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Research Paper

Investigating the MRI Lesions and Their Relationship With Cognition Condition for Multiple Sclerosis

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ABSTRACT

Background and Aim: Multiple sclerosis (MS) is a common inflammatory disease affecting the central nervous system, causing demyelination and axon loss. Cognitive impairment is also prevalent in patients. This study aims to measure magnetic resonance imaging (MRI) findings and their relation to cognitive impairments in MS patients.

Materials and Methods: This cross-sectional analytical study was conducted on 50 patients with a definite diagnosis of MS at Firoozgar Hospital in Tehran Province, Iran, from 2019 to 2021. MRI, complete neurological and psychological examinations, and information documented in the records were used to prepare a complete list of clinical, neurological, and psychological manifestations. The severity of these symptoms was assessed, and patients were scored according to the expanded disability status scale (EDSS), cholinergic pathways hyperintensities scale (CHIPS), and brief international cognitive assessment for multiple sclerosis (BICAMS) criteria.

Results: This study included 36 women and 14 men with a mean age of 34.14±9.4 years. Relapse and remission were observed in 70% of patients. CHIPS score had a significant relationship with spinal symptoms. Also, the BICAMS score of patients showed a significant relationship with limbic involvement in MRI. The third ventricular diameter and CHIPS score were positively correlated with the BICAMS score. Patients' EDSS score had a significant relationship with the symbol digit modalities test (SDMT) score.

Conclusion: In this study, a significant relationship is observed between the size of the third ventricle and the CHIPS score with decreased cognitive function in MS patients. Therefore, MRI can be used to suspect cognitive disorders in MS patients.

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Introduction

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system, causing demyelination and axon loss. This disease appears as focal and multifocal disorders of the brain, spinal cord, and optic nerve, of which sensory and motor symptoms are the most common. However, cognitive impairments are also relatively high due to brain changes in these patients [1-3]. Cognitive impairment is common in MS patients with a range of 8%-96%. It occurs early in the disease and worsens as it progresses. Self-efficacy plays a significant role in cognitive components, such as memory, processing speed, attention, executive functions, fluency, and learning. Cognitive impairment is a strong predictor of disease progression, including secondary progressive MS, depression, disability accumulation, poor sleep quality, unemployment, and low quality of life [2, 4, 5]. Cognitive disorders in MS patients are reported differently due to differences in disease subtypes and the use of different psychological tests. Neuropsychological tests can be affected by physical disability, while magnetic resonance imaging (MRI) is consistent and associated with cognitive disorders. Reduction of brain volume or specific brain lesions is also associated with cognitive disturbances [4, 6-10]. MRI is not widely used to determine cognitive disorders in MS patients due to its high cost. Instead, different Partial thromboplastin time (PTTs), including brief International cognitive assessment for multiple sclerosis (BICAMS) criteria, are used. BICAMS is an international initiative for cognitive assessment in MS patients. BECk is a psychometric test to evaluate depression severity [11, 12]. The prevalence of MS is on the rise worldwide, particularly among young adults who are active and productive members of society. The cause of the disease is uncertain, but genetics may play a role. MS can lead to disability, cognitive inactivity, fatigue, and mood disorders. MRI has proven to be an effective tool to identify neurodegenerative diseases but is underutilized in MS studies. A study using MRI can provide reliable information about the imaging characteristics of MS patients, leading to easier and faster diagnosis of the disease. This study can also determine the relationship between preliminary findings and MS prognosis in Iranian patients with cognitive disorders. This study was conducted to measure MRI and its relevance in MS patients with various cognitive disorders.

Material and Methods

This cross-sectional analytical study was conducted on 50 patients with a definite diagnosis of MS based on McDonald's criteria who were included in the study in Firoozgar Hospital, Tehran Province, Iran during 2019 and 2021. At the beginning of the study, based on the prepared checklist, personal information and clinical and behavioral characteristics of MS patients were referred to the neurology clinic of Firoozgar Hospital for follow-up and the cognitive and mood symptoms were collected. In the second part, a MRI was performed with the full consent of the patient to cooperate in this project and their information, including the report of the results of the patient's personal information, was added. Then, through a complete neurological and psychological examination and the information recorded in their records, a complete list of clinical, neurological, and psychological manifestations and the severity of these symptoms were prepared and the patients were scored according to the expanded disability status scale (EDSS), cholinergic pathways hyperintensities scale (CHIPS) and BICAMS criteria. After collecting all the data, the data were encoded and analyzed using SPSS software, version 22. To avoid loss to follow-up, all participants were taken from landline and mobile phone numbers and coordinated with participants to complete the information.

To calculate the CHIPS, anatomic major landmarks are used on four slices in the axial plan on fluid-attenuated inversion recovery (FLAIR) image according to the specific table (Figure 1). EDSS score is used to quantify the severity of inability due to MS. The test to measure BICAMS score consists of 3 subtests. The first test is the symbol digit modalities test (SDMT), the second test is the California verbal learning test (CVLT) and the third test is the brief visuospatial memory test (BVMT). This test was performed by an experienced psychologist from all participants and the results were reported.

Results

In this study, 14 men and 36 women participated. The Mean±SD age of 50 participants was 34.14±9.4 years. Table 1 shows different types of MS and regions of the brain involved in MRI in study participants. The Mean±SD duration of the disease was 5.2±4.2 years. Regarding the frequency of symptoms in the primary visit, the prevalence of sensory symptoms at the beginning of the visit was higher than other symptoms. Spinal symptoms were the least prevalent among participants (Figure 2).

Table 1. Type of MS and involvement of brain regions shown on MRI in study participants

Variables		No. (%)
Type of MS	RRMS	35(70)
	PPMS	3(6)
	SPMS	12(24)
Involvement of brain regions	Corpus callosum	34(68)
	Limbic system	22(44)
	Frontal subcortical	40(80)

Abbreviations: RRMS: Relapsing-remitting multiple sclerosis; PPMS: Primary progressive multiple sclerosis; SPMS: Secondary progressive multiple sclerosis; MS: Multiple sclerosis.

Table 2. Mean score of BICAMS in participants

BICAMS	Mean±SD
CVLT	46.3±11.9
BVMT	20.08±10.6
SDMT	37.2±14.3
Total	0.51±0.5

Abbreviations: SDMT: Symbol digit modalities test; CVLT: California verbal learning test; BVMT: Brief visuospatial memory test.

About three-quarters of the participants in the study mentioned the disease duration for >12 months.

The Mean±SD score of CHIPS was 30.34±16.4 the Mean±SD score of BICAMS was 0.51±0.5 (Table 2).

The relationship between qualitative variables and the gender of the participants was investigated using the chi-square test. Table 3 presents the results of this study. T-test was used to evaluate the difference between qualitative variables and age. In this evaluation, only the presence of spinal and ocular symptoms was significantly different from age (Table 3).

One-way analysis of variance (ANOVA) was used to evaluate the differences between the groups of MS form with quantitative variables. In this study, a significant relationship was observed between the form of MS and the EDSS and third ventricular diameter. None of the

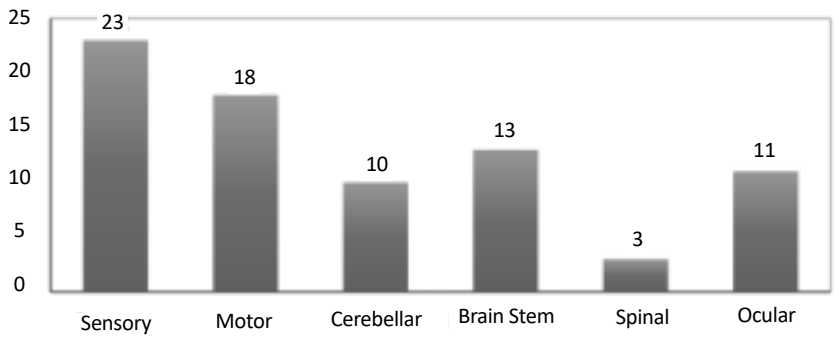

Figure 2. Status of participants in the study in respect of symptoms at the time of referral

Table 3. Comparison of qualitative variables based on gender and age of participants

Across Age	P	Across Gender	P
Sensory symptoms	0.128	Sensory symptoms	0.363
Motor symptoms	0.131	Motor symptoms	0.529
Cerebellar symptoms	0.647	Cerebellar symptoms	0.529
Brain Stem symptoms	0.383	Brain Stem symptoms	0.329
Spinal symptoms	0.028	Spinal symptoms	0.832
Ocular symptoms	0.030	Ocular symptoms	0.114
Corpus callosum involvement	0.282	Corpus callosum involvement	0.094
Limbic involvement	0.549	Limbic involvement	0.594
Frontal subcortical involvement	0.544	Frontal subcortical involvement	0.156
MS involvement	0.950	MS involvement	0.950

MS: Multiple sclerosis.

variables of MS form had a significant relationship with qualitative variables (Table 4).

T-test was used to evaluate the differences in MS manifestations at baseline with quantitative variables. It was shown that the duration of the disease has a significant relationship with spinal and brainstem symptoms at the onset. Also, age, CHIPS, and CVLT showed a significant relationship with spinal symptoms (Table 5).

T-test was used to evaluate the difference between MS involvement in MRI with quantitative variables. These studies showed that the third ventricular diameter was significantly associated with limbic and frontal subcortical involvement. Also, the CHIPS score showed a significant relationship with the involvement of all three regions of the corpus callosum, limbic, and frontal subcortical. However, the BICAMS score was significantly associated with limbic involvement (Table 6).

Table 4. Comparison of the MS type with quantitative and qualitative variables in participants

Qualitative Variables	P	Quantitative Variables	P	F
Sensory symptoms	0.216	Age (y)	0.877	0.131
Cerebellar symptoms	0.323	Third ventricular diameter	0.012	4.899
Motor symptoms	0.425	Disease duration	0.254	1.411
Brain Stem symptoms	0.499	CHIPS	0.522	0.659
Spinal symptoms	0.505	EDSS	0.019	4.333
Ocular symptoms	0.803	BICAMS	0.449	0.814
Corpus callosum involvement	0.381	CVLT	0.376	1.000
Limbic involvement	0.185	BVMT	0.821	0.198
Frontal subcortical involvement	0.812	SDMT	0.422	0.878

Abbreviations: EDSS: Expanded disability status scale; CHIPS: Cholinergic pathways hyperintensities scale; SDMT: Symbol digit modalities test; CVLT: California verbal learning test; BVMT: Brief visuospatial memory test; BICAMS: Brief international cognitive assessment for multiple sclerosis.

Table 5. Comparison of MS manifestations at baseline with quantitative variables in participants

Variables	Ocular	Spinal	Symptoms			Sensory
			Brain Stem	Cerebellar	Motor	
Age (y)	0.030	0.028	0.383	0.647	0.131	0.128
Disease duration (y)	0.381	0.001<	0.029	0.954	0.491	0.693
Third ventricular diameter (mm)	0.310	0.984	0.086	0.354	0.635	0.978
CHIPS	0.785	0.020	0.186	0.308	0.914	0.273
EDSS	0.696	0.074	0.584	0.710	0.163	0.952
BICAMS	0.409	0.070	0.899	0.184	0.384	0.787
CVLT	0.854	0.027	0.275	0.461	0.089	0.443
BVMT	0.373	0.141	0.717	0.185	0.501	0.669
SDMT	0.826	0.140	0.581	0.620	0.108	0.343

Abbreviations: EDSS: Expanded disability status scale; CHIPS: Cholinergic pathways hyperintensities scale; SDMT: Symbol digit modalities test; CVLT: California verbal learning test; BVMT: Brief visuospatial memory test; BICAMS: Brief international cognitive assessment for multiple sclerosis.

Discussion

MS is a disease that causes inflammation and damage to the central nervous system, resulting in a wide range of neurological symptoms. Cognitive symptoms are also common, affecting 40% to 70% of patients and impacting information processing speed, executive functions, and spatial visual abilities. This study aims to explore the correlation between lesions detected on MRI scans and cognitive impairment in MS patients. The BICAMS

Table 6. Comparison of MS involvement in MRI with quantitative variables in participants

Variables	Involvement		
	Frontalsubcortical	Limbic	Corpus Callosum
Age (y)	0.544	0.549	0.282
Disease duration (y)	0.631	0.249	0.569
Third ventricular diameter (mm)	0.018	0.008	0.119
CHIPS	0.001<	0.001<	0.006
EDSS	0.120	0.395	0.555
BICAMS	0.148	0.010	0.051
CVLT	0.146	0.605	0.601
BVMT	0.115	0.460	0.949
SDMT	0.502	0.235	0.324

Abbreviations: EDSS: Expanded disability status scale; CHIPS: Cholinergic pathways hyperintensities scale; SDMT: Symbol digit modalities test; CVLT: California verbal learning test; BVMT: Brief visuospatial memory test; BICAMS: Brief international cognitive assessment for multiple sclerosis.

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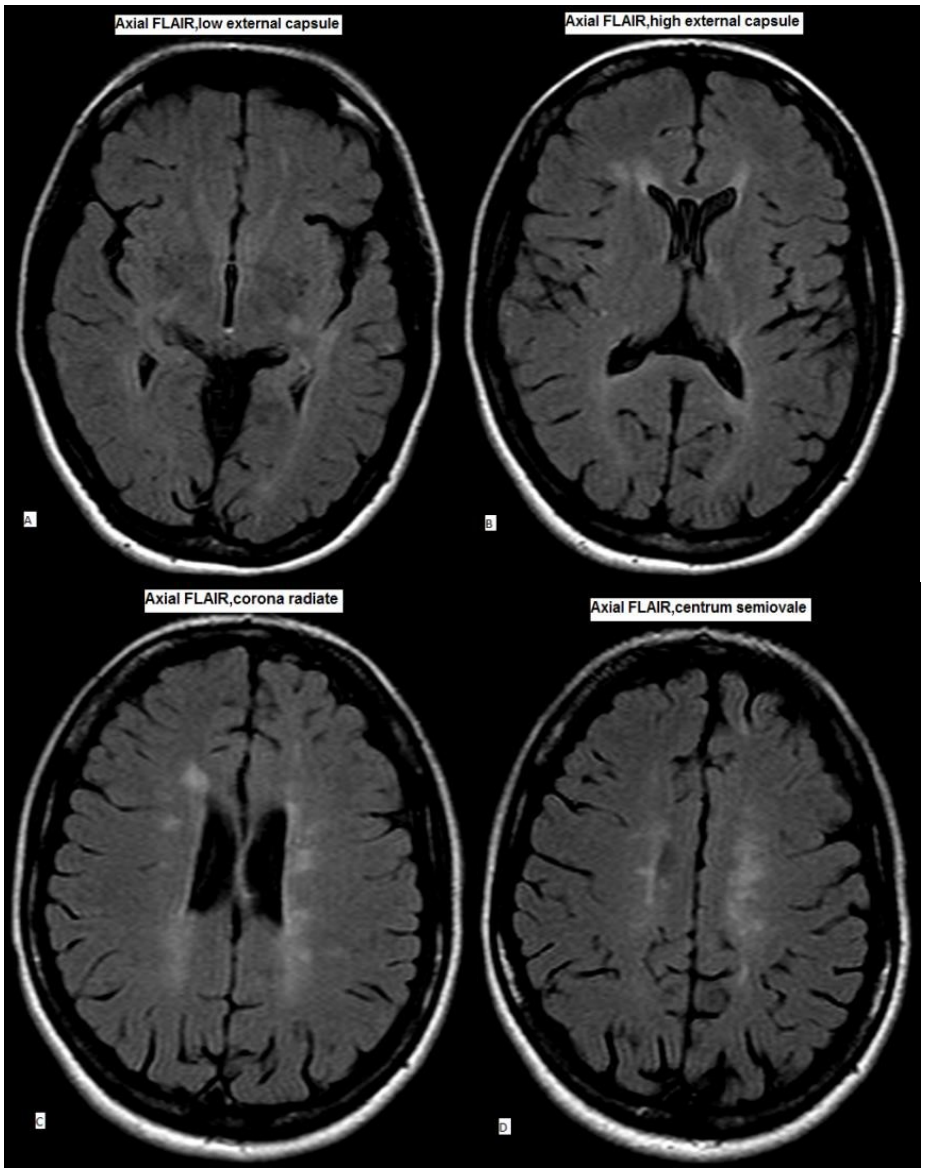

Figure 1. CHIPS scoring illustrated on a FLAIR sequence MR images

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A) Low external capsule, B) High external capsule, C) Corona radiate, D) Centrum semiovale

Note: To measure the CHIPS ratings, major anatomical landmarks on four index slices in the axial plane were selected on FLAIR sequence. Each region was weighted to account for the decreasing concentration of cholinergic fibers as they spread out from the nucleus basalis to neocortical regions (maximum weight of 4 for the first slice; minimal weight of 1 for the fourth slice).

questionnaire was utilized to evaluate patients' cognitive abilities. In this study, 50 patients with MS with a mean age of 34.14 years participated and 70% of the patients had relapsing and remitting MS. MRI scans showed subcortical frontal involvement of 80% of the patients, while 68% of the patients showed involvement in the corpus callosum and 44% in the limbic region. Statistical analysis showed that gender did not play a role in the early symptoms of the disease, but with increasing age, the initial spinal and ocular symptoms increased. The CHIPS score had a significant relationship with spinal symptoms, and the BICAMS score of patients with limbic involvement in MRI showed a significant relationship. Additionally, a negative correlation was observed between the third ventricular diameter and patients' CHIPS score with the BICAMS score. The patients' EDSS score was significantly related to their SDMT score. According to the analysis, the degree of disability of the patients measured by either the EDSS score or SDMT score showed a significant relationship. Artemiadis et al. conducted a study in 2018 to investigate the correlation between cognitive function and

MRI results in individuals with MS. The study revealed that a reduction in cognitive function was significantly linked to third ventricular diameter and corpus callosum involvement. Furthermore, third ventricular diameter had a significant relationship with BVMT score, while corpus callosum involvement was related to SDMT and CVLT [11]. In our study, a significant relationship was observed between the third ventricular diameter and patients' cognitive function score. However, corpus callosum involvement was not significantly associated with BICAMS or any of its subtests. Additionally, we found no independent relationship between the third ventricular diameter and BICAMS subtests in this study. It is worth noting that all patients in the report by Artemiadis et al. [13] had relapsing-remitting MS, while our study sample included other types of MS, which may account for the difference in results. Papathanasiou et al. [13] conducted a study in 2015 that involved examining 50 RRMS patients. The results of this study were consistent with those of Artemiadis et al. [13] indicating a correlation between cognitive impairment and third ventricular diameter as well as corpus callosum involvement. As a result, it can be inferred that cognitive impairment may not be associated with corpus callosum involvement in patients with different forms of MS. Sánchez et al. reported that patients with speech impairments, reduced information processing speed, and attention deficits have a larger third ventricle. The study also found that patients with corpus callosum involvement on MRI were associated with impaired visual memory [14]. In our study, we did not examine the external manifestations of cognitive impairment. However, we found a significant relationship between an increase in third ventricular size and a decrease in patients' cognitive function. Müller et al. conducted a cross-sectional study in 2013 on patients in the early stages of MS. They reported that the diameter of the third ventricle was associated with decreased cognitive function in MS patients. Additionally, after correcting for the effects of fatigue on this decrease in cognitive function, the size of the third ventricle still showed a significant relationship [15]. According to the literature review, no study was found in the field of using the CHIPS score to predict cognitive disorders in MS patients. This study showed that this criterion is correlated with the rate of cognitive dysfunction in patients. However, further studies are needed to prove this theory and compare the results with a control group before this criterion can be widely used.

Conclusion

In this study, it was stated that the size of the third ventricle and the CHIPS score were significantly associated with a decrease in patients' cognitive function. Therefore, MRI can be used to detect cognitive impairment in MS patients.

Limitations and suggestions

One limitation of this study is the lack of a control group for comparison. It is suggested that further studies utilize a control group to investigate the effect of CHIPS scores on the diagnosis of cognitive disorders. Additionally, this study did not compare each type of MS or different types of diseases. For future studies, it is recommended to include an equal and sufficient number of samples from each MS group.

Ethical Considerations

Compliance with ethical guidelines

This study has been approved by the Ethics Committee of the Iran University of Medical Sciences (Code: IR.IUMS.FMD.REC.1398.226).

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Authors' contributions

All authors participated equally in the design, execution, and writing of all parts of this research.

Conflict of interest

The authors declared no conflict of interest.

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