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ORIGINAL ARTICLE

Cortical activation during optokinetic stimulation – an fMRI study

MASAHIRO KIKUCHI[1], YASUSHI NAITO[1], MICHIO SENDA[2], TOMOHISA OKADA[1], SHOGO SHINOHARA[1], KEIZO FUJIWARA[1], SHIN-YA HORI[1], YOSUKE TONA[1] & HIROSHI YAMAZAKI[1]

[1]*Department of Otolaryngology, Kobe City Medical Center General Hospital, Kobe and* [2]*Department of Molecular Imaging, Institute of Biomedical Research and Innovation, Kobe, Japan*

Abstract

Conclusion: Activation of cortical areas related to visual motion processing and control of eye movement, and deactivation of parieto-insular vestibular cortices (PIVC) were revealed by functional magnetic resonance imaging (fMRI) with small-field optokinetic stimulation (OKS). The results agreed well with those of previous studies, which indicates that the current protocol is reliable enough to be used as a clinical examination. *Objectives:* To propose an fMRI set-up with OKS that is reliable and simple enough to be performed as a clinical test. *Subjects and methods:* Ten right-handed healthy volunteers participated in this study. fMRI was used to measure blood oxygen level-dependent (BOLD) signal increases (contrast: OKS – rest) and decreases (contrast: rest – OKS) during small-field OKS. Functional images were acquired using a standard clinical scanner operating at a magnetic field strength of 1.5 T. The data were analyzed by statistical parametric mapping (SPM2), and the significance level was set at $p < 0.001$, uncorrected. *Results:* BOLD signal increases were observed in the visual association area of both hemispheres (BA19) (MT/V5), primary visual cortex (BA17) of the right hemisphere, bilateral superior parietal lobules (BA7), and bilateral frontal eye fields (BA6). Decreases of BOLD signals were observed in the PIVC bilaterally.

Keywords: *Optokinetic nystagmus, visual cortex, vestibular cortex, functional MRI*

Introduction

Disorders of optokinetic nystagmus (OKN) have been reported to accompany disequilibrium due to central lesions involving the parietal and occipital cortices, brainstem, and cerebellum [1], and examination of OKN has been included in the routine equilibrium test battery. As a general rule, abnormalities of optokinetic slow components parallel abnormalities in smooth pursuit and those of fast components correlate with impairment in voluntary saccades [1], but precise correlation of OKN abnormalities with a certain cortical area is not always possible. Functional imaging studies using positron emission tomography (PET) [2] or functional magnetic resonance imaging (fMRI) [3–5] have been performed to visualize anatomical correlates of OKN, most of which, however, have been performed as basic physiological investigations, and the examination time and set-up may be too long and complex for a routine clinical test. The purpose of this study is to propose an fMRI set-up with OKS that is reliable and simple enough to be performed as a clinical test.

Subjects and methods

Ten healthy right-handed subjects (eight men, two women; age 34.0 ± 8.0 years, mean $\pm$ SD) participated in this study. The subjects had no history of visual, vestibular, or central nervous system disorders.

MRI scans were performed with a 1.5 T MR scanner (Signa Excite; General Electric Medical Systems, Milwaukee, WI, USA) with a quadrature birdcage head coil. Subjects lay supine watching a mirror attached to the head coil, which allowed

Correspondence: Yasushi Naito MD, Department of Otolaryngology, Kobe City Medical Center General Hospital, 4-6 Minatojima-Nakamachi, Chuo-ku, Kobe, Hyogo 650-0046, Japan. Tel: +81 78 302 4321. Fax: +81 78 302 7537. E-mail: naito@kcgh.gr.jp

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visual stimulation from outside the scanner. A white paper screen was placed in front of the MR scanner, at a distance of 0.8 m from the mirror. Black and white vertical stripes were projected to the screen so that the subjects could see the stripes through the mirror. The horizontal and vertical view angles were 20° and 15°, respectively. Rightward and leftward optokinetic stimulation (OKS) separated by a stationary rest condition, each lasting 24 s, was generated by a computer program made for the present experiment. The total session lasted 312 s, consisting of three right OKS, three left OKS, and seven rest conditions.

Functional images were acquired with a single-shot gradient echo (GE) echo planar imaging (EPI) sequence. The parameters were: TR 300 ms, flip angle 90°, field of view 22 cm, matrix size 64×64 in 26 axial planes of 4 mm thickness with a 1 mm gap. The first eight scans were discarded because of spin saturation effects.

Data were analyzed by SPM2 (Institute of Neurology, University College of London, UK) implemented in MATLAB (Mathworks, MA, USA), and blood oxygen level-dependent (BOLD) signal increases (contrast: OKS – rest) and decreases (contrast: rest – OKS) were measured. Significance level was set at $p < 0.001$, uncorrected.

Results

Group analysis

All the subjects completed the examination. The BOLD signal increases during OKS were observed in the BA19/37 of both hemispheres (motion-sensitive middle occipital and middle temporal area: MT/V5), right primary visual cortex (BA17), bilateral superior parietal lobule (BA7), and bilateral frontal eye field (BA6) (Figure 1A). The BOLD signal decreases during OKS were observed in the bilateral superior occipital gyrus (BA19), bilateral posterior insula (parieto-insular vestibular cortex: PIVC), bilateral cungulate gyrus (BA31), and the right middle temporal gyrus (BA21) (Figure 1B).

Individual analysis

Considerable individual differences were observed in BOLD signal changes among the present subjects. Two representative subjects are shown in Figure 2. Subject 5, whose total cluster volume above the threshold was the smallest among the subjects, exhibited significant BOLD signal increases only in bilateral MT/V5 (Figure 2A), while subject 2, whose total activated volume was the largest among the subjects, exhibited extensive BOLD signal increases in MT/V5 and occipital-parietal visual cortices and some frontal areas in both hemispheres (Figure 2B).

Discussion

OKN is an oculomotor reflex, which is driven by visual targets moving coherently across visual field or by self-motion when observing relative motion of the surroundings and contributes to the stabilization of the retinal image. This eye movement is characterized by a slow eye movement (smooth pursuit) in the same direction as the visual stimulus (slow phase) and a quick saccadic eye movement in the opposite direction. The frontal eye field (FEF), supplementary eye field, parietal eye field, middle temporal and middle superior temporal (MT/MST) areas, visual cortex, and the cerebellum have been reported to be cortical correlates of smooth pursuit, saccades, and OKN [3–12]. Although the present fMRI examination was performed using an ordinary clinical MR scanner operating at 1.5 T and the OKS was applied through a standard mirror system attached to the head coil, the current cortical activation pattern agreed well with previous results, suggesting that the present methods are reliable enough to be used in clinical examination. Additionally, the time required for the current examination (5 min) was shorter than those reported in previous reports (10 min [3], 8 min [4], and 22.4 min [5]), which may be another advantage for its possible clinical use.

The individual analysis of our results, on the other hand, revealed substantial individual variations in cortical activation pattern (Figure 2). However, MT/V5 was commonly activated in subjects with weakest and strongest OKS activation, suggesting that visual motion perception may be one of the most basic neuronal processes among those that drive OKN.

Friberg et al. [13] reported that the regional cerebral blood flow (rCBF) in the superior temporal region posterior to the auditory area increased during caloric vestibular stimulations, which corresponds to PIVC. The PIVC is now thought to be a core vestibular area among multi-sensory vestibular cortices [13–17], and a previous fMRI study [3] showed a decrease of BOLD signal in this area during small-field OKS. Significant deactivation of PIVC by OKS was also observed in the present investigation, which further supports the concept of 'inhibitory visual-vestibular interaction' discussed by Brandt et al. [17,18]. This interaction would be useful when there are contradictory visual and vestibular inputs, since it allows a potential mismatch between two incongruent or misleading sensory inputs to be suppressed by shifting the sensory weight to the dominant or more reliable modality. Cortical deactivation during sensory

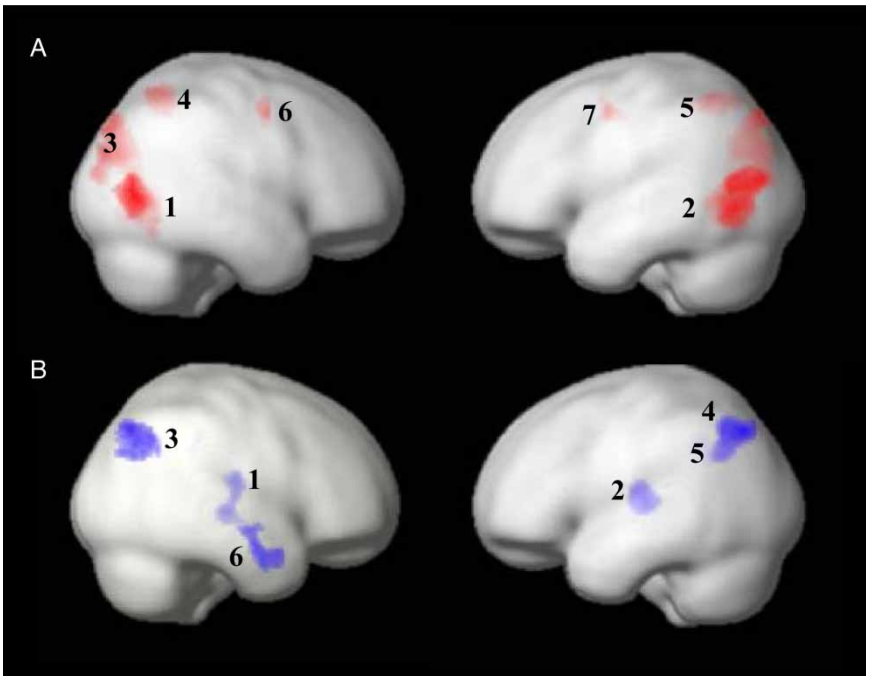

Figure 1. The cortical areas activated and deactivated by OKS (group analysis, SPM2, $p < 0.001$, uncorrected). (A) Activated regions. 1, right and 2, left MT/V5 (BA19/37); 3, right primary visual cortex (BA17); 4, right and 5, left superior parietal lobule (BA7); 6, right and 7, left frontal eye field (BA6). (B) Deactivated regions. 1, right and 2, left PIVC; 3, right and 4, left superior occipital gyrus (BA19); 5, bilateral cingulate gyrus (BA31); 6, right middle temporal gyrus (BA21).

stimulation has also been reported in the auditory system [19], suggesting the involvement of a number of both excitatory and inhibitory modulation and association relays, which might be common to various sensory systems.

In conclusion, the current fMRI with small-field OKS revealed significant activation of cortical areas related to visual motion processing and eye movement control, and deactivation of vestibular cortex (PIVC), which agreed well with previous studies. Future applications of the present method in various patients with dizziness and vertigo should elucidate whether it is useful as a clinical examination for vestibular disorders. Many questions, including its cost-effectiveness, may have to be answered before it is routinely used in daily clinic.

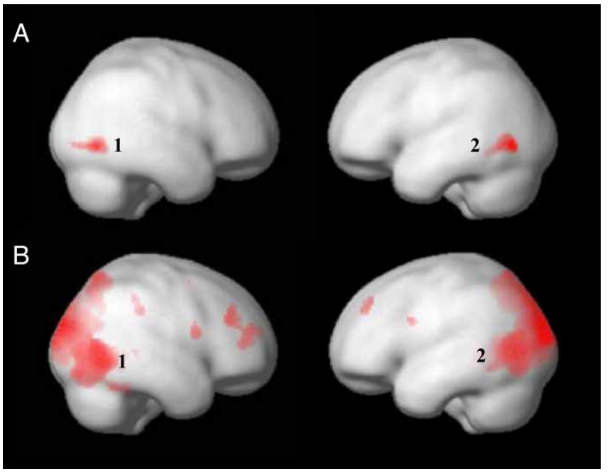

Figure 2. The cortical areas activated by OKS (individual analysis, SPM2, $p < 0.001$, uncorrected). (A) Subject 5, whose total cluster volume above the threshold was the smallest among the subjects, exhibited significant activation only in bilateral MT/V5 (1, 2). (B) Subject 2, whose total activated volume was the largest among the subjects, exhibited extensive activation in bilateral occipital-parietal visual cortices including MT/V5 (1, 2), and some frontal areas.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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