

Analysis of Event-related Response in Human Visual Cortex with fMRI

Ayesha Zaman, Tanvir Atahary, and Shahida Rafiq

Abstract—Functional Magnetic Resonance Imaging (fMRI) is a noninvasive imaging technique that measures the hemodynamic response related to neural activity in the human brain. Event-related functional magnetic resonance imaging (efMRI) is a form of functional Magnetic Resonance Imaging (fMRI) in which a series of fMRI images are time-locked to a stimulus presentation and averaged together over many trials. Again an event related potential (ERP) is a measured brain response that is directly the result of a thought or perception. Here the neuronal response of human visual cortex in normal healthy patients have been studied. The patients were asked to perform a visual three choice reaction task; from the relative response of each patient corresponding neuronal activity in visual cortex was imaged. The average number of neurons in the adult human primary visual cortex, in each hemisphere has been estimated at around 140 million. Statistical analysis of this experiment was done with SPM5 (Statistical Parametric Mapping version 5) software. The result shows a robust design of imaging the neuronal activity of human visual cortex.

Keywords—Echo Planner Imaging, Event related Response, General Linear Model, Visual Neuronal Response.

I. INTRODUCTION

EVENT-RELATED functional Magnetic Resonance Imaging (efMRI) procedures allow different trial types to be randomly intermixed for mapping brain function. [1] Such procedures greatly increase the flexibility of functional Magnetic Resonance Imaging (fMRI) by allowing for trials to occur in unpredictable sequences, for the response to rare event types to be selectively extracted and examined, and for post-hoc trial sorting based on subject performance. Rapid presentation allows for designs that are exactly matched to typical behavioral and electrophysiological studies. It also allows for improved statistical power, by increasing the number of event-related responses to be averaged per unit of time. [2]

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II. VISUAL CORTEX

The term visual cortex refers to the primary visual cortex (also known as striate cortex or V1) and extrastriate visual cortical areas such as V2, V3, V4, and V5. The primary visual cortex is anatomically equivalent to Brodmann area 17, or BA17 [3]. Neurons in the visual cortex fire action potentials when visual stimuli appear within their receptive field. By definition, the receptive field is the region within the entire visual field which elicits an action potential. The visual cortex receives its blood supply primarily from the calcarine branch of the posterior cerebral artery.

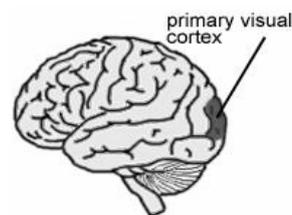


Fig. 1 Human Visual Cortex

Lesions to primary visual cortex usually lead to a scotoma, or hole in the visual field. Patients with scotomas are often able to make use of visual information presented to their scotomas, despite being unable to consciously perceive it. This phenomenon is called blindsight. Blindsight is caused by injury to the part of the brain responsible for vision. Types of visual attributes that can be discriminated by blindsight subjects in the absence of their experience of the stimuli include colour, different orientation of lines or gratings, simple shapes, motion, onset and termination of visual events. Good colour discrimination remains but there is a shift towards a relative increase in sensitivity of long wave-lengths (red) and a decrease of middle wave-lengths (green). The optimal stimuli for blindsight subjects lie in the low range of spatial frequencies (1 to 3 cycles/degree) combined with temporal oscillation in the range of 5-33 Hz.

III. PARTICIPANTS

Twelve participants took part in the fMRI experiment, each having given prior informed consent according to the Max-Planck-Institute guidelines. The study was approved by the local ethics review board at the University of Leipzig,

Germany. All participants were right handed as assessed by the Edinburgh Inventory (Oldfield, 1971). Due to technical problems, the data of one participant had to be discarded, resulting in 11 participants for the analyses. The age of the remaining 11 participants (5 women) ranged from 21 to 27 years, with an average of 24 years. All participants had normal or corrected to normal vision [4]

IV. STIMULI

Participants had to perform a visual three-choice reaction task. While lying in the fMRI scanner, participants were viewed a projection screen via a mirror.

V. VISUAL SINGLE TASK (VIS)

A trial in the VIS condition started with a blank green screen for 150 msec, followed by a fixation period of 850 msec is shown in Fig. 2. During this fixation period, three

black squares (each $1.6^\circ \times 1.6^\circ$) were presented on a green background, and the middle square contained a fixation cross ($0.38^\circ \times 0.38^\circ$). The middle square was located at the center of the screen and the two other squares horizontally to the left and right, each with a gap of 0.44° . After the fixation period, one of the three squares (the target) changed its luminance from black to a light gray for 300 ms, while the other two black squares remained on the screen, this happened randomly. After the presentation of the target stimulus, the screen was cleared and the participants had to respond during an interval of 1750 ms. Participants had to respond with the right index finger to the left, with the right middle finger to the middle and with the right ring finger to the presentation of the right target square. After responding, either a blank screen or a visual error feedback was presented for 250 ms [5].

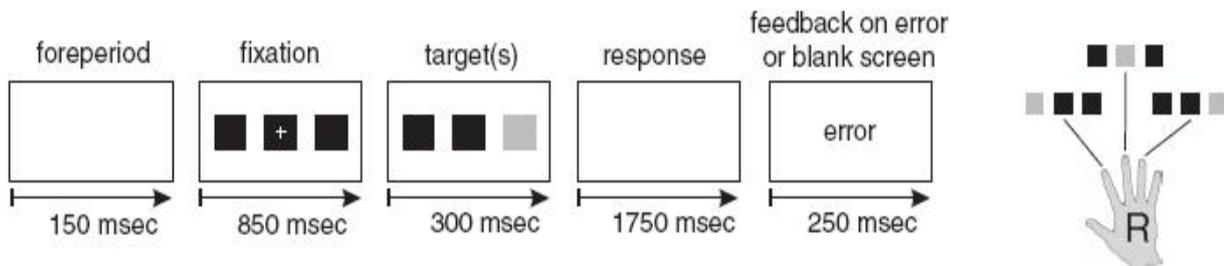


Fig. 2 Trial design for visual single task. The time courses are shown on the left, the stimulus-response mappings on the right, the trial lasted for 3300ms

VI. SCANNING PROCEDURE

Imaging was carried out with a 3T scanner (Medspec 30/100, Bruker, Ettlingen, Germany) equipped with a standard birdcage head coil. Participants were supine on the scanner bed, and cushions were used to reduce head motion. Fourteen axial slices (19.2 cm FOV, 64×64 matrix, 5 mm thickness, 2 mm spacing), parallel to the AC-PC plane and covering the whole brain were acquired using a single shot, gradient recalled EPI (Echo Planar Imaging) sequence (TR 20s, TE 30msec, 90° flip angle) sensitive to BOLD (Blood Oxygenation Level Dependent) contrast. Twenty two functional runs with 360 volumes each were administered, with each volume sampling all 14 slices. Prior to the functional runs, 16 anatomical slices and 16 EPI-T1 slices were acquired. Prior to the functional runs, 16 anatomical MDEFT slices and 16 EPI-T1 slices were acquired. In a separate session, high-resolution whole-brain images were acquired from each participant using a T1-weighted three-dimensional segmented MDEFT sequence. These images were linearly rotated and translated, but not resized, into the stereotactic space of Talairach and Tournoux (1988) [6][7]

VII. DATA ANALYSIS

a. Preprocessing

The fMRI data were analyzed using the software SPM5 (Statistical Parametric Mapping) (Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab 7.1 [8]. First, the functional data were preprocessed. The aim is primarily to remove movement artifact in fMRI time-series.[8]

b. Realignment (Motion Correction)

Realignment registers all images from a given subject. It is used to generate parameter files which can later be used to correct for head motion. Because of subject motion, different images are likely to have different patterns of zeros from where it was not possible to sample data. With masking enabled, the program searches through the whole time series looking for voxels which need to be sampled from outside the original image [9].

Image realignment

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1 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_001.i
2 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_002.i
3 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_003.i
4 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_004.i
5 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_005.i
6 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_006.i
7 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_007.i
8 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_008.i
9 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_009.i
10 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_010.i
11 C:\fmri_analysis\Single final\data1\0\session1\raws10_epir1_xoox10_epir1_011.i
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etc
    
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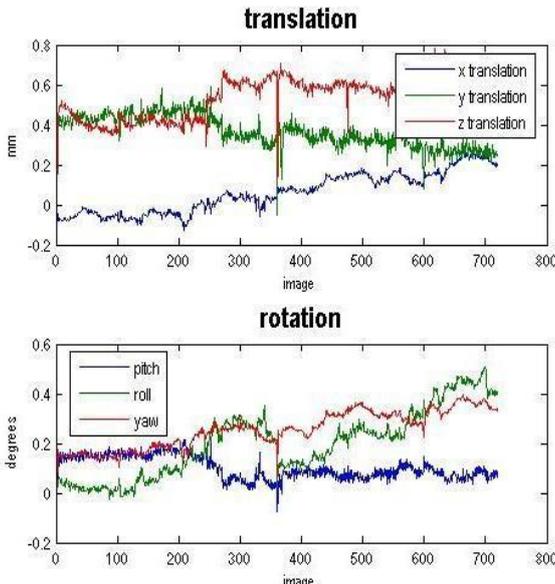


Fig. 3 Realignment for removing movement artifact in fMRI time series

Realignment produces text files that are stored in each session's directory. They contain 6 columns and each row corresponds to a x-file. The columns are the estimated translations in mm ("right", "forward", "up") and the estimated rotations in rad ("pitch", "roll", "yaw") that are needed to shift each V-file. These text files can be used later at the statistics stages, to enter the estimated motion parameters as user-specified regressors in the design matrix.

Here "translation", contains the estimated motion in the x-direction (left-to-right, blue line), y-direction (front-back, green line), and z-direction (bottom-top, red line).

c. Spatial Coregistration

Spatial coregistration refers to intrasubject registration, namely the alignment of functional and structural data from individual participants. After preprocessing, the functional and anatomical data were coregistered. After anatomical coregistration, the functional data were spatially rescaled to a resolution of 3 mm³ using trilinear interpolation.

d. Spatial Normalisation

Spatial normalisation refers to intersubject registration, namely the process of normalizing or scaling the data to a standard space.

A Gaussian spatial filter (FWHM 5.65 mm) was used for smoothing. The images are also smoothed slightly, as is the histogram [10].

Normalised Mutual Information Coregistration

$$\begin{aligned}
 X1 &= 0.998 * X - 0.028 * Y + 0.151 * Z + 0.476 \\
 Y1 &= 0.020 * X + 0.992 * Y + 0.288 * Z - 1.534 \\
 Z1 &= -0.029 * X - 0.052 * Y + 0.990 * Z + 3.732
 \end{aligned}$$

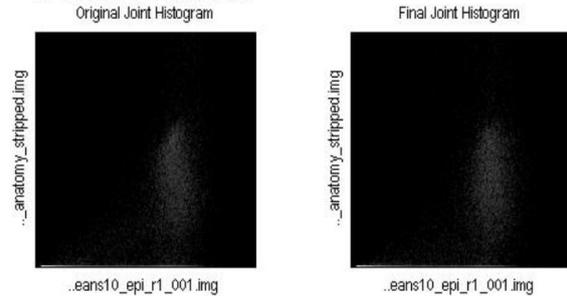


Fig. 4 Normalised Mutual Information Coregistration

In the Fig. 4 (Normalized mutual information coregistration) X1, Y1, Z1 indicates the normalized coregistered values of the selected structural data. Also X, Y, Z implies the realigned values of those raw dataset of the relevant patient.

At the end of coregistration, the voxel-to-voxel affine transformation matrix is displayed, along with the histograms for the images in the original orientations, and the final orientation.

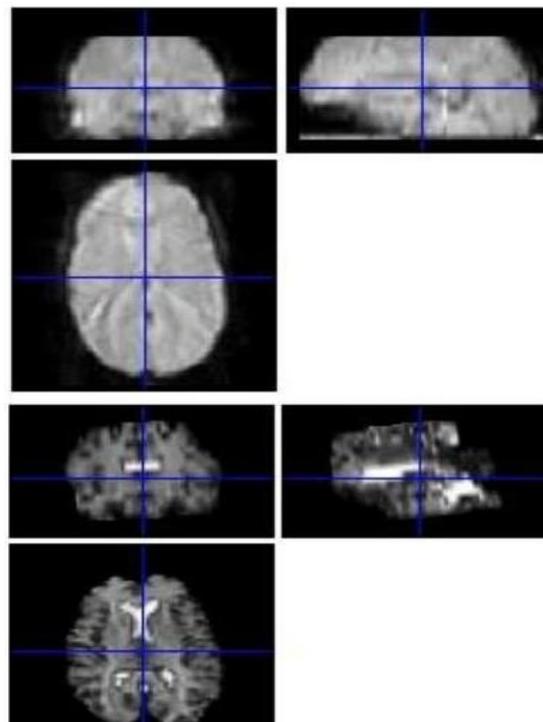


Fig. 5 Images after final Coregistration

e. Statistical Analysis

Statistical analysis was based on a voxelwise least squares estimation using the general linear model (GLM). Analysis of event-related data within the GLM requires that an explicit model is generated of the factors (i.e. effects) that are thought to contribute to variability in a data set. For each voxel in a data set, estimates of the response to each effect are calculated by representing each time point in the data set by a linear equation. For each time point in the data set the linear equation represents the measured BOLD(Blood Oxygenation Level Dependent) signal as the sum of the hemodynamic responses occurring at that point plus variance from noise. Low frequency signal drifts were controlled by applying a temporal high-pass filter with a cutoff frequency of 0.0036 Hz.

f. Modelling Categorical Response

While modeling the categorical response a sot.mat file was created containing the relevant Stimulus Onset Times(SOT) of the experiment . This ‘‘SOT’’ provides the sequential timing of the visual stimuli [11].

In the design matrix shown in Fig. 6, the conditions are assigned as ‘V1’, ‘V2’ ‘V3’ for three different types of random visual stimuli. There is a factor named ‘Visual’ with a ‘level’=3. The regressors comprise six columns of the design matrix.

g. Inference for Categorical Design

Here Canonical HRF (Hemodynamic response function) is used as the basis function. To determine the ‘Main Effect’ of ‘Visual Stimuli’ F-Contrast is used. During the experiment data are collected for each factor/level combination and then analyzed using One-Way-Within Subject Analysis of Variance (ANOVA) [12].

The ANOVA uses F-tests to examine a pre-specified set of standard effects. The f-contrast is used to pick out the linear combinations of the basis functions. The resulting f-statistics are f-to-z converted to produce spatial maps of pseudo-z-statistics. SPM{F} is essentially an extra-sum-of squares test , where the additional variance explained by a section of the model is compared with the error variance. In other words, the F-test is concerned with how much a given variable *uniquely* adds to explained variance. SPM{F} is spmF_***.img, computed by dividing the ess_***.img by the ResMS.img error variance estimate image, and scaling appropriately. The F-contrast signifies about how much a given linear contrast of parameter estimates (as a subset of such contrasts) contributes uniquely to explaining variance in the data. [13]

Calculation of ‘‘One-way Within Subject ANOVA’’

There are 720 observations for each level. Here V3, V1, V2 are the three levels of the factor ‘‘Visual ‘‘.First of all corresponding means are calculated.

$$\bar{V}_3 = \frac{1}{n} \sum V_{3i} \tag{1}$$

$$\bar{V}_1 = \frac{1}{n} \sum V_{1i} \tag{2}$$

$$\bar{V}_2 = \frac{1}{n} \sum V_{2i} \tag{3}$$

where $n = 720$

$$\bar{V} = \frac{\sum \bar{V}_p}{a} \Rightarrow \frac{\bar{V}_1 + \bar{V}_2 + \bar{V}_3}{a} \tag{4}$$

Where, $a = 3$

Now the between group some of squares (SS_B) is,

$$SS_B = n(\bar{V}_3 - \bar{V})^2 + n(\bar{V}_1 - \bar{V})^2 + n(\bar{V}_2 - \bar{V})^2 \tag{5}$$

$$df_b = (3 - 1) = 2 \tag{6}$$

Here df_b implies between group degrees of freedom and

MS = Mean Square, the subscript ‘‘ B’’ stands for between group

$$MS_B = \left(\frac{SS_B}{2} \right) \tag{7}$$

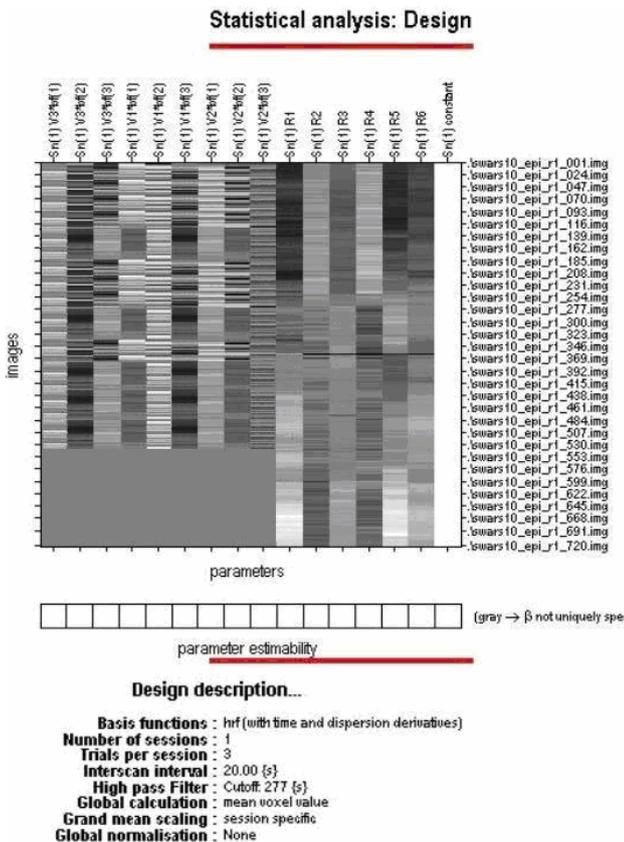


Fig. 6 Design Matrix

Calculate the within group some of squares (SS_w), begin by centering the data in each group

$$SS_w = \sum (V'_{3i})^2 + \sum (V'_{1i})^2 + \sum (V'_{2i})^2 \quad (8)$$

Now the within group mean square value :

$$MS_w = \left(\frac{SS_w}{df_w} \right) \quad (10)$$

Hence F-ratio is:

$$F = \left(\frac{MS_B}{MS_w} \right) \quad (11)$$

TABLE I
THE WITHIN GROUP SUM OF SQUARES OF ALL 2160 VALUES

V'_{3i}	V'_{1i}	V'_{2i}
$V_{3_1} - \bar{V}_3$	$V_{1_1} - \bar{V}_1$	$V_{2_1} - \bar{V}_2$
$V_{3_2} - \bar{V}_3$	$V_{1_2} - \bar{V}_1$	$V_{2_2} - \bar{V}_2$
\vdots	\vdots	\vdots
$V_{3_{720}} - \bar{V}_3$	$V_{1_{720}} - \bar{V}_1$	$V_{2_{720}} - \bar{V}_2$

All resulting SPMs were thresholded at $F=5.241912$ ($p<0.5$, uncorrected) to analyze the main effect of the factor 'Visual'. Since $(720*14*3=30240)$ number of voxels are tested here $P<0.5$ (FWE: Family Wise Error) and extended threshold value 0.0025 signifies it is expected that approximately 76 will activate by chance even if no stimulation is applied. During the experiment most of the neurons in the visual cortex were found in normal activation [14].

The within group degrees of freedom is

$$df_w = a(n-1) = 3(720-1) = 2157 \quad (9)$$

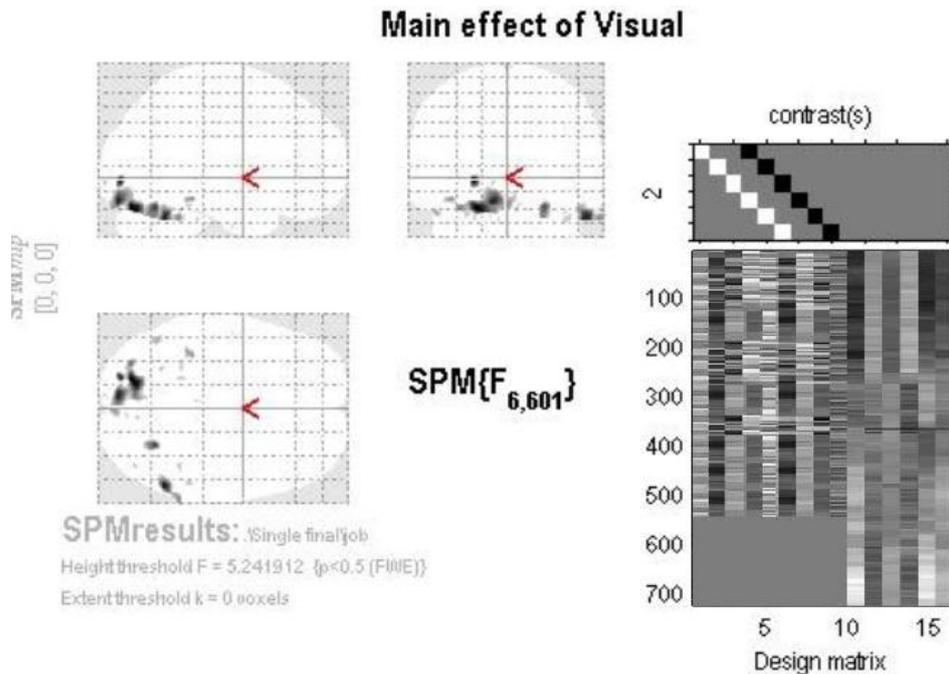


Fig. 7 Main effect of Visual Stimuli with F-Contrast

VIII. RESULT

During the experiment 11 participants were shown three types of visual stimuli. Their average behavioral response was found as the normal response of visual cortex. Proper neuronal activation was found by superimposing the functional data of each patient upon their relevant anatomical data.

Correlation between the activity of visual and motor cortex was found normal. The response of visual cortical areas

passed as a stimulus to the motor cortex. Also due to the proper functioning of the motor cortex each patient was able to indicate which of the box changed its color with their fingers as was asked to do. Also the participants could discriminate the change of colors and their response was obtained within about 2s after providing the visual stimuli. The black spots in Fig. 7 indicate all the active neurons of each patient's visual cortex which is necessary for its proper functioning.

IX. CONCLUSION

If any of the patients would have any sort of visual agnosia or dementia proper activation of maximum number of neurons within the visual cortex could not be diagnosed. Thus with the earlier detection of malfunctioning of visual cortex, further severe damage or blindsight can be diminished at an appreciable rate.

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