# Influence of Regular Astigmatism on the Human Visual Cortex. A Functional Magnetic Resonance Imaging Study

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**Abstract :**

**Purpose:** To describe a new functional magnetic resonance imaging (fMRI) method for measuring the influence of regular astigmatism, both against-the-rule (ATR) and with-the-rule (WTR), on the human visual cortex.

**Setting:** Department of Ophthalmology, Jikei University School of Medicine, Tokyo, Japan.

**Design:** Experimental study.

**Methods:** Images were acquired in two healthy volunteers using a 1.5 T scanner equipped for echo planar imaging. Horizontal and vertical sine wave grating flickering at a frequency of 8 Hz were simultaneously presented during the 20-second stimulation period. During the control period , subjects fixated on a control target. Stimulations were performed under three different conditions that included with hard contact lenses that were equal to emmetropia without astigmatism (condition 1); with hard contact lenses and cylindrical glasses of +6.00D at  0°, imitating WTR (condition 2); and with hard contact lenses and cylindrical glasses of +6. 00 D at 90°, imitating ATR (condition 3). Raw data were processed using in-house software with the significance of activation determined by Statistical Parametric Mapping (SPM 99).

**Results:** Although higher activation was found in the primary visual cortex for condition 1 versus conditions 2 and 3, activation in the dorsal pathway was higher in conditions 2 and 3 compared to condition 1. Dorsal pathway activation was also higher in condition 3 versus condition 2.

**Conclusions:** Study findings showed the potential influence of ATR and WTR on the human visual cortex , with fMRI able to detect the influence of regular astigmatism on the visual cortex. Our current results suggest that fMRI may be useful in exploring the influence of astigmatism on vision.

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## Introduction

Unlike in a normal eye that focuses rays of light on a single point, the astigmatic eye refracts two focal lines separated from each other by a focal interval (1). Furthermore, astigmatism is a typical refractive anomaly that can be roughly divided into regular astigmatism and irregular astigmatism. While regular astigmatism can be fully corrected by using a spectacle lens (2), irregular astigmatism is interrupted by a variety of alterations of the refractive corneal surface, thereby presenting different degrees of the astigmatism (3). Various studies performed in the field of ophthalmological surgery, especially studies involving surgeries of the anterior eye segment, have attempted to lessen induced cornea astigmatism (4-7). Furthermore, both regular astigmatism (8-11) and irregular astigmatism have recently become more treatable due to the progress that has been made in refractive surgery (12-14). The better medical treatments have also greatly contributed to achieving better diagnoses. For example, analysis of the radius of curvature and refractive power can be determined by kerato-refractometer (15-16), analysis of the form of the whole cornea by corneal videokeratoscopy (17-19), and measurement of the total ocular profile of refraction by wavefront analysis (20-22). However, the influence of astigmatism on the visual pathway has yet to be fully investigated. Several studies have recently reported using functional magnetic resonance imaging (fMRI) to diagnose the visual pathway (23-24). fMRI is a noninvasive method that can be used for human brain activity imaging (25-26). We used this methodology to investigate the influence of regular astigmatism on the visual cortex in addition to trying to determine the influence of astigmatism on the visual pathway.

## Subjects

Two normal healthy male volunteers (aged 27, 34 years) gave informed consent prior enrollment in the study. Both participants were right-handed, and had no history, past or current, of ophthalmologic, neurological, or psychiatric illness. Measurements were performed 6 times in each subject.

## Methods

Device for Refractive Correction and Simulation

The left eye of both subjects was covered with an eyepatch. In the right eye, each subject wore a hard contact lens, which was set to emmetropia. Moreover, +6.00 diopter (D) glasses were positioned at two different angles, one at 0 degrees and the other at 90 degrees. These three different conditions were used to create emmetropia (condition 1), with-the-rule (WTR) astigmatism (condition 2), and against-the-rule (ATR) astigmatism (condition 3), respectively.

## Visual Stimulation

Visual stimuli were back-projected onto a translucent screen placed at the subjects' feet. Subjects viewed the visual stimuli using the built-in mirror of a standard head coil. Stimuli were created using in-house software. The three types of visual stimulation used during the experiment are described below.

Stimulation 1

During the 20 second stimulation period, horizontal and

vertical sine wave gratings were presented for 15 minutes within a circle of 9 degrees, with the simultaneous flickering set at a frequency of 8 Hz (FIGURE 1). This phase was defined as 'activation'. During the control period, the subjects fixated on the control target. This target was a 50% grey circle of 9 degrees, with the fixation point located at the center (FIGURE 1). This phase was defined as the 'baseline'. The stimulation and control periods were alternated 5 times during the entire sequence. Each stimulation was performed under the three different conditions (used during the study (conditions 1-3).

Stimulation 2

Activation of stimulation 2 was created by removing the horizontal line activation factor of stimulation 1 (FIGURE 1). All other conditions were kept the same as in stimulation 1.

Stimulation 3

Activation of stimulation 3 was created by removing the

vertical line activation factor of stimulation 1 (FIGURE 1). All other conditions were kept the same as in stimulations 1 and 2.

fMRI Experimental Procedure

fMRI was performed on a 1.5 Tesla GE Signa Echospeed system (General Electric, Milwaukee, WI, USA) and Siemens Magnetom Vision (Siemens, Erlangen, Germany) using a standard quadrature head coil (repetition time (TR) = 2000 ms, echo time (TE) = 60 ms, field of view (FOV) = 32 cm, matrix = 64 x 64, thickness = 5 mm). T1-weighted images were acquired and used to obtain three-dimensional structural images that helped locate the activated areas. Visual stimuli were presented in a boxcar design (27).

## Data Analysis

After acquisition, images were converted from the native GE or Siemens format to the format used to analyze the data in the current study. After the image processing steps, data analysis was performed using statistical parametric mapping (SPM99; Wellcome Department of Cognitive Neurology, London, UK). After uniting the
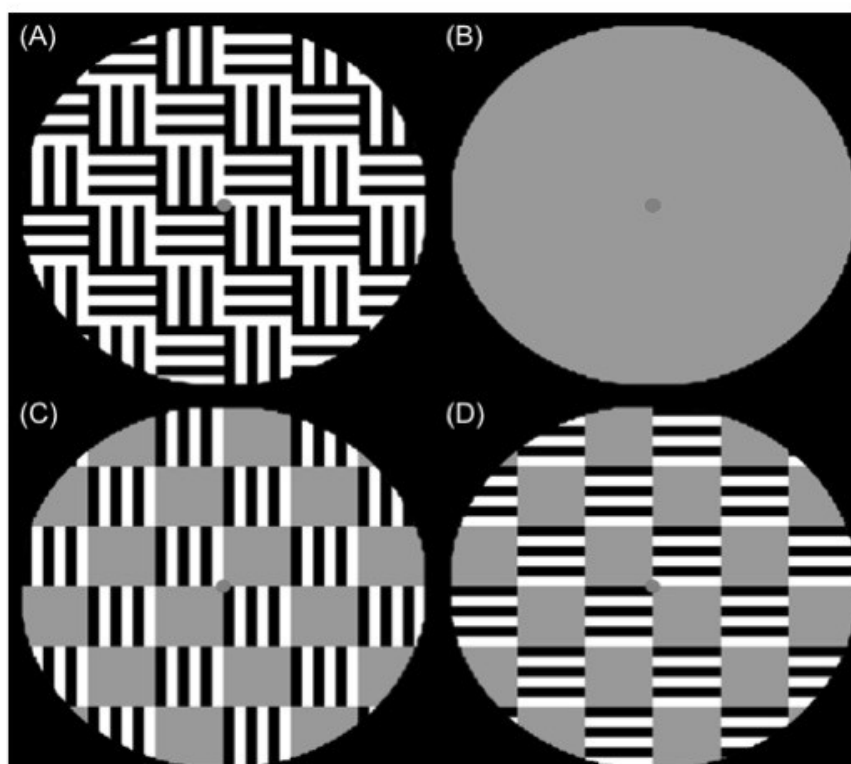


**FIGURE 1. Visual stimulations.**

(A) Activation phrase of stimulation 1. Presentation of horizontal and vertical sine wave gratings of 15 minutes in the circle of 9 degrees. (B) Control phrase of all stimulations. The control stimuli is the 50% grey circle of 9 degrees, with the fixation point at the center. (C) Activation phrase of stimulation 2. Stimulation was created by removing the ingredient of activation of stimulation 1 to horizontal lines. (D) Activation phrase of stimulation 3. Stimulation was created by removing the ingredient of activation of stimulation 1 to vertical lines.

position of each image, all volumes were realigned to the first volume. Spatial smoothing of the functional signal within each slice was performed prior to the analysis. We then defined a design matrix that consisted of contrast modeling of the alternating periods of 'baseline' and 'activation' when using a delayed boxcar reference vector (27) that accounted for the delayed cerebral hemodynamic response function after the stimulus presentation. Data were first analyzed for neural activations that were common to the experimental conditions relative to the baseline. To determine the statistical significance, we used a corrected significance level of the individual voxel of $P < 0.005$ and a cluster size of 26, with an AlphaSim-corrected cluster threshold of $P < 0.05$.

## Results

### Stimulation 1

Remarkably consistent activations were detected bilaterally for each condition in the primary visual cortex

(FIGURE 2). The amplitude of the vascular response for condition 1 was higher than that for conditions 2 and 3 in the primary visual cortex (FIGURE 3). For conditions 2 and 3, activation led to responses in the dorsal visual pathway (FIGURE 2). Furthermore, the range that showed activation was larger in condition 3 versus condition 2 (FIGURE 2). For the fitted response and PSTH (peri-stimulus time histogram), the condition 1 response was higher than that seen for conditions 2 and 3 in the primary visual cortex (FIGURE 4). Moreover, the fitted response and PSTH for the condition 2 and 3 responses were higher than that observed for condition 1 in the dorsal visual pathway (FIGURE 5)

### Stimulation 2

Although activation was bilaterally detected for conditions

1 and 2 in the primary visual cortex, (FIGURE 6), it was not detected for condition 3 (FIGURE 6). For condition 2,

**FIGURE 2. Result of stimulation 1.**

The black areas denote active brain regions ($P < 0.05$).

(A) Condition 1. Activations was detected in bilaterally primary visual cortex. (B) Condition 2. Activations was detected in bilaterally primary visual cortex and dorsal visual pathway. (C) Condition 3. Activations was detected
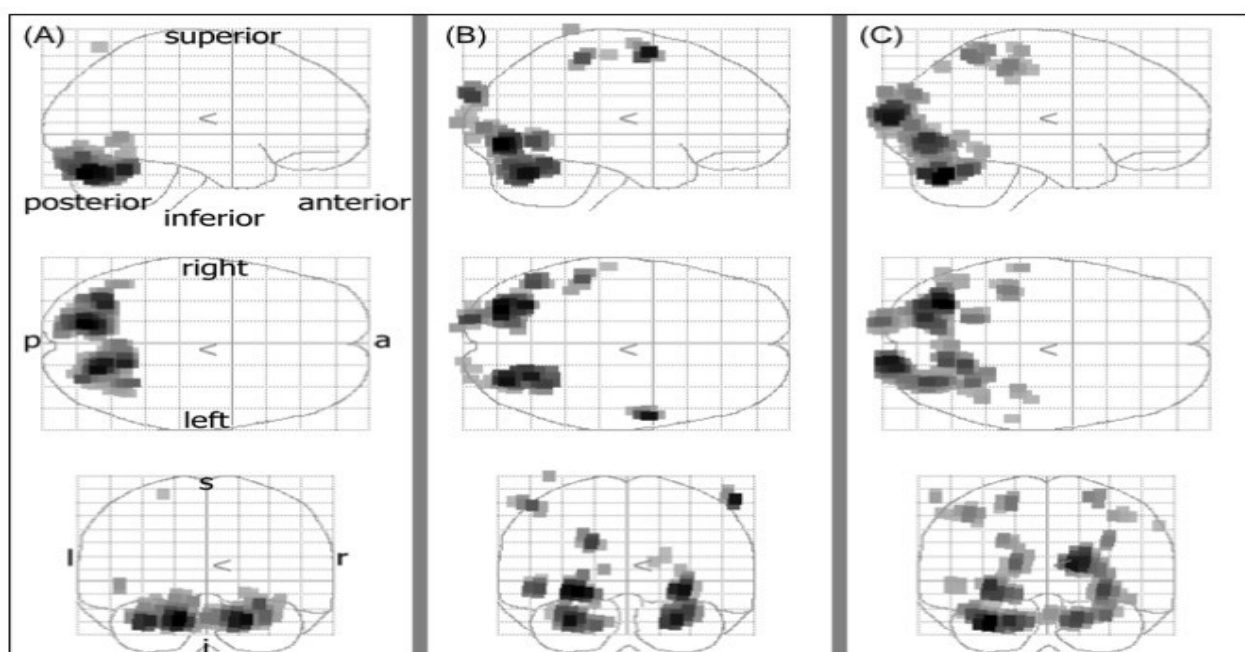
FIGURE 3. The amplitude of vascular response of primary visual cortex.

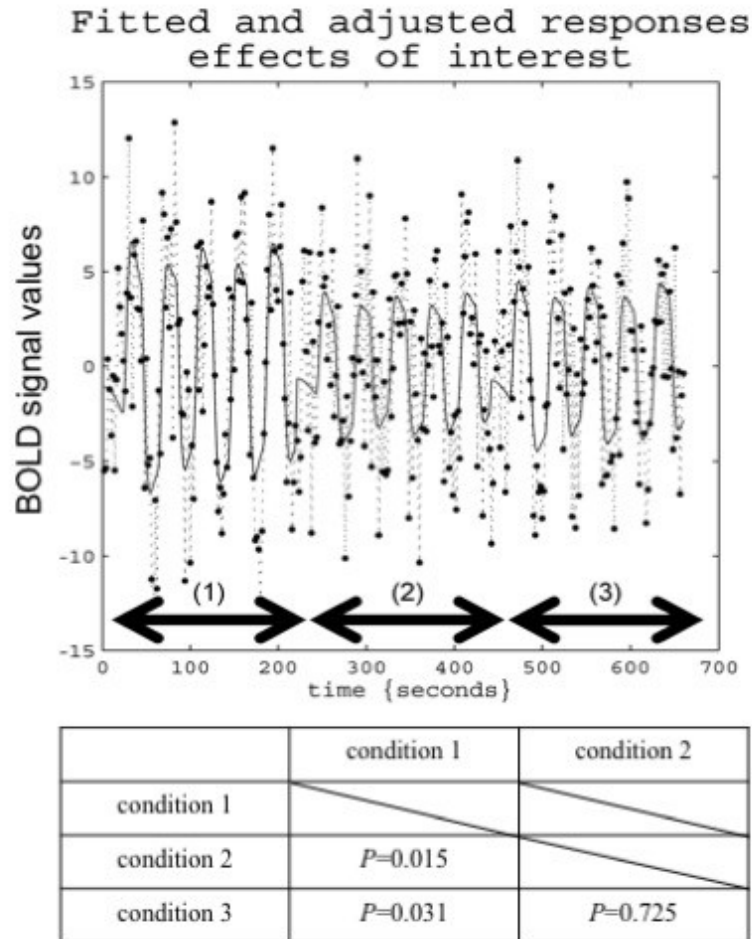The amplitude of vascular response of condition 1 (1) was higher than condition 2 (2) and 3 (3) ($P<0.05$).



**Fitted and adjusted responses effects of interest**

| | condition 1 | condition 2 |
|---|---|---|
| condition 1 | | |
| condition 2 | $P=0.015$ | |
| condition 3 | $P=0.031$ | $P=0.725$ |

FIGURE 4. Fitted response and PSTH in primary visual cortex.

The average response to an event type with mean signal +/- SE for each peri-stimulus time bin. Response of condition 1 (1) was higher than condition 2 (2) and 3 (3) in primary visual cortex ($P<0.05$).
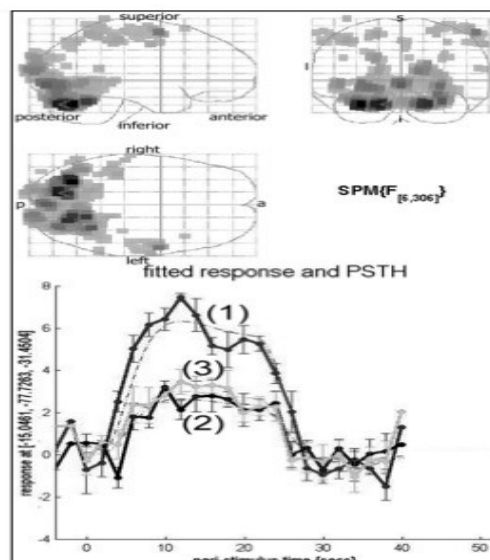
**FIGURE 5. Fitted response and PSTH in dorsal visual pathway**.

The average response to an event type with mean signal +/- SE for each peri-stimulus time bin. Response of condition 2 (2) and 3 (3) was higher than condition 1 (1) in dorsal visual pathway ($P<0.05$).
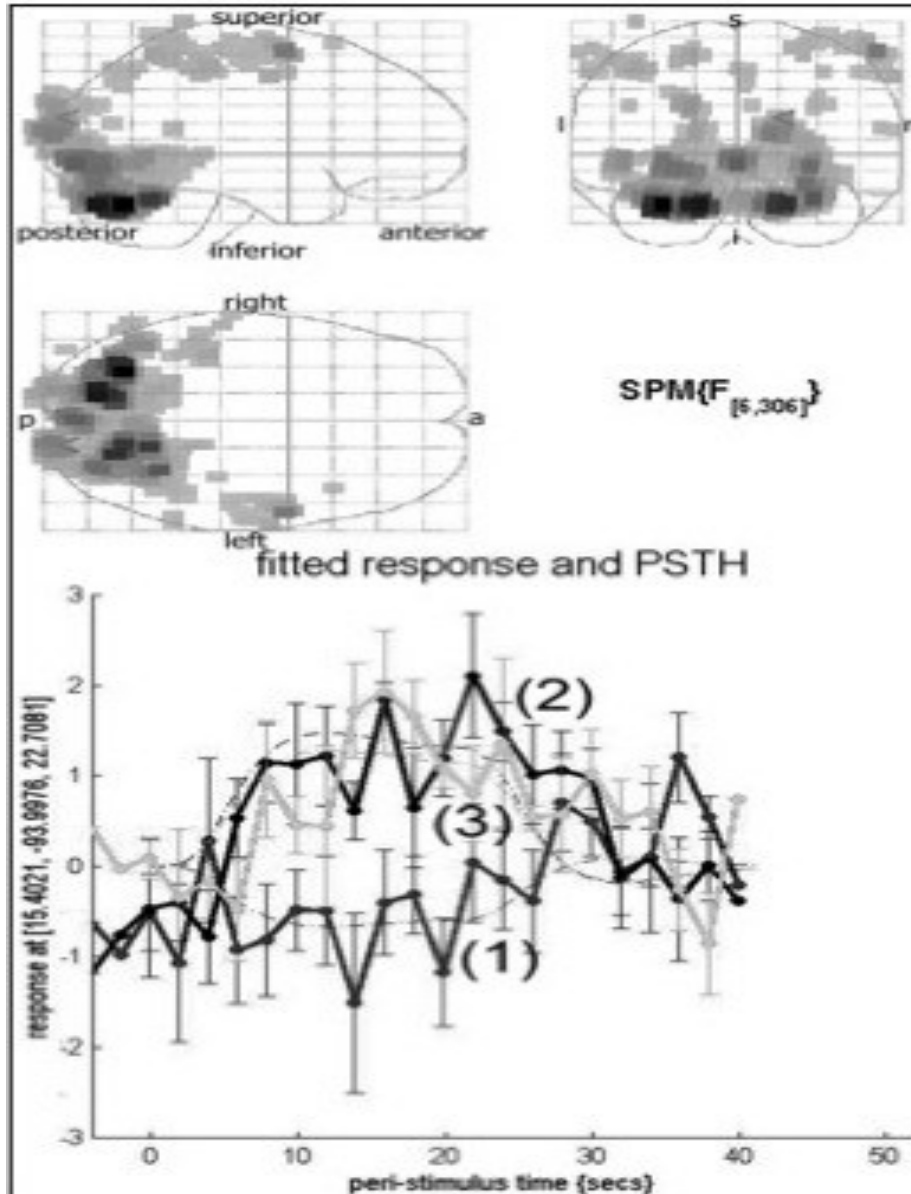
activation led to a response in the dorsal visual pathway (FIGURE 6).

Stimulation 3

Activation was bilaterally detected for conditions 1 and 3 in the primary visual cortex (FIGURE 7), but was not detected for condition 2 (FIGURE 7). For condition 3, activation led to a response in the dorsal visual pathway (FIGURE 7).

**Discussion**

Several studies have investigated both the influence of astigmatism on vision, and the evaluation methods used to examine astigmatism (28-29). However, these studies only examined the influence and the evaluation methods in the anterior and posterior eye segments. In the current study, we investigated astigmatism influence on the visual pathway located beyond the posterior eye segment.

Recent studies have reported using the fMRI cerebral functional appraisal method to evaluate the influence of regular astigmatism on the visual cortex. For more than ten years, fMRI has been used to evaluate cerebral function (25-26). This method calculates brain activity, by measuring the induction of regional cerebral blood flow changes. Although there are several different ways that the fMRI measurements can be made (30-32), we used the blood oxygenation level dependent (BOLD) method (30) in our study. This method determines the hemodynamic changes associated with the variations in the amount of blood flow that accompany the brain activity, which is partly based on the phenomenon of magnetic resonance. The amount or speed of the inflow of blood to a peripheral blood vessel floor increases in conjunction with the activity of cerebral cortex is anaerobic, there is a fall in the ratio of the deoxy hemoglobin / oxy hemoglobin relative to the blood vessel floor (33). In the human body, deoxy hemoglobin is a magnetic substance, and thus, is capable of creating a detectable magnetic resonance

signal. The BOLD fMRI method measures the rise and fall of this magnetic resonance signal, and thus, does not require the injection of a contrast media.. Since this method can be quickly performed and used to simultaneously measure the entire brain, there has been a rapid increase in the use of fMRI in many different types of studies

When a seeing on subject with WTR astigmatism views an object at a long distance, the image will be distorted perpendicularly, while a subject with ATR astigmatism will find the image to be distorted horizontally (34). In the current study, stimulation 1 was designed so that the subject would experience WTR and ATR astigmatism. we used stimulation 1. To achieve this stimulation, subjects were simultaneously presented with an image that contained the same quantity of vertical and horizontal lines. In a previous study that examined the developmental origins of visual perception, visual circuity involved with the processing of vertical and horizontal contours was found to be important in the enhanced visual capabilities of humans (35). Furthermore, since these contours and conditions are found throughout an image, our stimulations were designed to be circular in shape. The stimulation used in condition 1 resulted in a higher amplitude of vascular response as compared to that seen in conditions 2 and 3. It has been suggested that both WTR and ATR astigmatism can adversely influence the primary visual cortex. In conditions 2 and 3, activation led to a response in dorsal visual pathway. The dorsal visual pathway carries vision information going to the parietal association area from area V1. This pathway is roughly divided into two, with one section going to area 7 via the medial superior temporal area (MST) (36-37), ventral intraparietal area (VIP) (38), middle temporal area (MT) (39-40), etc. This pathway is involved in the analysis of visual motion. The other pathway goes to the lateral intraparietal area (LIP) or the caudal intraparietal sulcus area (cIPS) via the V3A and PO. areas. It is

FIGURE 6. Result of stimulation 2.

The black areas denote active brain regions ($P<0.05$).

(A) Condition 1. Activations was detected in bilaterally primary visual cortex. (B) Condition 2. Activations was detected in bilaterally primary visual cortex. (C) Condition 3. Activations was not detected in primary visual cortex.
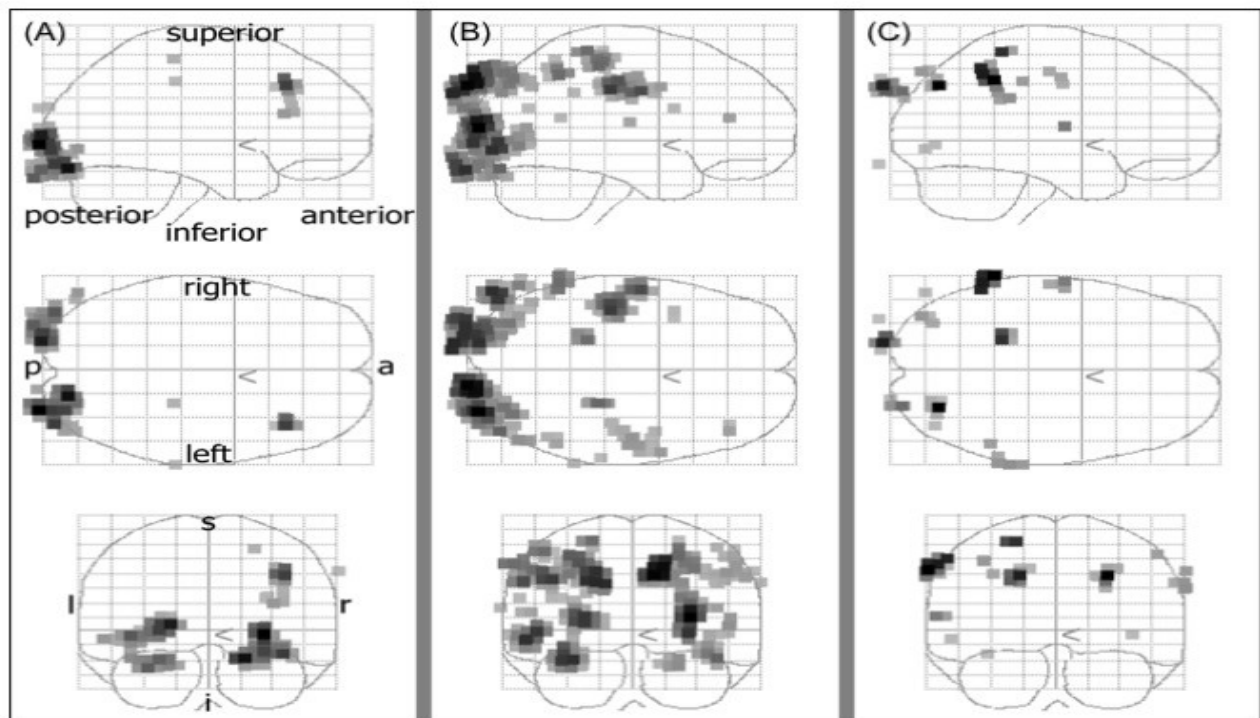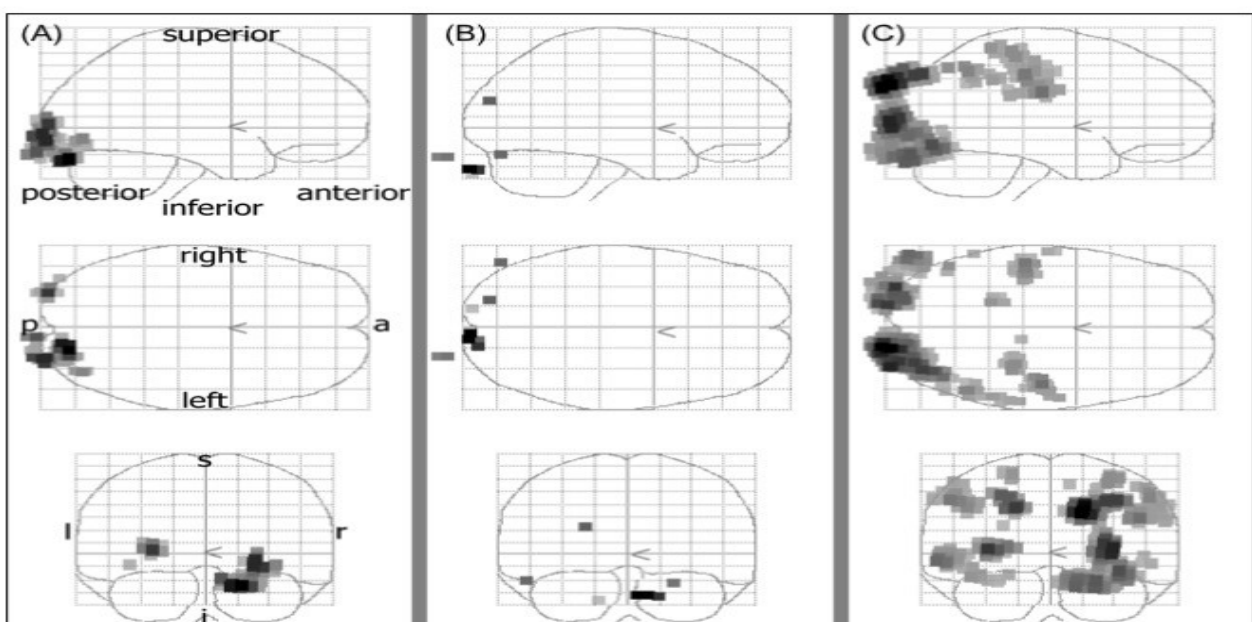


FIGURE 7. Result of stimulation 3.

The black areas denote active brain regions (P<0.05).

(A) Condition 1. Activations was detected in bilaterally primary visual cortex. (B) Condition 2. Activations was not detected in primary visual cortex. (C) Condition 3. Activations was not detected in primary visual cortex.

thought that this pathway is related to the objective position or the information processing of the three-dimensional form (41-42). However, the exact nature of this pathway has yet to be fully understood. The activation response in the dorsal visual pathway observed for conditions 2 and 3 suggests that astigmatism can influence activation whithin the dorsal visual pathway. However, the question of what the exact nature of this influence really is remains to be answered. If the direction of the line of the stimuli and the axis of the astigmatism are in agreement, then the line will be extended in this direction as it is projected on the retina. In contrast, when the directions of the line of the stimuli and the axis of the astigmatism differ, the line fades as it is projected on the retina. Thus, this suggests that this phenomenon is the visual factor responsible for generating noise on the retina can be considered. When stimulation 1 was presented through the range that resulted in activation, the response for condition 3 was larger than that for condition 2. However, there was no difference between stimulation 2 for condition 2 and stimulation 3 for condition 3. Moreover, the large difference seen between conditions 2 and 3 was not observed between stimulation 2 with condition 3 and stimulation 3 with condition 2. This suggests that ATR astigmatism may have a greater influence on the visual noise as compared to the WTR astigmatism.

In studies of ophthalmological surgeries, especially surgeries of the anterior eye segment, there have been several attempts to find ways to lessen induced cornea astigmatism if possible have been attempted (4-7). One study reported that a superior incision induced ATR astigmatism (43). Although the position of the incision during cataract surgery can be due to a variety of reasons (44-46), the overall outcomes seen in these cases have led to the creation of a defined protocol when performing these surgeries in the general population. Moreover, although there have been many reported cases of WTR astigmatism in young men,

there have been other studies that have found that aging can cause a large number of people to develop ATR astigmatism (47-49). Irregular astigmatism is commonly treated by laser in situ keratomileusis (LASIK), using the wavefront technique (12-14). After this medical treatment, the cornea temporarily becomes a perfect surface of a sphere. However, a large number of corneas could change to ATR astigmatism with aging. Thus, it will be necessary to closely follow these subjects in order to determine the validity of this hypothesis in the future.

Ophthalmologists need to pay close attention to basic fundamental abnormalities, such as WTR and ATR astigmatism, in order to ensure patients receive the best possible ophthalmological care.

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