Evaluation of optic neuropathy in multiple sclerosis using low-contrast visual evoked potentials

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ABSTRACT

Background: Contrast acuity (identification of low-contrast letters on a white background) is frequently reduced in patients with demyelinating optic neuropathy associated with multiple sclerosis (MS), even when high-contrast (Snellen) visual acuity is normal. Since visual evoked potentials (VEPs) induced with high-contrast pattern-reversal stimuli are typically increased in latency in demyelinating optic neuropathy, we asked if VEPs induced with low-contrast stimuli would be more prolonged and thus helpful in identifying demyelinating optic neuropathy in MS.

Methods: We studied 15 patients with clinically definite MS and 15 age-matched normal controls. All subjects underwent a neuro-ophthalmologic assessment, including measurement of high-contrast visual acuity and low-contrast acuities with 25%, 10%, 5%, 2.5%, and 1.25% contrast Sloan charts. In patients with MS, peripapillary retinal nerve fiber layer (RNFL) thickness was determined using optical coherence tomography. Monocular VEPs were induced using pattern-reversal checkerboard stimuli with 100% and 10% contrast between checks, at 5 spatial frequencies (8–130 minutes of arc).

Results: VEP latencies were significantly increased in response to low- compared with high-contrast stimuli in both groups. VEP latencies were significantly greater in patients with MS than controls for both high- and low-contrast stimuli. VEP latencies correlated with high- and low-contrast visual acuities and RNFL thickness. VEPs were less likely to be induced with low- than with high-contrast stimuli in eyes with severe residual visual loss.

Conclusions: Visual evoked potentials obtained in patients with multiple sclerosis using low-contrast stimuli are increased in latency or absent when compared with those obtained using high-contrast stimuli and, thus, may prove to be helpful in identifying demyelinating optic neuropathy. *Neurology*® 2009;73:1849–1857

GLOSSARY

IRB = Institutional Review Board; **MS** = multiple sclerosis; **OCT** = optical coherence tomography; **RNFL** = retinal nerve fiber layer; **VEP** = visual evoked potential.

Acute demyelinating optic neuritis commonly occurs in association with multiple sclerosis (MS).^{1,2} While it is well known to impair visual acuity, color vision, and the visual fields, it also frequently impairs contrast vision.^{3,4} Indeed, contrast vision often remains impaired, even if other visual functions recover, and correlates better with subjective visual complaints than do other measures of visual function.^{4–6} Abnormal contrast vision, or decreased ability to distinguish adjacent areas of differing luminance, can be quantified clinically using several psychophysical chart-based techniques in which low contrast optotypes are displayed on a white background.⁷ The Pelli-Robson chart consists of optotypes of the same size but with decreasing contrast, and can be used to obtain a measure of contrast sensitivity.⁸ Sloan charts consist of

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optotypes of decreasing size at one of several contrast levels, and thereby allow the measurement of a contrast acuity at each of these contrast levels.⁹ Several recent studies suggest that detection of abnormal contrast vision using Sloan charts might be the most sensitive means to identify afferent visual dysfunction in MS.¹⁰ In fact, contrast vision can be abnormal in patients with MS with no history of optic neuritis, suggesting subclinical demyelinating optic neuropathy or involvement of the retrochiasmal visual pathways.¹¹ Decreased contrast vision in patients with MS has also been found to correlate with decreased peripapillary retinal nerve fiber layer (RNFL) thickness and macular volume, as measured by optical coherence tomography (OCT), making it a potentially useful means for monitoring response to treatment in clinical trials.^{12,13}

Visual evoked cortical potentials (VEPs) have been used to identify optic nerve involvement in patients with suspected MS, ever since an increased latency of the positive peak seen in normal subjects at about 100 msec—the P100—was demonstrated in patients with optic neuritis.¹⁴ The increase in P100 latency in affected eyes is more marked with a high-contrast pattern-reversal (e.g., black-and-white checkerboard) stimulus than with a flash stimulus,¹⁴ and it persists following recovery from the acute episode.¹⁵ In the present study, we asked if P100 latency was further increased when using low-compared with high-contrast pattern-reversal stimuli in patients with MS compared with age-matched normal controls. We also aimed to determine if P100 latency correlated with other visual function parameters, such as contrast acuity, as measured with Sloan charts, and peripapillary RNFL thickness, as measured with OCT.

METHODS Subjects. We studied 15 patients with MS (13 male, 2 female; median age 59, range 37–68 years) recruited from the MS clinic of the Cleveland Veterans Affairs Medical Center. All patients fulfilled revised McDonald criteria for MS.¹⁶ We included patients with and without a history of optic neuritis, as patients with MS can have subclinical optic neuropathy.¹¹ No patient was studied during an attack of optic neuritis and serial clinical evaluations indicated stable visual function. We also studied 15 age-matched normal control subjects (12 male, 3 female; median age 51, range 30–71 years). All subjects were recruited and studied in 2008.

Standard protocol approvals and patient consents. The study protocol was approved by the Institutional Review Board

(IRB) of the Cleveland Veterans Affairs Medical Center. All subjects gave written informed consent in accordance with the Declaration of Helsinki and our IRB.

Clinical assessment. All subjects had a full neuroophthalmologic assessment, including monocular measurements of visual acuity (at 3 m) using a retroilluminated high-contrast ETDRS chart and of contrast acuity using 25%, 10%, 5%, 2.5%, and 1.25% contrast Sloan charts. Visual acuity was expressed as the logarithm of the minimum angle of resolution (logMAR). We also assessed color vision, confrontation visual fields (patients with MS also had Humphrey 24-2 SITA-fast fields), and performed ophthalmoscopy, pupillary, and ocular motor examinations. The level of disability was determined in all patients with MS using the Expanded Disability Status Scale.¹⁷ The clinical findings in patients with MS are given in the table. Normal subjects had no history of neurologic or ophthalmic disease, apart from refractive error, with best-corrected logMAR acuities of 0 (equivalent to 20/20) or better, and a normal neuroophthalmologic examination.

Optical coherence tomography. In patients with MS, the peripapillary RNFL thickness and macular volume was measured using OCT (Stratus 3000, Carl Zeiss, Dublin, CA). The fast RNFL scanning protocol was used to obtain measurements of RNFL thickness and the fast macular thickness map scanning protocol was used to obtain measurements of macular volume.¹³ OCT measurements were taken following pupillary dilation (with 1% tropicamide and 2.5% phenylephrine), to ensure optimal image quality. Signal strength of 7 or more was required for OCT data to be considered acceptable. Several of our patients with MS had RNFL thinning in only 1 or 2 quadrants. In the majority of these, the average RNFL thickness was also reduced, with only 3 of 30 eyes showing mild RNFL thinning in 1 quadrant and normal average RNFL thickness. Thus, focal RNFL thinning generally resulted in a reduced average RNFL thickness, so we used the average RNFL thickness (in μm) and total macular volume (in mm^3) for the correlations and statistical analysis.

Experiment protocol. VEPs were elicited in response to 2-Hz pattern-reversal checkerboard stimuli generated by a UTAS Visual Electrodiagnostic Testing System (LKC Technologies, Gaithersburg, MD), with an active electrode (Grass gold cup electrode, West Warwick, RI) fixed on the scalp at the Oz position, referenced to Fz. We studied the responses to stimuli with 5 spatial frequencies (check sizes of 130, 65, 33, 16, and 8 minutes of arc) and with 100% and 10% contrast between the shaded and white checks. Stimuli were presented on a color CRT monitor (NEC Multisync FE772M-BK), subtending an angle of $17^\circ \times 12^\circ$ at a viewing distance of 1 m, in dim ambient illumination conditions. Subjects were instructed to fixate on a target at the center of the display. The output signals from the electrodes were amplified and then passed through a bandpass filter with low and high cutoff frequencies of 0.3 Hz and 300 Hz, respectively. The output from the amplifiers was digitized at 2 kHz, for a duration of 256 msec after the onset of each stimulus, and displayed on a computer monitor, to allow immediate inspection of the waveform. When a poor waveform was obtained, adequate electrode contact was confirmed and a repeat study was undertaken.

Data analysis. VEP analysis was performed on the averaged waveform from 50 sweeps. The latency of the P100 peak of the VEP (hereafter referred to as VEP latency) was identified interactively for all waveforms with a distinct peak, with correction for

Patient	Age, y	MS subtype	EDSS	LogMAR visual acuity (R/L)	HRR color vision (R/L)	MD of Humphrey visual field (R/L)	RAPD	Optic atrophy (R/L)
1	68	SP	2.5	0/0	N/N	−6.19/−8.88	None	None/none
2	63	SP	6	0.1/3	RG, BY/−	−3.75/−30.57	L	Mild/severe
3	59	SP	8	0.4/0.4	RG/RG	−/−	None	Severe/severe
4	64	RR	3	0.4/−0.1	−/N	−11.12/−1.36	R	Mild/none
5	67	RR	1.5	0.1/0.2	N/RG	−2.47/−4.22	L	None/none
6	46	SP	6	0.1/0.1	RG/RG	−4.94/−4.39	L	Moderate/moderate
7	57	SP	7.5	0.2/0.3	−/−	−13.69/−13.39	None	Mild/mild
8	48	SP	7.5	0.2/0	RG/N	−3.19/−1.24	R	Severe/none
9	59	SP	6	0/0.8	RG/−	−3/−6.05	L	Mild/moderate
10	55	SP	7	0.1/0.1	N/N	−3.7/−3.47	L	Mild/moderate
11	44	SP	3	0/0.2	N/−	−2.02/−5.11	L	None/severe
12	65	SP	6.5	0.2/0.1	RG/RG	−2.61/−1.26	R	Moderate/mild
13	60	SP	7	0.1/0.1	N/N	−2.66/−3.56	None	None/none
14	37	RR	2.5	0/1	N/−	−0.67/−7.72	L	None/severe
15	54	SP	3	0/1.6	N/−	−0.85/−16.56	L	None/severe

EDSS = Expanded Disability Status Scale; HRR = Hardy-Rand-Rittler plates; MD = mean deviation (decibels); RAPD = relative afferent pupillary defect; SP = secondary progressive; N = normal; RG = mild red-green defect; BY = mild blue-yellow defect; − = unable to measure; RR = relapsing remitting.

baseline drift, using the EMWin software package (version 8.1.1, LKC Technologies). Further analysis was performed offline using custom-written software in S-plus (version 8.0, TIBCO Software, Palo Alto, CA). The Wilcoxon rank sum test was used to perform paired comparisons between data (the significance level was $p = 0.05$), as the data were not normally distributed. Correlations were assessed using linear least-squares regression with calculation of the correlation coefficient (r). Note that data from all MS eyes were grouped together for the analysis, regardless of whether there was a prior history of optic neuritis, since we often found signs of subclinical optic neuropathy (e.g., reduced contrast acuity or abnormal color vision) in patients without a history of optic neuritis.

RESULTS High- and low-contrast visual acuity.

Best-corrected visual acuity progressively declined as optotype contrast decreased in both the normal subjects and patients with MS; means $\pm$ standard deviations for logMAR acuity at each contrast level are plotted in figure 1. Note that in some patients with MS with severe visual loss due to previous optic neuritis, contrast acuities could not be obtained, in particular at the lower contrast levels, even when the chart was moved closer. Consequently, these data could not be included in the analysis. Despite this, the acuities were lower in the patients with MS than in the normal subjects at every contrast level ($p < 0.001$).

VEP responses. Measurable VEPs were not obtained in response to all stimuli in all subjects, especially in patients with MS with the lower contrast and highest spatial frequency stimuli (figure 2). VEPs were most likely to be absent when the eyes of the patients with

MS with the least residual vision (after optic neuritis) were stimulated, although a small percentage of normal subjects also had unidentifiable VEPs, even on repeat testing. As VEPs were most likely to be elicited in both groups with the 33 minutes of arc stimuli, these data were used to assess for correlations with other indices of optic nerve function and structure, as discussed below.

VEP latencies. VEP tracings from stimulation of a representative normal subject's eye and a typical eye of a patient with MS are plotted, for 1 spatial frequency (16 minutes of arc checks), in figure 3 (A and B). There was no prior history of optic neuritis in the eye of the patient with MS (figure e-1 on the *Neurology*[®] Web site at www.neurology.org). However, VEP latency was increased with stimulation of the eye of the patient with MS for both contrast levels, when compared with the responses from stimulation of the normal subject's eye. Furthermore, VEP latency with the 10% contrast stimulus was increased when compared with responses to the 100% contrast stimulus, in the eyes of both the normal subject and the patient with MS.

Across subjects, VEP latency was about 100 msec for normal subject eyes in response to 100% contrast stimuli for all spatial frequencies except the highest (smallest check size), where it was slightly prolonged (figure 3C). However, it was increased for MS patient eyes in response to 100% contrast stimuli for all spatial frequencies ($p < 0.01$), with the mean re-

Figure 1 Visual acuity as a function of optotype contrast in normal subjects and patients with multiple sclerosis (MS)

Means $\pm$ standard deviations of logMAR visual acuity are plotted as a function of optotype contrast (note logarithmic scale). (A) Normal subjects. Mean visual acuity at 100% contrast is slightly better than 0 (20/20), but progressively declines as the optotype contrast decreases to 1.25%. (B) Patients with MS. Visual acuity progressively declines, although at a slightly higher rate than for the normal subjects, as the optotype contrast decreases to 1.25%. The standard deviations are larger than in the normal subjects, since data from all MS patient eyes were grouped together. However, the acuities for patients with MS were lower at every contrast level, when compared to the normal subjects ($p < 0.001$). Note a higher logMAR value indicates a lower acuity; the equivalent Snellen acuities are indicated in parentheses next to the y-axis of (B), but the scales of the y-axes are identical.

sponses being 20–30 msec greater than those of normal subjects. It was also increased for both normal subject and MS patient eyes in response to 10% contrast stimuli for all spatial frequencies, when compared with the responses to 100% contrast stimuli ($p < 0.01$). Finally, latency was increased for MS patient eyes in response to 10% contrast stimuli for all spatial frequencies, except for the 65 minute of arc checks, when compared with the normal subject responses ($p < 0.05$). The means $\pm$ standard deviations of VEP latency for each check size and contrast level are listed in table e-1. Note that latency could not be determined when there was no identifiable VEP waveform. Consequently, these data could not be included in the calculations of the means or standard deviations, or in the statistical analyses. The number of eyes (of 30) in which there was an identifiable VEP waveform is indicated in figure 2 and table e-1.

We identified 4 patients with MS with normal latencies (within the 95% confidence intervals of the normal subject data) in response to 100% contrast stimuli, but increased latencies (outside the 95% confidence intervals of the normal subject data) in response to 10% contrast stimuli, for 2 or more spatial frequencies, in 1 or both eyes. There was no prior history of optic neuritis in the eye showing the discrepancy in 3 of these patients, while there was only a

possible history of optic neuritis (with excellent recovery of vision) in the fourth patient.

Correlations. High- and low-contrast visual acuities and VEP latencies (33 minute of arc data) were correlated with one another, peripapillary RNFL thickness, and macular volume. Visual acuities for 100% and 10% contrast optotypes were significantly correlated in both subject groups (figure 4A), being lower for the 10% contrast optotypes. The decline in acuity with the 10% contrast optotypes was more marked in patients with MS with lower 100% contrast acuities; the patients with the lowest 100% contrast acuities could not see the 10% contrast optotypes (plotted as “NR” in margins of figure 4A). Similarly, VEP latencies for 100% and 10% contrast checkerboard stimuli were significantly correlated in both subject groups (figure 4B), and were prolonged with the 10% contrast stimuli. While visual acuities and VEP latencies for 100% contrast optotypes and stimuli were significantly correlated in both subject groups (figure 4C), visual acuities and latencies for 10% contrast optotypes and stimuli were only significantly correlated in the MS patient group (figure 4D). Note that VEPs were more prolonged or absent in patients with MS with lower 100% and 10% contrast acuities. Visual acuities for both 100% and 10% contrast optotypes were significantly (negatively)

Figure 2 Percentage of eyes with an identifiable visual evoked potential (VEP) in response to 100% and 10% contrast checkerboard stimuli

(A) Percentage of eyes with an identifiable VEP waveform in response to 100% contrast stimuli is illustrated for normal subjects (N, blue bars, 30 eyes) and patients with multiple sclerosis (MS, red bars, 30 eyes) at each check size (spatial frequency). Stimulation of all normal eyes resulted in a VEP waveform, except for the smallest check size (highest spatial frequency). Stimulation of most, but not all, MS eyes resulted in a VEP waveform; responses were less likely to be seen in eyes with more severe visual loss at the 2 smallest check sizes (i.e., higher spatial frequencies). (B) Percentage of eyes with an identifiable VEP waveform in response to 10% contrast stimuli is illustrated for normal subjects (N, light blue bars) and patients with MS (MS, pink bars). Stimulation of most, but not all, normal eyes resulted in a VEP waveform. Some MS eyes did not show responses to 10% contrast stimuli, especially those eyes with more severe residual visual loss, at the smallest check size. The absolute number of eyes with an identifiable VEP (out of 30) is indicated in white at the base of each bar.

correlated with the peripapillary RNFL thickness in the patients with MS (figure 4E), but VEP latencies were only significantly (negatively) correlated with the RNFL thickness in patients with MS for the 100% contrast stimuli (figure 4F). Peripapillary RNFL thickness correlated with macular volume ($r = 0.7916$, $p < 0.001$). Macular volume was also (negatively) correlated with VEP latencies for 10% ($r = 0.4399$, $p < 0.05$), but not 100% contrast stimuli ($r = 0.2005$, $p > 0.05$).

DISCUSSION Abnormal contrast vision is a pervasive feature of demyelinating optic neuropathy, and is also common in patients with MS without a history of optic neuritis, where it suggests subclinical optic nerve or retrochiasmal visual pathway involvement.^{3-6,11} As contrast vision deficits are often more marked than visual acuity deficits, we studied VEPs using high- and low-contrast pattern-reversal checkerboard stimuli in patients with MS with a spectrum of visual dysfunction, compared with age-matched normal controls. We found that VEP latencies were significantly increased in patients with MS compared to controls for high-contrast stimuli, consistent with prior studies.^{14,15,18} However, VEP latencies were further increased in response to the

low-contrast stimuli in patients with MS and in some cases were absent, especially in eyes with greater visual loss. VEP latencies correlated with their corresponding high- and low-contrast visual acuities, RNFL thickness (for high-contrast stimuli), and macular volume (for low-contrast stimuli). There was a trend toward a correlation between VEP latencies with the low-contrast stimuli and RNFL thickness (see figure 4F), but it was not significant; the lack of correlation might be due to our small sample size and the larger number of patients with unidentifiable responses to the low- than to the high-contrast stimuli.

VEPs have been used as a means to detect optic nerve involvement in patients with suspected MS, ever since seminal studies demonstrated a persisting increase in the P100 latency when using high-contrast pattern-reversal checkerboard stimuli.^{14,15,18} The VEP in response to low-contrast stimuli has previously been studied in patients with MS using 2 approaches. First, in patients with MS with a prior history of optic neuritis, moving achromatic sine-wave gratings of varying spatial frequency were used rather than pattern-reversal checkerboard stimuli.¹⁹ The stimulus contrast was increased logarithmically

Figure 3 Visual evoked potential (VEP) P100 latencies in response to 100% and 10% contrast checkerboard stimuli

(A) VEP tracings from an eye of a representative normal subject for 1 spatial frequency (16 minute of arc checks). The P100 is indicated by the asterisk (*). VEP latency is slightly less than 100 msec with the 100% contrast stimulus, but is increased with the 10% contrast stimulus. Note that the traces have been offset on the y-axis for illustration purposes. (B) VEP tracings from an eye of a typical patient with multiple sclerosis (MS) for the same spatial frequency (left eye in figure e-1). VEP latency is increased at both contrast levels when compared with the latency on stimulation of the normal subject's eye. VEP latency with the 10% contrast stimulus is also increased when compared with the response to the 100% contrast stimulus. (C) Means $\pm$ standard deviations of VEP latencies in both subject groups for all stimuli. Stimulation of the normal subject eyes with the 100% contrast stimuli (blue bars) resulted in mean VEP latencies that were close to 100 msec. Latencies were increased ($p < 0.01$) in MS patient eyes (red bars) with the 100% contrast stimuli. Latencies were also increased ($p < 0.01$) in both normal subject and MS patient eyes with the 10% contrast stimuli compared with the 100% contrast stimuli (light blue bars for normal subjects, pink bars for patients with MS). Furthermore, latencies were increased in MS patient eyes compared with normal subject eyes with the 10% contrast stimuli for all check sizes, except the 65 minute of arc checks ($p < 0.05$). Means $\pm$ standard deviations for each condition are also listed in table e-1.

Figure 4 Correlations of visual acuity, visual evoked potential (VEP) latency (at 33 minutes of arc spatial frequency), and peripapillary retinal nerve fiber layer (RNFL) thickness

(A) Correlation of visual acuities with the 100% and 10% contrast optotypes. The correlation coefficients (r) from a linear least-squares regression and corresponding significance levels are indicated in blue for normal subjects and red for patients with multiple sclerosis. Data points plotted in the margins (outside the dashed lines) represent individual responses where visual acuity could not be obtained for either or both contrast levels. (B) Correlation of VEP latencies for 100% and 10% contrast stimuli. Data points plotted in the margins represent individual responses where a VEP waveform could not be identified for either or both contrast levels. (C) Correlation of visual acuities and VEP latencies for 100% contrast optotypes and stimuli. (D) Correlation of visual acuities and VEP latencies for 10% contrast optotypes and stimuli. (E) Correlation of visual acuities for 100% and 10% contrast optotypes with peripapillary RNFL thickness. The correlation coefficients and significance levels are indicated in red for 100% and in pink for 10% contrast optotypes. (F) Correlation of VEP latencies for 100% and 10% contrast stimuli with peripapillary RNFL thickness. Correlation coefficients and significance levels are again indicated in red for 100% and in pink for 10% contrast stimuli. NR = no response.

from 0.1%–20% over 20 s, and the threshold to evoke the VEP was determined. The authors found that an increased contrast threshold was required to evoke VEPs from eyes previously affected by optic neuritis, and that the contrast threshold was modulated by the spatial frequency and the orientation of the gratings.¹⁹ In a second study, VEP data collected from patients suspected to have optic neuritis or MS were analyzed retrospectively; VEPs were measured in response to pattern-reversal checkerboard stimuli with high (95%) and low (20%) contrast between checks, at 2 spatial frequencies (50 and 25 minute of arc checks), and the interocular latency difference was calculated for each stimulus condition.²⁰ A significant increase in the interocular latency difference with the lower contrast stimuli was found for only

the higher spatial frequency (25 minute of arc check) stimuli.²⁰ Unfortunately, the absolute latencies from stimulation of each eye were not reported or correlated with other parameters of visual function, such as high- or low-contrast visual acuity, or RNFL thickness. An important result from our study is that VEP latency to low-contrast stimuli may be increased in eyes without a previous history of optic neuritis and, thus, simple comparison of interocular differences in VEP latency may be misleading. Our study also emphasizes the need to interpret VEP latency measurements in the context of other parameters of visual function, such as contrast acuity, as well as RNFL thickness and macular volume.

The increased VEP latency in patients with MS results predominantly from demyelination of optic

nerve fibers, rather than axonal loss.^{21,22} We also noted a significant increase in VEP latency in response to low-contrast stimuli in our normal subject group. The change may result from differential conduction through the magnocellular and parvocellular visual pathways,^{23,24} as neurons in the magnocellular pathway are more sensitive to achromatic low-contrast stimuli than are those in the parvocellular pathway, whereas both are sensitive to achromatic high-contrast stimuli.²⁵⁻²⁷ Color vision information, in contrast, is relayed through the parvocellular pathway,^{26,27} whose function is known to be impaired in optic neuritis. Indeed, VEP latencies with equiluminant red-and-green chromatic (color) stimuli are prolonged in patients with MS and patients with prior optic neuritis.²⁸ VEP prolongation was greater with chromatic stimuli than with high-contrast achromatic (black-and-white) stimuli, suggesting there is predominantly parvocellular pathway involvement in optic neuritis.²⁸ Our finding of increased VEP latency with achromatic low-contrast and high spatial frequency stimuli in patients with MS, correlating with a decrease in contrast acuity, suggests that magnocellular pathway dysfunction is also likely. By combining color and low-contrast stimuli, future studies may tease out the relative degrees of involvement of the parvocellular and magnocellular pathways, revealing a specific signature of deficit in demyelinating optic neuropathy.

Although we found that VEPs were prolonged or absent with low-contrast stimuli in the patients with MS, the latency increase, when compared with normal responses to low-contrast stimuli, was similar to the latency increase with high-contrast stimuli (see figure 3C). Three of our patients with MS had an increased VEP latency with low-contrast stimuli, but a normal latency with high-contrast stimuli, in an eye with no history of optic neuritis. Thus, low-contrast stimuli may be more sensitive than high-contrast stimuli for detecting subclinical optic neuropathy; study of a larger subject group is required to confirm this. It is also possible that using low-contrast stimuli may help identify a contralateral subclinical optic neuropathy in patients with their first episode of acute idiopathic optic neuritis who have few or no white matter lesions on MRI. A prospective study of patients presenting with their first episode of acute idiopathic optic neuritis would clarify the role of low-contrast VEPs in this situation. There might also be a role for using low-contrast stimuli to evoke VEPs in established patients with MS, since they may be useful for assessing magnocellular pathway function in patients who have difficulty sustaining attention during testing of contrast acuity. Finally, they might prove to be useful for monitoring disease

progression and response to treatment in selected patients.²⁹

DISCLOSURE

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