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Optical coherence tomography versus visual evoked potential in multiple sclerosis patients

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Keywords
Optical Coherence Tomography, Multiple Sclerosis, Clinically Isolates Syndrome, Visual Evoked Potential

Abstract

Background: Optical coherence tomography (OCT) is a non-invasive instrument, which can be used to estimate the thickness of the retinal nerve fibre layer (RNFL) and provides an indirect measurement of axonal destruction in multiple sclerosis (MS). The main aim of this study was to find out any correlations between P100 latency in visual evoked potential (VEP) and RNFL thickness.

Methods: The patients with the definite history of optic neuritis regardless of the diagnosis of MS were included. The eyes with the history of blurred vision and increased VEP latency (> 115 milliseconds) were considered as cases and the eyes with normal latency were regarded as controls. RNFL thickness was compared between two groups of cases and controls. In addition, the correlation between VEP P100 latency and RNFL thickness in four quadrants of superior, nasal, inferior and temporal fields was estimated by spearman correlation coefficient. RNFL thickness between the patients with history of clinically isolated syndrome (CIS) was also compared to other two subgroups of RRMS and SPMS.

Results: There was significant negative correlation between VEP P100 latency and RNFL. In all four quadrants, with increasing VEP latency, RNFL thickness decreased. Furthermore, there was significant correlation between P100 latencies and mean RNFL thickness [Pearson correlation coefficient = -0.527, $P < 0.001$; RNFL (mean) = $(-0.44 \pm 0.087) \times P100 + (153.6 \pm 10.94)$]. Comparing RNFL thickness between three groups of CIS, RRMS, and SPSM, no significant difference was detected in RNFL thickness ($P > 0.05$). Power analysis demonstrated that RNFL average had the highest area under curve.

Conclusion: OCT does have good correlations with P100 latency, indicating retinal non-myelinated axonal involvement in early stages in addition to the myelinated axonal involvement. However, it cannot be used as the sole test in evaluating visual pathway in optic neuritis and complementary tests as VEPs are recommended.

Introduction

Multiple sclerosis (MS) is an inflammatory autoimmune disorder invading myelin sheath in central nervous system.[1-3] Optic neuritis (ON), a common manifestation of MS, frequently arises as

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the preliminary manifestation of central nervous system demyelination or develops throughout the course of the disease.[4,5] Since the retinal nerve fiber layer (RNFL) is composed of only unmyelinated axons, measuring RNFL thickness signifies a feasible technique of observing axonal loss in these patients.[4]

Optical coherence tomography (OCT) is a non-invasive instrument, which can be used to estimate the thickness RNFL[6,7] and provides an indirect measurement of axonal destruction in MS;[8] in other words, it may aid in elucidating the neuroretinal pathobiology of MS.[9] In MS, changes in the RNFL, ganglion cell layer, and inner nuclear layer have been detected,[10] and consequently, OCT has been more and more utilized in MS research.[11]

Some previous studies have elucidated reduced RNFL thickness in MS patients even in early course of the disease and others have criticized this notion. The main aim of this study was to find out correlation between P100 latency in visual evoked potential (VEP) and RNFL thickness.

Materials and Methods

In this cross-sectional study, the patients were recruited from Kashani Neurology Clinic of Isfahan University of Medical Sciences, Iran. The patients with the definite history of optic neuritis, regardless of the diagnosis of MS were included. The recruited patients comprised clinically isolated syndrome (CIS), relapsing remitting (RRMS) and secondary progressive (SPMS). Optic neuritis was approved provided that clinical features included retro-orbital pain worsening by eye movements, lessening color vision, and contrast sensitivity that may had progressed to severe visual loss, an afferent pupillary defect (Marcus-Gunn pupil), and in some cases optic disc hyperemia as well as swelling. The patients with the history of diabetes mellitus, uveitis, infections and granulomatous diseases of eyes were excluded.

The eyes with the history of blurred vision and increased VEP latency (> 115 milliseconds) were considered as cases and the eyes with normal latency were regarded as controls. RNFL thickness was compared between two groups of cases and controls. In addition, the correlation between VEP P100 latency and RNFL thickness in four quadrants of superior, nasal, inferior and temporal fields was estimated by spearman correlation coefficient. RNFL thickness between the patients with the history of CIS was also compared to other two subgroups of RRMS and SPMS.

Results

Thirty four patients with the history of MS were recruited in whom 3 (8.8%) patients were male and 31 (91.2%) patients were female. The mean age ± standard deviation (SD) of the patients was 33.4 ± 8.6. The mean disease duration was 5.09 ± 4.3. In addition, the mean EDSS was 1.84 ± 1.3 and the progression index (EDSS/Duration) was 0.48 ± 0.42. In terms of the disease course, 20 (58.9%) had RRMS, 18 (26.5%) had CIS and 10 (14.7%) had SP MS. The RNFL thickness of eyes with normal VEP and abnormal VEP is demonstrated in table 1 (abnormal VEP was defined as P100 latency > 115 milliseconds).

Table 1. RNFL thickness in four quadrants according to VEP results

Field	VEP	RNFL thickness Mean ± SD	P-value
Nasal	Normal	94.9 ± 22.7	0.023
	Abnormal	79.9 ± 22.4	
Inferior	Normal	126.8 ± 13.1	0.003
	Abnormal	112.0 ± 17.7	
Temporal	Normal	84.7 ± 16.4	0.023
	Abnormal	74.1 ± 15.7	
Superior	Normal	136.4 ± 14.8	< 0.001
	Abnormal	114.8 ± 19.2	

RNFL: retinal nerve fibre layer
VEP: visual evoked potential

There was significant negative correlation between VEP P100 latency and RNFL thickness (Table 2). The figure 1 demonstrates the regression plot between P100 latency and RNFL thickness in four quadrants. The equation between P100 latency and RNFL thickness is demonstrated below the figure 1. As indicated in the plot, in all four quadrants, RNFL thickness decreases with increasing VEP latency. Furthermore, there was significant correlation between P100 latency and mean RNFL thickness [mean RNFL= RNFL (nasal + inferior + temporal + superior)/4] (Pearson correlation coefficient = -0.527, P < 0.001) (Fig. 2).

Comparing RNFL thickness between three groups of CIS, RRMS and SPSM, no significant difference was detected in RNFL thickness (P > 0.05). Power analysis demonstrated that mean RNFL thickness had the highest area under curve (Fig. 3).

Table 2. Correlation between P100 latency and RNFL thickness

Field		Nasal	Inferior	Temporal	Superior
VEP and RNFL thickness	Pearson correlation coefficient	-0.26	-0.46	-0.30	-0.48
	P-value	0.029	< 0.001	0.027	< 0.001

RNFL: retinal nerve fibre layer
VEP: visual evoked potential

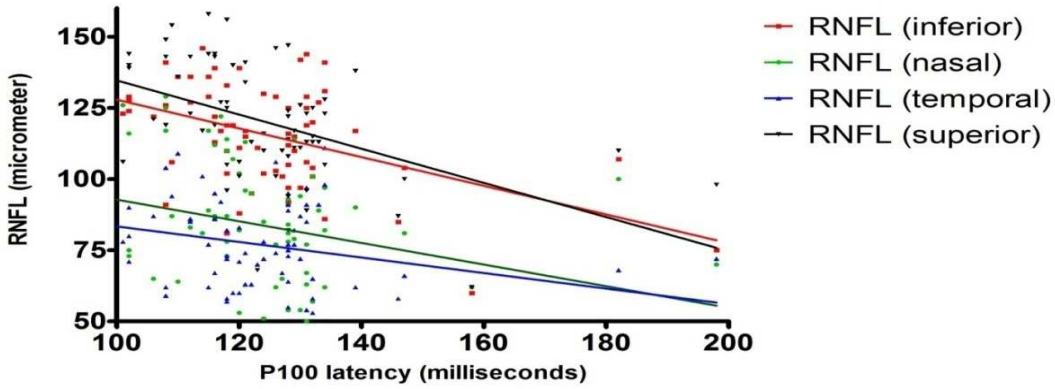

Figure 1. The regression plot between P100 latency and RNFL thickness in in four quadrants. The equations are noted as blow:
RNFL (inferior)= (-0.50 ± 0.12) × P100 + (178.2 ± 15.15) RNFL (nasal)= (-0.38 ± 0.17) × P100 + (130.8 ± 21.43)
RNFL (temporal)= (-0.27 ± 0.12) × P100 + (110.7 ± 15.12) RNFL (superior)= (-0.60 ± 0.14) × P100 + (194.7 ± 17.11)

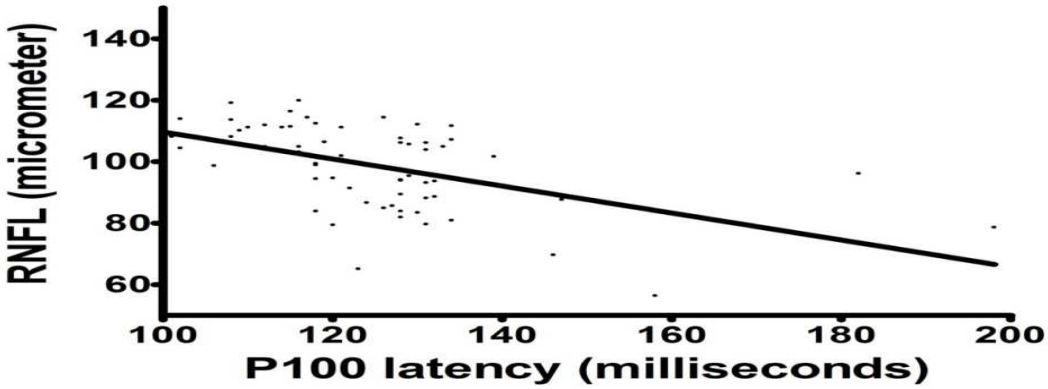

Figure 2. The regression plot between P100 latency and mean RNFL thickness [mean RNFL= RNFL (nasal + inferior + temporal + superior)/4]. The equation is RNFL (mean) = (-0.44 ± 0.087) × P100 + (153.6 ± 10.94).

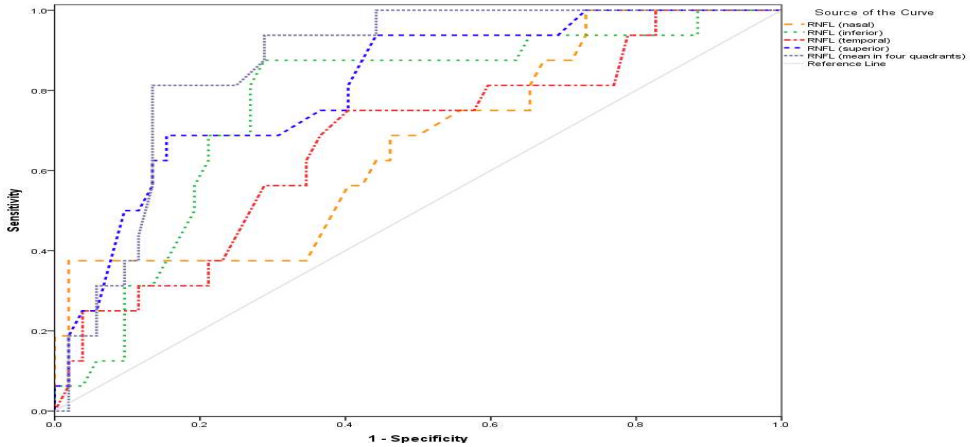

Figure 3. Power analysis of RNFLs in four quadrants of nasal, inferior, temporal and superior as well as RNFL mean in two groups of normal VEP versus abnormal VEP. Area under curve for nasal field was 0.664. It was 0.764 for inferior field, 0.671 for temporal field, 0.807 for superior field and 0.864 for mean RNFL.

Discussion

Based on our study, good association was found between RNFL changes in eyes with optic neuritis and P100 latency changes in VEP. This finding was regardless of MS subtype (RRMS, SPMS, or CIS). In addition, the highest decrement of RNFL thickness was observed in temporal field, followed by nasal,

inferior and superior fields. It seems that demyelinating disorders not only involve optic nerve sheaths in the optic nerve head or retrobulbar, but also retinal nerve fiber layer could be involved, and this involvement could be an early presentation.

In several studies, eyes with a history of optic neuritis had higher reduction of thickness in comparison with those patients without optic neuritis.[12-14] In a another study, 24 patients with CIS were prospectively studied.[8] Mean RNFL thickness was 101.6 ± 10.7 micrometers in retrobulbar of optic neuritis eyes and 96.9 ± 10.5 in unaffected eyes. Moreover, based on their results, the presence of at least one quadrant of an optic nerve with a RNFL thickness at a $P < 0.05$ cut-off value had a sensitivity of 75% and a specificity of 56% for predicting dissemination in space MRI and as a result, OCT could identify axonal damage in initial stages of the disease.

In another study,[15] the sensitivity of OCT RNFL after optic neuritis was 60%, diminishing further with mild onset and good recovery. VEP sensitivity was superior at 81% and RNFL was thinner with severe onset and disease recurrence. Comparing subtypes of MS, RNFL comparisons involving eyes without optic neuritis produced greater differences between MS subtypes than optic neuritis affected eyes.[16,17]

In one study,[18] no correlation between RNFL thickness and P100 response was discovered in patients with MS. Correspondingly, 56 consecutive CIS patients with clinically isolated syndrome (18 with optic neuritis and 38 without optic neuritis) and 32 control subjects were recruited.[19] Mean overall RNFL thickness and macular volume in the clinically isolated syndrome population were not significantly different in comparison with the controls.

According to MS subtypes, overall RNFL values in non-affected eyes were reduced in SPMS patients, relative to CIS and RRMS patients. Temporal RNFL atrophy was greater in RRMS eyes as compared to CIS eyes. Inversely, there was no significant change among MS subgroups in our study. In similar studies in progressive MS,[20] both the mean RNFL thickness and macular volume were decreased while compared with control values. Additionally, the average RNFL thickness and macular volume were significantly reduced in SPMS, but not in PPMS, when compared with control RNFL thickness.[20]

Conclusion

OCT does have good correlations with P100 latency, indicating retinal non-myelinated axonal involvement in early stages in addition to myelinated axonal involvement. However, it cannot be used as the sole test in evaluating visual pathway in optic neuritis and complementary tests as VEPs are recommended.

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