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Clinical Short Communication

Low-contrast visual evoked potential and early detection of optic demyelination

Jin Jun Luo[a,b,*], Favio Bumanlag[a], Nae Dun[b]

[a] Department of Neurology, Lewis Katz School of Medicine at Temple University, Philadelphia, PA 19140, USA
[b] Department of Pharmacology, Lewis Katz School of Medicine at Temple University, Philadelphia, PA 19140, USA

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ABSTRACT

Visual Evoked Potential (VEP) is a useful tool in identifying abnormality relative to the integration of optic pathways, and aids the diagnosis of central nervous system demyelinating disorders, such as multiple sclerosis (MS). However, the sensitivity of VEP in detecting early optic abnormality as a visual function surrogate remains questionable. Recent studies showed that low-contrast VEP increases sensitivity in early detection of optic demyelination. In order to evaluate the applicability of low-contrast VEP to our electrodiagnostic protocol, we tested whether low-contrast VEP may provide an improved sensitivity in identifying early optic demyelination. We performed low-contrast VEP with different stimulation intensities in 42 subjects. Twenty-three were patients (age: 44.0 ± 13.6 year-old, range 26–69) with a clinical diagnosis of clinically isolated syndrome, a subtype of MS, and 19 subjects were normal volunteers (age: 34.4 ± 14.3 year-old, range: 18–59) without any neurological disorders. Neither of them had a history of optic neuritis. Our preliminary data indicate that the low-contrast VEP is not superior over the conventional high-contrast VEP, and may not provide improved sensitivity in early detection of optic demyelination.

1. Introduction

Early recognizing the central nervous system demyelination and appropriately initiating treatment is essential in the management of multiple sclerosis (MS). Visual Evoked Potential (VEP), a conventional modality used clinically in aiding the diagnosis of MS, is a useful tool in evaluating visual pathways and serving as a visual function surrogate [1]. VEP is more sensitive than MRI in the evaluation of visual function and integration of visual pathway [2,3]. The ability of VEP to reveal clinically silent lesions at early disease stages that are not shown on MRI is a strong argument for employing VEP in addition to MRI early in the diagnosis of MS [3]. However, the sensitivity in early detecting optic abnormality as a visual function surrogate remains suboptimal. Recent clinical neurophysiologic studies showed that low-contrast VEP increases the sensitivity in identifying early optic demyelination. In an effort to improve VEP sensitivity in identifying early optic demyelination, we evaluated whether the low-contrast VEP can be incorporated into our electrodiagnostic protocol.

2. Methods

Normal volunteers without neurological disorders, and subjects with a diagnosis of clinically isolated syndrome (CIS), a subtype of early stage of MS, which is defined as the first clinical presentation of a disease that shows characteristics of inflammatory demyelination that could be MS but has yet to fulfill criteria of dissemination in time [4], were recruited. The subjects with CIS were chosen because 30% to 70% of patients with CIS later develop MS [5]. Those subjects with CIS were named as patients with MS in the following context of this manuscript. To better evaluate the early abnormality in the optic nerve, normal controls or patients with a history of optic neuritis or ophthalmologic diseases, such as retinal disorders or glaucoma, were excluded. Conventional pattern reversal VEPs using a video display were performed monocularly utilizing 28′ checkerboard stimuli (Viking Select 10.0.0, Nicolet, Madison, Wisconsin). The illuminate of the contrast stimuli was set up at 90%, 70%, 50%, 30% and 10% in intensity via a computer-controlled program provided by the manufacturer. Reversal rate was 1.1 Hz. Resultant responses of N75, P100, and N145 in the waveforms were recorded from LO-Fpz, MO-Fpz, RO-Fpz and Fpz-A1 derivations. Filters were set at LFF: 0.5 Hz, HFF: 100 Hz. Two trials were obtained from each eye. VEP analysis was performed on the averaged waveform from 100 sweeps. Statistical analysis was performed using an unpaired two-way Student's *t*-test. *P* value less than 0.05 was considered significant.

* Corresponding author at: Department of Neurology, Lewis Katz School of Medicine at Temple University, Philadelphia, PA 19140, USA.
E-mail address: jluo@temple.edu (J.J. Luo).

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Table 1
Low-contrast VEP.

	90%	70%	50%	30%	10%
P100					
Control	104.6 ± 7.7 ms	107.9 ± 5.9	113.8 ± 8.5	124.6 ± 28.9	134.8 ± 19.4
MS	110.5 ± 5.9 ms	115 ± 9.9	125.4 ± 24	132.4 ± 26.9	141.2 ± 29.6
p =	0.007	0.009	0.051	0.384	0.456
N75					
Control	71.1 ± 4.2 ms	73.9 ± 10.6	78.5 ± 8.9	89 ± 12	100 ± 12
MS	76.9 ± 9.8 ms	81.1 ± 9.9	88.2 ± 18.5	98.2 ± 28.9	105.8 ± 31.6
p =	0.02	0.03	0.04	0.20	0.47
N145					
Control	143.5 ± 11.8 ms	150.2 ± 15.7	151.3 ± 15	160.9 ± 19	168.4 ± 28.1
MS	149.8 ± 23.6 ms	154.4 ± 21.8	162.2 ± 26.8	172 ± 29.4	186.6 ± 31.6
p =	0.29	0.48	0.12	0.17	0.09

VEP: Visual evoked potentials.
ms: milliseconds.

3. Results

Nineteen normal volunteers (age: 34.4 ± 14.3 year-old, mean ± SD, range: 18–59 year-old) and 23 MS-patients (44.0 ± 13.6, range 26–69) were studied. Latencies were proportionally prolonged against the decrease in the intensity of low-contrast stimuli in N75, P100 and N145 waveforms in a similar slope in both MS-patients and normal controls (Table 1 and 2, Fig. 1). Notably, the variations of the waveform latency were also increased, particularly in the lower-contrast VEPs such as with the stimulation intensity at the 50% and below (Table 1). Unexpectedly, the statistically significant difference of the P100 latency between the MS group and controls was lost in the lower-contrast VEPs (Table 1), which may be due to the increased variations of the waveform (Fig. 1).

4. Discussion

Evoked potential tests are noninvasive and painless, and have excellent temporal resolution in the range of milliseconds (ms), permitting the study of dynamic changes occurring in the nervous system. VEP is the most sensitive diagnostic tool in suspected MS [1] and has been included in the diagnostic criteria for MS [3]. VEP abnormalities may uncover clinically silent lesions [1] and the proportion of clinically silent lesions revealed by VEP has been estimated at around 42–50% [6].

There are three identifiable waveforms in normal VEP recordings: N75, P100 and N145. The P100 is a positive potential at about 100 ms, and is the only one clinically used for VEP interpretation because the negative potentials at about 75 ms and 145 ms are too variable and inconsistent for routine interpretation. Abnormal P100 latency in conventional high-contrast VEP is present in approximately 90% patients with active MS and about 40% of patients with MS who do not have a history of optic neuritis [6]. As the sensitivity of conventional high-contrast VEP in identifying early optic abnormality as a visual function surrogate remained suboptimal [6], attempts were made in the past decades aiming at improving the sensitivity of VEP for early diagnosis of MS.

Comparisons in human were conducted using different techniques to deliver visual stimuli such as liquid crystal display (LCD) monitors versus cathode ray tube (CRT) monitors. The findings of different modalities using LCD versus CRT were discouraging, leading to the contention of the inability of LCD to replace CRT in VEP [7].

Subsequently low-contrast VEP was attempted and showed promising results relative to the evaluation of MS patients. Thurtell and colleagues reported that either increased latencies or absent waveforms were seen in MS patients when using a low-contrast VEP [8]. A similar observation has been obtained by Frohman and colleagues who used low-contrast multifocal VEP [9]. These findings suggested that low-contrast stimuli may be more sensitive than high-contrast stimuli in detecting optic neuropathy which is frequently seen in MS patients and, therefore, able to aid in the early diagnosis of MS. However, in their pilot low-contrast VEP studies, low-contrast were carried out only at 10% of the intensities in the former or 33.3% and below of the intensities in the latter studies [8,9]. Additionally, MS patients with a history of optical neuritis were included in those studies, which were not in their early stage but rather well established [8,9].

In our study we used a series of low-contrast at 90%, 70%, 50%, 30% and 10% in intensity and tested patients in an early stage of MS with clinically isolated syndrome [4]. We observed that low-contrast VEP produced prolongation of latencies inversely correlated with reduced stimulation contrast intensities (Table 1 and Fig. 1) in all waveforms. The observations of the fading out of the statistically significant difference in P100 latencies in the patients with CIS-MS versus controls were unexpectedly emerged, which may be due to the increased variations in such critical testing conditions (Table 1 and

Table 2
Demographic data of MS subjects.

MS	Age	Gender	Initial presenting symptoms
1	26	F	Diplopia, right side weakness
2	69	F	Numbness, sore, spams
3	30	F	Back pain, right leg weakness
4	29	F	numbness in upper extremities
5	53	F	Left hemi-paralysis
6	39	M	Ataxia, Spasm
7	59	F	Back pain, left leg numbness and weakness gait difficulty
8	47	M	Numbness, ataxia, imbalance
9	45	F	Left numbness and episodic right arm weakness
10	49	F	Numbness
11	26	M	Weakness, difficulty walking
12	31	F	Right leg weakness, urinary incontinence
13	27	F	Diplopia, right side weakness
14	67	F	Numbness, spams
15	32	F	Right leg weakness, urinary incontinence
16	55	F	weakness, numbness
17	41	M	Ataxia, Spastic gait
18	61	F	Left leg numbness, frequent fall, gait difficulty
19	51	M	Left sided numbness, ataxia, gait difficulty, imbalance
20	48	F	Numbness, arm weakness
21	51	F	Numbness
22	26	M	weakness, difficulty walking
23	49	F	Right leg weak, urinary incontinence
Mean ± SD	44.0 ± 13.6		

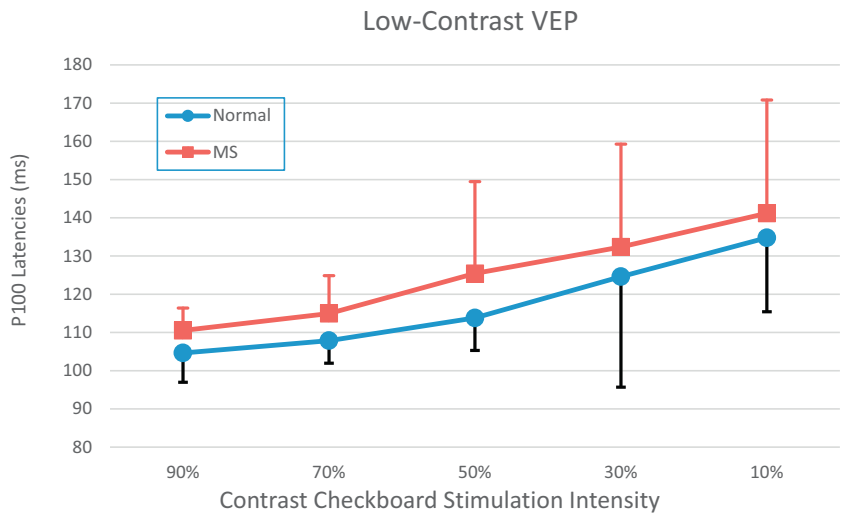

Fig. 1. Low-Conrast VEP. VEP: Visual evoked potentials; ms: milliseconds. Bars: for standard deviations.

Fig. 1). Notably, as observed in the previous pilot studies by Thurtell and colleagues and Frohman and colleagues, VEPs were less likely to be recorded with lower- than with higher-contrast stimuli to the eyes. In their studies, absence of VEP was seen in one third of clinically defined MS patients and in 10% of normal controls [7] in the low contrast VEP with 10% stimulation intensity. The fact that absence of recording of P100 waveforms was more frequently seen in low-VEP is a significant disadvantage in the evaluation of optical conditions. The inability to record a majority of P100 waveforms from the low-contrast VEP excluded the unobtainable true P100 values in their analyses [8,9], by which the analyzed data on P100 values may be inaccurate to reflect the true scenarios and, therefore, low-contrast VEP may be limited in clinical use for detecting early optic abnormality in MS patients. Moreover, low-contrast VEP consumes more time and efforts than high-contrast VEP in obtaining a reliable recording.

In summary, our study failed to confirm that the low-contrast VEP improves sensitivity in identifying early optic abnormality, even though we confirmed that the low-contrast VEP prolongs P100 latency. Our observations suggest that low-contrast VEP is not better than the conventional high-contrast VEP and may not provide improved sensitivity in early identification of optic abnormality.

Declarations of interest

None.

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