J. Biomed. Eng. Res : 477-483, 2007

The Influence of Eye Movement for Acquiring BOLD Signal in V1 : A Study of Simultaneous Measurement of EOG and fMRI

Jun-Young Chung[1], Hyo Woon Yoon[1], Young-Bo Kim[1], HyunWook Park[2]

[1]*Neuroscience Research Institute, Gachon University of Medicine and Science, Incheon, Republic of Korea.*
[2]*Department of Electrical Engineering, Korea Advanced Institute of Science and Technology, Daejeon, Republic of Korea.*
(Received June 7, 2007. Accepted July 6, 2007)

Abstract

We have measured EOG and fMRI simultaneously to investigate whether eye movement (blinking mechanism) might influence functional magnetic resonance imaging (fMRI) signal response in the primary visual cortex. T2*-weighted Echo-Planar Imaging (EPI) with concurrent electrooculogram (EOG) was acquired in four subjects while they viewed a fixation point and a checkerboard with a flickering rate of 8Hz. With the help of EOG information we divided the experimental blocks into two different conditions: fixation and moving eye. We have compared the fMRI data of these two conditions. Our results have shown that there is no difference between these two conditions. This might suggest that eye blinking does not affect BOLD signal changes in the primary visual cortex. This means further that eye blinking can be ignored in data processing.

Key words : EOG and fMRI simultaneous measurement: eye blinking

I. INTRODUCTION

There are several methodological approaches to measuring correlates of neuronal activation in the brain, e.g., Positron Emission Tomography (PET) or functional magnetic resonance imaging (fMRI). One of the preferred methods for this purpose is functional MRI which can detect the increased blood flow related to neuronal activity with relatively high spatial resolution. T2*-weighted MR imaging can reveal changes in blood oxygenation in activated brain areas[1]. Fast imaging sequences such as echo-planar imaging (EPI) can capture stimulus-evoked transient changes in blood oxygenation level-dependent (BOLD) contrast, which likely reflects hemodynamic responses[2-4]. The majority of fMRI studies are based on visual stimuli and eye movement could influence signal intensity of functional MR data, especially in the primary visual cortex. It has been reported that local eye movements influence whole-head motion correction procedures, resulting in inaccurate movement parameters and potentially lowering the activation detection sensitivity[5]. Eye movement also affected the magnitude of fMRI response in the extrastriate cortex during visual motion perception[6] and eye blinking in a dark environment evoked primary visual cortex's activation[7]. In this study, we have measured electrooculogram (EOG) data simultaneously with EPI data acquisition to detect the eye blinking signal while visual stimuli were being presented. The aim of our study is to find out if there are differences or correlations in the activation patterns of the primary visual cortex between a large and small frequency of eye blinking. However, hemodynamic response is only indirectly linked to the energy consumption of the neural population, and takes place on a timescale of more than 3 seconds after giving stimulus input. In order to compensate for temporal resolution and indirect measurement of neural activity, a direct measuring method of the electrical activity of neurons has been suggested. This can be done with using electroencephalogram (EEG) and this method features the millisecond timescale, which might represent underlying cognitive processes. The combination of EEG and fMRI or the simultaneous recording of the EEG and fMRI might be a promising tool for functional brain mapping, which provides physiological characteristics with both high spatial and temporal resolution.

Even though the advantages of this simultaneous measurement are well known, it is not so simple to acquire EEG waveforms during EPI sequences.

Corresponding Author : Young-Bo Kim
Neuroscience Research Institute, Gachon University of Medicine and Science, Incheon, Republic of Korea
Tel : +83-32-460-2602 / Fax : +82-32-460-8230,
E-mail : neurokim@gachon.ac.kr

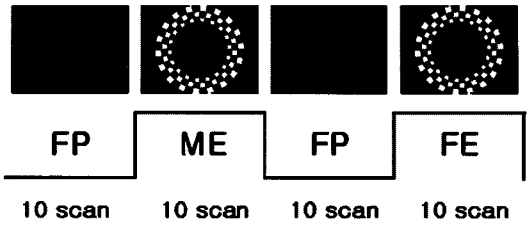


Fig. 1. The paradigm and stimuli, FP is fixed point's condition, ME is natural movement eye's condition, and FE is fixing eye's condition. Each condition has 3 sec. During FP and ME, flickering checkerboard pattern with a flicker rate of 8 Hz are presented.

In the present study, we aimed to complete the experiment using this combination. In particular, the acquisition of EOG is done for measuring the frequency of eye blinking in each subject.

II. MATERIALS AND METHODS

A. Subjects

Four right-handed healthy volunteers (mean age of 26 years with SD of 1.2 years, all males) participated as subjects in this study after giving their written informed consent. They were free of any neurological antecedent and had good vision. Before starting the scanning session, subjects put on the cap for recording EEG.

B. EEG (Electroencephalogram) Recording

A commercially available MR-compatible system (Brain Amp MR, Brain Products GmbH, Germany) was used for EEG recording and used along with a specially-designed electrode cap (BrainCap-MRI). The electrode cap contains 32 EEG channels and three additional channels dedicated to electocardiogram (ECG) and electrooculogram (EOG) acquisition. The reference electrode is located at the center between Cz and Fz. All the electrodes are ring-type sintered nonmagnetic Ag/AgCl electrodes. The impedance of each electrode site was maintained at 5k by injecting an electrode paste (ABRALYT 2000, FMS, Herrching-Breitbrunn, Germany). The amplifier was designed to be placed inside the magnet bore of the scanner and was connected to the host computer outside the MR room via a fiber optic cable. The resolution and dynamic range of the amplifier was 100 nV and 3.2 mV, respectively. The EEG and EOG waveforms were recorded with a sampling rate of 500 samples/s. Band pass filtering from 0.5 to 80 Hz was applied along with 60 Hz notch filtering. We recorded EOG in order to monitor the subject's blinking and eye movement. The gradient-induced artifacts on EEG signal were removed by digital filtering[8-10]. Detecting the blink signal on the EEG recording monitored eye movements.

C. Experiment Design

Visual stimuli were produced using custom designed software. Stimuli were presented with the aid of a video projecting on a screen to the subjects via a mirror. In experimental sessions visual stimuli had concentric circles shape. The fixation point at the center was static, while the surrounding field was flickered. These were circle type checkerboards which had a flickering rate of 8 Hz. Stimuli were presented to subjects with a viewing angle of 13 vertically, 17 horizontally and a viewing distance 5 m. During the experiment, subjects performed 24 blocks of condition with a duration of 30 sec alternating with visual center point fixation, as shown in Figure 1.

Images were acquired during three experimental conditions (natural eye movement, fixed eye, and rest). During the rest condition, subjects were asked to look at the fixation point. During natural eye movement's condition, they also should look at the fixation point and simultaneously the flickering checkerboard's pattern which was being presented. During the fixed eye condition, subjects were asked to keep eyes open and try to not to blink their eyes during stimuli presentation. Checkerboard stimuli were presented as the natural eye movement condition. These phases (as shown in Figure 1) were repeated six times in a run, which means the total duration time of an experimental run for 720 seconds.

D. fMRI Scanning

fMRI data was acquired with a 3 Tesla MR scanner (FORTE, Oxford magnet, Varian Console, built up by ISOL Tech., Korea). To acquire high resolution of Echo-planar images, a surface coil was used. Head movements were minimized with vacuum pillow and foam padding. Echo-planar images (128x128 matrix, over a 160 mm field of view) consisted of 15 consecutive axial sections (3 mm thickness, no gap, repetition time/echo time = 3000/37 ms, flip angle 70 degree). An experiment session consisted of 24 blocks of 30 seconds. The first 15 secs (8 volumes) of fMRI data were discarded to avoid the magnetic saturation effect.

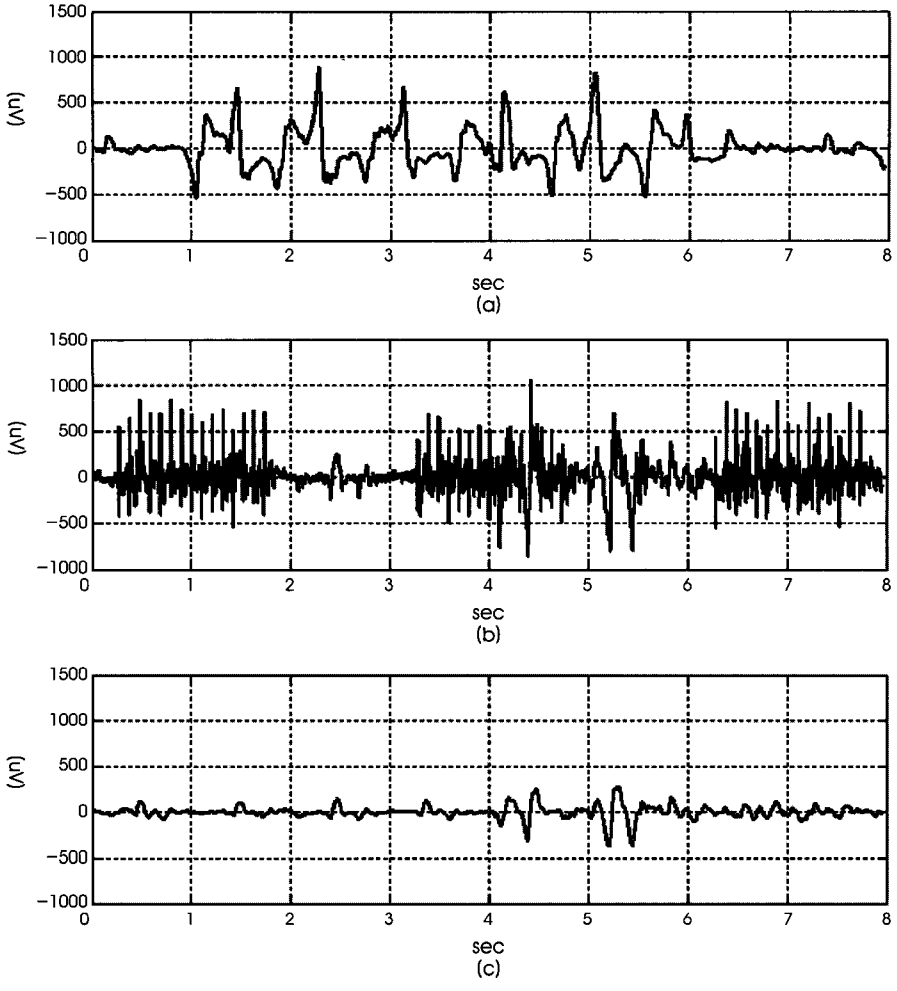


Fig. 2. The Electrooculography. (a) is reference data, (b) is acquired during fMRI scan and C is removed gradient-induced artifacts on (c). Calibration = 1 sec, 1500 μV.

The remaining 240 sec (40 volumes) were analyzed. Using a quadrature head coil (anatomic scan), high- resolution anatomic images were acquired using an MPRAGE sequence (TE = 3.7 ms, TR = 8.1 ms, Flip angle = 8 degree, FOV = 256 x 256 mm^2).

E. Data Analysis

Before scanning, we recorded each subject's EOG reference data (as shown in Figure 2(a)) and measured the amplitude, shape, and rate of reference data for detecting the eye's movement and blinking. During functional MR imaging, the switching of gradient magnetic field induced a series of artifacts into EEG whose amplitudes are 10 to 100 times lager than that of the EEG, data which was measured outside the MR-room. This makes the monitoring of EOG waveforms difficult when MR imaging is being simultaneously performed.

The correction method of gradient-induced artifact is to average the intervals in which the gradient changes of the scanner have taken place. The averaged gradient-induced artifact is then subtracted from the original EEG data in the affected intervals. The gradient-induced artifacts are generally not completely eliminated in this way. For this reason, different filters then were applied to the data in the corrected ranges. After gradient-induced artifacts on recorded EOG (Figure 2(b)) were removed by these methods (2), we detected the blink signal being similar to the each subject's reference EOG signal which has over 150μV and about 2~4 Hz frequency.

The EOG signals typically showed sustained spike wave during eye blinking as shown in Figure 2(c). To select adequate blocks for fMRI data analysis, we detected the blinking eye's signal and counted the number of eye blinks by the block (30 sec) as shown in Figure 3.

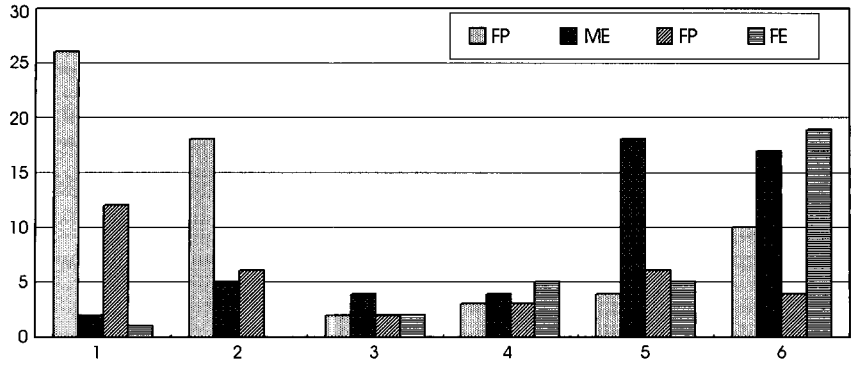


Fig. 3. Count of blinking eye in each condition's block. FP is center fixation point's blocks, ME is natural eye movement's condition block and FE is fixing eye's condition block.

To analyze fMRI data in adequate blocks, the first slice scan time within a volume was used as a reference for alignment by linear interpolation of the following slice of that volume to correct for the temporal slice scan time shifts. Data analysis and visualization were performed with the fMRI software package Brain Voyager (Brain Innovation, Maastricht, The Netherlands)[11]. Before the main analysis the following processing steps were carried out 1) motion correction, 2) spatial smoothing of EPI images with full width at half-maximum of 4 mm, 3) transformation into Talairach[12] coordinate space. The cortical sheets of individual subjects and a template brain were reconstructed as polygon meshes based on high-resolution T1-weighted structural three-dimensional recording. The white-gray matter boundary was segmented, reconstructed, smoothed, and morphed. A morphed surface always possesses a link to the folded reference mesh so that functional data can be correctly projected onto partially inflated representations. The ON and OFF phase were used for linear regression analysis of the BOLD signal time course. Using an empirically founded model[13] of the temporal dynamics of the fMRI signal, hemodynamic predictors were computed from the ON and OFF phase and a general linear model (GLM) was computed for every voxel. To exclude unspecific stimulus onset effects, the first perceptual phase (called dummy scans) was excluded. Especially, ROI (Region of interest) in this study was focused on the primary visual cortex of each subject.

Correlation (r_{xy}) between the number blinks (x_i) and the averaged BOLD-signal time course data(y_i) in each block of the FE and ME conditions is given by the covariance and variance of the two conditions' blocks. The covariance between those two conditions is given by the expression,

$$cov(x, y) = \frac{1}{n-1} \sum_{i=1}^{n} (x_i - \bar{x})(y_i - \bar{y}),$$

$\bar{x}$, $\bar{y}$ are average of data values
and the correlation (r_{xy}) is

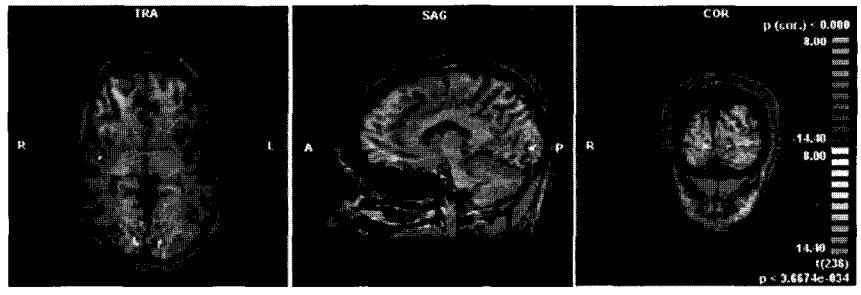
$$r_{xy} = \frac{cov(x,y)}{S_x S_y},$$

where S_x, S_y the standard deviations, are the square roots of the corresponding variance. Note that correlation (r_{xy}) is dimensionless and takes values limited to the range - 1 to +1.

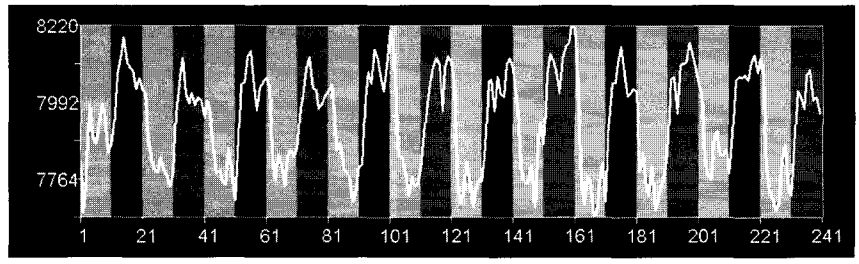
III. RESULTS

As shown in Figure 4, the results of one of four subjects indicates that the activation of primary visual cortex for both the fixed eye (FE) and natural eye movement (ME) conditions was observed. The indicated activation area was observed in the other three subjects. The averaged blinking frequency, which was detected by EOG, for the FE is condition 0.8 and 2.9 for the ME condition. Even though a larger blinking frequency can be observed by the ME condition compared to FE condition, the activation of the contrast 'ME minus FE', or 'FE minus ME' indicates that there were very few significantly activated voxels.

We proceed to correlation and consider that each data point consists of two measurements, the averaged blinking and BOLD-signal time course data in each block of the FE and ME conditions. Figure 5 shows each subject's number of blinks that were detected from EOG and averaged of MR-signal time course data in each block of the FE and ME conditions. The correlation between those two values is given by the covariance and variance of the two condition blocks. Correlation is dimensionless and takes values limited to the range of - 1 to +1. Figure 6 shows the correlation coefficient between the number of blinking eyes and the averaged MR signal intensity in four subjects. As we observe, correlation

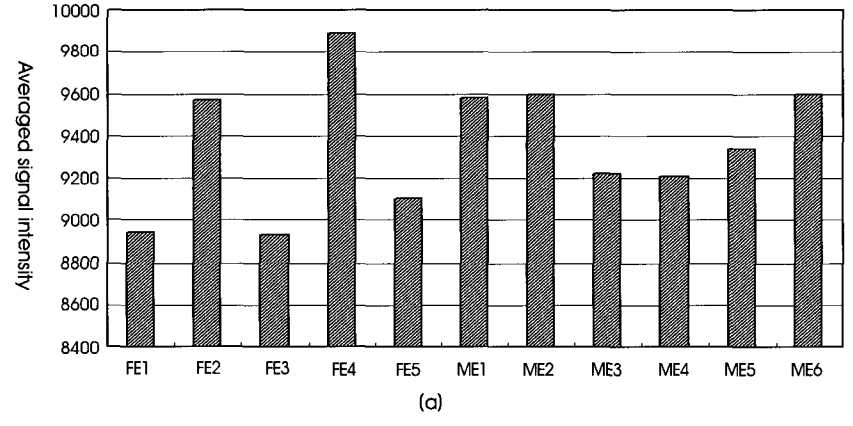


(a)

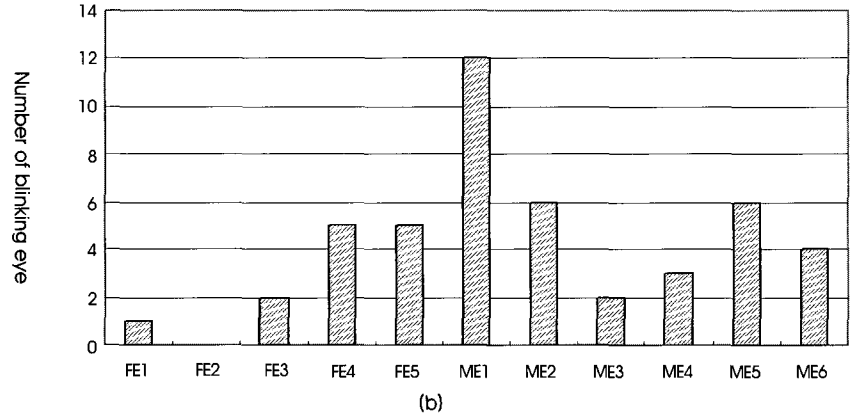


(b)

Fig. 4. Processing results of blinking eye (BE)'s condition. (a) is activated voxel on 'FE-FP's contrast ($p < 3.66E-34$). (b) is time course of MR signal intensity as a function of time in activated area. Green, blue, and red columns signify FE, BE, and FP's stimulation periods. The signal look like typical BOLD signal in all of BE (red columns) and FE (blue columns)'s stimulation periods.



(a)



(b)

Fig. 5. (a) is averaged signal intensity and (b) is number of blinking in subject 1's each FE and BE' s condition blocks.

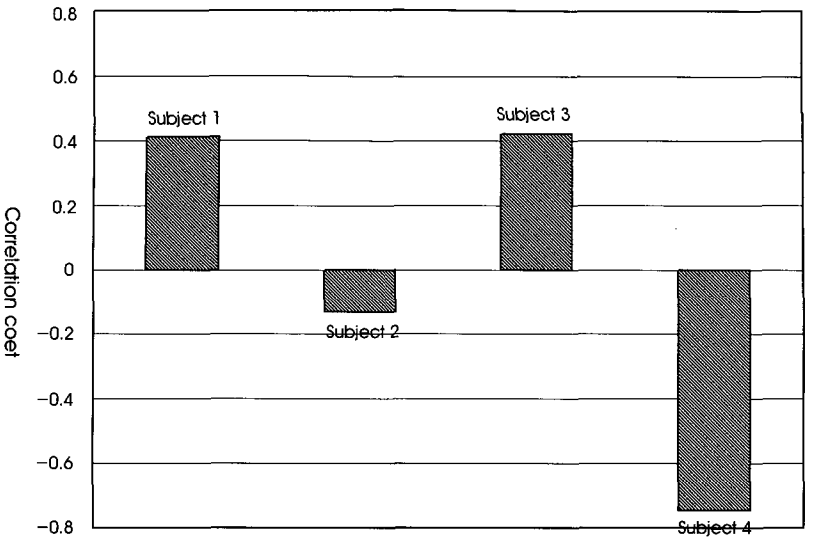


Fig. 6. Correlation coefficient between blinking eyes and averaged MR signal intensity in all of each condition's blocks.

between the number of blinks and the average MR-time course data are smaller. Therefore, eye blinking doesn't affect primary visual cortex activity in our experiment.

IV. DISCUSSION

Eye movements, both voluntary and involuntary, are the main focuses of this study. Due to their intrinsic nature, they can be possible sources of artifact and confound when interpreting functional MRI data. The blinking process is reported to be controlled in the orbitofrontal and visual cortices, including the anterior portion of the visual cortex and the primary visual cortex[7]. Local eye movements influence whole-head motion correction procedures, resulting in inaccurate movement parameters and potentially lowering the sensitivity to detect activations[5]. For this reason, during fMRI experimentation, infrared visible light video cameras or EPI data can be used for monitoring eye movement[14, 15]. While these methods appear simple to realize at first view, it is unfortunately not so simple to realize for technical reasons (i.e., synchronization of eye movement with pulse sequences and limited echo planar imaging time). Based on this, an MR-compatible EEG recorder might be a promising tool for monitoring the eye movement.

Our results indicate that eye blinking doesn't affect primary visual cortex and shows that the general fMRI study need not consider the effect of the eye blinking mechanism in data processing. It appears to be enough to instruct the subject to fix their eye on the stimuli in a general fMRI study.

REFERENCES

[1] S. Ogawa, T.M. Lee, A.R. Kay, and D.W. Tank et al., "Brain magnetic resonance imaging with contrast dependent on blood oxygenation," in *Proc. Natl. Acad. Sci.*, 1990, vol. 87, no. 24, pp.9868-9872.

[2] P.A. Bandettini, E.C. Wong, R.S. Hinks, R.S. Tikofsky, and J.S. Hyde, "Time course EPI of human brain function during task activation," *Magn. Reson. Med.*, vol. 25, no. 2, pp.390-397, 1992.

[3] T. Ernst and J. Hennig, "Observation of a fast response in functional MR," *Magn. Reson. Med.*, vol. 32, no. 1, pp.146-149, 1994.

[4] R.S. Menon, S. Ogawa, X. Hu, J.P. Strupp, P. Anderson, and K. Uğurbil, "BOLD based functional MRI at 4 Tesla includes a capillary bed contribution: echo-planar imaging correlates with previous optical imaging using intrinsic signals," *Magn. Reson.* Med., vol. 33, no. 3, pp.453-459, 1995.

[5] J.R. Tregellas, J.L. Tanabe, D.E. Miller, and R. Freedman, "Monitoring eye movements during fMRI tasks with echo planar images," *Hum. Brain Mapp.*, vol. 17, no. 4, pp.237-243, 2002.

[6] P. Freitag, M.W. Greenlee, T. Lacina, K. Scheffler, and E.W. Radü, "Effect of eye movements on the magnitude of functional magnetic resonance imaging responses in extrastriate cortex during visual motion perception," *Exp. Brain Res.*, vol. 119, no. 4, pp.409-414, 1998.

[7] K. Tsubota, K.K. Kwong, T.Y. Lee, J. Nakamura, and H.M. Cheng, "Functional MRI of brain activation by eye blinking," *Exp. Eye Res.*, vol. 69, no. 1, pp.1-7, 1999.

[8] P.J. Allen, G. Polizzi, K. Krakow, D.R. Fish, and L. Lemieux, "Identification of EEG events in the MR scanner: the problem of pulse artifact and a method for its subtraction," *Neuroimage*, vol. 8, no.3, pp.229-239, 1998.

[9] F. Kruggel, C.J. Wiggins, C.S. Herrmann, and D.Y. von Cramon, "Recording of the event-related potentials during functional MRI

at 3.0 Tesla field strength," *Magn. Reson. Med.*, vol. 44, no. 2, pp.277-282, 2000.

[10] P.J. Allen, O. Josephs, and R. Turner, "A method for removing imaging artifact from continuous EEG recorded during functional MRI," *Neuroimage*, vol. 12, no. 2, pp.230-239, 2000.

[11] L. Muckli, N. Kriegeskorte, H. Lanfermann, F.E. Zanella, W. Singer, and R. Goebel, "Apparent motion: event-related functional magnetic resonance imaging of perceptual switches and States," *J. Neurosci.*, vol. 22, RC219, pp.1-5, 2002.

[12] J. Talairach and P. Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*, New York, Thieme Medical Publishers, 1988.

[13] G.M. Boynton, S.A. Engel, G.H. Glover, and D.J. Heeger, "Linear systems analysis of functional magnetic resonance imaging in human V1," *J. Neurosci.*, vol. 16, no. 13, pp.4207-4221, 1996.

[14] H. Kimming, M.W. Greenlee, F. Huethe, and T. Mergner, "MR-Eyetracker: a new method for eye movement recording in functional magnetic resonance imaging," *Exp. Brain Res.*, vol. 126, no. 3, pp.443-449, 1999.

[15] M.S. Beauchamp, "Detection of eye movements from fMRI data," *Magn. Reson. Med.*, vol. 49, no. 2, pp.376-380, 2003.