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Signal change in BA17, 18 and 19: A comparative study of normal, glaucoma suspects and POAG patients

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Abstract. Magnetic resonance signal change is expected to be different between normal, glaucoma suspect (GS) and Primary Open Angle Glaucoma (POAG) subjects. Functional magnetic resonance imaging (fMRI) technique was employed to investigate the differences. This multiple subject studies were carried out to characterize the percentage of signal change (PSC) in Brodmann Area (BA) 17, 18 and 19 of the visual cortex. The block designed fMRI was implemented. The subjects were requested to focus on the black and white checkerboard stimulus of the visual world (A, B and CD), visual field (EF) and visual area (G). The data were analysed using Statistical Parametric Mapping (SPM8) via Matlab platform. results showed that GS subjects have the highest PSC, followed by normal and POAG subjects. However, no significant difference was observed in PSC between BA17, 18 and 19 for normal, GS and POAG groups with $p = 0.0869$, $p = 0.0688$ and $p = 0.2690$, respectively. In conclusion, none of the BA can be suggested to be the most dominant area in responding to the visual stimuli used in this study.

1. Introduction

Early diagnosis is important as a prevention and early treatment for glaucoma patient. One of the ways to evaluate glaucoma is by using functional magnetic resonance imaging (fMRI) technique. fMRI has been widely used to investigate the brain function and its abnormalities since 1990s. It is incredibly safe, non-invasive, no ionizing radiation and radioactive source involved as well as able to fabricate prompt and confidence results [1].

Percentage of Signal Change (PSC) analysis is very rarely used in evaluating the results of previous studies. The value of the signal change is measured by the intensity value rather than the number of activated voxel. Since early 90s when the fMRI scans and analysis were introduced, the assessment intensity signal cannot be determined directly using the session scan. However, the intensity changes are compared to the baseline which can be accurately evaluated through the effects of PSC[2].

PSC is the magnetic resonance signal change ratio in the brain while it is working, against the average change in magnetic resonance signal absorbed from the overall measurement. The PSC value is within 0.5% to 3% [3]. PSC is interpreted as the ratio of the average ratio of change in a trial to the average overall signal measurement of brain activity in fMRI study [4]. If referred to the definition, researchers are compulsory to select and designate areas to compare. Therefore, this study has selected BA17, 18 and 19 for PSC assessment analysis. Earlier studies using PSC analysis were conducted on fingertip study and for various conditions [4] as well as distance temporal sampling [5].



2. Materials and Methods

2.1. Subjects

Ages of all subjects were above 40 years old as suggested by [6]; group at risk for glaucoma. All the subjects went through complete ophthalmic tests to quantify visual acuity, intraocular pressure (IOP), cup to disc ratio (CDR) and visual field. The tests were conducted by ophthalmologist at Ophthalmology Clinic, PPUKM. Subsequently, the subjects underwent fMRI scans in the Department of Radiology, PPUKM. The entire fMRI scan was obtained using 3 Tesla MRI machine model Siemens Magnetom Verio with functional imaging protocol using planar resonance imaging pulse sequence (EPI). EPI pulse sequence parameters used were as follows: acquisition time (TA) = 3000 ms, echo time (TE) = 50 ms, field of view (FOV) = 192 x 192 mm, tilt angle (α) = 90°, matrix size = 3 x 3 x 3 and slice thickness = 3 mm. T1 images were acquired using pulse sequence multilayer reconstruction (MPR) with the following imaging parameters: TR = 1620 ms, α = 90°, matrix size = 3 x 3 x 3 and slice thickness = 1 mm. The subjects viewed a stimulus on the non-metallic screen (Figure 1).

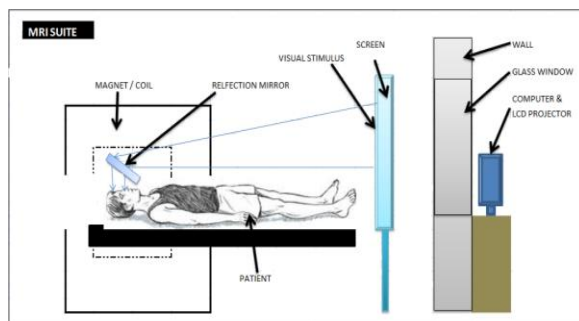


Figure 1. Cross-sectional view of the subject inside the magnet room

2.2. Data Analysis

All the data were analyzed at Diagnostic Imaging and Radiotherapy Program, Faculty of Health Sciences, UKM Kuala Lumpur. Analyses were executed using Statistical Parametric Mapping (SPM8) software (Functional Imaging Laboratory, Wellcome Department of Imaging Neuroscience, Institute of Neurology, University College of London), via Matlab (7.6 R2010a Mathworks Inc., Natick, MA, USA) platform. The analyses on the functional images endured realignment, normalization and smoothing process. General linear model approach was employed to identify an activated voxel and derive t statistical test for every single voxel. For recognizing the region of interest (ROI) of primary visual cortex (V1), The Wake Forest University (WFU) Pick Atlas toolbox was applied.

3. Results and Discussion

PSC value of normal subjects at BA17, 18 and 19 were in the range of 0.933 ± 0.198 to 1.254 ± 0.322 , with the highest value in BA18 for EF stimulus and the lowest was in BA19 for the A, B and CD stimuli. For the GS subject, the highest PSC was 1.201 ± 0.707 in BA18 and the lowest was in BA19 with value of 0.932 ± 0.386 , which both were for the same stimulus, EF. The same pattern was observed at the highest and lowest PSCs and with increasing progress. Both normal and GS groups gave high PSC values in BA18 when EF stimulation was shown. Different pattern was obtained for POAG subjects. When stimulated by EF, PSC values were only 0.431 ± 0.284 in BA17 and the highest value was in BA18 of 1.034 ± 0.072 for type A, B, and CD stimuli. A slight low signal pattern changes were observed among POAG subjects. The PSC of POAG subjects showed the highest values when the subjects viewed the stimulus of A, B, and CD at BA18 of 1.034 ± 0.072 . It was then followed by stimulus G at BA17 and 19 and the lowest was at BA17 when they viewed at the EF stimulus with the average PSC of 0.431 ± 0.284 .

The highest PSC was observed among GS subjects, followed by normal and POAG group of patients. The good visual acuity leads to better value of PSC in the selected region of interest. Higher PSC results among normal and GS subjects are expected due to its ability to response with the visual stimulus compared to POAG subject with visual abnormalities. Eventhough PSC results for GS

subjects were the highest, it was not significantly different with normal subjects ($p < 0.05$). This was because the GS subjects were not glaucoma patients although symptoms of glaucoma appeared slightly. The results were consistent for PSC value at the selected BA which increased the signal among the groups with better visual acuity.

All the recorded values were in the range of 0.4 to 1.5. The lowest value was less than the reference value reported by [3] from 0.5 to 3. The highest PSC value was at BA18 among normal subjects and the lowest was at BA17 among POAG group. This proved that BA18 and 19 contained more functions and working towards visual stimulus detection on pattern and moving objects as well as memory recognition. Figure 2 shows that the PSCs were scattered and not uniform for the three selected ROIs. The highest signal change was at BA17 and 18 for normal subjects and GS when they viewed at stimulus type of EF. The PSC showed a marked decrease in POAG subjects. The decline pattern was also found in BA19 with the highest PSC for normal subjects, followed by GS and POAG.

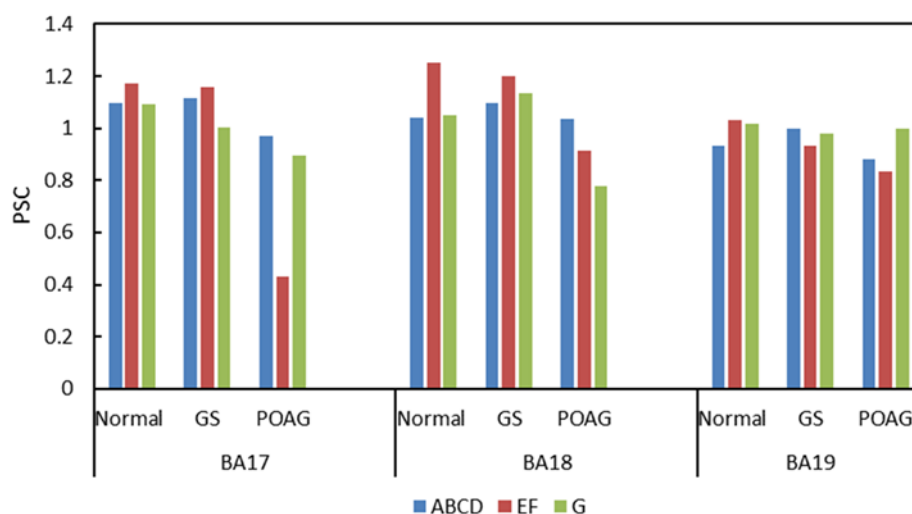


Figure 2. PSC among three group of subjects at BA17, 18 and 19

According to [7], this scenario happen due to glaucoma disease which affects a person's ability to detect low contrast patterns, patterns, low spatial frequency stimuli and attenuations. However, patients with POAG also show failure in detecting a static or stationary pattern. It should be noted that detecting a linear or moving pattern is more reliable than a static pattern. Therefore, it is suggested that POAG patients fail to detect visually stimulating, especially static stimuli. This has been proven in a previous study by [8].

The PSC values are being analysed by using analysis of variance (ANOVA) as well. This is to determine whether there are any statistically significant differences between the means of these three groups. ANOVA of ROI BA17, 18 and 19 for the normal, GS and POAG groups show values of $p = 0.0869$, $p = 0.0688$ and $p = 0.2690$ respectively. All values of $p > 0.05$ concluded that the change in PSC signal for the selected ROI did not differ significantly between the three study groups.

The various shapes and pattern of visual stimulus that being displayed to the subject are found to activate and cause signal change not just in visual area but in temporal and parietal lobes as well. The effects are cause assymetry in brain function and exhibit functional integration characteristic [9].

In a previous study by [10] on the neuro-fMRI response method for modulating regional brain activity, the neuroimaging signal was analysed using the PSC technique in assessing whether depressed patients would show increased amygdala responses to autobiographical memory or vice versa. The results showed that depressed patients can regulate their amygdala activation using autobiographical memory.

4. Conclusions

The PSC analysis showed uneven signal changes among the three groups on all the selected ROIs of BA17, 18 and 19. The highest PSCs occurred in BA17 and 18 for normal and GS subjects, while POAG showed the lowest signal change. POAG subjects were low on all ROIs, indicating that POAG subjects with retinal nerve fibre layer damage provided the least signal changes. However, when conducting ANOVA analysis to compare the three ROI areas, there was no significant difference among normal, GS and POAG subjects. As a result, no certain BA can be proposed to be the most dominant area of signal recognition as all the three Bas exposed random and almost similar pattern.

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