



The relationship between quantitative magnetic resonance imaging markers and clinical/cognitive assessments in patients with multiple sclerosis: A cross-sectional study

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Keywords

Disability; Multiple Sclerosis; Cognitive Assessment; Quantitative Magnetic Resonance Imaging Markers; Plaque Location

impact of MRI markers on disability, clinical status, and cognitive function.

Abstract

Background: This study examines the relationship between quantitative magnetic resonance imaging (MRI) markers and clinical/cognitive performance in patients with multiple sclerosis (MS), exploring the

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Methods: This cross-sectional study recruited patients with MS from the MS registry center of Rafsanjan University of Medical Sciences, Rafsanjan, Iran. Informed consent was obtained from all participants (8 men, 57 women). Patients with MS underwent neuropsychological and clinical assessments using a word-pair learning task, the Wisconsin Card Sorting test (WCST), Tower of London test (TOL), Paced Auditory Serial Addition Test (PASAT), Multiple Sclerosis Functional Composite (MSFC), and the Expanded Disability Status Scale (EDSS). MRI markers were assessed by the neurologist and radiologist. Statistical significance was set at $P < 0.05$.

Results: Patients with plaques in the basal ganglia and thalamus had significantly different MSFC ($P = 0.038$) and PASAT ($P = 0.010$) scores, while higher EDSS scores correlated with T2-weighted-fluid-attenuated inversion recovery (T2-FLAIR) hyper-intense plaques ($P = 0.025$). T1 black hole plaques were associated with increased depression ($P = 0.015$). WCST scores were significantly higher in patients with infratentorial plaques ($P = 0.006$) and those with T1 black hole lesions ($P < 0.05$). Total plaque volume positively correlated with EDSS score ($r = 0.386$, $P = 0.002$) and word-pair learning ($r = 0.254$, $P = 0.045$), and negatively correlated with PASAT scores ($r = -0.299$, $P = 0.017$). Enhanced plaques correlated positively with TOL performance ($r = 0.319$, $P = 0.010$).

Conclusion: Memory decline and increased disability in patients with MS are associated with brain volume loss, increased plaque volume, and plaque location in the infratentorial region, basal ganglia, and thalamus. Enhanced plaques or T1 black hole lesions also contribute to cognitive impairment.

Introduction

Multiple sclerosis (MS) is characterized as an inflammatory disease and destruction of myelin with the formation of lesions or plaques in the central nervous system (CNS), including the brain and spinal cord.¹ The disease is considered a permanent or progressive disability because it impacts the white and grey matter of the CNS.² Patients have a wide array of symptoms, including psychiatric, motor, and cognitive symptomatology.^{3,4} The Expanded Disability Status Scale (EDSS) is a MS quantifying disability method.⁵ However, it has some shortcomings in the measurement of upper organ disability and cognition. The Multiple Sclerosis Functional Composite (MSFC) is another disability measurement method with more emphasis on limb function and mental processing speed.⁶

The prevalence of cognitive disorders in

patients with MS is estimated from 43% to 70%.^{7,8} MS affects numerous cognition sites and it can occur during the course of the disease.⁷ Information processing speed (IPS), attention, executive function, working memory, and long-term memory are the most common cognitive deficits in patients with MS.^{7,9} The results of two studies have presented the association between brain lesion loads on T2-weighted images and impaired cognitive functioning in patients with MS.^{10,11} The results of other studies of MS utilizing neuroimaging described the relation between cognitive impairments and various measures of cerebral hemispheres, including T2 lesion burden, cerebral atrophy, third ventricle width, corpus callosum size, and cortical lesions.¹²⁻¹⁵ Brain atrophy has been found in primary progressive MS (PPMS) and secondary progressive MS (SPMS).^{16,17} The accumulation of hypo-intense lesions (black holes) may correlate with disease progression and disability.¹⁸⁻²⁰ Recent studies have reported that normalized total and cortical volume values were associated with depression and fatigue, disease duration, and disability in patients with MS.^{13,19} The results of one study showed that cerebellar grey matter damage and disruption of its connections contributed to cognitive dysfunction and physical disability in MS.²¹ A systematic review and meta-analysis presented that cortical lesion volume, brain volume, grey matter volume, and spinal cord magnetic resonance imaging (MRI) measurements might be reliable indicators of disability in patients with MS.²² Quantitative MRI markers at MS onset, specifically paramagnetic rim lesions and spinal cord lesions linked to physical disability and cortical lesions linked to cognitive impairment, can refine patient profiling and inform treatment decisions.²³

Previous MRI studies examining disability in MS have been limited by focusing on specific brain regions, lesions, and EDSS.^{24,25} A key limitation is the lack of separate analyses correlating diverse quantitative MRI markers with clinical assessments.²⁶ While prior research has established correlations between various brain and spinal cord regions with alternative disability measures like the Timed 25-Foot Walk (T25FW), Nine-Hole Peg Test (9-HPT), and MSFC, these associations with quantitative MRI markers remain largely unexplored.^{27,28} This study aims to comprehensively investigate the relationship between quantitative MRI markers and a broader range of clinical and cognitive assessments in patients with MS.

Materials and Methods

Participants: The patients were selected through the MS registry center of Rafsanjan University of Medical Sciences, Rafsanjan, Iran, from April to July 2024. The total number of patients in the registry was 250. Sampling was conducted by calling patients and obtaining their consent. Informed consents were collected from all patients (8 men and 57 women aged 18 to 50 years old) recruited before they participated in the study. The main reason for including such a high percentage of female patients was the significant preponderance of female patients with MS in comparison to male patients in our city (The ratio of female MS patients to male MS patients is more than 6 times higher), as well as the more agreement of female patients to be recruited in the study. Patients diagnosed with MS according to the revised McDonald diagnostic criteria as having relapsing-remitting MS (RRMS) or SPMS were admitted to this study.²⁹ A trained examiner administered cognitive tests and disability assessments over two days, after which the patient underwent an MRI. The radiologist and neurologist measured the MRI indices. Their disability status was evaluated with the EDSS scale (eight functional systems ranging from 0 to 10). Higher scores indicate greater disability.⁵ The MSFC comprises the average of the z-scores on the T25FW, the 9-HPT, and the Paced Auditory Serial Addition Test (PASAT) with a 3-second interstimulus interval. Higher scores indicate a lesser degree of disability.³⁰ The Ethics Committee

of Rafsanjan University of Medical Sciences approved the protocol of the study (ethical code: IR.RUMS.REC.1401.137).

Excluding criteria were: (a) comorbid clinical conditions other than MS affecting the CNS, (b) physical or cognitive impeditive disabilities secondary to conditions other than MS, such as drugs or toxins, (c) an impeditive psychiatric illness, and (d) in the last six weeks, an MS attack treated with corticosteroids at high doses, or untreated.

MRI measurement and image analysis: 1.5 Tesla (1.5T) Siemens scanner (Essenza, Germany) carried out MRI experiments in the Ali Ibn Abitaleb Hospital in Rafsanjan City, located in the south of Iran. The imaging protocol comprised standard precontrast axial T2-weighted, axial T1-weighted, sagittal fluid-attenuated inversion recovery (FLAIR), and post-contrast T1-weighted images in three orthogonal planes through 0.1 mmol/kg intravenous (IV) administration of gadolinium. The number of lesions on T2-weighted scans, the total volume of gadolinium-enhancing lesions, volumes of lesions on T2-weighted scans, and brain volume were segmented by the Lesion Segmentation Tool (LST) toolbox version 2.0.15 for statistical parametric mapping (SPM).³¹ From magnetic resonance (MR) images, the typical locations of MS plaques were identified by a radiologist and neurologist, which included: lesions at the basal ganglia and thalamus, the periventricular and juxtacortical areas, the corpus callosum, the callososeptal interface, the infratentorial region, and the cervical cord (Figure 1).

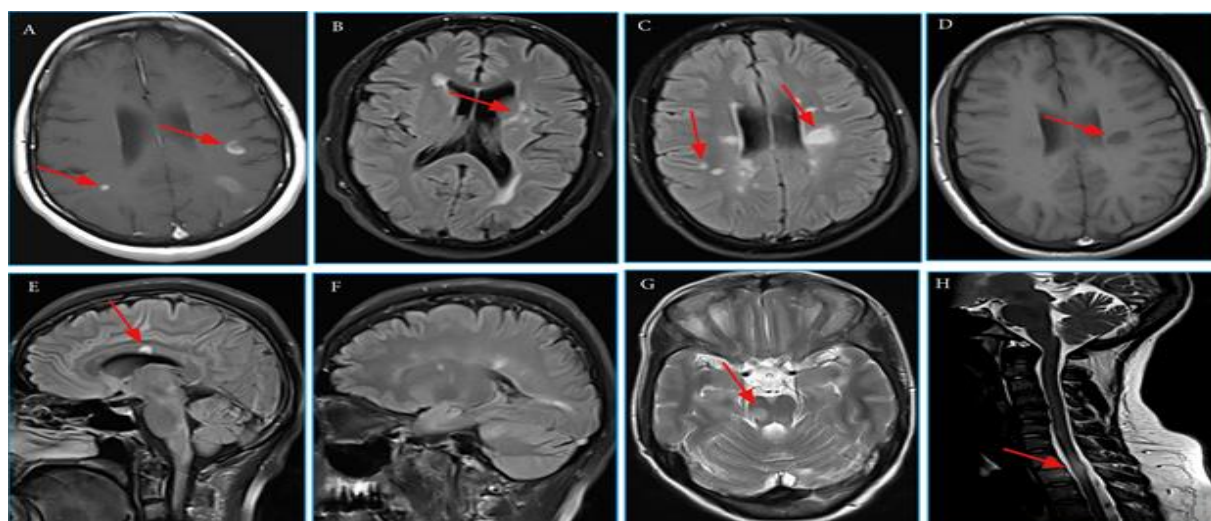


Figure 1. Typical locations of multiple sclerosis (MS) plaques. A) Enhanced plaques; B) Lesions at the basal ganglia and thalamus; C) Lesions at the periventricular and juxtacortical areas; D) Black hole; E) Involvement of the corpus callosum; F) Lesions at the callososeptal interface; G) Lesions at the infratentorial region; H) Lesion in the cervical cord

Procedures and evaluation tools: A trained assistant using the following tests conducted cognitive and neuropsychological assessments (all tests that have been evaluated for validity and reliability at Sina Institute of Cognitive Behavioral Sciences, Tehran, Iran):

(I) Word-pair learning task to measure verbal learning and working memory: There are seven pairs of unrelated words to read for participants, and then the participants must pronounce the pair of the first word. This test is repeated until the person can answer all pairs correctly. Higher scores indicate a memory performance impairment.³² The validity and reliability of this questionnaire have also been confirmed in Persian.³³

(II) The Wisconsin Card Sorting Test (WCST) is able to measure attention, working memory, executive functioning, and visual processing. In the present study, six indices were analyzed: 1) the number of categories completed, 2) the number of perseverative errors (PE), 3) the number of non-PE (NPE), 4) the total number of errors (NE), 5) trials to complete the first category (trial 1st), and 6) failure to maintain set (failure).³⁴

(III) The PASAT-3 is utilized to measure IPS and working memory. In this test, the numbers are read to a person in three seconds, and he/she must sum up both numbers. The maximum score is 60.³⁵

(IV) The Tower of London test (TOL) is able to measure planning abilities and problem-solving.³⁶ The patient must solve a series of 12 stages; time and error are measured at each stage. The test demonstrates acceptable construct validity for measuring planning and organization, with a correlation of 0.41 reported against the Porteus Maze test (PMT). Its reliability is established with a reported value of 0.79.³⁷

Depressive symptomatology was detected by the Beck Depression Inventory-Second Edition (BDI-II), a self-report instrument recommended for patients with MS, with 21 items rated on a scale from 0 to 3; the maximum total score was 63.³⁸ The validity and reliability of this questionnaire have also been confirmed in Persian.³⁹

The State-Trait Anxiety Inventory (STAI) was used to measure adult anxiety. It is also used to make a distinction between state anxiety and trait anxiety (feelings of anxiety and depression). The STAI contains 40 questions, which take 10-20 minutes to complete. The test is available in Persian.⁴⁰ The validity and reliability of this questionnaire have also been confirmed in Persian.⁴¹

We assessed fatigue using the Fatigue Severity Scale (FSS) as a self-report questionnaire consisting

of 9 items with a 7-point scale.²⁰ The reliability and validity of this questionnaire were confirmed by Krupp et al. concerning patients with MS.⁴²

Results were presented as mean $\pm$ standard deviation (SD) for numerical data and as number (percent) for categorical variables. The correlation between MRI indices and cognitive or clinical indices in patients with MS was evaluated using Pearson's correlation coefficient (r). The relationship between MRI indices (yes/no) and other factors was evaluated in a dependent t-test. Statistical significance was set at $P \leq 0.05$. The SPSS statistical software (version 15.0, SPSS Inc., Chicago, IL, USA) was used for the statistical analysis.

Results

Demographic results: Sixty-five patients with MS enrolled in this study. Table 1 shows the participants' clinical characteristics and demographic information. Of the 65 patients, 8 (12.3%) were men and 57 (87.7%) were women. The mean and SD of the patients' age was 33.34 ± 8.76 years, and their ages ranged from 18 to 49 years.

We demonstrated the location of plaques in all patients with MS. Figure 1 shows the anatomical localization of plaques. Due to the fact that there were lesions at the periventricular, juxtacortical, corpus callosum, and callososeptal interface areas in all patients, and also, T1 hyper plaque was present in only one patient, they were not mentioned in the results in the tables.

Neuroanatomical and clinical results: Table 2 compares the clinical indices with the characterization and anatomical localization of plaques in patients. According to the results, there was a marked difference in the MSFC score between patients who had a plaque in the basal ganglia and thalamus and those who did not, and the disability was higher in patients with plaque in the basal ganglia and thalamus ($P = 0.038$). Moreover, there was lower disability (EDSS score) in the patient who had T2 FLAIR hyper-intense plaques in the brain ($P = 0.025$).

In addition, there was a significantly higher depression in patients with T1 black hole plaque in the brain compared to those with no plaque ($P = 0.015$). Besides, there was a difference in the state anxiety in patients who had cervical cord plaques and those who did not ($P = 0.046$).

Neuroanatomical and neuropsychological results: Table 3 shows the relationship between neuroanatomical measurements and cognition in patients with MS.

Table 1. Demographic characteristics of the patients with multiple sclerosis (MS) (n = 65)

Characteristics	Value
Age (year) (mean $\pm$ SD)	33.34 $\pm$ 8.76
Median (range)	32.00 (18.00-49.00)
Age (year) [n (%)]	
≤ 30	26 (40.00)
31-40	22 (33.84)
> 40	17 (26.15)
Gender [n (%)]	
Men	8 (12.30)
Women	57 (87.70)
Education [n (%)]	
Elementary	7 (10.76)
Middle school	17 (26.15)
Diploma	28 (43.70)
College	13 (20.00)
Marital status [n (%)]	
Single	12 (18.46)
Married	53 (81.54)
Interval since first symptoms (year) (mean $\pm$ SD)	3.15 $\pm$ 3.73
Median (range)	1.00 (1.00-15.00)
Course of disease [n (%)]	
Relapsing-remitting	46 (70.76)
Secondary-progressive	19 (29.24)
Drug [n (%)]	
Any interferon beta	59 (90.76)
Glatiramer acetate	6 (9.24)
EDSS score* (mean $\pm$ SD)	1.50 $\pm$ 1.31
Median (range)	1.50 (0-3.50)
MSFC# (mean $\pm$ SD)	0.00 $\pm$ 0.76
Median (range)	0.10 (-2.38, 1.25)

*Scores range from 0 to 10, higher scores indicate a greater degree of disability; #Scores of MSFC are expressed as z-score, with higher scores indicating improvement in disability. EDSS: Expanded Disability Status Scale; MSFC: Multiple Sclerosis Functional Composite; SD: Standard deviation

Results showed that the number of trials to complete the first category (trial 1st) in WCST was significantly higher in patients who had plaques in the infratentorial ($P = 0.006$) area. Moreover, the score of PASAT was lower in patients who had plaque in the basal ganglia and thalamus ($P = 0.010$). Patients with T1 black hole lesions had high scores in trial 1st ($P = 0.016$) and low PE score ($P = 0.044$) in WCST, and other WCST indices had no significant differences.

MRI indices and neuropsychological/clinical results: Table 4 shows the correlation between cognitive and clinical measures with MRI indices in patients with MS. A positive correlation was found between the total volume of plaques with EDSS score ($r = 0.386$, $P = 0.002$) and word-pair learning ($r = 0.254$, $P = 0.045$) and a negative correlation with PASAT ($r = -0.299$, $P = 0.017$). Cognitive assessment and MRI measurements

showed a positive correlation between brain volume with PASAT ($r = 0.272$, $P = 0.031$). The total of enhanced plaques in the brain [total Enhanced plaques in the brain (EPB)] showed a correlation with TOL ($r = 0.319$, $P = 0.010$).

Discussion

This study focused on the relationship between the radiological indices with clinical variables and cognitive status in a sample of patients suffering from MS in Rafsanjan City. The main result of this study is that both cognitive and clinical measurements had a correlation with the neuroanatomical measurement of plaque in the brain and MRI indices in patients with MS.

Various studies have presented converging evidence that indicates the role of deep grey matter structures in the pathogenesis of IPS deficiency during MS. Some cross-sectional studies have presented a strong link between thalamic atrophy and PASAT,⁴³⁻⁴⁵ while diffusion tensor imaging and fractional anisotropy (FA) measures have illustrated an inverse correlation between IPS performance and microstructural alterations.^{44,46} Furthermore, there is some evidence claiming that damage to specific corticothalamic tracts is related to the pathology of direct thalamic atrophy, as well as the location of brain white matter lesions.^{46,47} However, only a limited number of studies have investigated the relationship between the anatomical location of the plaques and disability or cognition. Furthermore, we found that the anatomical location of plaques was important in cognition and disability status. Our results also showed that PASAT was affected by the dispersion of plaques in the basal ganglia and thalamus. It is noteworthy that our results showed that in addition to causing memory impairment, the presence of plaque in the basal ganglia and thalamus increased disability in patients and reduced the score of MSFC.

MS can affect all cognitive processes. In this regard, a study in 1991 identified characteristics of psychological impairment in adults with progressive forms of MS as well as in RRMS, including memory and learning, attention, and executive function.⁴⁸ Recently, other studies demonstrated that damage of the cerebellum could be associated with MS-related cognitive dysfunction especially impaired executive functioning⁴⁹ as cerebellar cortex circuits can also play an important role in specific cognitive functions.^{50,51}

Table 2. The relationship between neuroanatomical measurements and clinical indices in patients with multiple sclerosis (MS) (n = 65)

Indices	EDSS (mean ± SD)	P	MSFC (mean ± SD)	P	State anxiety (mean ± SD)	P	Trait anxiety (mean ± SD)	P	FSS (mean ± SD)	P	Depression (mean ± SD)	P
Anatomical localization of plaques												
Infratentorial		0.642		0.690		0.501		0.316		0.237		0.295
Yes	1.54 ± 1.25		0.03 ± 0.65		50.06 ± 13.78		48.73 ± 12.97		39.40 ± 10.36		18.62 ± 11.65	
No	1.34 ± 1.61		-0.11 ± 1.14		47.15 ± 14.11		44.85 ± 9.65		43.54 ± 14.10		14.77 ± 12.14	
Basal ganglia and thalamus		0.224		0.038*		0.862		0.306		0.382		0.139
Yes	1.69 ± 1.34		-0.19 ± 0.62		49.76 ± 14.37		49.47 ± 13.24		39.06 ± 11.16		19.91 ± 11.51	
No	1.29 ± 1.28		0.20 ± 0.86		49.16 ± 13.33		46.29 ± 11.41		41.52 ± 11.30		15.58 ± 11.79	
Cervical cord		0.525		0.880		0.046*		0.148		0.175		0.496
Yes	1.56 ± 1.32		-0.01 ± 0.73		47.46 ± 14.02		46.63 ± 13.04		39.10 ± 10.93		17.25 ± 12.53	
No	1.32 ± 1.36		0.02 ± 0.88		55.18 ± 11.64		51.71 ± 9.79		43.41 ± 11.69		19.53 ± 9.35	
Plaque characterization												
T1 black hole		0.691		0.423		0.517		0.296		0.422		0.015*
Yes	1.54 ± 1.25		-0.03 ± 0.70		49.98 ± 14.16		48.69 ± 12.86		39.72 ± 10.88		19.11 ± 12.09	
No	1.32 ± 1.69		0.17 ± 1.05		47.00 ± 12.01		44.36 ± 9.58		42.73 ± 12.99		11.64 ± 7.67	
T2 FLAIR hyper intense		0.025*		0.552		0.920		0.735		0.240		0.558
Yes	1.44 ± 1.30		0.01 ± 0.77		49.51 ± 13.87		48.05 ± 12.47		40.52 ± 11.15		18.00 ± 11.68	
No	3.25 ± 0.35		-0.32 ± 0.60		48.50 ± 14.85		45.00 ± 14.14		31.00 ± 12.73		13.00 ± 18.39	
Enhanced plaque		0.706		0.788		0.611		0.627		0.244		0.902
Yes	1.43 ± 1.24		0.03 ± 0.64		50.52 ± 13.09		48.85 ± 12.83		38.30 ± 9.59		17.63 ± 11.03	
No	1.55 ± 1.39		-0.02 ± 0.85		48.74 ± 14.37		47.32 ± 12.23		41.61 ± 12.17		18.00 ± 12.39	

*P < 0.05

EDSS: Expanded Disability Status Scale; MSFC: Multiple Sclerosis Functional Composite; FSS: Fatigue Severity Scale; FLAIR: Fluid-attenuated inversion recovery; SD: Standard deviation

Table 3. The relationship between neuroanatomical measurements and cognitive indices in patients with multiple sclerosis (MS) (n = 65)

Indices	Word-pair learning task (mean ± SD)	P	PASAT (mean ± SD)	P	TOL (mean ± SD)	P	WCST indices		
							PE (mean ± SD)	P	Trial 1 st # (mean ± SD)
Anatomical localization of plaques									
Infratentorial		0.510		0.752		0.291		0.808	0.006*
Yes	4.92 ± 3.05		28.02 ± 13.15		30.25 ± 2.80		5.40 ± 3.81		6.44 ± 0.73
No	4.31 ± 2.72		26.69 ± 14.88		29.38 ± 1.66		5.69 ± 3.77		6.08 ± 0.28
Basal ganglia and thalamus		0.372		0.010*		0.666		0.446	0.207
Yes	5.12 ± 3.20		23.74 ± 11.72		29.94 ± 2.79		5.12 ± 3.93		6.47 ± 0.75
No	4.45 ± 2.73		32.16 ± 13.91		30.23 ± 2.47		5.84 ± 3.63		6.26 ± 0.58
Cervical cord		0.955		0.100		0.974		0.114	0.345
Yes	1.56 ± 1.32		26.13 ± 14.05		30.08 ± 2.74		5.02 ± 3.51		6.42 ± 0.71
No	1.32 ± 1.36		32.35 ± 10.38		30.06 ± 2.33		6.71 ± 4.31		6.24 ± 0.56
Plaque characterization									
T1 black hole		0.598		0.149		0.818		0.044*	0.016*
Yes	4.89 ± 3.02		26.67 ± 13.86		30.11 ± 2.76		5.04 ± 3.65		6.43 ± 0.72
No	4.36 ± 2.87		33.09 ± 9.64		29.91 ± 1.92		7.55 ± 3.86		6.09 ± 0.30
T2 FLAIR hyper intense		0.124		0.473		0.296		0.353	0.783
Yes	4.70 ± 2.95		27.97 ± 13.54		30.02 ± 2.64		5.54 ± 3.77		6.37 ± 0.68
No	8.00 ± 2.83		21.00 ± 5.66		32.00 ± 1.41		3.00 ± 4.24		6.50 ± 0.71
Enhanced plaque		0.973		0.453		0.630		0.256	0.125
Yes	4.81 ± 3.01		26.26 ± 12.72		29.89 ± 2.31		4.85 ± 3.21		6.22 ± 0.58
No	4.79 ± 2.99		28.82 ± 13.94		30.21 ± 2.85		5.89 ± 4.12		6.47 ± 0.73

*P < 0.05; #Trials to complete the first category

PASAT: Paced Auditory Serial Addition Test; TOL: Tower of London test; WCST: Wisconsin Card Sorting Test; PE: Perseverative errors; FLAIR: Fluid-attenuated inversion recovery; SD: Standard deviation

Table 4. Correlation (r) between cognitive and clinical measures with magnetic resonance imaging (MRI) indices in patients with multiple sclerosis (MS) (n = 65)

Indices	Brain volume	P	Total VP	P	Total EPB	P	Total EPC	P	Total VEP	P	Total NP	P
EDSS	-0.079	0.540	0.386	0.002*	0.204	0.103	0.157	0.211	-0.081	0.529	-0.058	0.649
MSFC	0.156	0.221	-0.238	0.060	0.135	0.285	0.021	0.867	0.109	0.395	0.032	0.802
State anxiety	0.060	0.639	0.012	0.927	0.001	0.991	0.057	0.654	0.070	0.586	0.081	0.520
Trait anxiety	0.075	0.561	0.101	0.432	0.032	0.797	0.043	0.736	0.075	0.562	0.035	0.780
FSS	0.127	0.321	0.110	0.390	-0.176	0.161	-0.031	0.809	0.020	0.877	-0.134	0.286
Depression	0.038	0.768	0.152	0.234	0.065	0.605	0.072	0.570	0.092	0.471	0.079	0.529
Word-pair learning task	-0.216	0.890	0.254	0.045*	-0.219	0.079	0.039	0.758	-0.048	0.711	0.065	0.607
PASAT	0.272	0.031*	-0.299	0.017*	0.015	0.907	-0.025	0.845	0.070	0.588	-0.241	0.054
TOL	-0.128	0.318	0.234	0.064	0.319	0.010*	0.066	0.603	0.066	0.605	0.105	0.406
WCST, PE	0.085	0.506	-0.058	0.654	-0.173	0.169	-0.179	0.154	0.026	0.840	-0.075	0.555
WCST, trial 1 ^{st#}	-0.091	0.479	0.049	0.701	0.037	0.768	0.107	0.397	-0.033	0.796	-0.033	0.793

*P < 0.05; #Trials to complete the first category

VP: Volume of plaques; EPB: Enhanced plaques in the brain; EPC: Enhanced plaques in the cervical cord; VEP: Volume of enhanced plaques; NP: Number of plaques; EDSS: Expanded Disability Status Scale; MSFC: Multiple Sclerosis Functional Composite; FSS: Fatigue Severity Scale; PASAT: Paced Auditory Serial Addition Test; TOL: Tower of London test; WCST: Wisconsin Card Sorting Test; PE: Perseverative errors

Consistently, posterior lobule atrophy of the cerebellum can be associated with executive functioning impairment in patients with MS.^{52,53} We observed a decrease in executive functioning according to WCST performance in patients who had a plaque in the infratentorial region and T1 black hole plaque. On the other hand, our results showed that patients with T1 black hole plaque were more depressed, which could lead to impaired executive function. A high level of depression could also predict decreased executive functioning and ability.⁵⁴

Brain volume can affect cognitive function. Findings are very different from previous clinical trials on increasing brain volume and improving cognition with an anaerobic exercise.^{55,56} In addition, intellectual stimulation through social interaction was associated with increased brain volume as well as some cognitive enhancements.⁵⁷ These findings show that in addition to the rate of atrophy, the volume of the smaller regional grey matter, even 10 years earlier, is associated with an increase in cognitive decline.⁵⁸ Our study demonstrated a positive relationship between brain volume and cognitive performance, as tested by PASAT.

Neurological disability in SPMS has been shown to correlate with brain volume atrophy and plaques.⁵⁹ Additionally, volume of plaques correlated with neurological disability.⁶⁰ A strong relationship was observed between the number, size, volume, and site of MS plaques and neurological disability.⁶¹⁻⁶³ In accordance with the results of previous studies, our results showed that the increase of total volume of plaques was associated with the rate of disability (MSFC) and increased it.

Previous studies investigated the association between cognitive impairment and the burden of lesions in MS.^{64,65} The mean volume of T2-weighted plaques showed a tendency to associate with the total regional functional scoring scale.⁶⁶ Overall, our findings indicated that in

patients with MS, increased plaque volume correlated with greater memory impairment and reduced performance on both the word-pair test and the PASAT.

Limitations: A limitation of this study was its lack of evaluation of the lesion load. Another study limitation was three-dimensional (3D)-FLAIR sequences with 3-millimeter cuts and 1.5T MRI. The modest sample size for clinically recruited participants, without follow-up evaluation, was the third limitation. These findings have considerable clinical relevance. It is recommended that in future research, researchers and physicians select appropriate treatment methods after diagnosing the location of plaques in patients with MS and examine the effects of memory-enhancing drugs and disability reduction according to MRI indices. Despite limitations, our findings emphasize the importance of considering the coexistence of psychiatric, clinical, and cognitive disorders with MRI findings in MS.

Conclusion

Brain volume loss and increased plaque volume correlate with memory decline. Furthermore, plaque location in the infratentorial region, basal ganglia, and thalamus is associated with memory decline and increased disability. Enhanced plaques or T1 black hole lesions also contribute to cognitive impairment. These findings highlight the need for systematic clinical and cognitive screening to enable early pharmacological and rehabilitative interventions for managing disability, psychiatric issues, and cognitive impairment in a larger population of patients with MS.

Conflict of Interests

The authors declare no conflict of interest in this study.

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