Med Glas (Zenica) 2026;23(1)
https://doi.org/10.17392/1984-23-01

Med Glas (Zenica)

ORIGINAL ARTICLE

The impact of cognitive impairments on the quality of life of patients with multiple sclerosis

Aida Šehanović[1,2*], Suljo Kunić[2,3], Anida Šehanović[2,4], Dževdet Smajlović[1,2], Emir Tupković[2,3], Omer Ć. Ibrahimagić[1,2,]

[1]Department of Neurology, University Clinical Centre Tuzla, [2]School of Medicine, University of Tuzla, [3]Department of Neurology, Primary Health Care Centre Tuzla with Polyclinic Department, [4]University Clinical Centre Tuzla; Tuzla, Bosnia and Herzegovina

ABSTRACT

Aim Multiple sclerosis (MS) is a chronic, inflammatory, (auto)immune disease of the central nervous system. Cognitive impairments are common in MS patients and significantly affect their quality of life. This study aimed to assess the impact of cognitive disorders on the quality of life in MS patients.

Methods A prospective study included 135 MS patients and 50 healthy individuals. Participants were divided into three groups: 85 patients with MS lasting over one year, 50 newly diagnosed MS patients, and 50 healthy individuals. Clinical assessment included the Mini-Mental Status Examination and cognitive function tests (Wechsler Intelligence Scale, Revised Beta Test, Raven's Coloured Progressive Matrices, Wechsler Memory Scale, Audio-Verbal Learning Test, Rey-Osterrieth Complex Figure Test, Verbal Fluency Test, and the SF-36 quality of life scale).

Results Cognitive impairments were found in 40-60% of MS patients, with mnestic functions most affected (30-60%). Patients with longer disease duration had poorer visuospatial, visuoconstructive, and visuoperceptual abilities. Immediate working memory, attention, and logical memory were also more impaired. Quality of life was significantly reduced in both MS groups, with lower MMSE score correlating with greater impairment.

Conclusion Cognitive impairments in MS patients affect memory, executive function, and attention, with global intellectual decline occurring later. A strong link between cognitive dysfunction and reduced quality of life highlights the importance of cognitive assessment for evaluating disease severity and therapy effects.

Key words: cognition, executive function, neuropsychological tests

INTRODUCTION

Multiple sclerosis (MS) is a chronic, inflammatory, autoimmune disease of the central nervous system (CNS), characterized by inflammation, demyelination, gliosis, and neuronal loss (1). Although the exact etiology remains unknown, it is believed that a combination of genetic predisposition and environmental factors such as vitamin D deficiency, birth season, tobacco exposure, and Epstein-Barr virus, play a role in the disease development (2,3).

The prevalence of MS worldwide ranges from 5 to 300 per 100 000 people and increases at higher latitudes (4).

Although the overall prevalence of MS generally decreases with increasing proximity to the equator, recent epidemiological data indicate a rising incidence in certain regions, which may reflect changes in environmental exposure, genetic susceptibility, or improved diagnostic practices (5-7).

***Corresponding author:** Aida Šehanović
Department of Neurology, University Clinical Centre Tuzla
Prof. Ibre Pašića 1, 75000 Tuzla, Bosnia and Herzegovina
Phone: +387 61 721 171;
E-mail: aida.sehanovic@gmail.com
ORCID ID: https://orcid.org/0000-0001-6192-2680

The clinical course varies, with the relapsing-remitting form being most common, often progressing to a secondary-progressive form. Less common types include primary progressive and progressive-relapsing MS. Symptoms may present in episodes or as gradual progression (8,9).

Cognitive dysfunction is a common, yet often under recognized manifestation of MS, affecting up to 65% of patients (10). It typically involves deficits in working memory, attention, and executive functions, while global intellectual capacity often remains preserved in the early stages of the disease (11). These higher cognitive functions are supported by intricate neural networks encompassing the associative cortex and limbic structures particularly the hippocampus and anterior cingulate gyrus (12,13).

Disruption of these systems is closely associated with cognitive decline in MS and contributes significantly to reduced quality of life. Cognitive impairment interferes with daily functioning, including interpersonal relationships, work performance, and emotional well-being, and is frequently accompanied by other "invisible" symptoms such as fatigue and depression (14).

The World Health Organization defines quality of life (QoL) as an individual's perception of their position in life, within their

| Submitted: 10 Mar 2025. Revised: 24. Jun 2025, Accepted: 10 Aug 2025.

cultural context and value system, in relation to personal goals and expectations (15). QoL encompasses physical, psychological, social, and functional dimensions.

In routine clinical practice, an increasing number of patients with MS present with cognitive difficulties, including impairments in memory, attention, verbal expression, and concentration, despite being physically relatively stable (16).

These so-called "invisible symptoms" are frequently underdiagnosed and inadequately addressed, although they substantially compromise quality of life, occupational performance, and interpersonal relationships (17).

A deeper understanding of cognitive dysfunction in MS, along with its quantification and correlation with clinical manifestations, contributes to the advancement of individualized treatment, patient education, and rehabilitation strategies. Furthermore, cognitive decline may serve as an early predictor of MS progression (18).

The majority of available literature addresses cognitive impairments in patients with longer disease duration, often without comparative analysis involving control groups or longitudinal follow-up (19).

In the region of Southeast Europe such studies remain scarce. Notably, investigations that explore the association between objective neuropsychological findings and quality of life parameters are especially underrepresented.

The aim of this study was to examine the impact of cognitive impairments on the quality of life in patients with MS, emphasizing their effect on physical, psychological, and social functioning.

PARTICIPANTS AND METHODS

Participants and study design

This prospective study was conducted at the Clinic of Neurology, University Clinical Centre Tuzla, Bosnia and Herzegovina. The duration of the study was 2.5 years during the period June 2021 – December 2023.

A total of 185 patients were included in the study, comprising 135 patients diagnosed with multiple sclerosis (MS) and 50 healthy patients as controls. Patients were divided into three groups: Group I consisted of 85 patients with MS duration longer than one year, Group II included 50 patients newly diagnosed with MS with disease duration less than one year, and Group III consisted of 50 healthy patients, matched by age, gender, and education level to the MS groups. Patients were selected consecutively during the study period.

Inclusion criteria for Group I and Group II were a confirmed MS diagnosis based on the current McDonald criteria and in group I patients had to have a brain magnetic resonance scan no older than one year prior to the initial testing (20, 21). Group III included patients without a history or clinical signs of neurological or cognitive disorders. Exclusion criteria for MS patients included comorbid diseases and central nervous system (CNS) injuries, such as trauma, metabolic disorders, epilepsy, and vascular lesions. Demographic data including age, gender, and education level were collected for all patients. The approval from the Ethics Committee from University Clinical Centre Tuzla was obtained.

Methods

All MS patients underwent brain MRI at baseline. Neurological examinations were conducted by a neurologist, while neuropsychological testing was performed by both a psychologist and a neuropsychiatrist. Clinical evaluation included the Expanded Disability Status Scale (EDSS) (22), the Mini-Mental State Examination (MMSE) (23), and the SF-36 Quality of Life Scale (24). To assess cognitive functions, a comprehensive neuropsychological battery was used, consisting of the Wechsler Intelligence Scale WB-II (25), Revised Beta Test (26), Raven's Coloured Progressive Matrices (27), Wechsler Memory Scale (28), Audio Verbal Learning Test (AVLT) (29), Rey-Osterrieth Complex Figure Test (RCFT) (30), and the Verbal Fluency Test (FAS) (31). All participants underwent initial testing, with follow-up testing performed one year later.

Statistical analysis

The Mann–Whitney U test, Wilcoxon test, and $\chi 2$ test were used to examine differences between the groups. Associations among variables test scores, and scale domains were evaluated using regression analysis and Spearman's correlation coefficient. A $p< 0.05$ was considered statistically significant.

RESULTS

Group I included 85 MS patients (70.5% female; mean age 42.0±9.3 years), Group II included 50 newly diagnosed MS patients (82% female; mean age 37.5±10.8 years), and Group III included 50 healthy patients matched by age, gender, and education. Among MS patients, 121 (82%) had relapsing-remitting and 14 (18%) had secondary-progressive MS (Table 1).

Table 1. Demographic and clinical characteristics of the patients

Variable	Testing I			Testing II		
	Control	Group I	Group II	Control	Group I	Group II
Number of patients	50	85	50	50	80	45
RRMS	0	71	50	0	66	45
SPMS	0	14	0	0	14	0
Age (mean±SD) (years)	38±5.8	42±9.3	37.5±10.8	39±5.8	43±9.3	38.5±10.8
Gender (M/F) (N)	35 / 15	60 / 25	41 / 9	35 / 15	59 / 21	39 / 6
Education (mean±SD) (years)	16±1.8	12±2.5	12±2.4	16±1.8	12±2.5	12±2.4
EDSS (mean±SD)	0	2.5±2.3	1.9±1.8	0	3±2.6	1.6±1.5
Duration of disease (mean±SD) (years)	0	6±4.0	< 1	0	7±4.0	1

*Testing I, initial testing; Testing II, testing after one year; Control, patients without multiple sclerosis; Group I, patients with multiple sclerosis which lasted more than one year; Group II, patients with newly diagnosed multiple sclerosis; RRMS, relapsing remitting form of multiple sclerosis; SPMS, secondary progressive form of multiple sclerosis; EDSS, extended scale of disability status in multiple sclerosis

Table 2. Distribution of cognitive disorders, initial testing

Variable	No (%) of patients					
	Group I (N=85)			Group II (N=50)		
	Normal	Below average	Pathological	Normal	Below average	Pathological
WBac	50 (58.82)	12 (14.12)	23 (27.06)	40 (80.00)	4 (8.00)	6 (12.00)
WBc	33 (38.82)	46 (54.12)	6(7.06)	22 (44.00)	23 (46.00)	5 (10.00)
CPM	82 (96.47)	2 (2.35)	1 (1.18)	47 (94.00)	2 (4.00)	1 (2.00)
β	56 (65.88)	11 (12.94)	18 (21.18)	40 (80.00)	3 (6.00)	7 (14.00)
WB mc	33 (38.82)	28 (32.94)	24(28.24)	25 (50.00)	18 (36.00)	7 (14.00)
WB lm	35 (41.18)	9 (10.59)	41 (48.24)	23 (46.00)	8(16.00)	19 (38.00)
AVLT 1-5	42 (49.41)	18 (21.18)	25 (29.41)	27 (54.00)	11 (22.00)	12 (24.00)
AVLT 6	19 (22.35)	17 (20.00)	49 (57.65)	13 (26.00)	13 (26.00)	24 (48.00)
AVLT 7	18 (21.18)	15 (17.65)	52 (61.18)	14 (28.00)	16 (32.00)	20 (40.00)
RCFT rc	48 (56.47)	7 (8.24)	30 (35.29)	37 (74.00)	6 (12.00)	7 (14.00)
RCFT vm	31 (36.47)	8 (9.41)	46 (54.12)	24(48.00)	5 (10.00)	21 (42.00)
FAS	56 (65.88)	5 (5.88)	24 (28.24)	38 (76.00)	4 (8.00)	8 (16.00)

Wbac, Wechsler Bellevue scale form II -subtest: Assembling cubes; WBc, Wechsler Bellevue scale form II - subtest: Common terms; CPM, Raven's Coloured Progressive Matrices; β, Revised Beta test maze; WB mc, Wechsler Bellevue scale form II - subtest: mental control; WB lm, Wechsler Bellevue scale form II – subtest: logical memory; AVLT , Auditory-verbal learning test; RCFT rc, Rey Complex Figure Test - recognition trial; RCFT vm, Rey Complex Figure Test - visual memory; FAS, FAS verbal fluency tests

Significant differences in test performance were found between MS groups and healthy controls ($p<0.05$). Visuospatial and visuoconstructive abilities were more impaired in Group I than in Group II: cube subtest (WB ac) in 23 (27%) versus 6 (12%), crossing out subtest (RCFT re) in 30 (35.3%) versus 7 (14%) cases. Executive functions, as measured by the maze subtest, were preserved in 67 (79%) patients of Group I and 43 (86%) of Group II. Verbal fluency (FAS) was within normal range in 24 (28%) patients of Group I and 8 (16%) of Group II. Working memory, attention, and short-term memory were impaired in 24 (28.2%) patients of Group I and 13 (16%) of Group II, while logical memory was impaired in 41 (48.2%) and 19 (38%), respectively. Short-term verbal memory (AVLT A6) was impaired in 49 (57%) of Group I and 24 (48%) of Group II, while long-term verbal memory (AVLT A7) showed deficits in 52 (61%) of Group I and 20 (40%) of Group II patients. Non-verbal recall (RCFTvm) was impaired in 46 (54%) of Group I and 21 (42%) of Group II patients. Verbal fluency impairment due to demyelination was present in 24 (28.2%) patients of Group I and 8 (16%) of Group II (Tables 2, 3).

In Group I, all psychological tests correlated significantly with physical QoL ($p<0.05$); the mental and total QoL score correlated significantly with all tests except numerical memory. In Group II, SF-36 dimensions correlated significantly with all tests except the beta maze and numerical memory (Table 4).

At follow-up, Group I showed the strongest correlation between quality of life and the RCFT test. In Group II, the strongest correlation was with MMSE, WB mc, and RCFT. Physical and mental QoL dimensions, as well as total SF-36 score, correlated positively and significantly with MMSE in both MS groups. During the second testing, correlations in Group II remained significant for most psychological tests,

Table 3. Distribution of cognitive disorders, testing after one year

Variable	No (%) of patients					
	Group I (N=80)			Group II (N=45)		
	Normal	Below average	Pathological	Normal	Below average	Pathological
WBac	50 (62.50)	12 (15.00)	18 (22.50)	35 (77.78)	6 (13.33)	4 (8.89)
WBc	26 (32.50)	49 (61.25)	5 (6.25)	13 (28.89)	29 (64.44)	3 (6.67)
CPM	74 (92.50)	0 (0.00)	6 (7.50)	43 (95.56)	2 (4.44)	0 (0.00)
β	57 (71.25)	8 (10.00)	15 (18.75)	37 (82.22)	4 (8.89)	4 (8.89)
WB mc	23 (28.75)	31 (38.75)	26 (32.50)	20 (44.44)	14 (31.11)	11 (24.44)
WB lm	33 (41.25)	12 (15.00)	35 (43.75)	19 (42.22)	9 (20.00)	17 (37.78)
AVLT 1-5	34 (42.50)	17 (21.25)	29 (36.25)	19 (42.22)	15 (33.33)	11 (24.44)
AVLT 6	17 (21.25)	19 (23.75)	44 (55.00)	11 (24.44)	13 (28.89)	21 (46.67)
AVLT 7	17 (21.25)	16 (20.00)	47 (58.75)	8 (17.78)	13 (28.89)	24 (53.33)
RCFT rc	47 (58.75)	4 (5.00)	29 (36.25)	34 (75.56)	2 (4.44)	9 (20.00)
RCFT vm	29 (36.25)	13 (16.25)	38 (47.50)	24 (53.33)	6 (13.33)	15 (33.33)
FAS	57 (71.25)	6 (7.50)	17 (21.25)	32 (71.11)	7 (15.56)	6 (13.33)

Wbac, Wechsler Bellevue scale form II -subtest: Assembling cubes; WBc, Wechsler Bellevue scale form II - subtest: Common terms; CPM, Raven's Coloured Progressive Matrices; β, Revised Beta test maze; WB mc, Wechsler Bellevue scale form II - subtest: mental control; WB lm, Wechsler Bellevue scale form II – subtest: logical memory; AVLT , Auditory-verbal learning test; RCFT rc, Rey Complex Figure Test - recognition trial; RCFT vm, Rey Complex Figure Test - visual memory; FAS, FAS verbal fluency tests

Table 4. Correlation of psychological testing results with SF - 36 quality of life scale of two study groups, initial testing

Tests	Group I (N = 85)		Group II (N = 50)	
	b	p	b	p
MMSE	1.8715	0.0308*	1.7793	0.2432
Wbac	0.1448	0.9032	-0.7157	0.7833
WBc	1.2413	0.3767	0.2402	0.8874
CPM	-0.6093	0.5278	0.2281	0.8831
β	0.3079	0.8088	0.0432	0.9846
WB mc	-4.4289	0.0016*	-1.6309	0.4819
WB lm	1.3079	0.228	1.7972	0.3536
AVLT 1-5	0.9852	0.4016	-3.2439	0.2642
AVLT 6	2.2738	0.2714	2.6429	0.3723
AVLT 7	-1.2207	0.5215	-0.1473	0.9652
RCFT rc	0.1747	0.5549	0.9593	0.2157
RCFT vm	0.5844	0.0899	0.0259	0.9727
FAS	0.0195	0.9602	0.409	0.5703
D - W test	(R) = 0.6113	0.0005*	(R) = 0.5834	0.1915
	AC 2.1109		AC 2.0517	

b, Partial correlation coefficient of multiple regression correlation analysis; p, Possibility of random difference two-sided testing of the hypothesis; MMSE, Mini mental status examination; Wbac, Wechsler Bellevue scale form II -subtest: Assembling cubes; WBc, Wechsler Bellevue scale form II - subtest: Common terms; CPM, Raven's Coloured Progressive Matrices; β, Revised Beta test maze; WB mc, Wechsler Bellevue scale form II - subtest: mental control; WB lm, Wechsler Bellevue scale form II – subtest: logical memory; AVLT, Auditory-verbal learning test; RCFT rc, Rey Complex Figure Test - recognition trial; RCFT vm, Rey Complex Figure Test - visual memory; FAS, FAS verbal fluency tests; (R), multiple correlation coefficient; D - W test, Durbin Watson test; AC, autocorrelation

Table 5. Correlation of psychological testing results with SF - 36 quality of life scale of two study groups, testing after one year

Tests	Group I (N = 80)		Group II (N = 45)	
	b	p	b	p
MMSE	0.6482	0.4613	5.759	0.0018*
Wbac	-2.4887	0.1886	-9.1236	0.0038*
WBc	0.7909	0.6231	0.358	0.874
CPM	0.3813	0.4621	1.4019	0.3466
β	-0.0546	0.9706	0.6627	0.7973
WB mc	-0.2788	0.8991	-0.653	0.7925
WB lm	0.6237	0.7189	0.2282	0.9215
AVLT 1-5	-2.9256	0.1095	0.0268	0.9922
AVLT 6	1.9576	0.4079	-1.8345	0.6923
AVLT 7	-0.7322	0.683	2.0087	0.637
RCFT rc	1.3474	0.0188*	1.5841	0.0420*
RCFT vm	0.8836	0.061	0.0789	0.9163
FAS	0.1797	0.708	0.2756	0.7155
D - W test	(R) = 0.5986	0.0023*	(R) = 0.7285	0.0110*
	AC 2.0315		AC 1.4302	

b, partial correlation coefficient of multiple regression correlation analysis; p, possibility of random difference two-sided testing of the hypothesis; MMSE, Mini mental status examination; Wbac, Wechsler Bellevue scale form II -subtest: Assembling cubes; WBc, Wechsler Bellevue scale form II - subtest: Common terms; CPM, Raven's Coloured Progressive Matrices; β, Revised Beta test maze; WB mc, Wechsler Bellevue scale form II - subtest: mental control; WB lm, Wechsler Bellevue scale form II – subtest: logical memory; AVLT, Auditory-verbal learning test; RCFT rc, Rey Complex Figure Test - recognition trial; RCFT vm, Rey Complex Figure Test - visual memory; FAS, FAS verbal fluency tests; (R), multiple correlation coefficient; D - W test, Durbin Watson test; AC, autocorrelation

with fewer associations seen for the cube subtest, Raven's Coloured Progressive Matrices (CPM), beta maze, and logical memory (Table 5).

DISCUSSION

Multiple sclerosis (MS) is a neurodegenerative disease that most often affects women of reproductive and working age. In this study, women were more represented in both MS groups (70.5% and 82%, respectively), which is consistent with previous findings (4, 32). The majority of patients had the relapsing-remitting form of MS (82%), in line with the distribution reported in other studies (32, 33).

Cognitive impairments were identified in 50% of patients in Group I and 42% in Group II, which corresponds to the prevalence range of 40–70% reported in the literature (10, 11, 13, 34). These impairments mainly affected memory, attention, and executive functions, especially in patients with longer disease duration. Intellectual abilities and executive functions remained relatively preserved in the early stage, which supports previous findings (35) that executive deficits are less frequent in newly diagnosed patients.

Visuospatial and visuoperceptual functions were more impaired in Group I, while attention and short-term memory showed slightly worse outcomes in Group II. These results align with the study (36), which noted early difficulties in attention, concentration, and processing speed among MS patients. As multiple sclerosis progresses, memory difficulties tend to worsen. In the early stages, individuals often experience problems with retrieving information, while later stages are more commonly associated with challenges in acquiring new information (37). It was found that longer disease duration is linked to more severe impairments in verbal episodic memory and logical thinking (33, 34).

These findings support the observation in our study that verbal learning and memory are more significantly affected in patients with longer disease duration.

Our results showed the quality of life (QoL) of MS patients was significantly reduced across all measured dimensions and strongly correlated with both MMSE and cognitive test results; physical and mental dimensions of QoL showed statistically significant associations with most neuropsychological scores, especially in patients with more advanced disease. This relationship has been confirmed in previous studies emphasizing the link between cognitive status and social, emotional, and functional outcomes (34). Cognitive difficulties reported by patients with multiple sclerosis are strongly linked to poorer physical and mental quality of life, as well as a decreased likelihood of being employed, even when factors like age, fatigue, depression, and disability level are taken into account (38).

It is important to note that executive functions and non-verbal intelligence did not show a significant correlation with quality of life in the early stages of our study, suggesting that preserved higher-order functions may mask deeper cognitive decline. This finding aligns with longitudinal studies that have examined cognitive functions in MS patients and their association with quality of life, emphasizing that even mild cognitive deficits can substantially impact daily living, even among patients with minimal physical disability (35).

The limitations of this study include the absence of standardized neuropsychological protocols specifically designed for MS patients. The tests used were time-consuming and required

specialized examiner skills. Future studies should incorporate validated cognitive assessment tools tailored to MS populations and include larger samples to increase generalizability.

In conclusion, this study confirms that cognitive impairments are prevalent in MS and significantly reduce patients' quality of life. Our longitudinal comparison revealed that early cognitive decline primarily involves attention, working memory, and short-term verbal memory, whereas more advanced stages show greater impairments in verbal learning, logical memory, visuospatial abilities, and long-term memory.

The originality of this study lies in its longitudinal design, involving the assessment of cognitive functions at both early and advanced stages of the disease, in comparison with a control group of healthy individuals. Furthermore, the study introduces an innovative approach by integrating a broad range of validated neuropsychological tests along with the SF-36 questionnaire for quality of life assessment, enabling a multidimensional analysis of the impact of cognitive impairments on patients' functional status. Additionally, this research contributes to the existing body of literature by quantifying the relationship between cognitive status and subjectively perceived physical and mental health as an essential component in planning comprehensive care for patients with MS.

FOUNDING

No specific funding was received for this study.

TRANSPARENCY DECLARATION

Competing interests: None to declare.

REFERENCES

1. Ramaglia V, Rojas O, Naouar I, Becher B, Bar-Or A, Prat A, et al. The ins and outs of central nervous system inflammation—lessons learned from multiple sclerosis. Annu Rev Immunol 2021; 39:199–226.
2. Rasheed A, Khan G. Epstein-Barr virus, vitamin D and the immune response: connections with consequences for multiple sclerosis. Front Immunol 2024; 15:1503808.
3. Zarghami A, Li Y, Claflin SB, Van Der Mei I, Taylor BV. Role of environmental factors in multiple sclerosis. Expert Rev Neurother 2021;21(12):1389–408.
4. Browne P, Chandraratna D, Angood C, Tremlett H, Baker C, Taylor BV, Thompson AJ. Atlas of Multiple Sclerosis 2013: A growing global problem with widespread inequity. Neurology. 2014; 83(11):1022–4. doi: 10.1212/WNL.0000000000000768. PMID: 25200713; PMCID: PMC4162299.
5. Khan G, Hashim MJ. Epidemiology of multiple sclerosis: Global, regional, national and sub-national-level estimates and future projections. J Epidemiol Glob Health 2025; 15(1):21. doi: 10.1007/s44197-025-00353-6. PMID: 39928193; PMCID: PMC11811362.
6. Puthenparampil M, Perini P, Bergamaschi R, Capobianco M, Filippi M, Gallo P. Multiple sclerosis epidemiological trends in Italy highlight the environmental risk factors. J Neurol 2022; 269(4):1817–24. doi: 10.1007/s00415-021-10782-5. Epub 2021 Sep 27. PMID: 34580756; PMCID: PMC8940874.
7. Haki M, Al-Biati HA, Al-Tameemi ZS, Ali IS, Al-Hussaniy HA. Review of multiple sclerosis: Epidemiology, etiology, pathophysiology, and treatment. Medicine (Baltimore). 2024;103(8):e37297. doi: 10.1097/MD.0000000000037297. PMID: 38394496; PMCID: PMC10883637.
8. Arredondo-Robles AV, Rodríguez-López KP, Ávila-Avilés RD. Clinical Management in Multiple Sclerosis. Neuroglia. 2025; 6(1):6. https://doi.org/10.3390/neuroglia6010006
9. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol 2018; 17 (2):162–73. doi: 10.1016/S1474-4422(17)30470-2. Epub 2017 Dec 21. PMID: 29275977.
10. Portaccio E, Amato MP. Cognitive Impairment in Multiple Sclerosis: An Update on Assessment and Management. Neuro Sci 2022; 3(4):667–76.
11. Mirmosayyeb O, Nabizadeh F, Ghaffary E M, Panah M Y, Zivadinov R, Weinstock-Guttman B et al. Cognitive performance and magnetic resonance imaging in people with multiple sclerosis: A systematic review and meta-analysis. Multiple Sclerosis and Related Disorders 2024; 88, 105705.
12. Bush G, Luu P, Posner MI. Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn Sci 2000; 4(6):215-222.
13. Deldar Z, Gevers-Montoro C, Khatibi A, Ghazi-Saidi L. The interaction between language and working memory: a systematic review of fMRI studies in the past two decades. AIMS Neurosci 2020; 8(1):1-32. doi: 10.3934/Neuroscience.2021001. PMID: 33490370; PMCID: PMC7815476.
14. Kurt A Jellinger. Cognitive impairment in multiple sclerosis: from phenomenology to neurobiological mechanisms. Review J Neural Transm (Vienna) 2024; 131(8):871-99
15. The WHOQOL Group. The World Health Organization quality of life assessment (WHOQOL): position paper from the World Health Organization. Soc Sci Med 1995; 41:1403–9.
16. Chiaravalloti ND, DeLuca J. Cognitive impairment in multiple sclerosis. Lancet Neurol. 2008; 7(12):1139–51
17. Amato M P, Zipoli V, Portaccio E. Cognitive changes in multiple sclerosis', Expert Review of Neurotherapeutics 2008; 8(10):1585–96.
18. Eijlers AJC, van Geest Q, Dekker I, Steenwijk MD, Meijer KA, Hulst HE, et al. Predicting cognitive decline in multiple sclerosis: a 5-year follow-up study. Brain. 2018;141(9):2605–18. doi: 10.1093/brain/awy202. PMID: 30169585.
19. Sumowski JF, Benedict R, Enzinger C, Filippi M, Geurts JJ, Hamalainen P, et al. Cognition in multiple sclerosis: State of the field and priorities for the future. Neurology 2018; 90(6):278-88.
20. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol 2011; 69:292–302.

21. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol 2018; 17:162–73.
22. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 1983; 33:1444–52.
23. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12:189–98.
24. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. Med Care 1992; 30:473–83.
25. Ward LC. Prediction of verbal, performance, and full scale IQs from seven subtests of the WAIS-R. J Clin Psychol 1990; 46(4):436–40.
26. Kellogg RT, Morton JB. Beta III Test Manual. San Antonio, TX: The Psychological Corporation 1978.
27. Basso A, Capitani E, Laiacona M. Raven's coloured progressive matrices: normative values on 305 adult normal controls. Funct Neurol 1987; 2(2):189–94.
28. Prigatano GP. Wechsler Memory Scale: a selective review of the literature. J Clin Psychol 1978;34(4):816–32.
29. Paula JJ, de Sousa Magalhães S, Malloy-Diniz LF, Hamdan AC. Validity, convergent validity and test–retest reliability of the Rey Auditory Verbal Learning Test (RAVLT). Clin Neuropsychiatry. 2012; 9(3):129–37.
30. Deckersbach T, Savage CR, Henin A, Mataix-Cols D, Otto MW, Wilhelm S, Rauch SL, Baer L, Jenike MA. Reliability and validity of a scoring system for measuring organizational approach in the Complex Figure Test. J Clin Exp Neuropsychol. 2000; 22(5):640–8.
31. Vlaar AMM, Wade DT. Verbal fluency assessment of patients with multiple sclerosis: test–retest and inter-observer reliability. Clinical Rehabilitation. 2003; 17(7):756–64.
32. Hill J, Harrison J, Palmer K. Risk factors for relapsing remitting multiple sclerosis. Br J Neurosci Nurs 2021; 17(Suppl 1):S34–36.
33. Gich J, Salavedra-Pont J, Coll-Martinez C, Quintana E, Álvarez-Bravo G, Robles-Cedeño R et al. The nature of memory impairment in multiple sclerosis: understanding different patterns over the course of the disease. Front Psychol. 2024;14:1269794. doi: 10.3389/fpsyg.2023.1269794. PMID: 38298363; PMCID: PMC10828846.
34. Brochet B, Ruet A. Cognitive Impairment in Multiple Sclerosis With Regards to Disease Duration and Clinical Phenotypes. Front Neurol 2019; 10:261.
35. Rao SM, Leo GJ, Bernardin L, Unverzagt F. Cognitive dysfunction in multiple sclerosis: I. Frequency, patterns, and prediction. Neurology 1991; 41:685–91.
36. Benedict R, Amato M, DeLuca J, Geurts J. Cognitive impairment in multiple sclerosis: clinical management, MRI, and therapeutic avenues. Lancet Neurol 2020; 19:860–71
37. Lancia S, Marrie RA, Cutter G, Fox RJ, Salter A. Association of patient-reported cognitive impairment with quality of life and employment in multiple sclerosis. Mult Scler Relat Disord 2024; 87:105675. doi: 10.1016/j.msard.2024.105675.
38. Gómez-Melero S, Caballero-Villarraso J, Escribano BM, Galvao-Carmona A, Túnez I, Agüera-Morales E. Impact of Cognitive Impairment on Quality of Life in Multiple Sclerosis Patients-A Comprehensive Review. J Clin Med 2024; 13(11):3321. doi: 10.3390/jcm13113321. PMID: 38893032; PMCID: PMC11172944.