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**Original Article**

# Repeatability of Detecting Visual Cortex Activity in Functional Magnetic Resonance Imaging

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## Abstract

**Introduction**
As functional magnetic resonance imaging (fMRI) is too expensive and time consuming, its frequent implementation is difficult. The aim of this study is to evaluate repeatability of detecting visual cortex activity in fMRI.

**Materials and Methods**
In this study, 15 normal volunteers (10 female, 5 male; Mean age±SD: 24.7±3.8 years) attended. Functional magnetic resonance images were obtained during a visual task of sine-wave with spatial frequency of 1.84 cpd and temporal frequency of 8 Hz in three scan runs. Two runs of functional images were provided consecutively in a session, and the third run was provided 1-6 weeks later. The activation map was created using the data obtained from the block-designed fMRI study. Voxels whose Z value was above a threshold of 2.3, at a significance level p=0.05, were considered activated. After image processing, the blood oxygen level dependent (BOLD) signal changes and the number of activated voxels in response to visual stimuli were compared in different runs.

**Results**
The results of this study demonstrate no significant difference between the number of activated voxels and BOLD signal in first and second runs in one session (Paired t-test, p>0.05). Moreover, there is a considerable correlation between first and second scan runs (rsignal=0.74, p=0.006 and rvoxel=0.62, p=0.03), while the correlation between the runs in separate sessions is weak (rsignal=0.28, p=0.38 and rvoxel=0.32, p=0.31).

**Conclusion**
Since the repeatability of BOLD signal and number of activated voxels in one session is considerably better than that in the separate sessions, it is suggested that in fMRI visual studies that need repeated scanning, scans should be acquired during a single session.

**Keywords:** BOLD Signal, Functional Magnetic Resonance Imaging, Repeatability, Vision, Voxel Numbers

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## 1. Introduction

The study of brain function is one of the most fascinating pursuits of modern science [1]. Functional magnetic resonance imaging (fMRI) is a modern and non-invasive imaging technique to measure and localize specific functions of the human brain without applying radiation [2,3]. This provides the possibility of coordination and communication between physiologic activities and the anatomic position without using radiation [4]. In this method, brain function is assessed indirectly by high spatial resolution via detection of local hemodynamic changes in capillaries [5] and draining veins of so-called "functional areas" ,e.i., regions of the human brain which govern motor, sensory, vision, language, or memory functions [6].

fMRI measurements can be made using different methods, but the method of blood oxygen level dependent (BOLD) is the most common method used for the human brain [7-8]. In this method, blood is used as an intrinsic contrast [9-10]. In fact, when there is oxygen in blood hemoglobin, it would be diamagnetic but when oxygen is lost in response to a neural activity, it would be paramagnetic. Paramagnetic deoxy hemoglobin introduces a heterogeneity in a local magnetic field which can be measured in the T2*-weighted images, while oxy-hemoglobin has no interference with external magnetic field [11]. BOLD measurements usually run with echo planar imaging sequences such as single-phase gradient echo or spin echo [12]. Visual activity can be clearly seen by MR imaging. Moreover, details in the visual cortex may be well understood by functional MR imaging [13]. Therefore, it seems that the visual cortex in the brain region is ideal to be examined by fMRI. On the other hand, fMRI is useful in evaluating the brain activity in some disorders such as epilepsy, stroke, and behavioral problems [14]. Furthermore, this method is used for mapping functional regions in an injured brain and determining a mechanism to treat the injury [15].

Accordingly, fMRI is growing fast and its use is increasing day to day. However, the expensive and time-consuming nature of this approach makes it hard to use it frequently in a single patient. Therefore, it is very important to know about its repeatability. Various studies have been performed to check repeatability of visual cortex activity in fMRI [16-24].

Rombouts et al. using flash light as a visual stimulus showed a high repeatability for number and location of activated voxels in fMRI in the vision region [17]. On the other hand, Miki et al. expressed the repeatability of voxel numbers and signal [20]. Moreover, Peelen et al., using different pictures as visual stimuli, obtained very high repeatability [23].

Other researchers determined the repeatability in vision studies using different visual stimuli such as checkerboard [21-22], pictures of scene [19, 23-24], faces, tools, and bodies [19].

In fMRI results, two concepts are important. First concept is extension of visual activation including number and location of activated voxels. Second concept is percentage of BOLD signal changes as intensity of activation. As mentioned before, most studies measured location and number of activated voxels [16-17, 19, 21-22, 24]. There are few studies about BOLD signal changes [18, 20]. Another important point to mention is the variety of visual tasks used in the previous studies. The different features of visual task such as contrast and spatial frequency modulate the brain activation [25]. Hence, repeatability may be influenced by the type of stimulus used to elicit a response. For instance, the lower contrasts cause poor BOLD signals [26] and very high contrasts cause contrast saturation effects which exist in some visual areas in the cortex [27]. Additionally, checkerboards and square wave gratings have no pure spatial frequency due to having sharp edges. Therefore, it is necessary to design a study for investigating repeatability regarding these two aspects.

The aim of this study was to determine the repeatability of visual cortex activation

detection by fMRI, particularly in terms of signal intensity using a moderate spatial contrast sine-wave visual stimulus.

## 2. Materials and Methods

### *2.1. Subjects*

Fifteen healthy right-handed volunteers (10 females and 5 males from 19 to 33 years old, mean age±SD: 24.7±3.8) with no history of neurological disorders, with normal vision and no refractive error>±0.5D attended this study.

### *2.2. Visual stimulation*

#### 2.2.1. Visual stimulus design

In this study, a dark and light grating as a sine-wave visual stimulus was used. The distance between the eyes of volunteers and display screen was 528 cm. Visual field size on the screen was 115 cm×87 cm. Therefore, visibility on the screen in front of the volunteers had dimensions of 12.29°×9.35°. Afterward, based on these dimensions, the visual stimulus was created by MATLAB program so that a spatial frequency of 1.84 cycle per degree (cpd) was provided. A small red square was superimposed in the center of visual stimulus in order to help subjects to fix the center of image and keep their eyes stable.
This grating had a relative luminance level of 0.8 in the center of light stripes and a relative luminance level of 0.2 in the center of dark stripes. Hence, the contrast of luminance grating was calculated based on the Michaelson Equation [28] as below:

$$C = \frac{L\max - L\min}{L\max + L\min} \times 100 = \frac{0.8 - 0.2}{0.8 + 0.2} \times 100 = 60\%$$

In this equation, C is the contrast, $L_{max}$ is the relative luminance level in the center of bright stripes, and $L_{min}$ is the relative luminance level in the center of dark stripes. Therefore, the contrast of luminance grating was equal to 60%. Figure 1 shows the visual stimulus which was used at activation condition in this study. A gray surface with the same red square in the center was used at the resting condition.

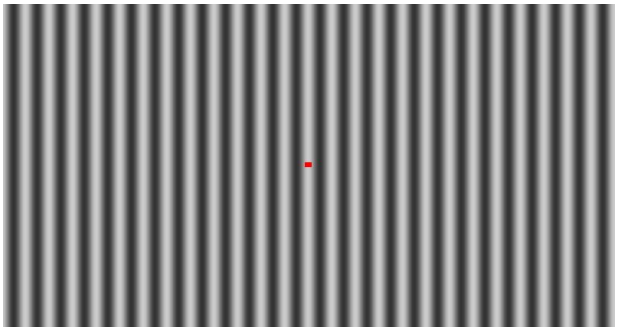

Figure1. Image used as visual stimulus with spatial frequency of 1.84 cpd.

#### 2.2.2. Visual task presentation

The visual stimulus was a 60% contrast sine-wave grating which counter-phased in a temporal frequency of 8 Hz. The visual stimulus was projected by a Sanyo video projector on the display screen. The subjects could see the visual stimulus through the non-magnetic mirror in front of their eyes while facing upward during image acquisition. The MRI room was kept as dark as possible so that the projected visual task was the only visual stimulation the subject could see. Each subject participated in three fMRI scanning runs. Runs 1 and 2 were done in one session. Run 3 was performed at a separated session after 1-6 weeks. In each run, activation condition lasted for 30 sec which was alternated with the resting condition of 30 sec, i.e., a 60 sec cyclic block design. This block design was repeated for four times, thus each run was done in 240 sec.

### *2.3. Data acquisition*

The functional data were acquired on a 1.5T Philips scanner using a four-channel head coil. The MRI system had been equipped with echo-planar (EPI) acquisition. Functional MR images were acquired using gradient echo T2*-weighted sequence with TR=3000 ms, TE=50 ms, flipe angle=90°, matrix size=64×64, number of slices=25, FOV=220×220 $mm^2$, voxel size=3.44×3.44×4 $mm^3$, and number of total volumes=80.
After functional image acquisition, an anatomical whole-brain image corresponding

to functional image was also acquired with a standard spin echo pulse sequence. Anatomical images were 3D T1-weighted image with pulse TR=25 ms, TE=4.60 ms, flipe angle=90°, matrix size=256×256, number of slices=150, FOV=220×220 $mm^2$, and voxel size=0.86×0.86×1 $mm^3$.

### *2.4. Data analysis*

Following data acquisition, we had a series of functional images in DICOM format (dcm) that should be converted to a format suitable for the analysis. We used MRICRO to convert DICOM images into img and hdr format data on which analysis processes were performed. Analysis was carried out using FEAT (fMRI Expert Analysis Tool) version 5.4, part of FSL (FMRIB's Software Library). The following pre-processing was applied: motion correction using MCFLIRT (Motion Correction FMRIB's Linear Image Registration Tool), non-brain removal using BET (Brain Extraction Tool), spatial smoothing using a Gaussian kernel of FWHM 5 mm, and mean-based intensity normalization of all volumes by the same factor. Z (Gaussianized T/F) statistic images were thresholded using clusters determined by Z>2.3 and a (corrected) cluster significance threshold of p=0.05. Registration to high resolution (anatomical) and standard images were carried out using FLIRT. Following registration, the activation maps including activated voxels whose Z value was above a threshold of 2.3, in significant level of p=0.05 were superposed on corresponding T1-weighted anatomical images.

Finally, the percentage of BOLD signal change and activated voxel numbers within the occipital lobe at each of the subjects were determined. Therefore, the Paired t-test and Pearson correlation analysis were used in order to evaluate repeatability of detecting visual cortex activity in the volunteers.

## 3. Results

Fifteen volunteers initially participated in this study. Two of the volunteers withdrew from continuing work and did not participate in the third scan. In addition, according to one of the volunteers, she was sleepy during MRI scans and did not show a desired activity. Therefore, the data of these three subjects were removed and all results were obtained based on the remaining twelve subjects.

Figure 2 shows the pattern of brain activity in visual cortex of one of the volunteers (The functional images were overlaid on the T1-weighted anatomical images).

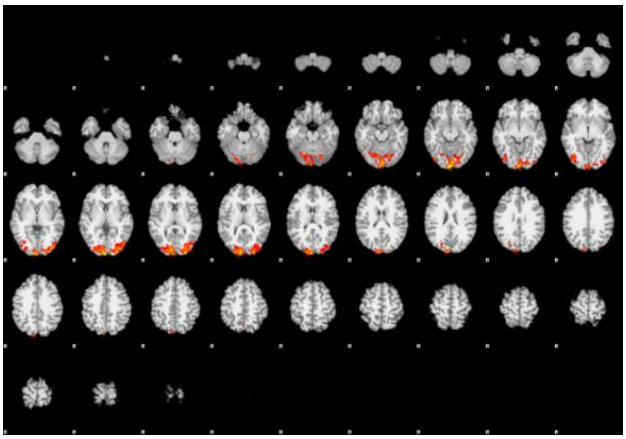

Figure 2. Image of activated regions of the visual cortex stimulated by visual task is shown with color code. (Z range of 2.3 to 8.5 )

The results of this study included the results related to Bold signal change percentage and activated voxel numbers visual stimulation.

### *3.1. BOLD signal results*

In this study, the BOLD signal change percentage was compared in three scanning runs; two runs were done in one session and the other run in a separate session. Figure 3 shows the mean value for BOLD signal change percentage in different scan runs in this experiment.

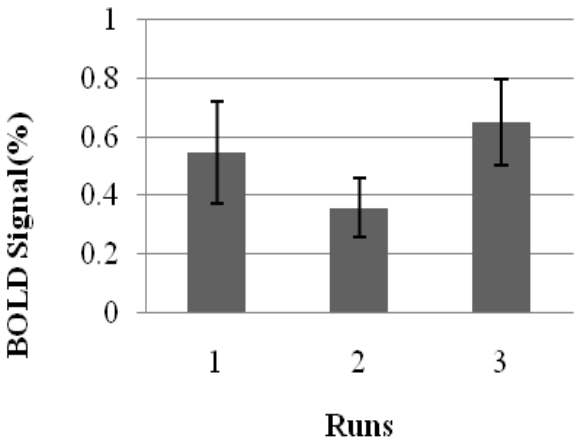


Figure 3. The mean value for BOLD signal change percentage obtained from twelve volunteers by visual stimulation in three runs repeated scans.

Although, according to Figure 3, the mean for BOLD signal change percentage decreases in the second run and increases in the third run, but the results of Paired t-test analysis showed that the difference in average in BOLD signal change percentage between the two scan runs (in one session) were 0.19, between two interval sessions were -0.10 and these differences between two scan runs in both cases were not significant ($p_{1,3}=0.60$, $p_{1,2}=0.14$).

Figures 4 and 5 show the scatter plots of BOLD signal change percentage in different scan runs.

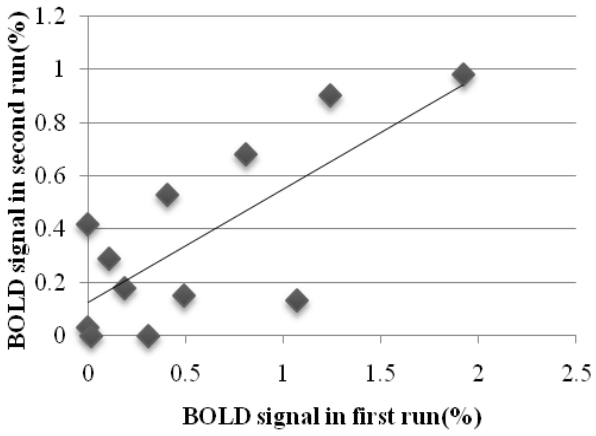


Figure 4. Scatter plot and regression line signal changes in two runs of scans, when done in one session.

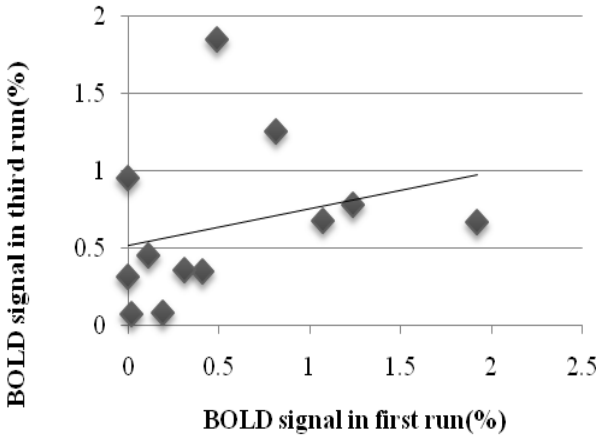


Figure 5. Scatter plot and regression line signal changes in two runs of scans, when done in two interval sessions.

The results of Pearson correlation test of the BOLD signal change percentage showed that there was a relatively good correlation between the first and the second runs ($r=0.74$, $p=0.006$) but the correlation between the runs one and three was considerably less ($r=0.28$, $p=0.38$).

### *3.2. Activated voxel numbers results*

Figure 6 shows activated voxel numbers mean affected by visual stimulation during three runs of scans for 12 volunteers.

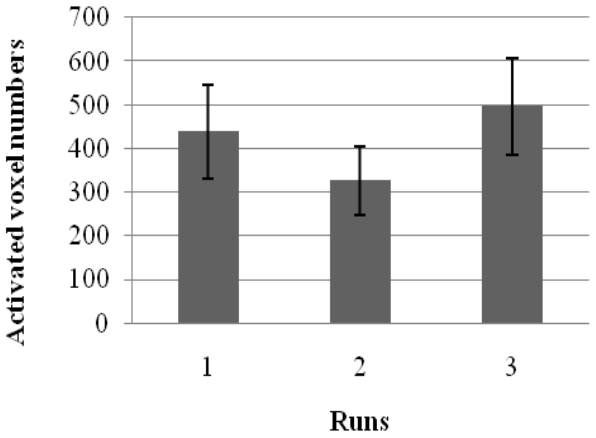


Figure 6. The mean value for activated voxel numbers affected by visual stimulation at three runs of scans in twelve volunteers.

As Figure 6 shows the activated voxel numbers as well as the BOLD signal change percentage decreased in the second run but again increased in the third run. The results of the Paired t-test analysis show that the difference average in the activated voxel numbers between two runs of scans in one session were 113.00 and two interval sessions were -56.83 and these differences between two runs of scans in both cases were not significant (p1,3=0.31, p1,2=0.21).

Figures 7 and 8 show the scatter plots of the activated voxel numbers in different scan runs.

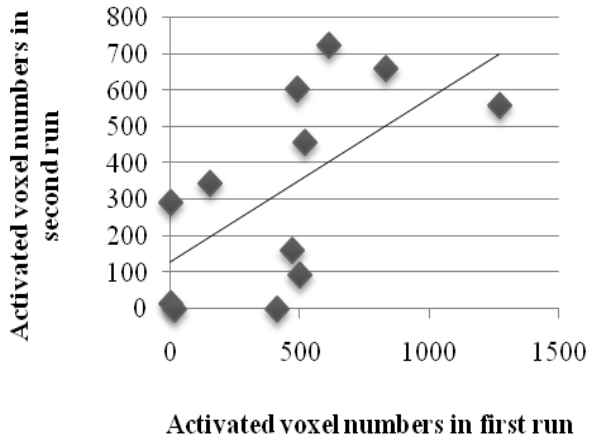


Figure 7. Scatter plot and regression line of activated voxel numbers in two runs of scans, when done in one session.

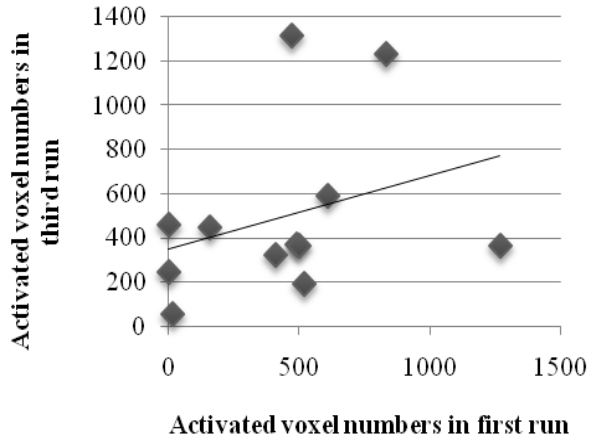


Figure 8. Scatter plot and regression line of activated voxel numbers in two runs of scans, when done in two interval sessions.

Pearson correlation test for activated voxel numbers showed that there was a moderate positive correlation between the first and second runs performed in one session(r=0.62, p=0.03) but the correlation between the first and third runs was considerably less (r=0.32, p=0.31).

## 4. Discussion and Conclusion

In the present study, the repeatability of detecting visual cortex activity by fMRI through 60% contrast sine-wave grating stimulation with a spatiotemporal frequency of 1.84 cpd/8Hz were investigated.

The measurements included the number of activated voxels and the BOLD signal change percentage that were tested in two runs with/ without time interval.

The results of this study show that when two runs of scans are done in one session, the repeatability of activated voxel numbers is higher than when two runs of scans are done in two different sessions. These results are in agreement with the results of Rombouts et al. that used a flash light as a visual stimulus [17] and Machilson et al. that applied the colour outdoor scenes pictures [19].

Although the nature of visual stimuli used in these studies was different from the present study, they showed higher repeatability when scans were done in a single session compared with two sessions. The visual stimulus used in the present study was a pattern visual stimulus with a spatiotemporal frequency of 1.84 cpd/8Hz while the visual stimuli used in the past studies varied from flash light to outdoor pictures, with different patterns and spatiotemporal frequencies.

Moreover, the results of this study indicated that there is a stronger significant correlation between the BOLD signal change percentage tested in two runs in one session than that of two sessions that is in agreement with the results of Cohen et al [18].

Repeatability testing showed that the correlation coefficient in the BOLD signal

change percentage and activated voxel numbers during one scanning session were 0.74 and 0.62, respectively. Moreover, the repeatability for the BOLD signal intensity slightly is better than that of activated voxel numbers as Cohen et al. [18] reported BOLD signal shows higher and more constant repeatability compared with activated voxel numbers.

An important point is that although the repeatability is better when scans are done in one session, the BOLD signal intensity in the second scan run decreases between 0.01 and 0.94 (average 0.30) and the decrease on the activated voxel numbers is between 15 and 410 (average 229.8). This reduction is observed in the scan results of the large number of subjects. The decrease of the BOLD signal intensity occurred in 67% and the activated voxel number in 58%. Regarding this reduction, it should be mentioned that since all features in these two measurements were equal, the difference between values may be related to priming [19, 29-30], fatigue [29], and lack of attention to the pictures [19].

According to these results, it seems that in order to compare functional scanning in visual studies, it is better to do scans in one session and use a correction factor to compensate the reduction in the BOLD signal intensity and activated voxel numbers in the second run. Based on the current study, these correction factors for the BOLD signal intensity and activated voxel numbers are 1.53 and 1.35, respectively. Obviously, further studies are required to determine the necessity and how to use this correction factor.

As a general outcome of this study, since the repeatability of two scan runs in one session is significantly better than those of two different sessions with a time interval between them, it is suggested that at visual fMRI studies, when scans should be repeated, it is better to do two scans during one single session.

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