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Optimization of Number of Scans for a Sparse Temporal Sampling (STS) Functional Magnetic Resonance Imaging (fMRI)

(Pengoptimuman Bilangan Imbasan untuk Pengimejan Resonans Magnet Kefungsian (fMRI) Pensampelan Temporal Berjarak (STS))

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ABSTRACT

High sensitivity signal detection for a sparse temporal sampling (STS) functional magnetic resonance imaging (fMRI) is compensated by the increase in the number of scans (N_s) and consequently the scan time. A long scan time would result in fatigue and restlessness in participants, while a short scan time is undesirable for an STS-fMRI due to insufficient N_s for averaging. The purpose of this study was to determine the N_s practically sufficient for a sparse fMRI study. Eighteen participants were presented with white noise during a sparse fMRI scan. The height extent of activation was determined via t *statistics and region of interest (ROI) based percentage of signal change (PSC). The* t *statistics and PSC for Heschl's gyrus (HG) and superior temporal gyrus (STG) during which the participants listened to the white noise were calculated for different number of scans which were 6, 12, 18, 24, 30 and 36. The* t *statistics and PSC values calculated for the bilateral HG and STG qualitatively indicated a minimal change over N_s = 12 to 36. Both ROIs showed a consistent common right lateralization of activation for all N_s, indicating the right-hemispheric dominance of auditory cortex in processing white noise stimulus. It was proposed that for a sparse fMRI study, N_s may practically fall between 12 and 36.*

Keywords: Auditory cortex; functional MRI; percentage of signal change; SPM; t *statistics*

ABSTRAK

Pengesanan isyarat berkepekaan tinggi bagi pengimejan resonans magnet kefungsian (fMRI) pensampelan temporal berjarak (STS) dipampas oleh peningkatan bilangan imbasan (N_s) dan seterusnya masa imbasan. Masa imbasan yang lama boleh mengakibatkan kelesuan dan resah gelisah dalam diri pesakit, manakala masa imbasan yang singkat tidak diterima dalam STS-fMRI disebabkan bilangan N_s yang tidak mencukupi untuk pemurataan. Tujuan kajian ini adalah untuk menentukan N_s yang secara praktiknya mencukupi untuk kajian fMRI berjarak. Lapan belas peserta kajian diperdengarkan bunyi hingar putih semasa imbasan fMRI berjarak. Takat tinggi pengaktifan ditentukan melalui statistik t *dan peratus perubahan isyarat (PSC) berasaskan kawasan diminati (ROI). Statistik* t *dan PSC untuk girus Heschl (HG) dan girus temporal superior (STG) semasa peserta kajian mendengar hingar putih dihitung untuk bilangan imbasan berbeza iaitu 6, 12, 18, 24, 30 dan 36. Statistik* t *dan PSC yang dihitung untuk HG dan STG bilateral secara kualitatif menunjukkan perubahan minimum merentasi N_s = 12 ke 36. Kedua-dua ROI memperlihatkan pengaktifan lateralisasi kanan biasa yang tekal untuk semua N_s, menunjukkan kedominanan hemisfera kanan bagi korteks auditori dalam memproses stimulus hingar putih. Dicadangkan bahawa untuk kajian fMRI berjarak, N_s secara praktiknya boleh mengambil nilai antara 12 dan 36.*

Kata kunci: Korteks auditori; MRI kefungsian; peratus perubahan isyarat; SPM; statistik t

INTRODUCTION

A commonly used technique in studying brain responses to auditory stimuli e.g. non-visual, non-verbal stimuli is sparse temporal sampling (STS) functional magnetic resonance imaging (fMRI) (Yusoff et al. 2011). This so called scanner noise - free technique applies a long repetition time (TR) of 10-15 s and an acquisition time (TA) of 2-3 s (Manan et al. 2012). The main advantage of using the STS-fMRI for a study using sound stimuli is that the interference of the scanner sound during stimulus presentation can be avoided (Hall et al. 1999). In an STS-fMRI, auditory stimulus is usually presented to the participant during the long silence between any two consecutive scans. This would prevent the occurrence of artificial activation on the statistical parametric maps (SPMs) e.g. due to the scanner sound, that will mask the activation due to the task of interest (Hall et al. 1999). According to Bandettini et al. (1995), a period of more than 12 s is required for mean signal in the auditory cortices to return to baseline after the stimulus offset. As a result of auditory stimulation, the individual hemodynamic response peaks at approximately 5 to 8 s post stimulus offset (Hickok 1997), although there are no direct estimates of the hemodynamic delay in the auditory cortices during stimulation period. This is due to the

difference in methods of various auditory neuroscience studies. The mean hemodynamic responses dip below the initial baseline following stimulus offset before returning to resting level of activation, taking even longer time than to rise to peak. An inter-scan interval of more than 11 s was suggested to be used with sparse imaging (Hall et al. 1999). The inter-scan interval provides ample time, long enough for the brain hemodynamic responses to reside before the commencement of the following scan.

The noise of scanner interferes with the increased blood to functionally-specialised brain regions corresponding to the task-dedicated auditory stimulation, resulting in an elevated baseline level of activation of certain brain regions, especially in the auditory cortices. In STS-fMRI, to reduce the impact of acoustic scanner noise on auditory activation, the interval between each set of data acquisitions is increased (i.e. increasing TR) to ensure that the measured activity in the auditory cortex is uncontaminated by its responses to the preceding burst of scanner noise. This rest period of no stimulus delivery which is in between the echo planar imaging (EPI) scan and the next stimulus presentation should be long enough for a complete recovery of hemodynamic response from the scanner sound (Gaab et al. 2007). A long inter-scan interval (long TR) can become a disadvantage in using STS-fMRI, from which it will result in a longer total examination time (Yusoff et al. 2013). In many functional imaging studies, for example in a study on cognition (Gaab et al. 2003), total scan time is crucial because subjects could become restless in a long scan time, especially if a long TR is used that could result in a long total scan time (in order to have relatively high N_s which are statistically reasonable). This could lead to suboptimal activation towards the end of the fMRI session. In contrast, an STS-fMRI with smaller N_s will shorten the scan time but at the same time, reduces the reasonable N_s for statistical analysis.

This study is a part of a comprehensive assessment of human cortical activation during the performance of a pitch memory task (Yusoff et al. 2013). In this work, the effects of the number of scan volumes (N_s = 6, 12, 18, 24, 30 and 36) on the *t* statistics and PSC values obtained from HG and STG were studied. The objective was to suggest a practically suitable range of N_s that can be implemented in a STS-fMRI study. The brain volumes were acquired using an STS-fMRI. Instead of acquiring the fMRI data separately for N_s = 6, 12, 18, 24, 30 and 36 through individual sessions, the desired N_s were randomly picked from the total scan volumes acquired. This method was thought to be a better option than to scan the participants separately for each desired N_s which would result in longer total scan time and burden the participants with multiple sessions of fMRI scan. Our hypothesis was that the *t* statistics and PSC values will reach a constant value following a higher number of volumes acquired and will remain constant thereafter regardless of the functional anatomy of the brain region and the condition during which the task was performed.

METHODS

PARTICIPANTS

Eighteen healthy 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) that have been confirmed to have normal hearing level for both ears by pure tone audiometric (PTA) test agreed to participate by filling in the informed consent and screening forms and signing them. The participants were given full explanation about the nature and risks of the research, as required by the Institutional Ethics Committee (IEC) (Reference no: NN-197-2010).

fMRI SCANS

A sparse temporal sampling functional magnetic resonance imaging (STS-fMRI) was used for this study to avoid the auditory paradigm interfering with the scanner sound. There were altogether 218 EPI 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 repetition time (TR) used was 13 s, comprising of an acquisition time (TA) of 3 s, a broad-band white noise stimulus of 6 s and a rest period of 4 s. The STS-fMRI session has 36 trials in which the participants were supposed to listen to white noise stimulus. Total scan time of white noise stimulation was 36 measurements × 13 s = 7.8 min. Details about the imaging parameters are given elsewhere (Yusoff et al. 2013).

DATA ANALYSIS

The fMRI data were analysed using MATLAB 7.4 - R2008a (Mathworks Inc. MA, USA) and Statistical Parametric Mapping (SPM8). Functional images in each scan 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 high-passed filter.

A general linear model was used to generate individual participant's activation map via a conventional first level group fixed-effects (FFX) analysis. Contrast images [Noise > Baseline conditions] for N_s = 36, 30, 24, 18, 12 and 6 obtained from all participants at the first level were then

entered into the second level analysis of random effects analysis (RFX). The final results are the group activation maps obtained from N_s = 36, 30, 24, 18, 12 and 6. Two regions of interest (ROIs) were chosen based on the significantly activated areas at the second level for N_s = 36, 30, 24, 18, 12 and 6. The chosen ROIs were left hemisphere superior temporal gyrus (L-STG), right hemisphere superior temporal gyrus (R-STG), left hemisphere Heschl's gyrus (L-HG) and right hemisphere Heschl's gyrus (R-HG). All the ROIs were later extracted from the brain activation maps using Wakeforest University (WFU) Pickatlas software based upon an automated anatomical labelling (Maldjian et al. 2003) at a significant level of 0.001, uncorrected for multiple comparisons. The *t* value for the respective voxel of maximum intensity from each ROI was recorded.

The ROI-based percentage of signal change (PSC) for each of the significantly activated areas were determined using MarsBar (Brett et al. 2002) toolbox for SPM. In order to obtain the PSC, the ratio between the condition-specific signal change and the mean signal during the session, was computed over a number of 33 voxels that contain a spherical volume of 4 mm radius with the ROIs' peak coordinates as the sphere center. Group's percentage of signal change (PSC) relative to the baseline for all the ROIs was then extracted from this 4 mm radius sphere using the toolbox. Both the *t* and PSC values were then plotted against N_s.

Due to the small number of data for comparisons (n = 5), non-parametric independent samples (Mann Whitney U) test was conducted to determine whether the median of the distribution of PSC for HG and STG is similar or not similar between the left and right hemisphere regions. The PSC values were averaged over all N_s prior to the tests. Significant level (α) and confidence interval (CI) used for both tests were 0.05 and 95%, respectively. Comparisons were conducted on PSC values but not on the *t* statistics since PSC values were obtained from a group of voxels neighboring the maximum intensity voxel, including the maximum intensity voxel itself and are more sufficient to represent a region, while the *t* statistics were obtained from only one voxel, which was the voxel with maximum intensity. Moreover, the *t* statistics were already the results of comparisons. The small number of n (referring to N_s = 36, 30, 24, 18, 12) may appear to be the limitation of these analyses. Nevertheless, the results may give valuable input on laterality and noise effect of the brain height extent of activation.

Results

Figure 1(a) shows the *t* statistics obtained from the random effects analysis (RFX) activation maps (t_{RFX}), plotted against the number of scan (N_s) for the selected regions of interest (ROIs) which are the bilateral Heschl's gyrus (HG) and bilateral superior temporal gyrus (STG). The

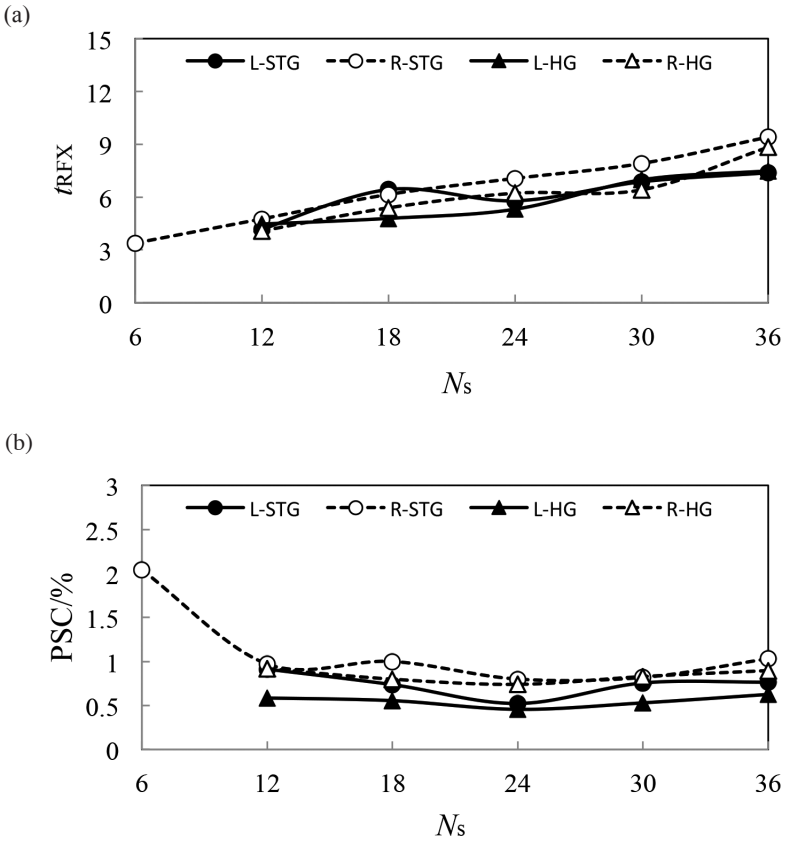

FIGURE 1. Plots of t_{RFX} and PSC as a function of number of scans (N_s) for the bilateral HG and STG

activation for L-STG, L-HG and R-HG is absent for $N_s = 6$. Nevertheless, all ROIs show a small increase in the *t*-values from $N_s = 12$ to $N_s = 36$. The results qualitatively indicated that for a particular N_s, the *t* statistics for all ROIs do not significantly differ from each other. Figure 1(b) illustrates the plots of PSC values for the selected ROIs against the number of scans. Similarly, all regions show a constant PSC for all number of scans above $N_s = 6$. Two participants were excluded in obtaining the *t* statistics and PSC values for $N_s = 6$ (for R-STG) due to the absence of activation at uncorrected significant level (α) = 0.001. The group RFX Montreal Neurological Institute (MNI) coordinates for both the bilateral HG and STG together with the *t* statistics and PSC values are given in Table 1 for all the respective N_s. The variability in the group MNI coordinates across N_s for all regions can be considered small.

Qualitatively, the change in the *t* statistics and PSC values for all ROIs are quite small across N_s especially for N_s larger than 6. These two quantities can be used in measuring the consistency of the height extent of activation in a sparse temporal sampling fMRI study that uses different number of scans for different conditions.

For the comparisons in the PSC values between the left and right hemisphere regions, the median PSC for R- HG was significantly higher ($p = 0.009$, 95% CI: 0.69(0.29), $n = 5$, $z = -2.611$) than the median PSC for L-HG. Similarly, the median PSC for the R-STG was significantly higher ($p = 0.018$, 95% CI: 0.88(0.24), $n = 5$, $z = -2.373$) than the median PSC for L- STG.

Discussion

Consistency in the PSC values (and a relatively small increase in the *t* statistic) for the bilateral HG and STG for $N_s > 6$, on the one hand, indicates the independence in the blood oxygenation level dependent (BOLD) signal intensity (also known as the height extent of activation) for the two regions on N_s. The PSC would probably remain constant with a further increase in N_s while the *t* statistic is expected to indicate a gradual increase. On the other hand, the similarity in the pattern of the *t* statistics and PSC plots for the left and right hemisphere HG and STG reflects a symmetrical respond of the two regions, which could be attributable to their equal function as processing center for various sound stimuli including for white noise used in this study. Previous study (Hall et al. 1999) reported that the HG and STG responses to auditory stimuli were usually significantly high with bilateral activations for stimuli that were delivered binaurally. One possible explanation for this behavior is related to the main function of the two regions as the processing center for the sensory input that was transmitted from the sub cortical level (Belin et

TABLE 1. The MNI coordinates for each ROI and N_s from which the corresponding *t* statistics and PSC were measured

ROIs	N_s	Group RFX (MNI) coordinates	*t* statistics	PSC
R-HG	6	-	-	-
	12	44/-14/4	4.07	0.92
	18	44/-14/4	5.39	0.80
	24	44/-14/4	6.22	0.74
	30	44/-16/6	6.41	0.83
	36	44/-16/6	8.83	0.90
L-HG	6	-	-	-
	12	-36/-28/6	4.46	0.59
	18	-36/-24/6	4.79	0.56
	24	-36/-28/6	5.31	0.46
	30	-36/-28/6	6.98	0.53
	36	-36/-26/6	8.83	0.63
R-STG	6	54/-14/6	3.39	2.04
	12	46/-16/2	4.76	0.97
	18	48/-18/6	6.15	1.00
	24	46/-16/2	7.06	0.80
	30	46/-16/2	7.91	0.88
	36	48/-18/6	9.41	1.03
L-STG	6	-	-	-
	12	-46/-20/4	4.17	0.91
	18	-38/-26/6	6.43	0.74
	24	-38/-26/4	5.79	0.52
	30	-46/-20/4	6.87	0.76
	36	-46/-20/4	7.38	0.77

L = left hemisphere; R = right hemisphere

al. 1999). From the results of this study, their sensitivity to the white noise can be said to be extremely high from which the height extent of activation can still be detected bilaterally for N_s as low as 12.

With regards to the brain activation due to listening to white noise, similar average temporal lobe activation has also been found in our previous studies using binaurally delivered white noise stimulus on five right handed male participants (Yusoff et al. 2011) and ten right handed mixed participants (Hamid et al. 2012). The absence of brain activation in the frontal and parietal regions during white noise listening indicates that listening to white noise is sensory in nature and does not involve any higher cognitive function. The activations in the primary auditory cortex, clearly indicate the important role played by the bilateral HG and STG in processing noise stimulus (Jamison et al. 2006) and that the participant's cortical auditory processing is working well in conjunction with the participant's good hearing condition which has been confirmed by the auditory test performed on the participant's left and right ears, prior to the fMRI scans.

The right lateralization of the PSC values for HG and STG was attributed to the auditory processing of white noise. White noise is much more complex than simple pure tone and has been known to evoke responses in the primary auditory cortex (PAC) bilaterally but with a larger activation in the right hemisphere PAC (Hwang et al. 2005). It was produced by adding together pure tones of different frequencies, levels and temporal alignments (phases) (Gockel et al. 2006). It has been known that the right PAC, containing HG and STG, is specialized in the processing of spectral information such as noise, effectively and has a high spectral resolution (Zatorre et al. 2002). Previous studies (Alcock et al. 2000; Murayama et al. 2004) demonstrated that lesion affecting the right temporal cortex impaired specific spectral processing skill. This is in agreement with the fact that right PAC is better in the processing of complex spectral information (Patterson et al. 2002) but at the expense of temporal resolution (Jamison et al. 2006). Moreover, 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). Another interesting explanation for the right lateralization is by referring to the analysis of the fine spectral structure of sound which was dedicated to music perception. Asymmetry towards the right hemisphere was found when the stimulus contains melodic (spectral) information as opposed to constant pitch stimuli which showed symmetrical bilateral activation of primary and non-primary auditory cortices (Zatorre et al. 2002).

This study has provided an alternative method to evaluate the consistency of the height extent of brain activation against the scan volumes obtained from an STS-fMRI sampling. By randomly selecting the desired scans from the total scan volumes for a particular N_s values, acceptable activation results have been obtained. Apart from having quite a consistent height extent of activation over several number of N_s, this study is limited by the way N_s is defined and collected. There is no doubt that as far as the experimental validity is concerned, the N_s is best obtained from actual fMRI experiment even though the main constraints revolve around the total scan time and cost.

Conclusion

White noise has been found to render the PAC right lateralized. The *t* statistics obtained from group RFX analysis are somewhat in good agreement with the PSC values as indicated by the consistency of the values across conditions and regions. The *t* statistics complement the PSC values in the presentation of height extent of activation in an STS-fMRI study. From this study, it was proposed that for a sparse imaging study that uses a non-jittered stimulus presentation, N_s for a certain experimental condition may practically fall in between 12 and 36.

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