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Functional magnetic resonance imaging evaluation of visual cortex activation in patients with anterior visual pathway lesions☆

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Abstract

The aim of this study was to examine the secondary visual cortex functional disorder in patients with glaucoma and large pituitary adenoma by functional magnetic resonance imaging, and to determine the correlation between visual field defect and primary visual cortex activation. Results showed that single eye stimulation resulted in bilateral visual cortex activation in patients with glaucoma or large pituitary adenoma. Compared with the normal control group, the extent and intensity of visual cortex activation was decreased after left and right eye stimulation, and functional magnetic resonance imaging revealed a correlation between visual field defects and visual cortex activation in patients with glaucoma and large pituitary adenoma. These functional magnetic resonance imaging data suggest that anterior optic pathway lesions can cause secondary functional disorder of the visual cortex, and that visual defects are correlated with visual cortex activation.

Key Words: functional magnetic resonance imaging; glaucoma; pituitary adenoma; anterior visual pathway; visual cortex

Abbreviations: MRI, magnetic resonance imaging; fMRI, functional MRI; MNI; Montreal Neurological Institute

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INTRODUCTION

Glaucoma represents a group of disease characteristics of optic nerve atrophy and visual field defects. Magnetic resonance imaging (MRI) has also shown the appearance of a thin optic nerve and a small ratio of height to diameter at the optic chiasm and the lateral geniculate body in patients with primary open-angle glaucoma[1-2]. Pituitary macroadenomas grow and cross through the diaphragm seal, then compress the optic chiasm, leading to visual field defects and visual loss. However, conventional MRI cannot detect abnormal changes in the optic radiation and the visual cortex in patients with glaucoma and pituitary adenoma. Further, although animal experiments show varying degrees of posterior visual pathway lesions[3-6], the majority of which are concentrated in the lateral geniculate body, the changes in the human brain are largely unknown. Functional MRI (fMRI) is a non-invasive approach for the assessment of visual cortex activation, and can be used to evaluate the influence of visual pathway lesions on the visual center[7-9]. Thus, in the present study we used fMRI to examine the secondary functional changes of the visual cortex in patients with glaucoma and pituitary adenomas, and to analyze the correlation between primary visual cortex activation and visual field changes.

RESULTS

Quantitative analysis of subjects

Both the left and right eyes of the study patients were analyzed because of different degrees of visual field defects between the two eyes. Head movement and mechanical noise were strictly controlled, and patients of normal monocular vision were excluded. A total of 30 patients were included in the final analysis, including two patients with glaucoma in both eyes.

Glaucoma patients were divided into left and right eye stimulation groups (n = 16 per group). The left stimulation group included 5 males and 11 females, aged 44–74 years (mean 61 ± 8 years), and the right stimulation group included 6 males and 10 females, aged 44–77 years (mean 64 ± 9 years). According to the differing degrees of visual field defects in the left and right eyes, the patients were assigned to the early visual field defect group (paracentral scotoma, nasal ladder) or the advanced visual field defect group (quadrantanopia, central visual field and temporal island). Each of the left and right eye stimulation groups comprised seven cases with early

visual field defect and nine cases with advanced visual field defect.

There were 23 patients with pituitary adenomas (one patient with pituitary adenoma in both eyes), which were divided into the left and right eye stimulation groups (n = 12 per group). The left stimulation group included six males and six females, aged 38–61 years (mean 52 ± 7 years). The right eye stimulation group included six males and six females, aged 38–64 years (mean 51 ± 8 years). The majority of visual field defects in both patients with glaucoma in both eyes were temporal visual field defects.

Thirty normal volunteers were selected for this study, and 16 cases were entered into the final study on the basis of visual stimulation data in both eyes under a strict control of head movement, mechanical noise, and other factors. This group included six males and 10 females, aged 38–72 years (mean 57 ± 8 years).

Visual cortex activation in normal volunteers after visual stimulation

Both left and right eyes of normal volunteers were analyzed as a control group. The activation area in the control group was most apparent in the primary visual cortex (anatomically equivalent to Brodmann 17 area), and frequently occurred in the posterior cortex of the cuneus gyrus, lingual gyrus, occipital gyrus, fusiform gyrus, and inferior temporal cortex (Brodmann 18 and 19 areas) (Table 1). The most activated brain area in patients after left and right eye stimulations was the right occipital lobe (Figure 1).

Table 1 Activated area, intensity, and Montreal Neurological Institute coordinate position of single eye stimulation in control group

Activated area	Brodmann area	*T*	Coordinate		
			X	*Y*	*Z*
Right cuneus gyrus	18	14.91	8	−96	−1
Left cuneus gyrus	18	11.44	−8	−94	−2
Left lingual gyrus	18	16.55	8	−90	−4
Right lingual gyrus	18	13.76	16	−76	−10
Right middle occipital gyrus	18	10.19	24	−90	20
Right inferior temporal gyrus	19	6.61	58	−56	−16
Left fusiform gyrus	19	8.38	−28	−76	−22

Visual cortex activation in glaucoma patients after visual stimulation

Both sides of the occipital visual cortex were activated in glaucoma patients following left or right eye stimulation. The intensity and range of activation in the bilateral occipital lobe visual cortex was reduced in glaucoma patients after left and right eye stimulation, particularly in the right occipital lobe, when compared with the control group (Figure 1). Further, these two indices of visual cortex activation in the nine patients with advanced visual field defect after left eye stimulation were significantly reduced, particularly in the right visual cortex, compared with the control group. Similar alterations were found in the nine patients with advanced visual field defect after right eye stimulation, mainly in the left visual cortex (supplementary Figures 1, 2 online).

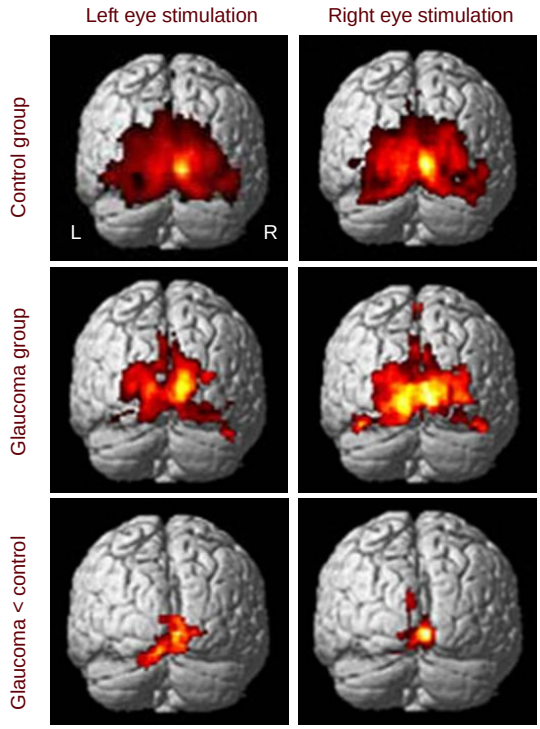

Figure 1 Activation mapping of single eye stimulation in the glaucoma group. The intensity and range of activation of the bilateral occipital lobe visual cortex were reduced in patients with glaucoma after left and right eye stimulation, especially in the right occipital lobe.

The two images in the last line were determined by subtraction of the glaucoma group from the control group (glaucoma < control). The fluorescence shades from red to yellow represent changes in activation intensity, with brighter colors indicating higher intensity of activation.

Visual cortex activation in patients with pituitary adenomas after visual stimulation

After left eye stimulation, the bilateral occipital lobes of patients with pituitary adenoma were activated, with the left side exhibiting significantly greater activation than the contralateral side. After right eye stimulation, the bilateral occipital lobes were also activated in patients, with the right side exhibiting significantly greater activation than the contralateral side. Compared with the control group, the occipital activation intensity and range were both decreased in the left and right stimulation groups. The decrease mainly occurred in the right occipital lobe of pituitary adenoma patients after left eye stimulation, and in the left occipital lobe after right eye stimulation (Figure 2, supplementary Figures 3, 4 online).

DISCUSSION

The visual pathway is typically divided into an anterior optic pathway (optic nerve, optic chiasm, and optic tract) and a posterior optic pathway (optic radiation and visual cortex), and the optic formation depends on the integrity of the visual pathway. Anterior optic pathway lesions such as optic neuritis and amblyopia have been shown to lead to structural and functional changes of the posterior optic pathway[7-11]. Werring *et al* [10] also demonstrated

that fMRI is more sensitive than visual electrophysiology and conventional MRI in the evaluation of visual pathway function.

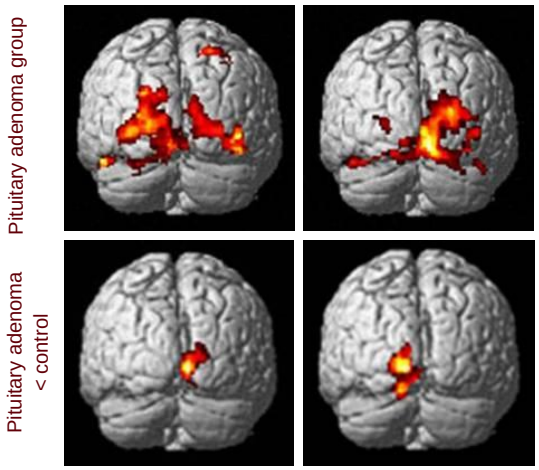

Figure 2 Activation mapping of single eye stimulation in the large pituitary adenoma group. The occipital lobe activation range and intensity were both decreased in pituitary adenoma patients, mainly in the contralateral occipital lobe after the monocular stimulation. The two images in the last line were determined by the subtraction of the pituitary adenomas group from the control group (pituitary adenomas < control). The fluorescence shades from red to yellow represent changes in activation intensity, with brighter colors indicating higher intensity of activation. The control group image is shown in Figure 1.

Glaucoma and pituitary tumors are both anterior optic pathway lesions. In the present study, we found that the intensity and range of bilateral occipital visual cortex activation were reduced after monocular visual stimulation in patients with anterior visual cortex lesions compared with the normal control group. These data suggest that anterior optic pathway lesions can cause secondary functional decline in the visual cortex, although this functional recovery should be confirmed in follow-up observations post-surgery. In addition to a decrease in visual cortex activation, fMRI studies have demonstrated functional recombination in the human visual cortex of some patients with different visual pathway lesions[12-15]. The pattern of changes in activation of the visual cortex can vary markedly depending on the pathogenesis of glaucoma and pituitary tumors, as well as with different patterns of visual field defects.

Similar to movement and language function, the visual cortex also exists in the dominant hemisphere, and the right visual cortex is generally considered to be the dominant hemisphere for vision[16-17]. We also demonstrated that the right occipital lobe exhibited the greatest decrease in activation area in patients with glaucoma, although it remained the dominant visual hemisphere. When the visional acuity and visional field are changed, the information input and conduction of nerve impulses are both reduced, leading to a significant affect on the visual cortex. In addition, the dominant visual cortical neurons may be more sensitive to detect abnormal vision, and more prone to induce secondary structure and functional changes.

With disease progression, we also found that the right hemisphere dominance of the visual cortex disappeared in glaucoma patients with advanced visual field defects, while the left and right eye stimulations caused different degrees of visual cortex activation. The patients with advanced vision field defects showed lesions in the tubular visional field and the temporal island of vision. Ultimately, only the intact cells at the nasal retina could elicit the light stimulus and conduct the nerve impulse from the optic chiasm to the contralateral visual cortex. As such, single eye stimulation mainly activates the contralateral visual cortex. These data also suggest that fMRI can reflect the topological correlation between the retina and the visual cortex, as previously described[18-21]. For example, Hirsch *et al* [18] analyzed the correlation between visual field defects and fMRI results in suspected patients, and found that fMRI results were fully consistent with the visual field examination. Sunness *et al* [19] also reported that atrophic macular degeneration caused visual field central scotoma, while the cortex corresponding to the macula was not activated. Pituitary adenomas can compress the optic chiasm and produce optic pathway conduction disorders, leading to visual field defects and vision loss. Compared with the control group, we found that activation in the hemisphere contralateral to the stimulated eye was significantly reduced or absent in patients; this reduced activation level is considered the hallmark of visual field defect. This result is consistent with the anatomy of the optic chiasm. The nasal retina receives projections from the temporal half field, and as this part of the fiber projections cross from the optic chiasm to the contralateral side, pituitary tumors can gradually compress the optic chiasm during disease progression. This compression first affects the nerve fibers below the nasal retina of both eyes, and then destroys the information pathway of the nasal optic nerve fiber, leading to a small amount or no information transfer to the contralateral visual cortex. The lesions mainly result in a temporal visual field defect, and the light stimulus from the temporal visual field cannot reach the central vision area. As such, activation of the contralateral visual cortex as visualized by fMRI is decreased or disappears. Some MRI studies examining the visual field and the optic chiasm found a correlation between activation of the visual cortex and visual field changes[22-25]. For example, using fMRI Victor *et al* [22] found activation of only the ipsilateral visual cortex in patients with non-decussation of the visual fibers using a simple light stimulation. Morland *et al* [23] also found that only the contralateral cortex showed a response to hemi-field monocular stimulation by fMRI in albino patients, suggesting that albino patients have an abnormal optic chiasm.

A potential limitation of the present study is the lack of point-to-point correspondence analysis in the activation of the visual cortex and the visual field defect. The recent development of fMRI retinal cortex mapping has allowed improved understanding of the topological correlation

between the visual cortex and the visual field, and this mapping technique has be used in clinical studies[11, 26-28]. However, this examination is time-consuming, and the experimental design and post-processing are complex. As an alternative approach, diffusion tensor imaging technology allows non-invasive evaluation of cerebral white matter fiber bundle abnormalities[29-32]. A combination of fMRI and diffusion tensor imaging may be useful to examine the anterior optic pathway lesion structure and function to help define the structural and functional changes in the visual pathway[33-35].

In summary, using fMRI we demonstrated that anterior optic pathway lesions can result in secondary visual cortex dysfunction in patients with glaucoma and large pituitary adenoma. Further, we found a correlation between the visual field defect and visual cortex activation.

SUBJECTS AND METHODS

Design

A case-control experiment.

Time and setting

Experiments were performed in the MRI Room, Tianjin Medical University, China from October 2007 to July 2010.

Subjects

A total of 30 patients with glaucoma and 23 patients with pituitary adenoma by MRI diagnosis were all from the General Hospital of Tianjin Medical University, China. Inclusion criteria: (1) Han population; (2) native in Tianjin; (3) clinical diagnosis as primary chronic angle-closure glaucoma or pituitary adenomas, and initial symptoms of changes in visual acuity and visional field; (4) central visual field corrected vision 0.3 or higher; (5) no abnormal signals in the posterior optic pathway and the remaining brain parenchyma by conventional MRI; and (6) patients signed informed consents. Patients of other eye diseases were excluded. Normal volunteers were recruited from the Tianjin Medical University General Hospital, China, as controls. They were all locals from Tianjin, matched the patients in gender and age, and gave informed consent. Experiments were performed in strict accordance with the Declaration of Helsinki.

Methods

Content and process of visual stimulation

The left and right eyes of all subjects were subjected to the monocular stimulation block design experiment by fMRI. The stimulating content was a full-screen black and white flip checkerboard at 8 Hz flip frequency. The control content was a black screen with static white dots in the center; the white dots were the fixed point of view (Figure 3). Six blocks of the control group and five blocks of the stimulation group were alternatively tested, each for 20 seconds. Subjects were fixed in a supine position with even breathing and focused concentration, and they watched the stimulation contents through a dedicated audio-visual stimulation system (RT Corporation, New York, NY, USA) with their eyes focused on the fixed point in the center of the screen.

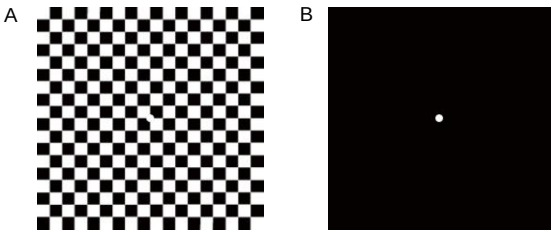

Figure 3 Schematic diagram of experimental stimulation.

(A) Full-screen black-white flip checkerboard at 8 Hz frequency.

(B) Control group: black screen, the fixed point of view in the center.

Whole-brain fMRI equipment and parameters

During stimulation, three-dimensional anatomical imaging and blood oxygen level-dependent fMRI testing were performed with the GE 1.5 T Twin Speed Infinity with Excite II MR scanner (GE, New York, NY, USA) and a quadrature head coil. Anatomical imaging was performed using a three-dimensional fast spoiled gradient echo recalled acquisition sequence, with the following parameters: repetition time 30 ms, echo time 5 ms, flip angle 45°, matrix 256 × 192, field of view 24 cm, slice thickness 1.2 mm, and spacing 0 mm, in the whole brain. Blood oxygen level-dependent fMRI scanning adopted a gradient recalled echo combined with single-shot echo planar imaging using the following parameters: repetition time 2 000 ms, echo time 40 ms, field of view 24 cm, matrix 64 × 64, slice thickness 5 mm, and spacing 1 mm, in the whole brain.

Data processing and statistical analysis

The fMRI data was input to offline workstations and processed with SPM2 (Welcome Laboratories, University of London, UK). In brief, data were motion corrected and those exceeding 1.0 mm over three-dimensional translation of the head and 1.0° over three-dimensional rotation were discarded. The fMRI images were then standardized to a standard SPM template brain, and the images were smoothed with a 5 mm full width at half maximum of Gaussian kernel function. The corrected data were analyzed using the linear model method, and the statistical probability threshold was set $P < 0.05$ (corrected). The activation threshold range was set at 10 pixels, and an area with greater than 10 continuous activated pixels was considered as activation. The activation anatomical location and intensity were recorded with the *t*-test (the higher the *t*-value the greater the activation strength) and Montreal Neurological Institute coordinates.

A single-sample *t*-test was performed with the SPM2 basic model to examine the activation of the left and right eyes after stimulation in the patient and control groups. Comparison between the two groups was conducted with a two-sample *t*-test using the SPM2 basic model to determine differences in the left and right eyes after stimulation in the patient group and the control group.

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Author contributions: Xiufeng Song was responsible for the study concept and design, contact with subjects, had full access to fMRI data, performed statistical analysis, and wrote the manuscript. Guohua Wang was responsible for statistical analysis and supervised the manuscript. Tong Zhang, Lei Feng, Peng An, and Yueli Zhu were responsible for post-processing of fMRI data.

Conflicts of interest: None declared.

Ethical approval: This experiment was approved by the Medical Ethics Committee, Tianjin Medical University, China.

Supplementary information: Supplementary data associated with this article can be found, in the online version, by visiting www.nrronline.org, and entering Vol. 7, No. 9, 2012 item after selecting the “NRR Current Issue” button on the page.

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