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Memory in Polish multiple sclerosis patients – correlations with mood and fatigue

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Summary

Aim. Assessment of the selected aspects of memory in Polish patients with multiple sclerosis (MS) and the associations between memory and clinical course, neurological status, mood, fatigue, and employment status.

Material and methods. The initial five learning trials of the *California Verbal Learning Test* (CVLT), the initial three learning trials of the *Brief Visuospatial Memory Test-revised* (BVMT-R), the *Hospital Anxiety and Depression Scale* and *Modified Fatigue Impact Scale* were administered to 100 MS patients and 150 healthy participants (HP).

Results. The MS group performed worse than the HP group on both the CVLT and the BVMT-R. The lowest scores were obtained by secondary progressive MS patients. There were significant differences between the MS and HP group on fatigue and depression, but not anxiety. Multivariate analysis showed worse neurological status was the only clinical predictor of memory disturbances. CVLT scores were significantly associated with employment status.

Conclusions. Memory impairment occurs in patients with MS and affects employment status. Depressive symptoms, anxiety and fatigue, unlike neurological status, were not directly related to memory status.

Key words: multiple sclerosis, cognitive dysfunction, memory

Introduction

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system, associated with the presence of disseminated demyelinating lesions and axonal injury in the brain and spinal cord. MS is the most common cause of disability in young adults [1–3].

Neuropsychiatric symptoms, including cognitive impairment (CI), are one of the most common symptoms. CI affects 43–70% of patients with MS [4–6]. CI in the course of MS concerns mainly memory, information processing speed, attention, executive functions, and visual-spatial dysfunctions [6]. CI has been observed in all MS clinical courses, affecting patients at all stages, even rarely as a first manifestation of MS. CI is most common and severe in patients with primary progressive multiple sclerosis (PPMS) and secondary progressive multiple sclerosis (SPMS). The incidence and severity of cognitive deficits are typically associated with duration of the disease. This partly explains the highest prevalence and severity of CI in SPMS [7–10].

Memory impairment is one of the most common cognitive symptoms in MS. It affects 40–65% of patients. 20% of relapsing remitting MS (RRMS) patients have memory dysfunction in the context of intact information processing speed [11]. The nature of the memory deficits is not entirely clear. Early data suggested that memory impairment results from inefficient retrieval process in long-term storage with preserved encoding. However, more recent data suggest a problem in learning new information and processing it, rather than a primary long-term storage problem [5, 12]. Both verbal episodic memory impairment and visual-spatial dysfunctions are observed in MS. Memory difficulties occur in all clinical courses [13].

Mood disorders and fatigue are also frequent symptoms found in patients with MS. Up to 50% of people with MS experience clinical depression [14]. Anxiety affects 40% of patients [15], whereas fatigue has been reported in up to 83% of patients with MS [16]. The influence of mood disorders on memory disturbances is not entirely clear [17]. It seems that depression has a negative impact on the information processing speed and working memory [18]. It was suggested that episodic memory impairment at least partially results from decreased information processing speed, attention and working memory deficits [19, 20].

Most studies did not show a significant relationship between fatigue and CI, although there was little effect on verbal and visual memory impairment [21, 22]. The newer data indicate that there is a complex relation between fatigue and memory function in MS [23].

Assessments of cognitive impairment in MS, including memory deficits, should be carefully chosen because of the subtle and selective character of MS cognitive dysfunction and in the context of physical disability. For this reason targeted test batteries are used. The most widely used are the *Brief Repeatable Battery of Neuropsychological Tests* (BRB-N) [24], the *Minimal Assessment of Cognitive Function*

in MS (MACFIMS) [25] and the *Brief International Cognitive Assessment in Multiple Sclerosis* (BICAMS) [26]. There is no Polish adaptation available for these methods. The BICAMS includes the initial five learning trials of the *California Verbal Learning Test-II* (CVLT-II) [27] measuring verbal memory and the initial three learning trials of the revised *Brief Visuospatial Memory Test* (BVMT-R) [28] assessing visual memory. International standards for validation have been agreed [29] and the BICAMS has been shown to be feasible and valid in many countries [30].

The aims of this study were to assess memory status among Polish patients with MS using components of the BICAMS in the context of clinical course, depressive symptoms, anxiety, and fatigue, and to verify whether memory impairment is associated with employment status.

Material and methods

One hundred patients over 18 years of age with a diagnosis of MS based on the revised McDonald's criteria [31] were included in the study. Patients were treated at the Department of Neurology and Clinical Neuroimmunology of Regional Specialist Hospital in Grudziadz, Poland. The study was conducted in 2017. Patients were recruited cross-sectionally, no selection for cognitive impairment was performed before enrollment. Exclusion criteria were as follows: evidence of other neurological, psychiatric, systemic diseases or taking medications affecting cognitive function, alcohol or drug abuse (current or in the past), motor, sensory, vision or hearing dysfunction which could influence the test performance, MS relapse or glucocorticosteroid treatment in the last 4 weeks. 150 healthy volunteers with no evidence of neurological, psychiatric or systemic diseases affecting cognitive function were also assessed. The first language of all participants was Polish.

Structured demographic and clinical interview was performed, and subjects completed these self-administered questionnaires*: Hospital Anxiety and Depression Scale* (HADS) and *Modified Fatigue Impact Scale* (MFIS). Then the following neuropsychological tests were administered: the initial five learning trials of the CVLT and the initial three learning trials of the BVMT-R, as it was recommended by the BICAMS committee. Finally, the neurological examination with the *Expanded Disability Status Scale* (EDSS) assessment was performed. All participants were examined by the same clinical psychologist and neurologist.

The CVLT is a tool for measuring verbal memory. The Polish adaptation of the CVLT [32] was used in this study. The initial five learning trials of the CVLT were administered. The score was the total number of correct responses recorded across the five trials.

The BVMT-R [28] is a tool to evaluate visual memory. The initial three learning trials of the BVMT-R were administered. The total score was the sum of all 3 trials. The instructions were given in a standardized Polish translation.

The HADS [33] is a quick self-reported questionnaire containing 14 items, seven questions probing anxiety (HADS-A) and seven for depression (HADS-D). The HADS has been validated in MS [34]. The Polish version of the HADS [35] was used in this study.

The Polish version of the *Modified Fatigue Impact Scale* (MFIS) was used to measure fatigue [36]. The MFIS is a modified form of the *Fatigue Impact Scale* [37]. The MFIS contained 21 items, 9 questions related to physical fatigue, 10 questions to cognitive fatigue, and 2 questions to psychosocial fatigue. Each item was rated on a scale from 0 to 4. The scoring ranged between 0 and 84, a higher score reflected greater impact of fatigue. A cut-off value of 38 was used to discriminate fatigued from non-fatigued patients.

The study was approved by the Bioethical Committee at the Regional Chamber of Physicians and Dentists in Bydgoszcz, Poland (no. 39/2017 of 19.09.2017). Written informed consent was obtained from all participants.

Statistical analysis

Statistical analysis was performed using licensed software Statistica 13.1, StatSoft. The statistical significance value was set at $p < 0.05$. Normal distribution of data was verified using the Shapiro–Wilk test. The mean (with standard deviation) was used as a measure of central tendency for data with normal distribution. Otherwise, the median (with 25 and 75 percentile) was presented. The comparison between two groups for continuous variables was performed using: *t*-test for independent variables – for variables with normal distribution and homogenous variance in the groups (the homogeneity of variance was tested using Levene's test), *t*-test for independent variables with Welch's correction – for variables with normal distribution but unequal variances in the groups, Mann–Whitney *U* test – for variables not meeting the assumption of normality. The comparison between more than two groups for continuous variables was performed using Kruskal–Wallis *H* test. The chi-square test was used to compare between two groups for categorial variables. To assess correlation between two variables parametric test (Pearson's correlation) or nonparametric test (Spearman rank correlation) was used, depending on the character of variable's distribution. In the analysis regarding more than one predictor of independent variable, multiple regression model was applied.

Results

The main characteristics of patients with MS and healthy participants (HP) are detailed in Table 1. MS patients performed significantly below HP on both the CVLT and BVMT-R (Table 2). 7 MS patients and 5 HP did not complete the HADS, whereas the MFIS was not completed by 4 MS patients and 6 HP. The depression subscale

and anxiety subscale of the HADS were analyzed separately. In the case of the MFIS, overall MFIS score and subscale for cognitive aspect of fatigue were analyzed (Table 2). Statistically significant differences between MS patients and HP were demonstrated regarding the depression subscale of the HADS, the MFIS total score and the MFIS cognitive fatigue subscale. There was no significant difference in the case of anxiety symptoms. Significant anxiety symptoms were reported by 35 MS patients (37.6%) and 42 HP (29%). Significant depressive symptoms were reported by 15 MS patients (16.1%) and 11 HP (7.6%). 42 MS patients (43.8%) and 18 HP (12.5%) reported significant fatigue.

Table 1. **Demographic and clinical characteristics of the study population**

	MS patients (n = 100)	Control group (n = 150)	p-value
Age (years)	40 (33–49)	37 (29–48)	0.15
Female-to-male ratio	71/29	109/41	0.77
Duration of education (years)	13 (12–17)	15 (12–17)	0.02
Employment status (employed/unemployed)	72/28	150/0	<0.001
Disease duration (years)	8 (3–14)		
Clinical course			
RRMS	68 (68%)		
SPMS	23 (23%)		
PPMS	9 (9%)		
EDSS	3.25 (2–4)		

Values are presented as medians (25–75th percentile) or *n* (%). MS – multiple sclerosis; RRMS – relapsing-remitting MS; SPMS – secondary progressive MS; PPMS – primary progressive MS; EDSS – Expanded Disability Status Scale. Mann–Whitney *U* test was used to assess differences in age and duration of education, whereas a chi-square test was used to assess female-to-male ratios and employment status.

Table 2. **CVLT, BVMT-R, HADS, and MFIS scores in MS and HP groups**

	MS patients	Control group	p-value
CVLT	49.8 ± 11.9	54.1 ± 10.3	0.003
BVMT-R	24 (18.5–30.0)	29 (24–32)	<0.001
HADS-A	6 (3–8)	5 (2–8)	0.08
HADS-D	3 (1-6)	2 (1–5)	0.02
MFIS total score	34 (22.0–44.5)	17.0 (7.0–28.5)	<0.001
MFIS cognitive fatigue	15.5 (6.0–20.5)	9 (4–13)	<0.001

Values are presented as mean ± SD or medians (25–75th percentile). MS – multiple sclerosis; CVLT – California Verbal Learning Test; BVMT-R – Brief Visuospatial Memory Test – Revised; HADS-A

– anxiety subscale of the Hospital Anxiety and Depression Scale; HADS-D – depression subscale of the Hospital Anxiety and Depression Scale; MFIS – Modified Fatigue Impact Scale. *T*-Test was used to assess the difference for CVLT. For other variables Mann–Whitney *U* Test was used.

In the MS group, both the CVLT and BVMT-R results correlated with age ($R = -0.27$, $p = 0.008$; $R = -0.52$, $p < 0.001$, respectively) and duration of education ($R = 0.48$, $p < 0.001$; $R = 0.31$, $p = 0.002$, respectively). Similar associations were demonstrated in the HP group for age ($R = -0.34$, $p < 0.001$; $R = -0.47$, $p < 0.001$) and duration of education ($R = 0.42$, $p < 0.001$; $R = 0.38$, $p < 0.001$). Only the CVLT scores differentiated gender in the MS group – women performed better in this test (females 55.1 ± 11.6; males 44.2 ± 11.0; $p = 0.002$). However, in the control group no association with gender was observed. Unemployed patients with MS performed worse than employed subjects on the CVLT (45.5 ± 12.2; 51.4 ± 11.5, respectively, $p = 0.03$). There was no relationship between employment status and BVMT-R performance. Association between the employment status and disability was not observed – the median value of EDSS in the employed subjects was 2.75 (Q25–Q75: 2.00–4.00), while in the unemployed ones it was 3.50 (Q25-Q75: 2.75–4.00; $p = 0.07$).

Table 3 presents demographic and clinical characteristics and memory tests results of patients with MS by disease course. Significant differences in performance on both memory tests were observed between RRMS and SPMS ($p = 0.05$ for the CVLT; $p = 0.002$ for the BVMT-R) as well as between SPMS and HP ($p = 0.002$ for the CVLT; $p < 0.001$ for the BVMT-R). There was no difference between RRMS and PPMS, RRMS and HP, SPMS and PPMS, PPMS and HP. Patients with higher EDSS performed worse on both the CVLT and BVMT-R ($R = -0.38$, $p < 0.001$; $R = -0.46$, $p < 0.001$, respectively). Both memory tests were also negatively correlated with duration of the disease ($R = -0.26$, $p = 0.01$; $R = -0.27$, $p = 0.007$, respectively).

Table 3. **Demographic and clinical characteristics, and memory tests results of patients with MS by disease course**

	RRMS (n = 68)	SPMS (n = 23)	PPMS (n = 9)
Age (years)	35.5 (30–43)	50 (40–55)	45 (42–50)
Female–to–male ratio	49/19	19/4	3/6
Duration of education (years)	13 (12–17)	12 (12–16)	12 (12–17)
Duration of the disease (years)	5 (3–10)	19 (11–23)	6 (2–10)
EDSS	2.5 (2.0–3.5)	5 (4.0–6.5)	4 (3.5–5.5)
CVLT	53 (43–61)	47 (33–52)	49 (29–52)
BVMT–R	26 (19.5–32.0)	21 (14–25)	23 (19–30)

Values are presented as medians (25–75th percentile) or *n*. RRMS – relapsing-remitting MS; SPMS – secondary progressive MS; PPMS – primary progressive MS; EDSS – Expanded Disability Status Scale; CVLT – California Verbal Learning Test; BVMT-R – Brief Visuospatial Memory Test – Revised.

The anxiety subscale of the HADS was not significantly correlated with the memory tests in the MS group. The depression subscale of the HADS correlated significantly only with the CVLT score in this group ($R = – 0.21$, $p = 0.05$), whereas the MFIS total score was significantly associated with both the CVLT and BVMT-R ($R = – 0.34$, $p < 0.001$; $R = – 0.36$, $p < 0.001$, respectively). The MFIS cognitive fatigue score also correlated with the CVLT and BVMT-R ($R = – 0.28$, $p < 0.006$; $R = – 0.23$, $p = 0.02$, respectively).

We also analyzed the CVLT and BVMT-R scores within the MS group in a multiple regression model that included several demographic and clinical factors: age, duration of the disease, the EDSS, the HADS depression subscale, and the MFIS total score (Table 4). This analysis revealed that the EDSS was the only predictor for CVLT scores, whereas both age and the EDSS were predictors of BVMT-R scores.

Table 4. **Predictors of memory impairment in MS patients – multiple regression model**

	CVLT		BVMT-R	
	F = 4.16; corrected R^2 = 0.15; p = 0.002		F = 10.21; corrected R^2=0.38; p <0.0001	
	Standardized B	p	Standardized B	p
Age	-0.11	0.35	-0.39	<0.001
Duration of the disease	-0.06	0.57	-0.04	0.71
EDSS	-0.28	0.02	-0.25	0.01
HADS-D	0.02	0.86	-0.14	0.23
MFIS total score	-0.19	0.14	-0.07	0.55

CVLT – California Verbal Learning Test; BVMT-R – Brief Visuospatial Memory Test – Revised; EDSS – Expanded Disability Status Scale; HADS-D – depression subscale of the Hospital Anxiety and Depression Scale; MFIS – Modified Fatigue Impact Scale.

Discussion

Cognitive impairment, including memory deficits, is a significant clinical problem in patients with MS, which has been intensively studied in recent years. Cognitive impairment affects daily life activity of patients and is not less important than the progression of physical disability [26, 38, 39]. Therefore it is a significant benefit to identify a tool for clinical assessment of memory dysfunction, which will be feasible for routine use in everyday work in centers providing diagnosis and treatment for patients with MS. In this study we used only the initial learning trials of the CVLT and BVMT-R. The CVLT contains also recall trial after distraction and long-delay recall task (free-recall and cued-recall), as well as recognition task. The BVMT-R contains also long-delay recall task. It is stated in the recommendation of the BICAMS committee

that the initial five learning trials of the CVLT and the initial three learning trials of the BVMT-R are the most sensitive for memory impairment assessment in patients with MS, whereas other measures do not significantly increase the sensitivity of these tools [29]. Using the CVLT and BVMT-R in the short version, we found a significant differences in memory functioning between patients with MS and healthy participants. Our findings are consistent with the results of studies conducted in other countries[40–44].

We found more severe verbal and visual memory disturbances in the SPMS group than in PPMS and RRMS. Our data confirm previously described differences in memory deficits related to the clinical courses of MS with the most severe changes in progressive forms, especially SPMS [8, 10, 13, 45, 46]. This means that patients with progressive forms of MS are a group that requires a special attention and monitoring of increasing cognitive deficits, which may affect compliance with therapeutic recommendations and rehabilitation.

Negative correlations of both CVLT and BVMT-R test scores with age in patients with MS and healthy participants confirm the previous data that age-related memory decline affects verbal memory and visuospatial abilities [47]. We observed a significant association between the duration of education and memory tests scores in MS patients as well as in the HP group. A correlation of the CVLT with the duration of education was already described in the Polish and Italian populations [32, 48]. However, earlier data do not corroborate such relationship between education and the BVMT-R [28, 48]. Parallel observations on gender effect on the CVLT were only made on Italian population [48]. In both the Italian [48] and our study the test results were higher in female subjects, but in our population this was significant in MS patients only. Previous data indicate more severe cognitive decline in male patients with MS compared to females [49]. We found that unemployed patients with MS performed worse on the CVLT. This may indirectly indicate that verbal memory impairment limits employment among patients with MS or professional activity supports verbal memory efficiency. Similar observation was made in the Czech validation of the BICAMS and MACFIMS [40], as well as in the Irish study [44]. Moreover, verbal memory functioning was associated with the employment status independently from disability assessed with the EDSS in our study. This observation is consistent with the results of other study on relation of cognitive impairment with employment and social functioning of MS patients [38] and highlights the importance of cognitive dysfunction in a wide spectrum of clinical symptoms of MS.

Our data confirm earlier findings of correlation between cognitive impairment, motor disability as assessed by the EDSS and the duration of the disease [10, 43]. In the current study, a higher EDSS score was significantly associated with decreased memory functioning in MS patients, while duration of the disease positively correlated with the severity of memory deficits. Moreover, we established the EDSS as the strongest predictor of worse results in tests assessing memory using a multiple regression model.

Regarding mood disorders severity, the difference between patients with MS and healthy participants was significant for depression only. Compared to previous studies, in which clinically significant depression was observed in 30–50% of patients, in our dataset both prevalence and severity of depression were notably lower [50–54]. In our study the correlation between depression and memory performance was present only for the CVLT. A relationship between depressive symptoms and verbal memory deficits was described earlier [55, 56]. However, a multiple regression analysis allowed us to rule out the direct impact of depressive symptoms on verbal memory efficiency in patients with MS. The link between the anxiety symptoms and memory disturbances in MS is less known. Both CVLT and BVMT-R scores did not correlate with anxiety in the current study, which was also described previously [57].

One of the potential factors influencing the performance in neuropsychological tests in patients with MS is fatigue. Fatigue was more prevalent in MS patients compared to controls. Approximately 45% of MS patients presented significant symptoms of fatigue, which is less than it was observed in the earlier study [16]. In some studies an association between fatigue and cognitive impairment was shown, especially in tasks requiring prolonged attention [56]. Nevertheless, a recent study on a large group of patients did not confirm the effect of fatigue on processing speed, attention, executive function, and memory [58]. Similarly to the Hungarian BICAMS validation [41], we observed a strong correlation of fatigue with performance on the CVLT and BVMT-R. However, this relation was not confirmed using the multivariate analysis, with the EDSS remaining as the only clinical predictor of the CVLT and BVMT-R performance. Thus the independent effect of fatigue on the memory function was not confirmed. This suggests a simple co-occurrence of fatigue and a memory decline, with no causal relation.

Conclusions

Memory function in patients with MS is decreased compared to healthy population. It was found using the initial five learning trials of the Polish version of the CVLT and the initial three learning trials of the BVMT-R. Depression, anxiety and fatigue do not affect memory directly, but there is a co-occurrence of memory disturbances with depressive symptoms and fatigue. Memory impairment is more severe in patients with greater disability and in SPMS. We found worse verbal memory functioning in unemployed patients.

References

1. Compston A, Coles A. *Multiple sclerosis*. Lancet 2008; 372(9648): 1502–1517.
2. Hollenbach JA, Oksenberg JR. *The immunogenetics of multiple sclerosis: A comprehensive review*. J. Autoimmun. 2015; 64: 13–25.
3. Grzegorski T, Losy J. *Cognitive impairment in multiple sclerosis – A review of current knowledge and recent research*. Rev. Neurosci. 2017; 28(8): 845–860.
4. Amato MP, Zipoli V, Portaccio E. *Multiple sclerosis-related cognitive changes: A review of cross-sectional and longitudinal studies*. J. Neurol. Sci. 2006; 245(1): 41–46.
5. Chiaravalloti ND, DeLuca J. *Cognitive impairment in multiple sclerosis*. Lancet Neurol. 2008; 7(12): 1139–1151.
6. Langdon DW. *Cognition in multiple sclerosis*. Curr. Opin. Neurol. 2011; 24(3): 244–249.
7. Amato MP, Ponziani G, Siracusa G, Scorbi S. *Cognitive dysfunction in early-onset multiple sclerosis: A reappraisal after 10 years*. Arch. Neurol. 2001; 58(10): 1602–1606.
8. Achiron A, Polliack M, Rao SM, Barak Y, Lavie M, Appelboim N et al. *Cognitive patterns and progression in multiple sclerosis: Construction and validation of percentile curves*. J. Neurol. Neurosurg. Psychiatry 2005; 76(5): 744–749.
9. Glanz BI, Holland CM, Gauthier SA, Amunwa EL, Liptak Z, Houtchens MK et al. *Cognitive dysfunction in patients with clinically isolated syndromes or newly diagnosed multiple sclerosis*. Mult. Scler. 2007; 13(8): 1004–1010.
10. Amato MP, Portaccio E, Goretti B, Zipoli V, Hakiki B, Giannini M et al. *Cognitive impairment in early stages of multiple sclerosis*. Neurol. Sci. 2010; 31(2): 211–214.
11. Leavitt VM, Tosto G, Riley CS. *Cognitive phenotypes in multiple sclerosis*. J. Neurol. 2018; 265(3): 562–566.
12. Thornton AE, Raz N, Tucke KA. *Memory in multiple sclerosis: Contextual encoding deficits*. J. Int. Neuropsychol. Soc. 2002: 8(3): 395–409.
13. Benedict RH, Cookfair D, Gavett R, Gunther M, Munschauer F, Garg N et al. *Validity of the minimal assessment of cognitive function in multiple sclerosis (MACFIMS)*. J. Int. Neuropsychol. Soc. 2006; 12(4): 549–558.
14. Feinstein A, Magalhaes S, Richard JF, Audet B, Moore C. *The link between multiple sclerosis and depression*. Nat. Rev. Neurol. 2014; 10(9): 507–517.
15. Korostil M, Feinstein A. *Anxiety disorders and their clinical correlates in multiple sclerosis patients*. Mult. Scler. 2007; 13(1): 67–72.
16. Minden SL, Frankel D, Hadden L, Perloffp J, Srinath KP, Hoaglin DC. *The Sonya Slifka Longitudinal Multiple Sclerosis Study: Methods and sample characteristics*. Mult. Scler. 2006; 12(1): 24–38.
17. Whitehouse CE, Fisk JD, Bernstein CN, Berrigan LI, Bolton JM, Graff LA et al. *Comorbid anxiety, depression, and cognition in MS and other immune-mediated disorders*. Neurology 2019; 92(5): e406–e417.
18. Arnett PA, Barwick FH, Beeney JE. *Depression in multiple sclerosis: Review and theoretical proposal*. J. Int. Neuropsychol. Soc. 2008; 14(3): 691–724.
19. DeLuca J, Barbieri-Berger S, Johnson SK. *The nature of memory impairments in multiple sclerosis: Acquisition versus retrieval*. J. Clin. Exp. Neuropsychol. 1994; 16(2): 183–189.

20. Archibald CJ, Fisk JD. *Information processing efficiency in patients with multiple sclerosis*. J. Clin. Exp. Neuropsychol. 2000; 22(5): 686–701.
21. Morrow SA, Weinstock-Guttman B, Munschauer FE, Hojnacki D, Benedict RH. *Subjective fatigue is not associated with cognitive impairment in multiple sclerosis: Cross-sectional and longitudinal analysis*. Mult. Scler. 2009; 15(8): 998–1005.
22. Bol Y, Duits AA, Hupperts RM, Verlinden I, Verhey FR. *The impact of fatigue on cognitive functioning in patients with multiple sclerosis*. Clin. Rehabil. 2010; 24(9): 854–862.
23. Andreasen AK, Iversen P, Marstrand L, Siersma V, Siebner HR, Sellebjerg F. *Structural and cognitive correlates of fatigue in progressive multiple sclerosis*. Neurol. Res. 2019; 41(2): 168–176.
24. Rao SM. *A manual for the Brief, Repeatable Battery of Neuropsychological Tests in Multiple Sclerosis*. New York: National Multiple Sclerosis Society; 1991.
25. Benedict RH, Fischer JS, Archibald CJ, Arnett PA, Beatty WW, Bobholz J et al. *Minimal neuropsychologyical assessment of MS patients: A consensus approach*. Clin. Neuropsychol. 2002; 16(3): 381–397.
26. Langdon DW, Amato MP, Boringa J, Brochet B, Foley F, Fredrikson S et al. *Recommendations for a brief international cognitive assessment for multiple sclerosis (BICAMS)*. Mult. Scler. 2012; 18(6): 891–898.
27. Delis DC, Kramerm JH, Kaplan E, Ober BA. *California Verbal Learning Test Manual: Second Edition, Adult Version*. San Antonio: Psychological Corporation; 2000.
28. Benedict RH. *Brief Visuospatial Memory Test – Revised: Professional Manual*. Odessa: FPAR Inc.; 1997.
29. Benedict RH, Amato MP, Boringa J, Brochet B, Foley F, Fredrikson S et al. *Brief International Cognitive Assessment for MS (BICAMS): International standards for validation*. BMC Neurol. 2012; 12(1): 55.
30. Corfield F, Langdon D. *A systematic review and meta-analysis of the Brief Cognitive Assessment for Multiple Sclerosis (BICAMS)*. Neurol. Ther. 2018; 7(2): 287–306.
31. 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(2): 292–302.
32. Łojek E, Stańczak J. *Podręcznik do Kalifornijskiego Testu Uczenia się Językowego*. Warsaw: Psychological Test Laboratory of the Polish Psychological Association; 2010.
33. Zigmond AS, Snaith RP. *The hospital anxiety and depression scale*. Acta Psychiatr. Scand. 1983; 67(6): 361–370.
34. Honarmand K, Feinstein A. *Validation of the Hospital Anxiety and Depression Scale for use with multiple sclerosis patients*. Mult. Scler. 2009; 15(12): 1518–1524.
35. Karakuła H, Grzywa A, Śpila B, Baszak J, Gieroba A, Kosikowski W et al. *Zastosowanie Skali Lęku i Depresji – HADS w chorobach psychosomatycznych*. Psychiatr. Pol. 1996; 30(4): 653–668.
36. Gruszczak A, Bartosik-Psujek H, Pocińska K, Stelmasiak Z. *Analiza walidacyjna wybranych aspektów psychometrycznych polskiej wersji Zmodyfikowanej Skali Wpływu Zmęczenia (Modifed Fatigue Impact Scale) – wyniki wstępne*. Neurol. Neurochir. Pol. 2009; 43(2): 148–154.
37. Fisk JD, Pontefract A, Ritvo PG, Archibald CJ, Murray TJ. *The impact of fatigue on patients with multiple sclerosis*. Can. J. Neurol. Sci. 1994; 21(1): 9–14.

38. Rao SM, Leo GJ, Ellington L, Nauertz T, Bernardin L, Unverzagt F. *Cognitive dysfunction in multiple sclerosis. II. Impact on employment and social functioning*. Neurology 1991; 41(5): 692–696.
39. Sartori E, Edan G. *Assessment of cognitive dysfunction in multiple sclerosis*. J. Neurol. Sci. 2006; 245(1–2): 169–175.
40. Dusankova JB, Kalincik T, Havrdova E, Benedict RH. *Cross cultural validation of the minimal assessment of cognitive function in multiple sclerosis (MACFIMS) and the brief international cognitive assessment for multiple sclerosis (BICAMS)*. Clin. Neuropsychol. 2012; 26(7): 1186–1200.
41. Sandi D, Rudisch T, Füvesi J, Fricska-Nagy Z, Huszka H, Biernacki T et al. *The Hungarian validation of the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery and the correlation of cognitive impairment with fatigue and quality of life*. Mult. Scler. Relat. Disord. 2015; 4(6): 499–504.
42. Polychroniadou E, Bakirtzis C, Langdon DW, Lagoudaki R, Kesidou E, Theotokis E et al. *Validation of the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) in Greek population with multiple sclerosis*. Mult. Scler. Relat. Disord. 2016; 9: 68–72.
43. Sousa C, Rigueiro-Neves M, Miranda T, Alegria P, Vale J, Passos AM et al. *Validation of the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) in the Portuguese population with multiple sclerosis*. BMC Neurol. 2018; 18(1): 172.
44. O'Connell K, Langdon DW, Tubridy N, Hutchinson M, McGuigan CA. *Preliminary validation of the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) tool in an Irish population with multiple sclerosis (MS)*. Mult. Scler. Relat. Disord. 2015; 4(6): 521–525.
45. Huijbregts SC, Kalkers NF, de Sonneville LM, de Groot V, Reuling IE, Polman CH. *Differences in cognitive impairment of relapsing remitting, secondary, and primary progressive MS*. Neurology 2004; 63(2): 335–339.
46. Planche V, Gibelin M, Cregut D, Pereira B, Clavelou P. *Cognitive impairment in a population-based study of patients with multiple sclerosis: Differences between late relapsing-remitting, secondary progressive and primary progressive multiple sclerosis*. Eur. J. Neurol. 2016; 23(2): 282–289.
47. Harada CN, Natelson Love MC, Triebel K. *Normal cognitive aging*. Clin. Geriatr. Med. 2013; 29(4): 737–752.
48. Goretti B, Niccolai C, Hakiki B, Sturchio A, Falautano M, Minacapelli E et al. *The Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS): Normative values with gender, age and education corrections in the Italian population*. BMC Neurol. 2014; 14: 171.
49. Beatty WW, Aupperl RL. *Sex differences in cognitive impairment in multiple sclerosis*. Clin. Neuropsychol. 2002; 16(4): 472–480.
50. Sadovnick AD, Remick RA, Allen J, Swartz E, Yee IM, Eisen K et al. *Depression and multiple sclerosis*. Neurology 1996; 46(3): 628–632.
51. Siegert RJ, Abernethy DA. *Depression in multiple sclerosis: A review*. J. Neurol. Neurosurg. Psychiatry 2005; 76(4): 469–475.
52. Beiske AG, Svensson E, Sandanger I, Czujko B, Pedersen ED, Aarseth JH et al. *Depression and anxiety amongst multiple sclerosis patients*. European J. Neurol. 2008; 15(3): 239–245.
53. Solaro C, Trabucco E, Signori A, Martinelli V, Radaelli M, Centonze D et al. *Depressive symptoms correlate with disability and disease course in multiple sclerosis patients: An Italian multi-center study using the Beck Depression Inventory*. PLoS One 2016; 11(9): e0160261.

54. Gay MC, Bungener C, Thomas S, Vrignaud P, Thomas PW, Baker R et al. *Anxiety, emotional processing and depression in people with multiple sclerosis*. BMC Neurol. 2017; 17(1): 43.
55. Nocentini U, Pasqualetti P, Bonavita S, Buccafusca M, De Caro MF, Farina D et al. *Cognitive dysfunction in patients with relapsing-remitting multiple sclerosis*. Mult. Scler. 2006; 12(1): 77–87.
56. Heesen C, Schulz KH, Fiehler J, Von der Mark U, Otte C, Jung R et al. *Correlates of cognitive dysfunction in multiple sclerosis*. Brain. Behav. Immun. 2010; 24(7): 1148–1155.
57. Karadayi H, Arisoy O, Altunrende B, Boztas MH, Sercan M. *The relationship of cognitive impairment with neurological and psychiatric variables in multiple sclerosis patients*. Int. J. Psychiatry Clin. Pract. 2014; 18(1): 45–51.
58. Golan D, Doniger GM, Wissemann K, Zarif M, Bumstead B, Buhse M et al. *The impact of subjective cognitive fatigue and depression on cognitive function in patients with multiple sclerosis*. Mult. Scler. 2018; 24(2): 196–204.

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