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Original Article

Functional Magnetic Resonance Imaging Findings in Meares-Irlen Syndrome: A Pilot Sudy

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Purpose: To investigate patterns of functional magnetic resonance imaging (fMRI) activation during sentence reading before and after wearing color-tinted lenses.

Methods: A total of 15 Meares-Irlen syndrome patients with a mean age of 23.4 years (range, 13 to 42 years) with no history of neurological or psychiatric disorders were scanned using a 3T MR scanner (Siemens, Tim-Trio, Germany). Each patient underwent two sessions of fMRI imaging (before and after MISViS color-tinted lens application). The fMRI paradigm included a block design of 20 seconds of rest (cross), 20 seconds of activation (sentence reading), and ten blocks (a total of 200 echo-planar image volumes) repeated for each session. Data preprocessing and analyses were performed using the SPM8 software package.

Results: The reading speed of patients improved more than 20% while wearing the selected lenses. When compared to the before-lens session, the after-lens session identified significant regions of activation in the left middle and superior temporal gyri (paired *t*-test; maximal z score, 5.38; Montreal Neurological Institute coordinate, -60 / -39 / 0; threshold at $p < 0.05$; corrected for multiple comparisons using family-wise error). No region of activation at the same threshold was found in the before-lens session as compared to the after-lens session.

Conclusions: In the current study, we confirmed activation in the left middle and superior temporal gyri during sentence reading after wearing color-tinted lenses. These results could explain the effectiveness of color-tinted lenses in patients with Meares-Irlen syndrome.

Key Words: Left temporal gyrus, Magnetic resonance imaging, Meares-Irlen syndrome

Meares-Irlen syndrome (MIS) is a disorder characterized by reading difficulties that are mitigated by wearing colored filters of a specific tint [1,2]. The reading difficulties include symptoms of eye strain, headache, and visual perceptual distortions such as blurring, doubling, patterns, and movement of print on the page [3]. MIS is considered to be a magnocellular system disorder that induces visual stress and distortion; however, there is not yet a clear consensus on the etiology of this disorder [4,5].

A key diagnostic criterion for MIS is alleviation of somatic symptoms and perceptual distortions by use of colored overlays or precision tinted lenses [6,7]. The diagnosis and treatment of MIS begins with patient complaint that may be one or more of several on a long list of symptoms. The patient is then asked to read text through a series of tinted overlays used alone and in combination. The patient

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is finally asked to select the tint that allows for the most comfortable vision. To date, reports of successful treatment of reading disorders using tinted lenses are based on anecdotal information and testimonials. To our knowledge, no study has been undertaken to objectively document improvement in reading difficulties following the use of tinted lenses in patients with MIS.

In the current study, we investigated patterns of functional magnetic resonance imaging (fMRI) activation during sentence reading, before and after wearing color-tinted lenses, to demonstrate the effectiveness of color-tinted lenses in patients with MIS.

Materials and Methods

Patient enrollment

A total of 15 MIS patients with no history of neurological or psychiatric disorder were recruited. All patients were selected through a detailed questionnaire including any symptoms of eye-strain or visual perceptual distortion and other associated symptoms to determine if the described reading difficulties were due to MIS. A complete ophthalmologic evaluation including visual acuity, refractive errors, slit lamp examination, tear break-up time, strabismus, and retinal findings was performed prior to inclusion in the study. Exclusion criteria were the following: 1) any ophthalmologic disorder other than MIS, 2) history of proven neurological or psychiatric disorder, 3) history of significant head injury, 4) patients who were younger than nine years of age, and 5) patients who were linguistically, intellectually, or mentally challenged. All participants gave written informed consent prior to study inclusion and the local ethics committee approved the study protocol of the institutional review board at Korea University Medical Center.

Examination for dyslexia

We conducted a thorough examination for dyslexia via the Reading Writing Speed Meter, which was developed in Korea to evaluate both reading and writing abilities [8-10]. Patients were asked to read paragraphs aloud written in different font sizes, with letter spacing and vocabulary level that was dependent on the age group. The number of words read in one minute were determined and recorded. Different paragraphs were provided for those in grades 4 to 6, middle school, and high school. To eliminate the possibility of guessing words based on the context, the wording was randomized so that the presented sentences were meaningless. Statistical analysis of the reading speed before and after use of tinted lenses was conducted using the Wilcoxon signed-rank test. Statistical significance was set at $p < 0.05$ (SPSS ver. 13.0; SPSS Inc., Chicago, IL, USA).

Selection of tinted lenses

MISViS filters consist of a variety of lens colors. Each color provides four to five lenses with differences in the degree of darkness (Fig. 1). Patients first wore the lightest lens of each color group to be sure they were comfortable with the color group. Within the selected color group, subjects with a reading speed that improved more than 20% compared to their base line speed without selected lenses or those with marked alleviation of subjective visual symptoms with color-tinted lenses were considered to have MIS (Table 1) [8-10].

Functional magnetic resonance imaging acquisition and analysis

fMRI acquisition was performed using a Trio 3T scanner (Siemens, Erlangen, Germany) equipped with a

Fig. 1. MISViS filters consist of diverse colors of lenses. Each color family includes four to five lenses with differences in the degree of darkness.

Table 1. Patients profiles

Patients no.	Age	Sex	Word per minute		
			Before	After	After-before
1	17	F	119	125	6
2	32	F	100	130	30
3	22	M	115	124	9
4	24	M	105	126	21
5	32	M	102	130	18
6	36	M	125	159	34
7	23	M	107	107	0
8	13	M	96	112	16
9	41	M	124	137	13
10	13	F	103	145	42
11	18	M	132	157	25
12	19	M	73	73	0
13	19	M	141	167	26
14	21	M	105	105	0
15	21	M	114	130	16
Mean	23.4		110.7 ± 15.9	128 ± 23.1	17.1 ± 12.4

$p < 0.002$ by Wilcoxon signed rank test.

12-channel phased array head coil. We acquired gradient echo T2-weighted echo-planar images with blood-oxygenation-level-dependent (BOLD) contrast as an index of brain activity [11]. A functional image volume consisted of 38 continuous axial slices of 3 mm thickness (repetition time, 2,000 ms; echo time, 21 ms; field-of-view, 220 × 220; matrix, 64 × 64; in-plane resolution, 3.4 mm × 3.4 mm). A total of 400 functional volumes were acquired for each participant (200 in each session, as described below). To co-register echo-planar images and facilitate the anatomical localization of statistically significant activations, a high-resolution 3D MP-RAGE sequence was acquired with the following parameters: repetition time, 1,780 ms; echo time, 2.34 ms; number of excitation, 1; matrix, 256 × 256; FOV, 256 × 256 mm; voxel size, 1 mm. Axial T2-weighted images (3-mm-thickness) were also acquired to identify structural abnormalities. Structural magnetic resonance images of all participants were reviewed by a board-certified neuroradiologist to identify any structural abnormalities and were reported as normal.

Each participant wore eyeglasses without metal frames that were specifically designed for the fMRI study. The fMRI paradigm used a block design comprised of alterations of 20-s rest epochs of passive viewing of an on-screen black cross with 20-s activation epochs during which patients were previously instructed to make their best effort to soundlessly read sentences on the magnetic resonance imaging-compatible LCD screen. This rest-activation procedure was repeated for a total of ten cycles for each session. Each patient underwent two sessions of fMRI experimentation, before and after application of color-tinted lenses.

Pre-processing and analysis of fMRI data were performed using SPM8 (Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm). Functional images were realigned to correct for head movements and co-registered with the high-resolution structural image from each participant. The structural image was then segmented into grey matter, white matter, and cerebrospinal fluid partitions and normalized to the Montreal Neurological Institute standard brain. The resulting transformation matrix was then applied to all functional volumes, which were resampled to a voxel size of 3.0 mm × 3.0 mm × 3.0 mm. Finally, the functional images were smoothed with an 8-mm full-width at half-maximum isotropic Gaussian kernel.

Changes in BOLD contrast associated with the performance of the sentence reading task were assessed on a pixel-by-pixel basis using the general linear model and the theory of Gaussian fields [12]. Each boxcar stimulus function was convolved with a canonical hemodynamic response function, and data were high-pass filtered with a cutoff period of 128 seconds. For two sessions in each subject, a first-level design matrix was built, in which motion parameters were used as regressors. Specific effects to identify areas of brain activation were then tested by defining the contrast of sentence reading versus resting conditions. Significant hemodynamic changes for this contrast (1, 0) were assessed, and resulting contrast images were submitted to a second-level random-effect analysis. A within-group paired *t*-test was then used to identify brain activations of sentence reading with application of a color-tinted lens condition compared to those without the application of a color-tinted lens. We report activations with a threshold of $p < 0.05$, corrected for multiple comparisons for the whole brain using family-wise error (FWE).

Results

A total of 15 patients completed the study (3 females; mean age, 23.4 ± 8.3 years; range, 13 to 42 years). Demographic and clinical data of the patients are detailed in Table 1. Of the 15 patients, 12 (80%) selected blue-tinted lenses. The median reading speed, expressed as word per minute (WPM), before wearing color-tinted lenses was 107 (interquartile range, 102 to 124). The median WPM after wearing color-tinted lenses was 130 (interquartile range, 112 to 145). The difference in WPM before and after wearing tinted lenses was statistically significant (Wilcoxon signed-rank test, $p < 0.002$).

Compared to the before-lenses session, the after-lenses session identified significant regions of BOLD activation in the left middle and superior temporal gyri (paired *t*-test; maximal *z* score, 5.38; Montreal Neurological Institute coordinate, -60 / -39 / 0; threshold at $p < 0.05$; corrected for multiple comparisons using FWE). No region of significant activation at the same threshold was found in the before-lenses session as compared to the after-lenses session (FWE-corrected $p < 0.05$) (Fig. 2).

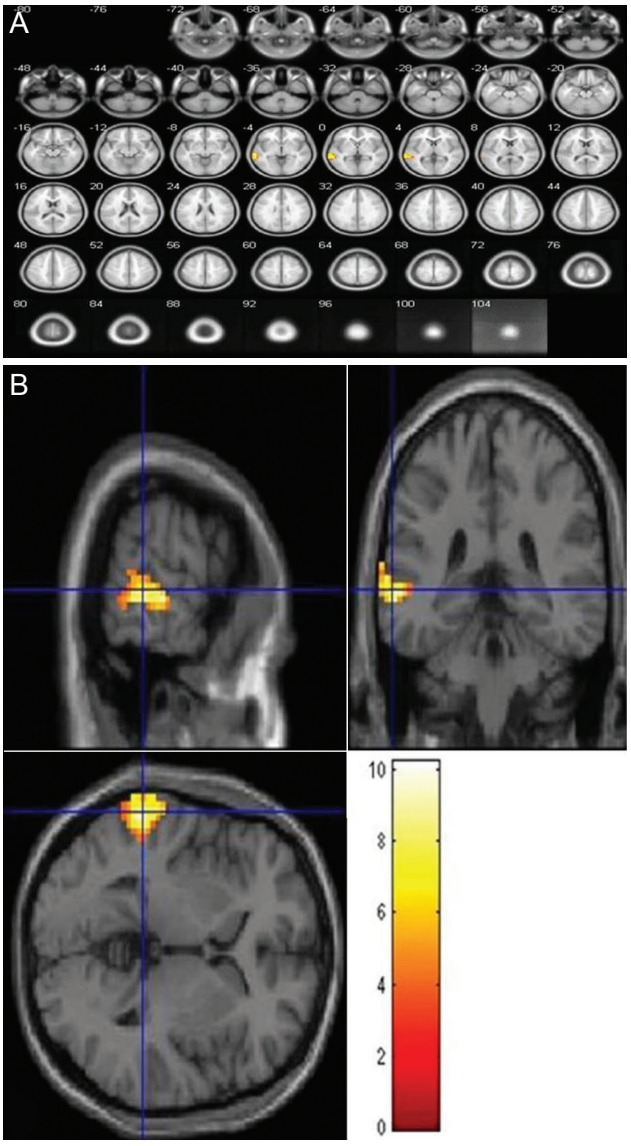

Fig. 2. Statistical parametric maps showing a significant blood-oxygenation-level-dependent activation in the left middle and superior temporal cortices in patients with Meares-Irlen syndrome during sentence reading with color-tinted lenses compared to reading without color-tinted lenses (paired *t*-test, $p < 0.05$, corrected for multiple comparisons using family wise error). The left side of each picture is the left side of the brain (A). The color bar represents the t-value (B). The images show mean differences in the activated regions before and after wearing different lenses.

Discussion

MIS (previously known as scotopic sensitivity syndrome) is considered a magnocellular system disorder that induces visual stress and distortion, causing reading difficulties by hypertransmission of a specific light wave [13]. The use of color-filtered lenses is useful for improving visual symptoms. Colored overlays and tinted lenses are purported to improve reading ability and visual perception and eliminate symptoms associated with reading, such as light sensitivity, eyestrain, headaches, blurring of print, loss of place, and watery eyes [14-16].

In the present study, we found significant regions of fMRI activation in the left middle and superior temporal cortices during sentence reading with color-tinted lenses compared to reading sessions without color-tinted lenses. These temporal regions are well known to be involved (engaged) in sentence comprehension and, more specifically, semantic and syntactic integration at the sentential level [17,18]. In line with BOLD activations, the finding of a 21% improvement in reading speed with color-tinted lenses suggests a beneficial effect of color-tinted lenses on sentence reading.

Recently, Chang et al. [8] reported that doubling and difficulty moving between lines are specific visual distortion symptoms observed in MIS patients. We believe that the results of the fMRI suggest the possibility of the existence of MIS and explain the effectiveness of color-tinted lenses

in patients with MIS. Further large studies on the activated region in MIS are required to provide strong evidence for the existence of a physiological basis of MIS, and, moreover, to provide an explanation for the improvements in reading with colored lenses.

There are several limitations to the present study. First, the sample size was small. Second, age-matched investigation was not performed. Third, lack of diagnostic criteria for MIS in this study was an inherent limitation. Finally, this study was a pilot study because the experiment lacks an appropriate control condition. Several previous studies reported that control groups had a prevalence of MIS ranged from 25% to 34% [6,18]. This indicates that increasing reading speed with tinted lens is not an absolute diagnostic criteria but a suggestive finding in MIS. At present, comparisons are made between reading without and with different lens tints.

Significant regions in the left middle and superior temporal gyri were shown to be activated after wearing a specific color filter in patients with MIS.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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