Functional connectivity in strabismic adults during saccadic eye movements

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Introduction

Strabismus is a visual disorder in which the patients suffer from misalignment of the eyes in any direction. The etiology of strabismus is commonly believed to be due to the maldevelopment of visual pathways which mediate eye movements and motion in brain [1]. Studies in strabismic monkeys and humans showed a striking loss of binocular vision, reduced disparity sensitivity, directional asymmetry in tracking moving object and abnormal oculomotor processing [2-4]. However, little work had been done on the functional correlations between the visual and oculomotor processing regions in response to the challenges of visual deficits for functional adaptations in strabismic adults. In this study, functional connectivity in strabismic brains as well as healthy brains was assessed with visually saccade eye movement tasks to observe the correlations between different brain regions. The aims of this study were to investigate the possible differences of functional connectivity among the brain regions between strabismic and healthy subjects during the visually guided saccade tasks.

Materials and Method

A total of 26 Chinese adults aged 20-40 years were included. 13 of them had constant strabismus and the remaining 13 subjects were free from any vision disorders which were confirmed by comprehensive eye examinations. All of the strabismic subjects had the eye deviation of 20-prism-diopter or above in the cover test with prisms. MRI brain scanning was performed on a 1.5 Tesla scanner (Siemens Medical, Germany) in the conjunction with a standard 12-channel head coil at the Queen Elizabeth Hospital. 4 imaging datasets from each subject were acquired: 1) sagittal images acquired with volumetric T1 weighted 3D-FLASH sequence as anatomical reference for functional images; 2) T2*-weighted sequence for the identification of possible brain lesions; 3) two sets of BOLD fMRI images acquired with gradient-echo echo planar imaging (EPI) sequence (TR=2000 ms, TE=60 ms, flip angle=90°, FOV=200 mm, matrix=64×64, thickness=5 mm, gap=1 mm) while the subject performed the visually guided saccade task. Each fMRI session lasted 3 min 40 s and was preceded by 4 dummy scans for equilibration of MRI signals. The visually guided saccade task consisting of 5 activation and 6 fixation blocks was presented by a LCD projector. In each activation block, the subject was required to follow a visual cue precisely which jumped in an unpredictable direction to a position 25º left or right of a central fixation for 20 seconds. The fixation block only had a cross-hair in the center of the screen lasting 20 seconds.

Functional connectivity analysis

Using general linear modeling analysis (GLM), the region of interests (ROIs) showing the highest brain activations and deactiviations individually in strabismic and control groups were identified. We used the approach of context-dependent correlation analysis in the software AFNI for the functional connectivity analysis. Before the connectivity analysis, all imaging data were motion corrected, normalized and warped to standard Talairach space. For each set of the BOLD images, the average time series of each ROI with the highest activation or deactivation at the center and 4 mm in radius was extracted. Each time series was then detrended to remove the drifting effect in MR scanning. The detrended time series underwent deconvolution to obtain the neuronal response. The neuronal response in each ROI then convolved with the paradigm for the interaction time series at the ROI. There were two imaging datasets for the visually guided saccade tasks, hence the normalized imaging data and regressors for two imaging datasets were concatenated separately for connectivity analysis. The concatenated normalized imaging data from each subject were regressed with a total of 9 regressors (task paradigm, ROI time series, interaction time series and 6 motion parameters) for each ROI. The correlation coefficient value for interaction of each ROI with each brain voxel was then derived and transformed to Z score through Fisher transformation for group analysis. In each of the strabismic and control groups, group analysis was separately performed using single sample t-test on the z scores derived in regression analysis. The significance level was at $p<0.05$. Z score at the brain voxels showing $p<0.05$ in group analysis was converted back to correlation coefficient R to indicate the functional connectivity between ROI and brain voxels in groups and group connectivity maps were constructed for the brain regions showing significant correlation in activity.

Results and Discussion

The brain regions showing significant functional correlations ($p<0.05$) were presented in Fig.1 for both strabismic and control groups during the visually saccade task. Positive correlations were found to be dominant in the control group whereas negative correlations were found to be dominant in strabismic group. The ROIs which were identified by GLM and the correlated regions identifiable only by connectivity analysis are consistent with those areas previously reported to be structurally different between strabismic subjects and healthy controls [5]. The present connectivity findings imply that the modulation of the functional connectivity for saccadic eye movements is different between strabismic adults and healthy controls among a complicated network of brain regions in which include the frontal eye field, supplementary eye field, prefrontal cortex, parietal eye field, occipital eye field and midbrain.

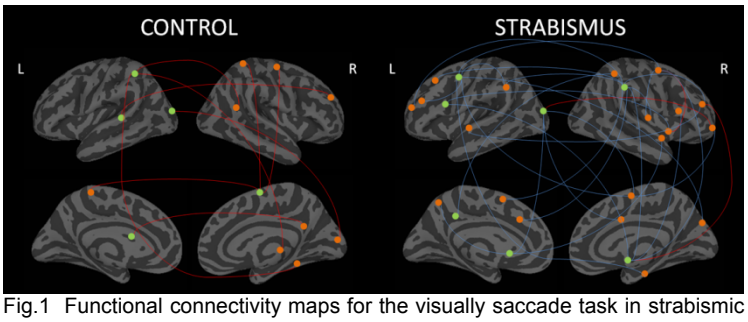

Fig.1 Functional connectivity maps for the visually saccade task in strabismic and healthy subjects. Red and blue lines between 2 brain regions represent the positive and negative correlations respectively. Green dots indicate the ROIs identified by GLM and orange dots indicate the correlated regions identified in functional connectivity analysis.

References

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