Evaluation of the relationship between retinal nerve layer thickness and corpus callosum atrophy in MRI with memory impairment in patients with multiple sclerosis

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Abstract

Introduction: Multiple sclerosis (MS) is a chronic neurological disease in which demyelination and loss of axons lead to disruption of communication between neurons in the central nervous system. Cognitive impairment occurs in a significant proportion of patients with MS. Therefore, the aim of this study was to investigate the relationship between retinal nerve fiber layer (RNFL) thickness and corpus callosum atrophy in magnetic resonance imaging with memory disorders in patients with MS. Methods: This descriptive analytical study was performed on patients with a diagnosis of relapsing-remitting multiple sclerosis referred to the clinic of Ali Ibn Abi Talib Hospital in Zahedan, Iran. An information form that includes a Mini–Mental State Examination was first prepared, by which the patient’s memory impairment is measured. After recording the data, the data were collected using an information form and finally analyzed by SPSS software version 22 using an independent t-test. Results: In this study, 80 patients with MS primary progressive multiple sclerosis were included in the study, of which 53 were female and 27 were male. The mean age of patients was 45.1 ± 5.9 years, which did not show a statistically significant difference (P = 0.536). The mean RNFL thickness in patients with memory impairment was significantly lower than that in patients without memory impairment. The mean corpus callosum thickness was found to be significantly lower in patients with memory impairment than in patients without memory impairment. Conclusion: All in all, the results of this study showed that the thickness of RNFL and the corpus callosum in patients with memory impairment was significantly lower than that in patients without memory impairment.

Keywords: Corpus callosum, memory impairment, multiple sclerosis, RNFL thickness

Introduction

Multiple sclerosis (MS) is an inflammatory demyelinating/autoimmune disease of the central nervous system in which the immune system attacks the protective sheath, leading to a
wide range of signs and symptoms. MS is the most common auto-immune disease of the central nervous system that affects young people and women. Researchers believe that following chronic inflammation, the blood-brain barrier loses its permeability and allows the body’s defense cells to enter the brain tissue. Under these conditions, the process of damage to the myelin sheath begins in susceptible individuals who have self-reactive cells or anti-myelin antibodies in their body, causing a wide range of neurological symptoms. The most common age for onset of the disease is 20 to 40 years. Women are twice as likely as men to develop the disease. This disease includes a heterogeneous group of symptoms and findings. MS can present with a variety of symptoms, including ocular symptoms (optic neuritis, inter-nuclear ophthalmoplegia, and nystagmus); peripheral sensory symptoms (paraesthesia, dizziness balance disorders, movement disorders); gastrointestinal and urinary disorders; and depression, seizures, and cognitive disorders. Expanded Disability Status Score (EDSS) is a measure of severity of the disease. It is very difficult to diagnose the disease, and only the symptoms can determine the disease. Optical coherence tomography (OCT) or cross-sectional radiography is able to measure the thickness of the back layer of the eye. This scan can be capable of measuring the thickness of nerve fibers inside the retina. These nerve fibers do not have a myelin sheath and may therefore be able to show the earliest signs of MS damage. During MS development, nerve conduction is severely slowed in areas without myelin nerves because of destruction of myelin sheaths.

Magnetic resonance imaging (MRI) images can usually show myelin damage to the brain tissue, but these images are perfectly normal in some MS patients and show no problems or deficiencies. MRI imaging shows the size, distribution, and number of lesions with plaques on the brain and sometimes the spinal cord. Progressive depletion of the brain and spinal cord tissue appears to begin at the onset of the disease. This possibility is supported by recent reports of an increased cerebral ventricular size and a decreased corpus callosum area and brain width between 1 and 2 years from onset in MS patients with recurrence.

This descriptive and analytical study was performed on patients with a diagnosis of relapsing–remitting multiple sclerosis (RRMS) referred to the clinic of Ali Ibn Abi Talib Hospital in Zahedan, Iran. Patients with inclusion and exclusion criteria were included in the study.

Inclusion criteria
All patients with definite diagnosis of RRMS without past history of optic neuritis according to history, medical records, previous imaging and neurologic examinations, single-eye patients, and evidence of ophthalmologic diseases such as glaucoma.

Exclusion criteria included: History or evidence of optic neuritis, history of trauma associated with loss of consciousness, drug abuse, and sedative or anticholinergic use.

Sample size
According to Grazioli et al., the sample size was calculated at 95% confidence level based on the thickness of the retinal neural layer. Therefore, 71 patients were calculated using the following formula. Finally, the sample size was considered to be 80 patients because of the sample dropouts.

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N = \left( \frac{Z_{1-\alpha}}{d} \right)^2 \times S^2
\]

Procedure
An information form that includes a Mini–Mental State Examination (MMSE) was first prepared, by which the patient’s memory impairment is measured. This form also contains information such as age, sex, duration of disease, retinal nerve fiber layer (RNFL) thickness obtained by OCT in both eyes, and corpus callosum thickness obtained by 1.5 tesla MRI.

The MMSE is a 30-point questionnaire, consisting of three items of five-point questions, three items of three-point questions, one item of two-point questions, and four items of one-point question. Its five-point items include orientation to time and place and serial sevens. Its three-point items include three-step command (get up, walk, sit), recent memory, and instant memory. Its two-point item is calling two objects, with each object containing a point. Its one-point items include reading, writing, repetition, and drawing a certain symbol.

The minimum score for patients with higher education is 29, followed by secondary education (27), primary education (25), and illiterate (19). The patient was considered to have a memory impairment if the score was less than the required minimum score.

Data analysis
Descriptive statistics methods, determination of central indices and dispersion, tables, frequency distribution, graphs, analytical statistics, Pearson correlation test, and independent t-test were
used to analyze the data. Data analysis was performed using SPSSS software version 22 at 95% confidence level.

**Ethical considerations**

A letter of introduction and a written letter of intent were obtained from the relevant authorities. The information of all patients remained confidential. In all stages of the research, all declarations of Helsinki and ethics research committees of the University of Medical Sciences were considered.

**Results**

In this study, 80 patients with MS primary progressive multiple sclerosis (PPMS) were included in the study, of which 53 were female (66.25%) and 27 (33.75%) were male. The mean age of patients was 45.1 ± 5.9 years, which did not show a statistically significant difference (P = 0.536). The mean thickness of the RNFL in MS patients was assessed. The mean thickness of RNFL in the left and right eyes was 85 ± 3.2 and 85.9 ± 3.3 µm, respectively. Table 1 shows the average thickness of the corpus callosum in patients.

In this study, the frequency of memory impairment in MS patients was determined to be 42.5% [Table 2]. The normality of the data was assessed using Kolmogorov–Smirnov test, by which the data distribution was found to be normal (P > 0.05).

The relationship between RNFL and the rate of memory impairment in MS patients is shown in Table 1. According to the independent t-test, the mean RNFL thickness in patients with memory impairment was significantly lower than that in patients without memory impairment. The relationship of corpus callosum thickness with the degree of memory impairment in MS patients was investigated in the present study [Table 3]. As shown by the independent t-test, the mean corpus callosum thickness was significantly lower in patients with memory impairment than in patients without memory impairment.

**Discussion**

MS is a primary disease of the central nervous system that has different clinical manifestations. Although the main lesion in MS is myelin nerve involvement, axonal degeneration is also important in the early stages of the disease. Involvement of the visual system in MS is in the form of optic neuritis, so central nervous system axonal degeneration can be observed through the eye examination. Therefore, the aim of this study was to determine the relationship between RNFL thickness and corpus callosum atrophy on MRI with memory impairment in patients who suffered from MS.

In this study, 80 patients with PPMS MS were studied, of which 53 were female (66.25%) and 27 were male. The mean age of patients was found to be 45.1 ± 5.9 years. In the present study, the prevalence of memory impairment in MS patients was found to be approximately 42.5%. The results also showed that the mean RNFL thickness and mean corpus callosum thickness in patients with memory impairment were significantly lower than those in patients without memory impairment. The results of this study are consistent with other studies conducted in this field. In 2015, Ashたり et al. studied 100 MS patients in Isfahan to determine the relationship between RNFL and MRI findings at the macula and head of the optic nerve and Wechsler Adult Intelligence Scale-Revised (WAIS-R). They reported that the mean RNFL of the macular area in these patients was 250.5 ± 15.1 µm and its thickness in the optic nerve head was 92.5 ± 10.2 µm. In the afore-mentioned study, there was only a positive and significant relationship between the mean RNFL thickness at the macula and verbal IQ and full IQ; additionally, a significant relationship was found between the rain atrophy and verbal IQ.

Another study conducted by Danko Coric et al. (2017) in the Netherlands on 217 patients with MS and 59 healthy individuals reported that the rate of cognitive impairment in patients with MS was significantly higher than that in the control group. The rate of cognitive impairment was not statistically significant between MS patients with and without a history of optic neuritis. In this study, the mean thickness of RNFL in the peripapillary retinal nerve fiber layer (pRNFL) in MS patients was significantly lower than that of healthy individuals in the
control group (83.16 ± 11.18 versus 91.67 ± 6.82). Also, pRNFL in patients without a history of optic neuritis was found to be significantly higher than that in patients with a history of optic neuritis, and the mean pRNFL thickness in patients with cognitive impairment was significantly lower than that in patients without cognitive impairment.\[18\]

Another study by Yildiz et al. (2014) on 44 patients with MS in Switzerland reported that 39% of patients had cognitive impairment. In this study, the overall mean annualized corpus callosum index (aCCI) change was −0.72% ± 0.96%. The rate of aCCI reduction was significantly higher in patients with cognitive impairment than in patients without cognitive impairment. Multi-variate analysis demonstrated that corpus callosum atrophy was an independent predictor of cognitive impairment and the progression of atrophy was also associated with the development of cognitive dysfunction in MS patients.\[19\]

In another study conducted by Papathanasiou et al. (2017) on 30 patients with secondary progressive MS, the frequency of cognitive impairment in these patients was 80%. In this study, corpus callosum level was associated with cognitive flexibility, processing speed, composite memory, executive functions, psychomotor speed, and reaction time. Corpus callosum area was the most sensitive MRI marker for memory and processing speed.

**Conclusion**

The frequency of memory impairment in patients with MS was found to be 43%, and the RNFL thickness and corpus callosum thickness in patients with memory impairment were significantly lower than those in patients without memory impairment.

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**Conflicts of interest**

There are no conflicts of interest.

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