reference tone or target tone. Several brain areas have been associated with AP perception including the motor and premotor cortices which were described as being involved in early component of pitch processing (Gaab et al. 2003; Schulze et al. 2009). Other multisensory and different network components (such as inferior parietal lobe, Broca's area, dorsolateral prefrontal cortex and parietal regions) which had been activated in auditory perception were also thought to have their own specific roles in pitch discrimination although some are only partially understood (Zatorre et al. 2007).

The right lateralization of the main effect of background in this study was subjected to the presence of white noise. White noise is much more complex than simple pure tones. It is produced by adding together pure tones of different frequencies, levels and temporal alignments (phases) (Gockel et al. 2006). It is therefore appropriate to assume that white noise has a variety of spectral form of wave and may likely to cause right lateralization of activation in the PAC during the pitch discrimination task. It has been known (Zatorre et al. 2002) that the right PAC is specialized in processing spectral information effectively and has a high

spectral resolution. Previous studies (Alcock et al. 2000; Hyde & Peretz 2004; Murayama et al. 2004) demonstrated that lesion affecting the right temporal cortex impaired specific spectral processing skill. This is in line with the facts that right PAC is better in the processing of complex spectral information (Johnsrude et al. 2000; Patterson et al. 2002) but at the expense of temporal resolution (Jamison et al. 2006). As opposed to left PAC, the right PAC appears to be denser with more interconnected columnar structure within it which are close together making it appears more conducive in evaluating and coding fine frequency distinctions (Anderson et al. 1999; Morand et al. 2001). Another interesting explanation for the right lateralization of the main effect of background is by referring to the analysis of the fine spectral structure of sound which is dedicated to music perception. Asymmetry towards the right hemisphere was found when the stimulus contains melodic information as opposed to constant pitch stimuli which showed symmetrical bilateral activation of primary and non-primary auditory cortices (Zatorre et al. 2002).

Asymmetrical bilateral activation in the PAC due to various stimulus presentations has been observed in many previous studies (Celsis et al. 1999; Griffiths et al. 1999; Hwang et al. 2005; Platel et al. 1997; Zatorre et al. 1994). Listening to melodies had caused increasing blood flow to the bilateral superior temporal cortex in particular the STG with right lateralized activation, while discriminating pitches resulted in additional right lateralized prefrontal cortex (PFC) (Zatorre et al. 1992) and inferior frontal gyrus (IFG) (Zatorre et al. 1994). In another pitch memory experiment, an extensive right lateralized

network comprising of posterior temporal gyrus (pSTG), cerebellum and IFG was observed (Griffiths et al. 1999). In contrast, more left hemispheric activities in precuneus, STG and superior frontal gyrus (SFG) were observed when the participants were required to detect changes in pitch (Platel et al. 1997). When the participants were presented with deviances in tonal sequences, a rightward asymmetry was observed in PAC and secondary auditory cortices (SAC) while the posterior temporal lobe regions indicated a leftward asymmetry (Celsis et al. 1999). In this study, the main effects of frequency were obtained when the participants discriminated pure tones. In contrast to the asymmetry of the main effects of background explained earlier, symmetrical bilateral activation in the PAC was observed in terms of the height and spatial extent of activation at a corrected significant level ($p < 0.05$), see Table 3 and Figure 3. Similar results were obtained in a previous study that used pure tones as stimuli (Gaab & Schlaug 2003) in which musician and non-musician were compared in terms of their brain activation during a pitch memory task. Non-musician showed more right primary and left secondary auditory cortex activation as compared to musician, while this study which was conducted on non-musician participants revealed significant activation in the right HG and left STG. These results suggest the equal sensitivity of the bilateral PAC in pitch memory processing when the frequency is taken as the factor, as opposed to their unequal role in response to the same task when background noise is taken as the factor. Despite the presently accepted dichotomy that the left PAC is more sensitive to tonal processing, this study reveals that PAC showed no hemispheric preference. The results also suggest that normal participants rely on these brain regions, which were widely known for their sensory role, for pitch memory processing.

During the pitch discrimination task, the bilateral activation in response to discriminating tonal frequencies is attributable to the low frequency tones rather than high frequency tones. This is supported by the results of our previous study using a t-test which indicated that regions that show more activation in discriminating low frequency tones as compared to high frequency tones were bilateral STG, left HG and right insula, while regions that show more activation in discriminating high frequency tones as compared to low frequency tones were putamen and hippocampus (Yusoff et al. 2013). In addition, behavior analysis results showed that participants were found to be better in discriminating low frequency tones as opposed to high frequency tones. An explanation pertaining to this is described elsewhere (Glasberg & Moore 1986). The study implemented a model of pitch perception for complex tones such as voiced speech which used a combination of both spatial and temporal information. In the model, initial frequency analysis divided up the spectrum into frequency bands or channels (the auditory filters). The temporal information (fiber firing rates) of each channel was then processed separately. It follows later that the

temporal analysis of fundamental frequency of the tone was most accurate in the low frequency region where the harmonics were resolved, permitting temporal analysis of a single harmonic per auditory filter thus explaining why the participants were better in discriminating low frequency pure tones. Furthermore, the auditory cortex is specialized at resolving those low frequency harmonic and thus enabling the temporal processing and coding.

Another asymmetrical behavior shown by the PAC due to the main effects of background and frequency is in the coordinates of the maximum intensity voxel, which is thought to be the processing center (Table 3 & Figure 3). The processing center in the left and right hemisphere PACs seem to be in different anatomical area but are still located in the PAC. In comparison with the results obtained by (Gaab & Schlaug 2003) which found right PAC and left SAC as the processing centers, this study indicated right HG and left STG as the processing centers for both the main effects of background and frequency. Since both ears received the stimuli bilaterally equal, which in turn projected symmetrical bilateral activation in both hemispheres, the results probably indicated different specialized area in each hemisphere to undertake the same task or they could be due to similar functional specialization of HG and STG in pitch memory processing, at least in the context of this study.

There are several limitations in the study design that may have adversely affected the results (Yusoff et al. 2013). The first concern is about the potential habituation of each participant. Varied individual personality, comfort-level in the scanner and exposure to past scans could potentially introduce additional physiological noise into the fMRI results, affecting habituation and leading to erroneous conclusions. Possible solutions to habituation would be prior and repeated exposure to the entire experimental paradigm (including sensations and sounds) in a mock-scanner setup to at least minimize the “initial novelty” of this experience. In addition, the participants could be put through an initial period of exposure at the beginning of the experiment to ensure habituation prior to recording actual data. This first concern is about the duration of dead time during which the participant’s brain is supposedly recovering from the scanner sound. This rest period of no stimulus delivery which is in between the EPI scan and the next stimulus presentation should be made longer for a complete recovery of hemodynamic response from the scanner sound. Secondly, subjects’ hand dominance might have confounded the results. Hand dominance has been shown to cause different activation in cognitive regions. Future studies should select subjects that have same hand dominance.

CONCLUSION

The main effect of action is in accordance with the contralateral voluntary behavior of PCG in motor coordination. The PCG is well known for its function as

a site for preparatory and execution of a movement and may also act as one of the pitch centers in pitch memory processing. The pitch discrimination task used in this study revealed certain points regarding the asymmetry in auditory cortex. Right lateralization of PAC for the main effects of background clearly demonstrated its functional specialization while for the symmetric main effect of frequency indicated equal specialization of the bilateral PAC which was undertaken by different brain area particularly the right HG and left STG as shown by the asymmetry of the processing center in the right and left PAC. It can therefore be concluded that the right and left PAC may have different or similar perceptual functionality in terms of spectral and temporal processing respectively at the expense of one another. HG and STG, in particular, are believed to act not only as the pitch center but also as the center for pitch memory processing, similar to PCG. This study has shown that the temporal-spectral lateralization dichotomy is not especially rigid. Future studies should focus on the differentiation of the low and high frequencies brain activation the methods in measuring it.

ACKNOWLEDGEMENT

The authors would like to thank Sa'don Samian, the MRI Technologist of the Universiti Kebangsaan Malaysia Medical Centre (UKMMC), for his assistance in the scanning, the Department of Radiology, UKMMC for the permission to use the MRI scanner and the Audiology Program, Faculty of Health Sciences UKM for conducting hearing test on the participants. This work was supported by the research grant eScience Fund 06-01-02-SF0548, the Ministry of Science, Technology and Innovation of Malaysia.

REFERENCES

- Alcock, K. J., Wade, D., Anslow, P. & Passingham, R. E. 2000. Pitch and timing abilities in adult left-hemisphere-dysphasic and right-hemisphere-damaged subjects. *Brain Lang* 75(1): 47-65.
- Alho, K., Vorobyev, V. A., Medvedev, S. V., Pakhomov, S. V., Roudas, M. S., Tervaniemi, M., van Zuijen, T. & Naatanen, R. 2003. Hemispheric lateralization of cerebral blood-flow changes during selective listening to dichotically presented continuous speech. *Brain Res Cogn Brain Res* 17(2): 201-211.
- Anderson, B., Southern, B. D. & Powers, R. E. 1999. Anatomic asymmetries of the posterior superior temporal lobes: a postmortem study. *Neuropsychiatry Neuropsychol Behav Neurol* 12(4): 247-254.
- Bangert, M., Peschel, T., Schlaug, G., Rotte, M., Drescher, D., Hinrichs, H., Heinze, H. J. & Altenmuller, E. 2006. Shared networks for auditory and motor processing in professional pianists: evidence from fMRI conjunction. *Neuroimage* 30(3): 917-926.
- Bernal, B. & Altman, N. R. 2001. Auditory functional MR imaging. *AJR Am J Roentgenol* 176(4): 1009-1015.
- Boatman, D. F. 2006. Cortical auditory systems: speech and other complex sounds. *Epilepsy Behav* 8(3): 494-503.
- Burton, H., Firszt, J. B., Holden, T., Agato, A. & Uchanski, R. M. 2012. Activation lateralization in human core, belt, and parabelt auditory fields with unilateral deafness compared to normal hearing. *Brain Res* 1454: 33-47.
- Celsis, P., Boulanouar, K., Doyon, B., Ranjeva, J. P., Berry, I., Nespoulous, J. L. & Chollet, F. 1999. Differential fMRI responses in the left posterior superior temporal gyrus and left supramarginal gyrus to habituation and change detection in syllables and tones. *Neuroimage* 9(1): 135-144.
- Colebatch, J. G., Deiber, M. P., Passingham, R. E., Friston, K. J. & Frackowiak, R. S. 1991. Regional cerebral blood flow during voluntary arm and hand movements in human subjects. *J Neurophysiol* 65(6): 1392-1401.
- Ehrsson, H. H., Fagergren, A., Jonsson, T., Westling, G., Johansson, R. S. & Forssberg, H. 2000. Cortical activity in precision- versus power-grip tasks: an fMRI study. *J Neurophysiol* 83(1): 528-536.
- Gaab, N., Gaser, C., Zaehle, T., Jancke, L. & Schlaug, G. 2003. Functional anatomy of pitch memory – an fMRI study with sparse temporal sampling. *Neuroimage* 19(4): 1417-1426.
- Gaab, N. & Schlaug, G. 2003. The effect of musicianship on pitch memory in performance matched groups. *Neuroreport* 14(18): 2291-2295.
- Galaburda, A. M. & Pandya, D. N. 1983. The intrinsic architectonic and connectional organization of the superior temporal region of the rhesus monkey. *J Comp Neurol* 221(2): 169-184.
- Glasberg, B. R. & Moore, B. C. 1986. Auditory filter shapes in subjects with unilateral and bilateral cochlear impairments. *J Acoust Soc Am* 79(4): 1020-1033.
- Gockel, H., Moore, B. C. J., Plack, C. J. & Carlyon, R. P. 2006. Effect of noise on the detectability and fundamental frequency discrimination of complex tones. *J Acoust Soc Am* 120(2): 957-965.
- Grefkes, C., Eickhoff, S. B., Nowak, D. A., Dafotakis, M. & Fink, G. R. 2008. Dynamic intra- and interhemispheric interactions during unilateral and bilateral hand movements assessed with fMRI and DCM. *Neuroimage* 41(4): 1382-1394.
- Griffiths, T. D., Johnsrude, I., Dean, J. L. & Green, G. G. 1999. A common neural substrate for the analysis of pitch and duration pattern in segmented sound? *Neuroreport* 10(18): 3825-3830.
- Hamid, K., Yusoff, A., Rahman, M., Mohamad, M. & Hamid, A. 2012. Effective connectivity between superior temporal gyrus and Heschl's gyrus during white noise listening: linear versus non-linear models. *Biomed Imaging Interv J* 8(2): e13.
- Hwang, J. H., Wu, C. W., Chou, P. H., Liu, T. C. & Chen, J. H. 2005. Hemispheric difference in activation patterns of human auditory-associated cortex: an FMRI study. *ORL J Otorhinolaryngol Relat Spec* 67(4): 242-246.
- Hyde, K. L. & Peretz, I. 2004. Brains that are out of tune but in time. *Psychological Science* 15(5): 356-360.
- Jamison, H. L., Watkins, K. E., Bishop, D. V. & Matthews, P. M. 2006. Hemispheric specialization for processing auditory nonspeech stimuli. *Cereb Cortex* 16(9): 1266-1275.
- Johnsrude, I. S., Penhune, V. B. & Zatorre, R. J. 2000. Functional specificity in the right human auditory cortex for perceiving pitch direction. *Brain* 123 (Pt 1): 155-163.

- Langers, D. R. & van Dijk, P. 2012. Mapping the tonotopic organization in human auditory cortex with minimally salient acoustic stimulation. *Cereb Cortex* 22(9): 2024-2038.
- Langers, D. R., van Dijk, P. & Backes, W. H. 2005. Lateralization, connectivity and plasticity in the human central auditory system. *Neuroimage* 28(2): 490-499.
- Manan, H. A., Franz, E. A., Yusoff, A. N. & Mukari, S. Z. 2015. The effects of aging on the brain activation pattern during a speech perception task: an fMRI study. *Aging Clin Exp Res* 27(1): 27-36.
- Morand, N., Bouvard, S., Ryvlin, P., Mauguier, F., Fischer, C., Collet, L. & Veillet, E. 2001. Asymmetrical localization of benzodiazepine receptors in the human auditory cortex. *Acta Otolaryngol* 121(2): 293-296.
- Murayama, J., Kashiwagi, T., Kashiwagi, A. & Mimura, M. 2004. Impaired pitch production and preserved rhythm production in a right brain-damaged patient with amusia. *Brain Cogn* 56(1): 36-42.
- Obleser, J., Eisner, F. & Kotz, S. A. 2008. Bilateral speech comprehension reflects differential sensitivity to spectral and temporal features. *J Neurosci* 28(32): 8116-8123.
- Patterson, R. D., Uppenkamp, S., Johnsrude, I. S. & Griffiths, T. D. 2002. The processing of temporal pitch and melody information in auditory cortex. *Neuron* 36(4): 767-776.
- Platel, H., Price, C., Baron, J. C., Wise, R., Lambert, J., Frackowiak, R. S., Lechevalier, B. & Eustache, F. 1997. The structural components of music perception. A functional anatomical study. *Brain* 120 (Pt 2): 229-243.
- Roland, P. E. & Zilles, K. 1996. Functions and structures of the motor cortices in humans. *Curr Opin Neurobiol* 6(6): 773-781.
- Romanski, L. M., Bates, J. F. & Goldman-Rakic, P. S. 1999. Auditory belt and parabelt projections to the prefrontal cortex in the rhesus monkey. *J Comp Neurol* 403(2): 141-157.
- Schulze, K., Gaab, N. & Schlaug, G. 2009. Perceiving pitch absolutely: comparing absolute and relative pitch possessors in a pitch memory task. *BMC Neurosci* 10: 106.
- Specht, K. & Reul, J. 2003. Functional segregation of the temporal lobes into highly differentiated subsystems for auditory perception: an auditory rapid event-related fMRI-task. *Neuroimage* 20(4): 1944-1954.
- Tervaniemi, M. & Hugdahl, K. 2003. Lateralization of auditory-cortex functions. *Brain Res Brain Res Rev* 43(3): 231-246.
- Wengenroth, M., Blatow, M., Heinecke, A., Reinhardt, J., Stippich, C., Hofmann, E. & Schneider, P. 2014. Increased volume and function of right auditory cortex as a marker for absolute pitch. *Cereb Cortex* 24(5): 1127-1137.
- Yusoff, A. N., Abdul Hamid, K., Mohamad, M., Abdullah, A., Abdul Hamid, H. & Mukari, S. Z. M. 2013. Assessing human cortical activation and network during pitch discrimination task in quiet and in noisy background. *Modern Applied Science* 7(10): 42-59.
- Yusoff, A. N., Mohamad, M., Hamid, A. I. A., Wan Abdullah, W. A. K., Hashim, M. H. & Zulkifli, N. Z. 2010. Functional specialisation and effective connectivity in cerebral motor cortices: An fmri study on seven right handed female subjects. *Malaysian Journal of Medicine and Health Sciences* 6(2): 71-92.
- Yusoff, A. N., Mohamad, M., Hamid, K. A., Abd Hamid, A. I. & Mukari, S. Z. M. S. 2011. Acquisition, Analyses and Interpretation of fMRI Data: A Study on the Effective Connectivity in Human Primary Auditory Cortices. *Sains Malays* 40(6): 665-678.
- Zatorre, R. J. 2003. Absolute pitch: a model for understanding the influence of genes and development on neural and cognitive function. *Nat Neurosci* 6(7): 692-695.
- Zatorre, R. J., Belin, P. & Penhune, V. B. 2002. Structure and function of auditory cortex: music and speech. *Trends Cogn Sci* 6(1): 37-46.
- Zatorre, R. J., Chen, J. L. & Penhune, V. B. 2007. When the brain plays music: auditory-motor interactions in music perception and production. *Nat Rev Neurosci* 8(7): 547-558.
- Zatorre, R. J., Evans, A. C. & Meyer, E. 1994. Neural mechanisms underlying melodic perception and memory for pitch. *J Neurosci* 14(4): 1908-1919.
- Zatorre, R. J., Evans, A. C., Meyer, E. & Gjedde, A. 1992. Lateralization of phonetic and pitch discrimination in speech processing. *Science* 256(5058): 846-849.
- Zatorre, R. J. & Gandour, J. T. 2008. Neural specializations for speech and pitch: moving beyond the dichotomies. *Philos Trans R Soc Lond B Biol Sci* 363(1493): 1087-1104.
- Ahmad Nazlim Yusoff,
 Khairiah Abdul Hamid
 Farah Nabila Ab Rahman
 Mazlyfarina Mohamad
 Diagnostic Imaging and Radiotherapy Program
 School of Diagnostic and Applied Health Sciences
 Faculty of Health Science
 Universiti Kebangsaan Malaysia
 Jalan Raja Muda Abdul Aziz
 50300 Kuala Lumpur, Malaysia
- Khairiah Abdul Hamid
 Medical Imaging Program
 School of Health Science
 KPJ Healthcare University College
 Lot PT 17010, Persiaran Seriemas
 Kota Seriemas, 71800 Nilai
 Negeri Sembilan, Malaysia
- Siti Zamratol-Mai Sarah Mukari
 Institute of Ears, Hearing and Speech (I-HEARS)
 Universiti Kebangsaan Malaysia
 Jalan Temerloh, 53200 Kuala Lumpur
- and
- Audiology Program
 School of Rehabilitation Sciences
 Faculty of Health Science
 Universiti Kebangsaan Malaysia
 Jalan Raja Muda Abdul Aziz
 50300 Kuala Lumpur, Malaysia
- Corresponding author: Ahmad Nazlim Yusoff
 E-mail address: nazlimtrw@ukm.edu.my
- Tel: 03-9289 7295
 Fax: 03-2692 9032
- Received: December 2016
 Accepted for publication: July 2017