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Functional Magnetic Resonance Imaging by Visual Stimulation

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Abstract We evaluated functional magnetic resonance images obtained in 8 healthy subjects in response to visual stimulation using a conventional clinical magnetic resonance imaging system with multi-slice spin-echo echo planar imaging. Activation in the visual cortex was clearly demonstrated by the multi-slice experiment with a task-related change in signal intensity. In addition to the primary visual cortex, other areas were also activated by a complicated visual task. Multi-slice spin-echo echo planar imaging offers high temporal resolution and allows the three-dimensional analysis of brain function. Functional magnetic resonance imaging provides a useful noninvasive method of mapping brain function.

Key words: Functional mapping, Magnetic resonance imaging, Echo planar imaging, Visual stimulation, Occipital lobe

Introduction

Functional activation of the brain has been visualized with magnetic resonance imaging (MRI) in recent years. Its basis is that deoxygenated hemoglobin acts as an endogenous paramagnetic contrast agent. Ogawa et al. referred to this as the "BOLD (blood oxygenation level dependent)" contrast theory [1)2)]. We used a conventional clinical MRI system with multi-slice spin- echo echo planar imaging (EPI) to produce functional magnetic resonance images in response to visual stimulation.

Methods

Imaging studies were performed with a 1.5 tesla MRI system (Magnetom Vision; Siemens -Asahi Medical, Germany) equipped with a spin-echo version of the EPI sequence (repetition time, 3.3 msec; echo time, 18 msec; flip angle, 90°; matrix, 90×128; field of view, 300 mm; slice thickness, 3 mm; scan time, 0.1 sec/slice). A standard head coil was used. Full -field visual stimulation was provided by an MRI video system (Resonance Technology, U. S.A.). Eight right-handed healthy volunteers (5 men and 3 women, age ranged from 24 to 37 years old, mean 28.5 years) underwent examinations using visual stimulation with a varying (10Hz) black-and- white checkerboard-pattern and with colored computer -graphic video images. Initially, T1 weighted sagittal images were obtained to identify the calcarine sulcus (Fig.1-a). Five-slice axial EPI sequential images were obtained in parallel with the plane that included the calcarine

sulcus(Fig.1-b). These five images were pooled as one study. Five such studies were carried out continuously during a resting period ("OFF" data). Next, five studies were performed during a stimulation period ("ON" data). A total of six data sets alternating between resting and stimulated states were obtained (Fig.2). The interval between "OFF" and "ON" periods was 20 sec. The first image in each period was excluded from averaging, because these images were displayed more brightly compared with other images. The average image in the resting state was subtracted from the average image in the stimulated state. The z-score from software image analysis programs was applied to visualize signal changes. For each pixel in activated region, the mean and standard deviation(SD) of the signal intensity were calculated for the prestimulation control images. The mean was subtracted from the pixel intensity of the activated state. The result was divided by the SD to calculate the z-score for each pixel. These z-score images, which indicate the areas of increased signals (Fig.3-a), were superimposed on the anatomical images (Fig.3-b). To evaluate the significance of these signal changes in the activation images and to quantify the percentage of signal changes, we observed the time courses of signal intensity changes for regions of interest (ROI).

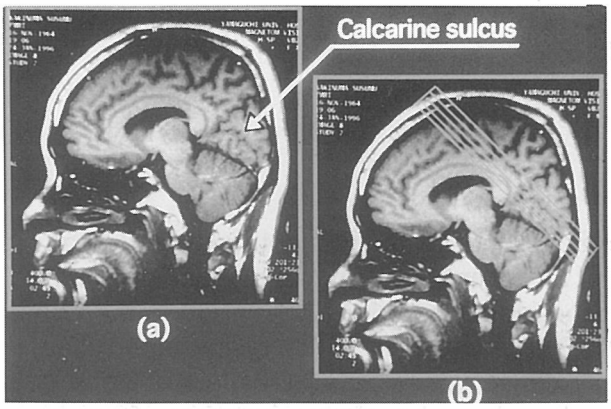

Fig.1 Anatomic definition of the brain section used for functional imaging of the visual cortex. (a) Sagittal T1 weighted MRI image. The arrow points to the calcarine sulcus. (b) The obliquity of the transverse slices was chosen to include a large part of the calcarine sulcus.

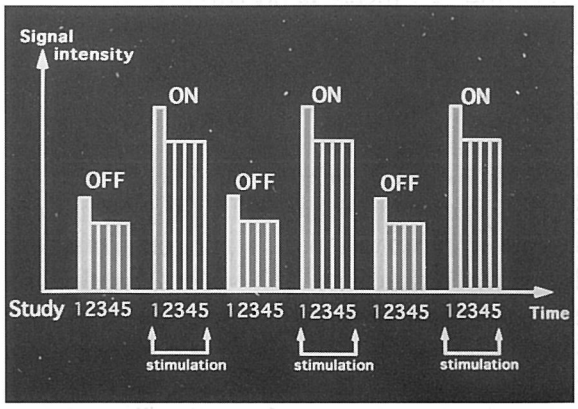

Fig.2 Protocol for functional imaging study. A total of six data sets alternating between resting(OFF) and stimulated(ON) states were collected.

Results

In all 8 examinations with full-field checkerboard-pattern visual stimulation, increased signal changes were found in the visual cortex of the occipital lobes. Functional activation maps of two volunteers are

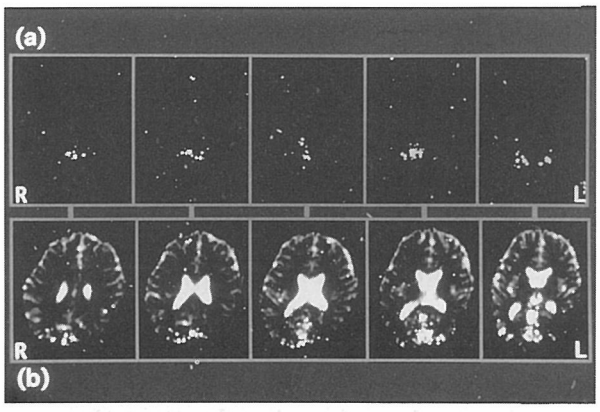

Fig.3 (a)Z-score images obtained by subtracting the average image during visual stimulation from the average image during the resting state. (b) Functional images obtained by superimposing z-score images from (a) on the anatomical images.

shown in Fig. 4. The signal changes in the occipital lobes are seen clearly in several sequential slices. In each subject, the greatest changes were observed in the medial-posterior regions of the occipital lobes along the calcarine sulcus, which was equivalent to the primary visual cortex (Brodmann's area 17). The authors found an increased signal in the visual cortex in all 8 examinations involving full-field visual stimulation with computer graphic images. Areas outside the primary visual cortex also showed significant signal changes in several subjects. In addition to activation within the visual cortex, activation was demonstrated in four subjects in the temporo-occipital cortex (the posterior part of the middle temporal gyrus and the lateral occipital gyrus), in two subjects in the left frontal cortex (the posterior part of the middle frontal gyrus and the inferior frontal gyrus). Slightly different activation patterns were observed depending on the type of visual stimulation. The activated area was relatively larger with checkerboard-pattern stimulation than with computer-graphic images (Table 1).

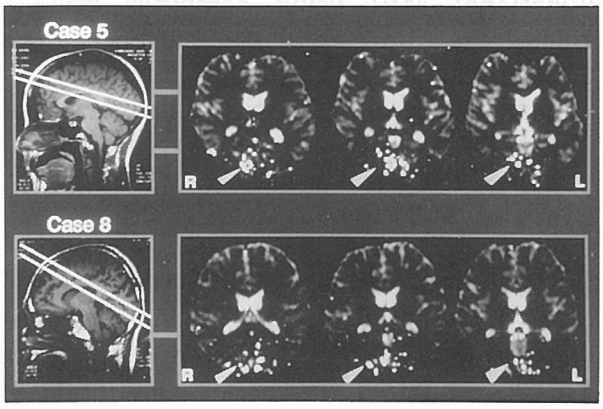

Fig.4 Functional images in response to visual stimulation in two volunteers. The increased signal in the occipital lobes is shown in several sequential slices (arrowheads). Interindividual differences in the anatomy of the calcarine sulcus were observed.

Comparing the time courses of the signal intensity for the right occipital lobe (ROI 1) and a randomly selected, increased-signal region outside the visual cortex, ROI 1 evidenced an increased signal by visual stimulation (Fig.5). The time-intensity curve for ROI 1 showed clearly cyclical changes in relation to the visual stimulation, whereas no task-related signal change was seen in ROI 2. The increased signals of ROI 1 were significant signal changes for visual stimulation, whereas those of ROI 2 were apparently artifacts.

Discussion

Various methods have been used to evaluate brain function, including electroencephalography, single photon emission computed tomography, positron emission tomography (PET), and magnetoencephalography. Recently, functional mapping of the brain by MRI became possible, a technique that has been termed "functional MRI". On the basis of PET observations, it was demonstrated that

Table 1. Summary of results.

Case	Age/Sex	Size of activated area with two types of stimulation	Activated area outside primary visual cortex <P.R.>	<C.G.>
1	30 / M	P. R. = C. G.		left temporo-occipital
2	37 / M	P. R. > C. G.		
3	31 / M	P. R. = C. G.		
4	25 / F	P. R. > C. G.		left frontal
5	24 / M	P. R. > C. G.	right temporo-occipital	right temporo-occipital
6	26 / M	P. R. = C. G.		left frontal, left temporo-occipital
7	30 / F	P. R. = C. G.		
8	25 / F	P. R. > C. G.		bilateral temporo-occipital

Abbreviations: M= male; F= female; P.R.= pattern reversal; C.G.= computer graphic.

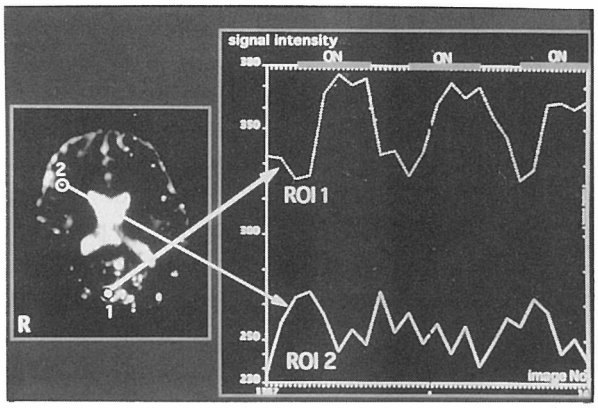

Fig.5 The time courses of signal intensity changes for regions of interest (ROI 1) and randomly selected, increased signal region outside the visual cortex (ROI 2). The time-intensity curve for ROI 1 shows a task-related signal change in the gray matter of the right occipital lobe.

activated areas of the human brain showed increased regional cerebral blood flow[3]. The methods for functional mapping by MRI using such focal changes in regional cerebral blood flow accompanying neuronal activation can be divided into two categories. One involves measuring blood volume based on signal changes after injection of an exogenous contrast agent, a method first carried out by Belliveau et al[4]. The other method detects concomitant changes in hemodynamic parameters. Among these parameters, the state of oxygenation of capillary and venous blood, which has been called the BOLD contrast, is particularly useful for functional brain imaging. This MRI technique has many advantages compared with other techniques to evaluate brain function. It is noninvasive and does not require the injection of radioactive tracers or of exogenous contrast agents, so that repeated studies in the same individual are possible. Oxygenated hemoglobin has the same susceptibility as water, whereas deoxygenated hemoglobin is paramagnetic and acts as an intravascular endogenous contrast agent. In the presence of deoxygenated hemoglobin, local magnetic-field inhomogeneities or "T2* susceptibility" are created between blood and the surrounding tissues; thus, the intensity of the MRI signal decreases. In the pre-activated resting state, the signal intensity of the brain decreases due to capillary and venous deoxygenated hemoglobin. An elevation in venous oxygenation during brain activation leads to a decrease in the amount of the intravascular endogenous paramagnetic contrast agent, deoxygenated hemoglobin, relative to the amount that is observed in the resting state. This decreases T2* susceptibility and causes the signal intensity to increase.

There are several reports of functional MRI using visual stimulation[5),6)]. Those studies used a stroboscopic flashing light or a checkerboard-pattern for visual stimulation. Functional MRI using computer graphic video images for visual stimulation has not been previously reported. We compared the activated pattern of functional images in the visual cortex with computer-graphic stimulation and with checkerboard-pattern stimulation, and found that the activated area with checkerboard stimulation was generally larger. Thus, the checkerboard-pattern seemed to be more intense and to have a greater influence on the visual cortex than computer -graphic stimulation.

The computer-graphic visual stimulation not only resulted in activation within the visual cortex but also increased the signal intensity in the temporo-occipital cortex and left frontal lobe, whereas, with the checkerboard-pattern stimulation, activation outside the visual cortex was seen only in one case. Apparently, the volunteers observed the complicated shapes and the colorful, moving objects and also recognized the space and contents of those images. This complex visual task may have stimulated areas beyond the usual visual area. In 4 volunteers, the temporo -occipital cortex was activated (Fig.6). This cortical area corresponds with the area which was previously reported as the movement vision-sensitive cortex (the junction of Brodmann's areas 19 and 37) in the PET study [7]. This area is also known as area V5 [8]. In 2 volunteers with computer- graphic visual stimulation, the frontal cortex (the posterior part of the middle frontal gyrus and the inferior frontal gyrus) was activated. This cortical area seemed to correspond with the

frontal eye field (Brodmann's area 8). This area is considered as one of the cortical oculomotor centers [9]. It is known that the frontal eye field activity precedes purposive saccadic eye movements, particularly saccades directed at visual targets [10),11)]. Additionally, it is reported that the neurons in the prefrontal association area play one part of the function which focuses and maintains attention to the space [12)]. Future studies should investigate how the size of the activated area in the visual cortex changes, and how other areas outside the primary visual cortex are activated in response to different contents of video images.

The BOLD effect in the activated brain parenchyma is the best known mechanism of the increases in signal in a functional MRI. However, other factors for such increases exist. The BOLD effect inside the relatively large vessels overlying the neighboring activated cortical region produces local increases in signal. Motion-related subtraction artifacts also produce signal changes in functional MRI [13)]. Fig.7 illustrates artificially activated images related to eye movement and head motion during the stimulation. On repeatedly exciting a single slice using a short repetition time and large flip angle, unsaturated water that flows into the observed plane from neighboring regions represents a large fraction of the signal intensity [14)]. Contrast in functional MRI using gradient-echo images may be more strongly affected by this in-flow effect than by the BOLD effect, particularly with the combination of a large flip angle and a thin slice [15),16)]. In such cases, the increased signal regions do not always correspond to the activated cortical region because the flow velocity in the large vessels may lead to an increase in signal intensity. Theoretically, however, there is little in-flow effect in functional MRI using multi-slice EPI.

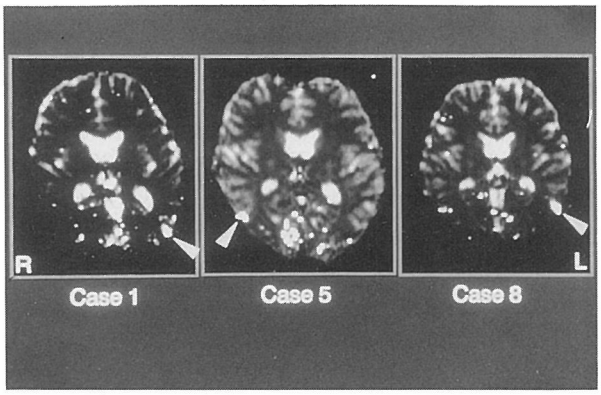

Fig.6 Functional images activated in the lateral temporo-occipital cortex (arrowheads).

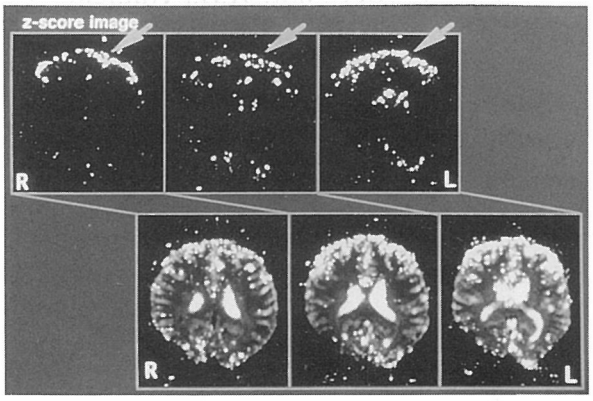

Fig.7 Artificially activated images related to eye movement and head motion during visual stimulation (arrows).

Multi-slice EPI provides a high temporal resolution and allows for the three-dimensional analysis of brain function. To detect small changes in the local magnetic field accompanying brain activation, adjustment of the field homogeneity in the pre-activated state for each subject is indispensable. Because of individual differences in the anatomy of the calcarine cortex, the choice of the most suitable imaging planes to include the activated region is important. There is a need for stringent control of head motion to reduce changes in signal related to artifacts. Functional MRI provides a useful noninvasive method of mapping brain function, and will find wide application in clinical assessment as well as in physiological research.

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