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Kertas Asli/*Original Article*

Bilateral Heschl's Gyrus Display Non-Reciprocity in Connectivity during the Performance of Simple Arithmetic Addition Task

(Girus Heschl Bilateral Menunjukkan Kehubungan Tak Bersaling Semasa Perlaksanaan Tugasan Aritmetik Mudah)

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ABSTRACT

Heschl's gyrus (HG) is known to interact with other auditory related areas of the same hemisphere during the performance of an auditory cognitive task. However, the information about how it interacts with the opposite HG is still lacking. The aim of this study was to investigate the psychophysiologic interaction (PPI) between the bilateral HG during a simple arithmetic addition task and to verify the role of noise as an experimental factor that would modulate the PPI. Functional magnetic resonance imaging (fMRI) scans were performed on eighteen healthy participants, in which a single-digit addition task were solved during in-quiet (AIQ) and in-noise (AIN) conditions. The fMRI data were analysed using Statistical Parametric Mapping (SPM8). The interaction between the bilateral HG was investigated using PPI analysis. The response in right HG was found to be linearly influenced by the activity in left HG, vice-versa, for both in-quiet and in-noise conditions. The connectivity from right to left HG in noisy condition seemed to be modulated by noise, while the modulation is relatively small oppositely, indicating a non-reciprocal behavior. A two-way PPI model between right and left HG is suggested. The connectivity from right to left HG during a simple addition task in noise is driven by a higher ability of right HG to perceive the stimuli in a noisy condition. Both the bilateral HGs took part in the cognitive processes of arithmetic addition from which the interactions between the two were found to be different in noise.

Keywords: Psychophysiologic interaction; auditory cortex; fMRI; SPM; random-effects analysis; reciprocal

ABSTRAK

Girus Heschl (HG) diketahui berinteraksi dengan kawasan berkaitan auditori lain dalam hemisfera yang sama semasa perlaksanaan tugasan auditori kognitif. Walau bagaimanapun, maklumat mengenai bagaimana ia berinteraksi dengan HG bertentangan masih kurang. Matlamat kajian ini adalah untuk menyelidiki interaksi psikofisiologi (PPI) di antara HG bilateral semasa tugasan penambahan aritmetik mudah dan untuk mengesahkan peranan hingar sebagai faktor uji kaji yang boleh memodulasi PPI. Imbasan pengimejan resonans magnet kefungsian (fMRI) dilakukan ke atas lapan belas subjek sihat, bila mana tugasan penambahan digit tunggal diselesaikan dalam keadaan senyap (AIQ) dan hingar (AIN). Data fMRI dianalisis menggunakan Pemetaan Statistik Berparameter (SPM8). Interaksi di antara HG bilateral diselidiki menggunakan analisis PPI. Respons HG kanan didapati dipengaruhi secara linear oleh aktiviti HG kiri, dan juga sebaliknya, untuk kedua-dua keadaan senyap dan hingar. Kehubungan dari HG kanan ke HG kiri dalam keadaan hingar seperti dimodulasi oleh hingar, sementara modulasi adalah kecil secara relatif dalam arah bertentangan, menunjukkan kelakuan tak bersaling. Satu model PPI dua hala di antara HG kanan dan HG kiri dicadangkan. Kehubungan dari HG kanan ke HG kiri semasa tugasan penambahan mudah dalam hingar dipacu oleh kebolehan HG kanan yang lebih baik untuk mengamati stimulus dalam keadaan hingar. Kedua-dua HG berperanan dalam proses kognitif penambahan aritmetik daripada mana interaksi di antara keduanya di dapati berbeza dalam hingar.

Kata kunci: Interaksi psikofisiologi; korteks auditori; fMRI; SPM; analisis kesan rawak; bersaling

INTRODUCTION

Heschl's gyrus (HG), also known as transverse temporal gyrus (TTG), is located in the primary auditory cortex. Both the right and left hemisphere HG have the same general functional role i.e. to receive and to process the incoming auditory information, before sending it to other related areas (Boatman 2006; Humphries et al. 2010; Langers & van Dijk 2012). Studies showed that the auditory cortices have developed asymmetrically to cater for specialized functions, both in normal (Hwang et al. 2005) and unilateral deaf individuals (Burton et al. 2012). The left auditory areas for instance, have a better ability in temporal processing, while the right auditory areas have a better ability in spectral processing (Boemio et al. 2005; Zatorre et al. 2002). In addition, most of the temporal regions in the left hemisphere showed extended activation during a task performance involving speech and cognitive processing such as arithmetic working memory (Hamid et al. 2011), while the right hemisphere regions were activated comparatively higher than the left hemisphere regions when listening to non-verbal stimulations (Hwang et al. 2005). However, the knowledge on how the left and right hemisphere auditory regions interact during the accomplishment of a task and how noise influence the interaction is still lacking, for example the psychophysiologic interaction (PPI) between the bilateral primary auditory cortices (HG).

PPI is defined as the contribution of the activity in one region to the response of another that is altered significantly with the presence of an experimental factor or a psychological context (Friston et al. 1997). A PPI also means that the contribution of one area to another, changes significantly with the presence of experimental manipulations (Friston et al. 1997; Friston et al. 1995; Smith et al. 2012). PPI is considered to exist if there is a significant difference in the regression slope for both 'in the absent' and 'in the presence' of the psychological factors such as in quiet and in noise (Yusoff 2014) or with low-speed or high-speed action (Yusoff 2013). The response in one area can be predicted based on the activity in another area, that corresponds to the contribution of the psychological factor in the interaction. PPI analysis can be used to investigate which voxels in a brain region that increase their covariance with a seed area of interest in a given event (O'Reilly et al. 2012). The brain areas whose activity is influenced by an interaction between psychological factors and physiological factors (O'Reilly et al. 2012) can thus be determined. In our previous study, PPI was found to exist with the speed of the action influences the interaction between the right pre-central gyrus and superior parietal lobule (Yusoff 2013). In short, PPI is an example of effective connectivity, which can be defined as the influence that one neural system exerts over another (Friston et al. 1997). The objective of an effective connectivity analysis is to estimate parameters that represent influences among regions that may change with respect to experimental tasks.

Apart from investigating the PPI between the bilateral HG, this work also investigated the influence of noise in the activation of the bilateral HG. An increase in the activation of an area is associated with a higher processing demand and a higher attention during the performance of a task. In the presence of background noise, the increase in activation is a result of the brain response to overcome this interference (Hanani et al. 2013). In another study, it was found that the performance of simple arithmetic addition task with the presence of background noise stimulated a higher cognitive process in working memory and attention (Hamid et al. 2011) as correspond to in quiet. To date, it is not known whether the increase in activation in one region following an increase in activation in another due to the presence of noise correlates with the results obtained from connectivity analysis between the two particular regions. If the relationship exists, it can be suggested that brain activation has some influence on the magnitude of connection between the regions.

The general objective of this study was to investigate the interaction characteristics between the bilateral HG. The two specific objectives include 1) to determine the existence of psychophysiologic interaction (PPI) between the bilateral HG during an arithmetic working memory task performance in quiet and in noisy conditions, and 2) to subsequently determine whether noise plays an important role as an experimental factor that influence the interaction between the bilateral HG. The importance of this study lies on the fundament of the investigation of the PPI between bilateral HG and the outcome of this work would contribute to the rehabilitation strategy of patients with brain disorders. The present study investigated the PPI of the specific structure in auditory cortices which is HG during the performance of an arithmetic working memory e.g. the simple addition task. This simple arithmetic addition task involved processing of numbers, recalling of numerical knowledge, calculating of numbers given and working memory (Hamid et al. 2011). The PPI was hypothesised to exist non-reciprocally between the right and left HG when the participants perform the simple arithmetic addition tasks. The interaction between the bilateral HG is hypothesised to be influenced by noisy background which is the experimental factor used in this study.

METHODS

PARTICIPANTS

Eighteen native, Malay-speaking, male adults participated in the present study. All the participants agreed to participate by filling in the informed consent and screening forms and signing them, after being given full explanation of the nature and risks of the research, as required by the Institutional Ethics Committee (IEC) NN-049-2009. The participants were conveniently recruited from Universiti Kebangsaan Malaysia (UKM) Kuala Lumpur campus and were screened by of the Malaysian Certificate of Education to obtain a group of participants who could perform simple mathematical operations. Only those who passed their mathematics papers were enrolled in this study. None of the participants were professional mathematician or actively involved in teaching mathematics. The participants were interviewed on their health condition prior to the scanning session. All the participants were tested for handedness using the Edinburgh Handedness Inventory (Oldfield 1971). The participants were also tested for their middle ear condition and hearing level using a tympanometer (Model Grason Stadler Inc. GSI33) and a pure-tone audiometer (Model Grason Stadler Inc. GSI61) respectively, by a qualified Audiologist. Pure tone audiometry (PTA) was conducted in the frequency range of 250 Hz to 8000 Hz.

DEMOGRAPHICAL DATA

The average age and standard deviation of the participants were 23.2 ± 2.5 years (ranged between 20 to 28 years). All participants reported no history of psychiatric or neurological disorder and no current use of any psychoactive medications. All participants were confirmed to be right handed with average laterality index (LI_{ave}) of 87 in the range of sixth to seventh right. In a study by Deutsch (1978), left-handed participants have been found to perform the pitch discrimination tasks significantly better than the right-handed. Based on this finding and on the fact that both arithmetic and pitch memory processing would involve working memory, it is important that the participants should not be mixed in terms of their handedness to avoid confounding effects. The participants were found to have no hearing impairment and no history of long time exposure to loud noise to be inappropriate for auditory stimulus presentation. The participants' hearing levels for both ears are not greater than 30 dB (HL) in the respective range of frequency used for the PTA test.

EXPERIMENTAL TASKS

The experimental tasks consisted of simple arithmetic addition problems that need to be solved by the participants. Each arithmetic addition problem consisted of four digits that were randomly selected from numbers 0 to 9, e.g. (2 + 1 + 5 + 4). Each digit may appear twice such as (6 + 2 + 4 + 2) but not more than twice. The arithmetic addition problems were recorded in a CD ROM using a male voice. Prior to the recording, the voice was verified by a Speech Pathologist for a correct pronunciation and intonation. There were altogether 60 sets of an arithmetic addition problem that were recorded as stimuli. The recordings were alternately done in quiet (known as Addition in Quiet - AIQ) and in the presence of white noise as background (known as Addition in Noise - AIN). For AIN, the 83-dB stimuli were embedded in 80-dB noise to obtain a signal-to-noise ratio (SNR) of 3dB. The alternating sequence of the 30 arithmetic addition problems in quiet and 30 arithmetic addition problems in the noisy background was fixed so that all participants attended to the same experimental task. A complete arithmetic addition problem set is given elsewhere (Abd Hamid et al. 2011).

fMRI EXPERIMENT

Prior to the functional magnetic resonance imaging (fMRI) scans, all the participants were given detailed instructions on how to respond to the stimuli and were allowed to practice. The participant to be scanned was laid down supine in the MRI gantry. The participant was required to put on the MRI headphones (transmission of sound stimulus through an air tube) for the delivery of instructions and stimuli and the radiofrequency (RF) head coil for signal transmission and reception. The participants were also instructed not to move their head during the scan as it can cause signal intensity changes over time from any one voxel and present a serious confound in fMRI studies. To minimize head movement, immobilizing devices were used together with the head coil.

A sparse fMRI paradigm was used for this study (Abd Hamid et al. 2011). This type of paradigm had previously been used in auditory studies (Binder et al. 2004; Hall et al. 1999). The recorded stimuli were presented using a digital playback system during the silent gaps between volume acquisitions and did not overlap with the sound produced by the scanner. Thus, the effects of the scanner sound on the MRI images were avoided. The duration of the stimuli was 6 s.

As mentioned above, each participant was subjected to two different conditions, which were AIQ and AIN. The participants were instructed to listen carefully to the 6-s stimuli and were required to start performing the calculations (imaginary) immediately after hearing the first digit. The participants were required to provide an answer verbally to the addition tasks in 3 - 5 s after the last digit. Participant's response in answering is important in order to evoke responses in the respective brain areas, and to ensure that the participants remain alert and focused throughout the scanning session.

The functional imaging session consisted of 120 series of trials (or measurements); 30 trials for AIQ, 30 trials for AIN and 60 trials for baseline (stimulus not given). The sequence was AIQ-BASELINE-AIN-BASELINE-AIQ. A long (11 s) inter-measurement interval was used to allow for the hemodynamic response to decline after each given stimulus. The acquisition time was 5 s, with each functional measurement producing 35 axial slices in the 5-s duration (one image slice per 143 ms). The measurement started with AIQ. The imaging time for each session was 32 minutes, which produced 120 × 35 = 4200 images in total.

DATA ACQUISITION

The fMRI scans were conducted in the Department of Radiology, UKM Medical Centre. Functional images were acquired using a 1.5T magnetic resonance imaging (MRI) system (Siemens Avanto, Erlangen, Germany) equipped with blood oxygenation level-dependent imaging protocol, echo-planar imaging capabilities, and radiofrequency head coil used for signal transmission and reception. Echo-planar imaging (EPI) pulse sequence was used to produce T2*-weighted images. The imaging parameters are repetition time (TR) = 16000 ms, acquisition time (TA) = 5000 ms (interval between two scans = 16000 ms − 5000 ms = 11000 ms), echo time (TE) = 50 ms, field of view (FOV) = 192 × 192 mm, flip angle = 90°, matrix size = 128 × 128, and slice thickness = 3 mm. In addition, high resolution anatomical images of the entire brain were obtained using a T1-weighted multiplanar reconstruction (MPR) spin-echo pulse sequence with the following parameters: TR = 1620 ms, FOV = 250 × 250 mm, flip angle = 90°, matrix size = 128 × 128, and slice thickness = 1 mm.

POST-PROCESSING

All the T2*- and T1-weighted images were analyzed at the Diagnostic Imaging & Radiotherapy Program, Faculty of Health Sciences, UKM Kuala Lumpur. Image analyses were performed using a personal computer. Matlab (7.8 R2009a Mathworks Inc., Natick, MA, USA) -based Statistical Parametric Mapping (SPM8) (Functional Imaging Laboratory, Wellcome Department of Imaging Neuroscience, Institute of Neurology, University College of London) was used in the analysis. The T1 and T2*-weighted images which were initially in DICOM (.dcm) formats were transformed into Analyze (.hdr, .img) format using SPM8. Functional images from each measurement were realigned using the 6-parameter affine transformation translationally (*x*, *y*, and *z*) and rotationally (pitch, roll, and yaw) to reduce artefacts from participant movement and to make within- and between-participant comparisons meaningful.

Following realignment, a mean image of the series was used to estimate some warping parameters that mapped it onto a template that conformed to a standard anatomical space, i.e., EPI template provided by the Montreal Neurological Institute (MNI). The normalization procedure used a 12-parameter affine transformation, where the parameters constituted a spatial transformation matrix. The images were then smoothed using a 6-mm full-width-at-half-maximum Gaussian kernel. The activated voxels were identified by the general linear model approach by estimating the parameters of the model and deriving the appropriate test statistic (*t* statistic) for every voxel. Statistical inferences were finally obtained based on Gaussian random field theory.

GROUP ANALYSES

The Wakeforest University (WFU) Pickatlas, an SPM toolbox (Maldjian et al. 2003), was used in obtaining the activation for the bilateral HG from the random effects analysis (RFX) statistical parametric maps. For AIQ and AIN, statistical inference was made at $\alpha = 0.05$, corrected for multiple comparisons. The anatomy of the activated brain regions were confirmed using Anatomy toolbox (Eickhoff et al. 2005).

PSYCHOPHYSIOLOGIC INTERACTION (PPI) ANALYSIS

Bilateral HG was chosen for PPI analysis due to their important roles as processing centre in a task involving auditory function. However, we found that not all participants showed significant activations ($p_{FWE} < 0.05$) in the bilateral HG. Therefore, PPI analyses were conducted only on participants who showed significant activation in bilateral HG. The PPI analysis was undertaken separately for each condition. The response in one region of interest (ROI), known as the target region, in terms of an interaction between the influence of another ROI, known as the source region and the background condition was investigated. A 4-mm radius sphere (VOI = volume of interest) with the point of maximum intensity as the centre was drawn from each ROI in both quiet and noisy backgrounds. In this study, the R-HG and L-HG were the interchangeable set of the source and target regions.

The PPI response in the target region was then plotted as a function of the activity in the source region, assumed to be interacting with the experimental factor (noise) and thereby influencing the response in the target region. PPI is considered to exist if there is a significant change in the slope of the regression line, which is the plot of the response in a target region vs. the activity in the source region, either with or without the interaction with the experimental factor (Friston et al. 1997).

A simple linear regression analysis was performed using IBM SPSS Version 20 to investigate the interaction between the ROIs in quiet and noisy backgrounds at p = 0.05 (95% confidence interval). Individual participant's regression coefficients for the above-mentioned plots were also determined and were compared using a paired *t* test to test for any significant difference in the regression coefficient values between in-quiet and in-noise conditions.

RESULTS

BRAIN ACTIVATION

Figure 1(a) shows the brain activation in the bilateral HG during AIQ. The activation maps were overlaid onto the standard axial T1 images at selected cross sections. R: right, L: left. Color codes represent increasing *t* statistics from blue to red. Figure 1(b) is the activation during AIN. The activation maps were obtained from group random effects analysis (RFX) ($t > 4.07$, $p_{FWE} < 0.05$ corrected for multiple comparisons) using the WFU Pickatlas toolbox (Maldjian et al. 2003). Leftward height extent of activation can be clearly observed based upon the colour codes. The corresponding activated areas, together with their number of activated voxels (*NOV*), coordinates of maximum intensity, and the respective *t* statistics were presented in Table 1. The maximum intensity voxel for both AIQ ($t = 8.15$) and AIN ($t = 8.96$) were observed at the same coordinates, -42/-22/6, which were in the left HG. The total *NOV* in the left and right HG were 140 and 90 during AIQ and, 128 and 123 during AIN respectively. In the one hand, asymmetrical leftward (left higher than right) height extent of activation is observed in the left HG during both the AIQ and AIN. However, the spatial extent of activation indicates leftward activation during AIQ but is almost equals during AIN. On the other hand, the right HG shows an increase in the height and spatial extent of activation during AIN as compared to AIQ, while the left HG indicates a decrease in spatial extent of activation during AIN but an increase in the height extent of activation when compared with AIQ.

TABLE 1. Activated bilateral HG during AIQ and AIN ($p < 0.05$ corrected for multiple comparisons) with their number of activated voxels (NOV), coordinates of maximum intensity (x, y, z) and the t statistics

Condition	Region	NOV	*x*	*y*	*z*	*t*
AIQ	L-HG	140	-42	-22	6	8.15
	R-HG	90	52	-14	4	6.22
AIN	L-HG	128	-42	-22	6	8.96
	R-HG	123	52	-12	4	7.15

Abbreviations: AIQ = addition in quiet, AIN = addition in noise, HG = Heschl's gyrus

PSYCHOPHYSIOLOGIC INTERACTION

The Psychophysiologic interaction (PPI) between the bilateral HG is presented graphically by plotting the PPI data obtained from the target region against the PPI data obtained from the source region, during the AIQ and AIN tasks. Figure 2(a) illustrates the PPI between right HG (target region) and left HG (source region) while Figure 2(b) shows the PPI plots between the left HG (target region) and right HG (source region). The best-fit line equation, the R^2 value and the number of participants involved (N) are shown on both of the PPI figures. For both plots, the response over the target region (vertical axis) increased linearly and significantly ($p < 0.05$) with the increase in the activity within the source region (horizontal axis) for both AIQ and AIN conditions. The activity in the left HG had an almost a similar effect upon the response in the right HG in quiet and in noisy conditions based on the small difference in the regression coefficient values that were obtained (Figure 2(a)). It can be said that the influence that the left HG has on the right HG during the performance of a simple arithmetic addition task in noise is comparable to that in quiet. A relatively small change in the slope is observed when left HG acts as the source region from which the slopes are 0.35 and 0.38 for both the AIQ and AIN lines respectively.

In Figure 2(b), the response in the left HG is plotted against the activity in the right HG, illustrating different results as compared to Figure 2(a). The activity in the right HG had a different influence upon the response in the left HG in quiet and in noise. The red regression line (AIN) shows a steeper slope than the black regression

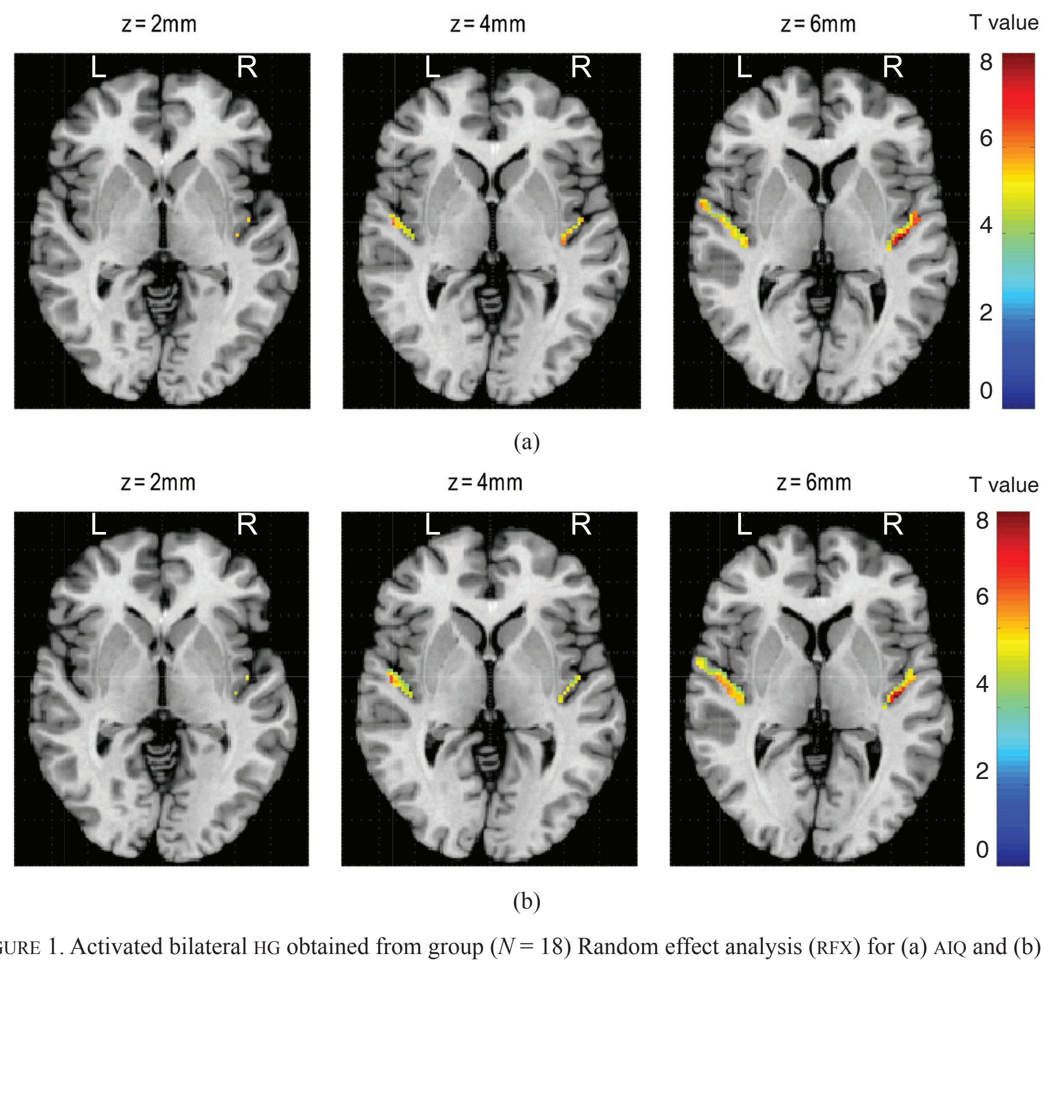

FIGURE 1. Activated bilateral HG obtained from group (N = 18) Random effect analysis (RFX) for (a) AIQ and (b) AIN

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line (AIQ) (Figure 2(b)). The findings from the two plots suggest that noisy condition increased the influence of the source region upon the response in the target region during the performance of simple addition task. From Figure 2(b), it can be seen that there is an increase in the slope (gradient) of the line from 0.39 for AIQ to 0.52 for AIN, when the right HG acts as the source region.

Comparisons made on the individual participant's regression coefficient values between AIQ and AIN using two-sample *t* test revealed a higher coefficient for AIN as compared to AIQ. However, the difference is not significant ($p > 0.05$). This lack of significant difference could possibly be due to insufficient number of participants that have shown significant activation in the bilateral HG at a corrected threshold. Nevertheless, it is worth noting that despite the insignificant difference between the regression coefficient values, the group results shown in Figure 2(a) and (b) indicate a significant ($p < 0.05$) correlation between the activity of the source region and the response of the target region for the bilateral HG during the performance of the simple addition tasks in quiet and in noise.

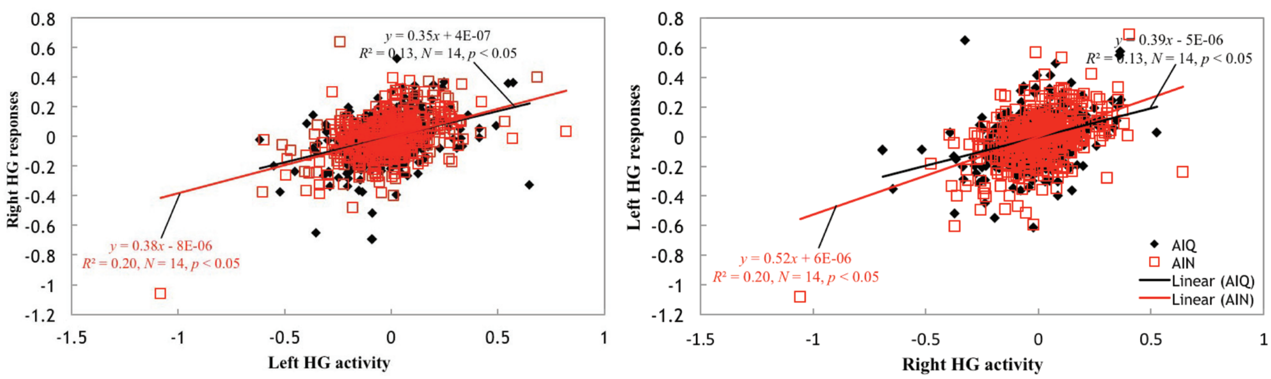
Figure 3 (a) and (b) show the suggested PPI model that can be used to explain the effective connectivity between the bilateral HG during AIQ and AIN respectively. The values indicated in the figures are the regression coefficient values taken accordingly from Figs. 2(a) and (b). The magnitude of the regression coefficient presumably reflects the strength of the connection. It can be seen that in a quiet condition, the connectivity between the left and right HG is reciprocal with an almost similar strength of connection between the two regions. In the presence of noise as the experimental factor, the connectivity from left HG to right HG is similar to that in a quiet condition but the connectivity from right HG to left HG is increased with noise modulating the connection, indicating non-reciprocity. Noise, however, imposed a direct influence on both the bilateral HG.

DISCUSSION

BRAIN ACTIVATION PATTERN

From the brain activation results shown in Table 1 and Figure 1, both the AIQ and AIN were found to significantly activate the HG bilaterally, in addition to other cognition-related areas (Abd Hamid et al. 2011). The results suggest that the arithmetic addition task activated the bilateral HG as both tasks involved the processing of auditory information that was delivered binaurally through both ears, regardless of whether the task is performed in a quiet or in a noisy condition. AIQ and AIN used the same method of stimulus delivery and should activate the HG bilaterally. The activation in the HG could be due not only to the processing of auditory stimuli but also to the execution of cognitive processing by the participants. This is supported by a previous study (Abdul Manan et al. 2013) that indicated the role of HG in cognitive function, from which it was found that the functional networks that underlie STG, HG and cerebellum undergo reorganization to compensate for the cognitive decline.

The maximum intensity voxel for both AIQ and AIN (Table 1) was observed at the same coordinates which is in the left HG. The left HG showed a higher number of activated voxels (*NOV*) as compared to the right HG during AIQ, while the *NOV* for the left and right HG are almost equals during AIN. 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 (Hwang et al. 2005; Tervaniemi & Hugdahl 2003; Zatorre et al. 1992). During AIQ, there was no background noise in the stimuli. The participants only hear the presentation of the arithmetic addition problems which were recorded in a CD ROM using a male voice which in this case a speech-related stimuli and should activate the left HG wider than



(a) (b)

FIGURE 2. Results of psychophysiologic interaction (PPI) analysis during AIQ and AIN between right HG and left HG for (a) left HG as the source region and (b) right HG as the source region

the right HG. During AIN, the stimuli were delivered in the presence of background noise. According to a previous study (Hwang et al. 2005), the presence of noise plays a role in increasing the *NOV* in the right hemisphere. Thus, the combined effects of stimuli and noise during AIN equalized the extent of activation in the left and right HG. However, for the height extent of activation (*t* statistics), the value is always higher for the left HG, either the task was performed in quiet or in a noisy background. While the spatial extent of activation indicates the extent of brain areas that are involved in a task, the height extent of activation is related to the sensitivity of a particular area to a particular task. From the results of this study, it can be said that the left HG is relatively more sensitive to verbal stimuli as compared to the right HG regardless of whether the stimuli were delivered in quiet or in the presence of background noise. The asymmetry of the locations of the point of maximum intensity for the left and right HG during both the AIQ and AIN clearly indicates different locations of processing centre in the left and right HG for the processing the same stimuli and the locations are not influenced by the presence of noise.

Comparing the spatial extent of activation of a particular region in different background, the left HG shows a decrease in *NOV* in noisy background as compared to in quiet. These mean that a wider brain area or more brain cell was recruited in the left HG in quiet than it was in noisy background, indicating a reduction in its involvement when the noise is present. It can be said that the activation in the left HG is more likely to be suppressed by noise. In contrast, for the right HG, more voxels are activated when the noise is present as compared to in quiet. It can be said that the activation in the right HG is more likely to be enhanced by noise. This is in good agreement with the present dichotomy that the right temporal lobe regions are more specialized for non-verbal stimuli such as noise and music while the left temporal lobe regions are more specialized for verbal stimuli. In terms of the height extent of activation (*t* statistics), both the left and right HG show a higher value in noisy condition as compared to in quiet. These indicate the increase in the sensitivity of each particular area when the task is performed in noisy condition, at least in the context of this study. This was done by the brain, perhaps, in order to give more attention to the given stimuli in the presence of background disturbance.

PSYCHOPHYSIOLOGIC INTERACTION

Figure 2(a) and (b) show the responses over the target region that increases linearly against the increase in the activity within the source region, regardless of whether the task was being performed in quiet (dark line) or in noise (red line). The slope on a line reflects the influence that the source region exerted over the target region. The change in the slope on a plot indicates the presence of PPI, with noise (presumably the increase in attention) as the experimental factor that modulates the influence that the activity within the source region has on the response over the target region. Thus, a steeper plot slope means that a small change in the activity of the source region results in a relatively larger response over the target region.

Figure 2(a) shows that the slope of the AIQ line is almost equals that of the AIN line (left HG as the source region and right HG as the target region). Thus, PPI is not observable in the plots of the response of the left HG against the activity of the right HG. These results indicate that the connectivity from left HG to right HG is not influenced by any experimental factors that exist, which is noise in this case, see the suggested PPI model shown in Figure 3(a). As mentioned earlier, the left auditory

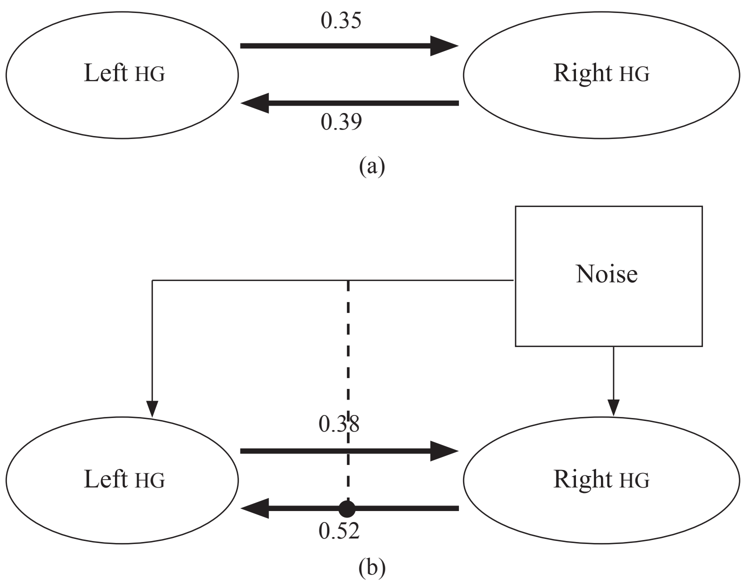


FIGURE 3. PPI models indicating a) reciprocity and b) non-reciprocity in connectivity between the left and right HG during AIQ and AIN respectively. Dotted line indicates modulation of connection by noise. The regression coefficient values are depicted for comparisons

cortex was found to be more responsive to verbal stimuli but less responsive to non-verbal stimuli as compared to the right auditory cortex (Mari Tervaniemi & Kenneth Hugdahl 2003; Yusoff et al. 2008). Thus, the transmission of signal to other cortical areas, such as the auditory cortex in the right hemisphere, is less influenced by the noisy condition. The experimental factor, however, exerts a direct influence on the respective regions.

In Figure 2(b), the presence of PPI is noticeable with noise as the experimental factor that modulates the influence that the activity within the right HG has over the response of the left HG. Regions in the right auditory cortex have been found to be more responsive to noise as compared to the regions in the left auditory cortex. Thus, the activity in the right HG could possibly be influenced by the noisy background during the transmission of auditory signal to the left HG. In addition, the disturbance in the right HG would also demand more efforts to overcome the interference and to accomplish the task. Consequently, in the course of interaction between the activities in the right HG with the experimental factor (noise), a larger influence is conveyed onto the response of the left HG, which is the target region.

PPI models (Figure 3) constructed from the results shown in Figure 2 schematically explains the difference in the response of the bilateral HGs in the absent and presence of noisy background during the performance of the arithmetic addition task. The bilateral HGs clearly indicate a reciprocal characteristic of connectivity when the task is performed by the participants in a quiet condition. A non-reciprocal behaviour of connectivity is observed when the task is performed in a noisy condition from which a stronger influence is imposed by the right HG onto the left HG in accomplishing the task. Noise, as the psychological or experimental factor can be thought of as modulating the contribution of one area to another in terms of neuronal activity (Friston et al. 1997). This can be understood as a condition or context sensitive change in the contributional aspects of connectivity between the two areas (Friston et al. 1997). Thus, Figure 3 has provides another experimental evident in accordance to the temporal-spectral lateralization dichotomy of the primary auditory cortex which explains the well-known ability of the right hemisphere regions in responding to spectral type of stimuli.

CONCLUSION

In conclusion, simple arithmetic (single-digit) addition task used for this study in which the stimuli were presented verbally, evoked extended activation in the bilateral HG, regardless of whether the task was performed in a quiet or in a noisy background. HG was found to be activated mainly due to its functional role in auditory processing. PPI results indicated that in noisy condition, the connectivity from the left HG to the right HG is not influenced by the experimental factor. In contrast, the connectivity from the right HG to the left HG is modulated by the interaction between the activity of the right HG and the experimental condition, e.g. noise. The steeper slope of the regression line in noisy condition points to an argument which suggests that the persisting interaction when the right HG acts as the source region is modulated by the noise which could be due to the relatively larger influence of noise on the right hemisphere auditory cortex. In quiet, the connectivity between the left and right HG is reciprocal with an almost similar strength of connection between the two regions. In the presence of noise as the experimental factor, the connectivity from left HG to right HG is similar to that in a quiet condition but the connectivity from right HG to left HG is increased with noise modulating the connection, indicating non-reciprocity.

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REFERENCES

Abd Hamid, A.I., Yusoff, A.N., Mukari, S.Z. & Mohamad, M. 2011. Brain activation during addition and subtraction tasks in-noise and in-quiet. *Malays. J. Med. Sci.* 18(2): 3-15.

Abdul Manan, H., Yusoff, A.N., Franz, E.A. & Sarah Mukari, S.Z. 2013. Early and late shift of brain laterality in STG, HG, and cerebellum with normal aging during a short-term memory task. *ISRN Neurol* 2013: 892072.

Binder, J.R., Liebenthal, E., Possing, E.T., Medler, D.A. & Ward, B.D. 2004. Neural correlates of sensory and decision processes in auditory object identification. *Nature neuroscience* 7(3): 295-301.

Boatman, D.F. 2006. Cortical auditory systems: speech and other complex sounds. *Epilepsy Behav.* 8(3): 494-503.

Boemio, A., Fromm, S., Braun, A. & Poeppel, D. 2005. Hierarchical and asymmetric temporal sensitivity in human auditory cortices. *Nature Neuroscience* 8(3): 389-395.

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.

Eickhoff, S.B., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K. & Zilles, K. 2005. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *Neuroimage* 25(4): 1325-1335.

Friston, K., Buechel, C., Fink, G., Morris, J., Rolls, E. & Dolan, R. 1997. Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage* 6(3): 218-229.

Friston, K.J., Buechel, C., Fink, G.R., Morris, J., Rolls, E. & Dolan, R.J. 1997. Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage* 6(3): 218-229.

Friston, K.J., Frith, C.D., Frackowiak, R.S. & Turner, R. 1995. Characterizing dynamic brain responses with fMRI: a multivariate approach. *Neuroimage* 2(2PA): 166-172.

Hall, D.A., Haggard, M.P., Akeroyd, M.A., Palmer, A.R., Summerfield, A.Q., Elliott, M.R., Gurney, E.M. & Bowtell, R.W. 1999. Sparse temporal sampling in auditory fMRI. *Human brain mapping* 7(3): 213-223.

Hamid, A.I.A., Yusoff, A.N., Mukari, S. Z.-M. S. & Mohamad, M. 2011. Brain activation during addition and subtraction tasks in-noise and in-quiet. *The Malaysian Journal of Medical Sciences: MJMS* 18(2): 3.

Humphries, C., Liebenthal, E. & Binder, J. R. 2010. Tonotopic organization of human auditory cortex. *Neuroimage* 50(3): 1202-1211.

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.

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.

Maldjian, J.A., Laurienti, P.J., Kraft, R.A. & Burdette, J.H. 2003. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage* 19(3): 1233-1239.

Manan, H.A., Franz, E.A., Yusoff, A.N. & Mukari, S.Z.M.S. 2013. Age-related laterality shifts in auditory and attention networks with normal ageing: Effects on a working memory task. *Neurology Psychiatry and Brain Research* 19(4): 180-191.

Manan, H. A., Franz, E. A., Yusoff, A. N. & Mukari, S. Z. M. S. 2014. The effects of aging on the brain activation pattern during a speech perception task: an fMRI study. *Aging Clinical and Experimental Research*.

Manan, H.A., Yusoff, A.N., Franz, E.A. & Mukari, S.Z.-M.S. 2013. The effects of background noise on brain activity using speech stimuli on healthy young adults. *Neurology, Psychiatry and Brain Research* 19(4): 207-215.

O'Reilly, J.X., Woolrich, M.W., Behrens, T.E., Smith, S.M. & Johansen-Berg, H. 2012. Tools of the trade: psychophysiological interactions and functional connectivity. *Social Cognitive and Affective Neuroscience* 7(5): 604-609.

Oldfield, R.C. 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9(1): 97-113.

Smith, S.M., Miller, K.L., Moeller, S., Xu, J., Auerbach, E.J., Woolrich, M.W., Beckmann, C.F., Jenkinson, M., Andersson, J. & Glasser, M.F. 2012. Temporally-independent functional modes of spontaneous brain activity. *Proceedings of the National Academy of Sciences* 109(8): 3131-3136.

Tervaniemi, M. & Hugdahl, K. 2003. Lateralization of auditory-cortex functions. *Brain Res. Brain Res. Rev.* 43(3): 231-246.

Tervaniemi, M. & Hugdahl, K. 2003. Lateralization of auditory-cortex functions. *Brain Research Reviews* 43(3): 231-246.

Yusoff, A., Mohamad, M. & AI, A.H. 2008. The acquisition, analyses and interpretation of fMRI data: a study on functional specialisation in primary auditory cortices. *Medicine & Health* 3(2): 300-317.

Yusoff, A.N. 2013. Psychophysiologic interaction between right precentral gyrus and superior parietal lobule. *Sains Malaysiana* 42(6): 765-771.

Yusoff, A.N. 2014. Brain activation and psychophysiologic interaction in association with a phonological working memory task. *Mal. J. Health Sci.* 8(5): 97 – 114.

Zatorre, R.J., Belin, P. & Penhune, V.B. 2002. Structure and function of auditory cortex: music and speech. *Trends in Cognitive Sciences* 6(1): 37-46.

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.

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