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Association of Cognitive deficits with Optical Coherence Tomography changes in Multiple Sclerosis Patients

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Abstract

Background: Multiple Sclerosis (MS) is a neurodegenerative disorder affecting myelinated axons. Cognitive impairments have been observed in patients with MS. Although there are some methods to examine the progress of MS, a tool hasn't been developed to fully correlate MS symptoms with cognitive deficits.

Methods: Among patients referring to Kerman-Iran Shafa Hospital, 60 MS patients were chosen to be included in the study. Their demographic data was obtained and patients filled the Brief International Cognitive Assessment for MS (BICAMS) questionnaire and then underwent OCT. The Chi-square test was used to analyze the frequency of patients with normal and abnormal OCT in the impaired and unimpaired cognition groups. $P<0.05$ was considered as statistically significant.

Results: 20 % of the patients with cognitive impairments had normal OCT, while 71.4% who were cognitively healthy had normal OCT. the difference between the two groups was statistically significant ($p<0.001$). 20% of patients with impaired cognition had physical disabilities, while only 2.9% with normal cognition had physical disabilities, the statistical difference between these two groups was also statistically significant ($p=0.029$).

Conclusions: Results of our study indicates that OCT can be used as a screening tool to evaluate the cognitive status of MS patients with 66.6% and 83.3%sensitivity and specificity, respectively.

Keywords: Multiple Sclerosis; Optic Coherence Tomography; BICAMS

Introduction

Multiple Sclerosis (MS) is a debilitating immune mediated illness which has both economic and social burdens [1- 4]. It includes both degenerative and inflammatory components and is manifested by the axonal loss at different levels in the CNS [3-5] which can be diagnosed in its early stages using different methods [6].

MS usually manifests with cognitive deficits [5,7-9], although recently neurologists have become aware of these manifestations [10]. 65-40% of MS patients show cognitive impairments and these deficits would be observed at any stage of the disease in any progress stage [11]. Cognitive deficits have a great impact on patients' quality of life, thus, measuring the effectiveness of therapeutic agents on these deficits would help in the assessment of treatment progress [1,6,11].

The optic nerve is affected in nearly 50% of patients [3,12]. Axonal loss in the anterior visual pathway is usually a consequence of ON, which could be identified as a thinning of the retinal nerve fiber, measured by methods such as Optic Coherence Tomography (OCT) [3,4,12-14]. This method is easy to use and is an effective way to measure retinal nerve thickness and axonal loss at the retina [3].

Therefore, the objective of this study is to assess the association of cognitive deficits with OCT changes in recently diagnosed MS patients. This would help evaluate if OCT could predict cognitive impairments in MS patients.

Methods and Materials

Among relapsing-remitting MS patients referring to the MS clinic of Shafa Hospital (Kerman, Iran), 60 subjects with at least two years history of disease were chosen for this study. Patients were initially examined by the ophthalmologist and patients with concomitant ophthalmic diseases such as Glaucoma and Cataract and refractory impairments and those with a history of Optic Neuritis were excluded from the study.

The Brief International Cognitive Assessment for MS (BICAMS) initiative which is optimized for small centers, with perhaps one or few staff members, who may not have NP training, was undertaken in order to recommend a brief and cognitive assessment for MS. BICAMS is particularly focused on international use, to facilitate comparison across settings. An expert committee of twelve

neurologists and neuropsychologists representing the main cultural groups that contributed a lot of data about cognitive dysfunction in MS, was convened. The opinions generated from the meeting were published elsewhere. In brief, the panel recommended one particular test with high reliability and good sensitivity, the Rao adaptation of the revised Brief visuospatial Memory Test (BVMTR), the Symbol Digit Modality Test (SDMT), Consensus was also achieved on optimal measures for the learning and memory criteria in MS patients, time permitting: the initial learning trials of the second edition of the California Verbal Learning Test (CVLT2) [15]. Patients impaired on two or more tests were defined as cognitively impaired [16]. An ROW Score of 9was considered as the cutoff point. To assess optic nerve thickness, OCT was performed by an expert ophthalmologist. The Optovue device (RTVue, USA) was used for the tests [3]. Demographic data including age, sex and education was gathered using a questionnaire. The Expanded Disability Status Scale (EDSS) (Kurtzke, 1983) was used to score patients impairments [17,18]. Scores more than 6 on EDSS were considered as physically impaired.

After evaluating the axonal loss in the retina and performing BICAMS, data were analyzed using the SPSS software version16 (IBM, USA). To compare the categorical variables among the two groups of unimpaired and impaired patients, the chi-square or Fischer's exact test was used.

Ethical code: K/92/67

Results

From 60 patients who were evaluated by the BICAMS test for cognitive function, the results are shown in table 1.

Variables	Cognition		Age		Gender		Education		Duration		EDSS		OCT	
	Normal	Impaired	<40	≥40	Female	Male	<Diploma	≥Diploma	<6yr	≥6yr	<6	≥6	Normal	Abnormal
Number	35	25	35	25	51	9	26	34	25	35	54	6	30	30

Table 1: The number of each variables.

Of the patients in the impaired cognition group, 15 (60%) were younger than 40, while on the normal cognition group, 22 (62.9%) were younger than 40. The impaired cognition group consisted of five female subjects (20%), while the normal group included four female subjects (%11.4). 13 (52%) patients with cognitive disorders and 21 (60%) normal patients had an education higher than diploma. The difference in terms of disease duration between the impaired group in comparison with the non-impaired group was not statistically significant (p=0.070) (table 2).

Variables	Age		Gender		Education		Duration	
	<40 yr	≥40yr	Male	Female	<Diploma	≥Diploma	<6yr	≥6yr
Normal cognition	22(62.9%)	13(37.1%)	4(11.4%)	31(88.6%)	14(40%)	21(60%)	18(51.4%)	17(48.6%)
Impaired cognition	15(60%)	10(40%)	5(20%)	20(80%)	12(48%)	13(52%)	7(28%)	18(72%)
P-Value	0.8		0.4		0.538		0.070	

Table 2: The baseline information of the patients in the two groups.

Variables	EDSS		OCT	
	<6	≥6	Normal	Abnormal
Normal cognition	34(97.1%)	1(2.9%)	25(71.4%)	10(28.6%)
Impaired cognition	20(80%)	5(20%)	5(20%)	20(80%)
P-Value	0 .002		0.001	

Table 3: Frequency of patients with physical disability and abnormal OCT in the impaired and the non-impaired cognition groups.

The frequency of the physical disability, evaluated by the EDSS, was compared among the cognitively impaired and the normal group. Results showed that the frequency of physical disability in the impaired group was statistically more when compared to the normal group (p=0.029).

Comparing the OCT in the two groups showed that normal OCT was statistically more in the group with normal cognition in comparison to the group with impaired cognition (p<0.001) (Table 3).

Quantitative analysis

The relation between the BICAMS (SDMT, CVLT-2, and BVMT-R) and the OCT was assessed using the multiple regression analysis. Regarding the accounted P values, we can say that the OCT predicts the SDMT component (processing speed) of the BICAMS test at a rate of 64.6%, while BVMT-R and CVLT-2components are not predictable in this way (Table 4).

Variables	Standard error	Standard estimate	t Value	P Value
Constant	6.507	-	11.289	0.000
SDMT	0.116	0.646	3.228	0.002
CVLT	0.181	-0.003	-0.017	0.986
BVMT-R	0.282	0.112	0.649	0.519

Table 4: Coefficients regression model of BICAMS(SDMT,CVLT-2,BVMT-R) and OCT.

Data analysis using the Pearson correlation coefficient showed that there is significant difference between the OCT and the BICAMS. (P=0.000) (Table 5).

P	n	rxy
0.000	60	-0.567

Table 5: Pearson correlation coefficient between BICAMS and OCT.

Discussion

Many methods and tests have been introduced to evaluate the progress of Multiple Sclerosis (MS) [6,10,18]. While some are invasive and costly [3], others are non-invasive and less costly, such as Optical Coherence Tomography (OCT). We used this method to document whether there is an association between OCT changes and cognitive impairments in MS patients. We observed that only 20% of MS patients with cognitive impairment had normal OCT, while 71.4% of the patients with non-impaired cognition had normal OCT, therefore we conclude that OCT changes could predict the presence of cognitive impairments in MS patients.

MS patients suffer from cognitive impairments, as shown by previous studies [5,6,8-11], but the extent of these impairments and the methods of measuring them are costly and sometimes invasive, therefore, finding a novel method for the testing of cognitive impairments in MS patients would help clinicians increase the precision of their diagnosis. In a review by Chiaravalloti and DeLuca (2008), they showed that MS patients suffer from: cognitive deficits in their complex attention, efficiency in processing information, executive functioning, processing speed and long-term memory [5]. We used BICAMS in the study to evaluate the cognitive functioning of MS patients [16]. This screening tool was used to split the MS patients into two groups: the cognitively impaired and the non-impaired groups. The Persian version of this test is shown to have good reliability and validity [16]. The presence of more patients with abnormal OCT in the cognitively impaired group compared to the non-impaired group showed that patients suffering from abnormal OCT are at a higher risk of developing cognitive impairments.

There is a vast body of evidence supporting the finding that OCT can detect neuronal axon loss in MS patients [3,4,13,14]. In a systematic review by Petzold et al. (2010), showed that MS patients have a lower Retinal Nerve Fiber Level (RNFL) compared to the control group, and patients suffering from Optic Neuritis have a lower RNFL compared to the MS patients without optic neuritis [4]. The current study included patients without a history of optic neuritis, therefore the criteria for the thinning of RNFL was 112.78 ± 13.2 micrometer.

There was a significant difference between the cognitively impaired and the non-impaired group in their physical disability, which was measured by the EDSS. While 20% of the former had physical disability, only 2.9% of the latter showed signs of physical disability, which might indicate another possible association between cognitive impairments and physical disabilities.

Generally the sensitivity and specificity of the OCT in the prediction of cognition is %66.6and 83.3% respectively.

Conclusion

MS patients with abnormal OCT are at a higher risk of developing cognitive impairments compared to patients with normal OCT. This finding is of clinical value since it can introduce a new method of assessing cognitive impairments which is easy to use and non-invasive in comparison to other applied methods.

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