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BRIEF COGNITIVE MONITORING IN MULTIPLE SCLEROSIS PATIENTS IN LATVIA

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Cognitive changes are common in people with multiple sclerosis (MS). The neuropsychological testing requires specialised trained staff, time-consuming expert analysis and complicated test result interpretation. An expert committee recommended the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS), which is optimised for small centres. We conducted the Symbol Digit Modalities Test (SDMT) and Brief Visuospatial Memory Test (BVMT), for which the results were comparable with similar results in literature. Most MS patients showed decreased attention and processing speed, while visual memory was generally normal. Cognitive impairment occurrence is not strongly related to Expanded Disability Status Scale (EDSS) score.

Key words: *cognitive defects, cognitive monitoring, BICAMS, multiple sclerosis, MS.*

INTRODUCTION

Cognitive function is one of the eight brain functional system parts used in the Expanded Disability Status Scale (EDSS) to quantify disability in MS. Cognitive dysfunction can be identified by self-reported evaluation performed by the MS patient or his relative or using special neurocognitive tests. Tests minimise the influence of subjective features and provide comparable results in the evaluation of cognitive decline in stages of the disease. Cognitive impairment is found in 40–65% of MS patients (Rao *et al*., 1991; Benedict *et al*., 2006; Feinstein *et al*., 2013). Even light cognitive deficits can affect a person's ability to perform normal daily activities and diminish the quality of life.

Mostly cognitive defects are connected with reduced information processing speed, impaired attention, short-term memory, spatial orientation abilities and task execution rate (Strober *et al*., 2009; Guimaraes and Sá, 2012). In contrast, general intelligence and language abilities are relatively spared (Rao *et al*., 1991). The correlation of early cognitive impairment in MS predicts disability outcome several years later (Deloire *et al*., 2010).

The neuropsychological testing require specialised trained staff, time-consuming expert analysis of the patient's condition and test result interpretation; this complicates the assessment of cognitive status in small MS centres that have no access to specialised trained personnel and substantial resources. For research purposes and in clinical practice, two widely popular and validated cognitive batteries are used — the Brief Repeatable Battery of Neuropsychological tests (BRBN) and the Minimal Assessment of Cognitive Function in MS (MACFIMS) (Rao, 1990; Benedict *et al*., 2002). Both batteries are quite similar: composed of several tests that are found to be most sensitive and reliable to the cognitive impairment in MS, but they have different memory tests, and in comparative study by Strober *et al.* (2009), both batteries were found to have similar sensitivity. MACFIM can be administered in about 90 min, but BRBN in about 45 min. Ideally, the neuropsychological tests and batteries should be sensitive, consistent, reliable, with no language barrier, easy to administer and could be fulfilled in short time.

In 2012, an expert committee recommended BICAMS, which is optimised for MS centres with one or a few staff members, who may not have neuropsychological training. It does not require any special equipment, beyond paper, pen and stop watch. The committee recommended the 5 min Symbol Digit Modalities Test (SDMT), and the California

Verbal Learning Test – Second Edition (CVLT2) with the Brief Visuospatial Memory Test – Revised (BVMTR) learning trials if a further 10 minutes could be allocated for testing (Langdon *et al.,* 2012). The tests are easy to administer and evaluate in everyday practice, but still expert evaluation and MS specialist cognitive assessments would be beneficial.

The aims of the study were (1) short assessment of cognitive state in MS patients, EDSS 0.5–6.0, using BICAMS recommended tests: SDMT; BVMT-R; (2) comparison of test results with demographically corrected normative scores.

MATERIALS AND METHODS

Patients meeting McDonald's criteria for MS and attending the Rīga East Clinical University Hospital "Gaiļezers" and Latvian Maritime MS centre were recruited from January 2013 to March 2015. Sixty-nine patients completed a standardised test — BVMTR and SDMT oral form. Unfortunately, we could not use CVLT2 due to necessity for test translation, validation and associated high expenses.

We used two tests: (1) SDMT form: patient substituted a number orally for randomised presentations of geometric figures, test duration: max 5 min; and (2) BVMTR T1-3 form: 6 geometric figures in a 2×3 array. Patient inspected a 2×3 stimulus array of abstract geometric figures in three learning trials of 10 seconds and drew the array from memory after each learning trial. Test duration: max 10 minutes (Benedict, 1997; Parmenter *et al*., 2010).

The SDMT shows visual, manual motor, speech, learning, speed and accuracy functions (Smith, 2011). BVMTR measures short and long-term visuospatial memory and attention, t scores show respondent's performance relative to the respondent's age group average in the normal population (Benedict, 1997).

Cognitive impairment was defined as ≤ -1.5 standard deviations from the mean for a given age at a particular education level at SDMT performance and ≤ 39 t score range according to demographically corrected normative scores at BVMTR T1-3 performance. Statistical data were processed using guidelines and normative scales developed by the test authors.

All participants gave their written informed consent before entering the study. The study was approved by the Rīga Stradiņš University Ethics Committee and performed according to the Declaration of Helsinki.

Inclusion criteria were:

- MS patient who visited the Latvian Maritime MS centre or hospital "Gaiļezers" MS centre;
- patient age 18 ≤ 60 years;
- patient could write, read and had no significant vision problems (patient could read test symbols).

Exclusion criteria were:

- patient had any known psychiatric condition, alcohol or drug dependence, or presence of a neurological disease other than MS;
- patient had any progressive somatic, oncologic, or infectious disease.

RESULTS

Demographic features. The group included 69 MS patients. Table 1 shows the demographic and clinical data for the group. A control group consisted of healthy adults with comparable demographic characteristics. Comparison in test results is seen in Table 2.

Cognitive performance. The largest patient group (33/69 patients; 47.8%) had very low scores on the SDMT test and 28 of 69 patients (40.6%) had low scores. Table 3 shows test results for the group.

Overall, the largest group (33/69; 47.8%) had average or normal results on the BVMTR T1-3 test with average or normal results, and 15 of 69 (21.7%) patients showed borderline or mild impairment, 9 of 69 (13.0%) — inferior results or moderate impairment and only 2/69 (2.9%) performed very inferior. Table 4 shows group results for total recall (TR).

Table 1

DEMOGRAPHIC AND CLINICAL DATA OF PATIENTS, n = 69

Parameters		Patients
Gender (male/female)		26/43
Age (mean ± SD[1]; years)		37.1 ± 9.7 years
Education 12 years or less/ 13 years or more		21/48
Disease duration (mean ± SD; years)		6.4 ± 6.2
EDSS:		
_	0.0–2	_ 32 (46.4%)
_	2.5–4	_ 17 (24.6%)
_	4.5–6	_ 20 (29.0%)

[1] Standard Deviation

Table 2

RESULTS OF SDMT AND BVMTR TR TESTS FOR PATIENTS AND CONTROLS

	Patients	Controls
Group	69	SDMT[2] = 292
		BVMTR[3] = 1009
Age mean ± SD[1], years	37.1 ± 9.7	SDMT[2] = 34.7
		BVMTR[3] = 38.91 ± 1.37
SDMT[2] score ± SD[1]	44.5 ± 12	51.65 ± 7.8
BVMTR TR[4] score ± SD[1]	23.3 ± 6.9	25.85 ± 4.83

[1] Standard Deviation
[2] Symbol Digit Modalities Test
[3] Brief Visuospatial Memory Test Revised
[4] Brief Visuospatial Memory Test Revised Total Recall

Table 3

COGNITIVE ASSESSMENT DATA FOR PATIENTS, SDMT[1], n = 69

Classification for scores SD[2]	Patients	Interpretation
1	2 (2.9%)	-
0	6 (8.7%)	-
-1	28 (40.6%)	Low scores
-1.5	0	Moderately low scores
-2	14 (20.3%)	}Very low scores
-2.5	0	
-3	19 (27.5%)	

[1] Symbol Digit Modalities Test

[2] Standard Deviation

Table 4

COGNITIVE ASSESSMENT DATA FOR PATENTS BVMTR TR[1], n = 69

t score range	TR[2]	Normative
≥ 81	0	Very superior
71–80	1 (1.4%)	Superior
61–70	9 (13.0%)	Above average
40–60	33 (47.8%)	Average
30–39	15 (21.7%)	Below average
20–29	9 (13.0%)	Inferior
≤ 19	2 (2.9%)	Very inferior

[1] Brief Visuospatial Memory Test Revised Total Recall

[2] Total Recall

Cognitive impairment and EDSS correlation. In the SDMT test, 33 of 69 (47.8%) patients had impaired cognitive skills and we found that cognitive impairment in the SDMT test (n = 33) was distributed evenly among the three EDSS groups. The BVMT-R TR test showed that 26 of 69 (37.7%) patients had memory impairment. Regarding Impaired patient distribution in the EDSS groups (n = 26), 11 of 26 (42.3%) of patients had EDSS 2.5–4.0; 10 of 26 (38.5%) had EDSS 0.5–2.0 and the smallest group 5 of 26 (19.2%) of patients had EDSS 4.5–6.0. Table 5 shows cognitive impairment assessed by the EDSS test.

DISCUSSION

The Symbol Digit Modalities Test (SDMT) score for chronic lesions, according to the manual, is mean SDMT score = 22.8 ± 11.75, which is twice lower than in our study (Benedict, 2007). New validation of scores should be undertaken. It is unclear how to use the presented neurologic patient scores in the BVMTR manual; it describes different types of dementia, but not primary neurodegenerative dementias. More recently, Parmenter *et al.* (2010) and Benedict *et al.* (2006) published normative data for MS on the MACFIMS battery (Benedict *et al.*, 2006; Parmenter *et al.*, 2010). Table 6 provides a comparison of these data.

Table 5

COGNITIVE IMPAIRMENT AND EDSS[1] RELATION

EDSS[1] group	SDMT[2] ≤ -1.5, n = 33	BVMTR TR[3] t score range ≤ 39, n = 26
0.5–2.0	11 (33.3%)	10 (38.5%)
2.5–4.0	10 (30.3%)	11 (42.3%)
4.5–6.0	12 (36.4%)	5 (19.2%)

[1] Expanded Disability Status Scale

[2] Symbol Digit Modalities Test

[3] Brief Visuospatial Memory Test Revised Total Recall

Table 6

COMPARISON, COHEN'S d

	Parmenter *et al.*, 2010, results	Benedict *et al.*, 2006, results	Current study
SDMT[1]	d = 1	d = 1.3	d = 0.7
BVMTR[2]	d = 0.9	d = 1.0	d = 0.4

[1] Symbol Digit Modalities Test

[2] Brief Visuospatial Memory Test Revised

The difference in effect size was medium/large, which might be explained by the incomplete test control group used. The results should be recalculated when testing of the the control group is completed.

Two studies regarding BICAMS validation have recently been published: German and Argentinean (Penner *et al.*, 2015; Vanotti *et al.*, 2015). Comparison data show that effect size difference of test results is small. Results for the different tests are comparable, as shown in Table 7.

Cognitive impairment assessed by EDSS shows that cognitive impairment may be unrelated to neurologic disability status where function problems predominate. Howeveer, this has not been much studied. Lynch *et al.* (2005), found that cognitive impairment was correlated with the rate of disability progression, but it was equivalent for patients with shorter (years) versus longer (10 years) disease duration (Lynch *et al.*, 2005). A large number of MS patients showed decreased elements of attention, visuoperceptual processing working memory and psychomotor speed detected by SDMT, while visual memory tested by the BVMTR T1-3 test was normal or below average in most MS patients.

Table 7

TEST COMPARISON COHEN'S d

	German study (15)	Argentina study (16)	Current study
SDMT[1]	d = 0.5	d = 0.8	d = 0.7
BVMTR[2]	d = 0.6	d = 0.5	d = 0.4

[1] Symbol Digit Modalities Test

[2] Brief Visuospatial Memory Test Revised

It is important to include cognitive evaluation of MS patients in clinical routine, since these cognitive deficits may be present in early phases of disease; the standardisation of cognitive profile evaluation seems to be mandatory in MS patients. Short assessment of cognitive impairment in MS patients is possible in MS centres without a trained neuropsychologist. The Symbol Digit Modalities Test and Brief Visuospatial Memory Test – Revised T1-3 are easy to perform and fast to administer. Translation and validation of the CVLT-II test is needed to include complete international cognitive assessment for the MS recommended battery in Latvia.

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KOGNITĪVO FUNKCIJU MONITORINGS MULTIPLĀS SKLEROZES PACIENTIEM LATVIJĀ

Multiplās sklerozes (MS) pacientiem kognitīvie traucējumi attīstās samērā bieži. Neiropsiholoģiska testēšana ir laikietilpīgs process, kas ietver datu analīzi un sarežģītu testu rezultātu interpretāciju, kam ir nepieciešams speciāli apmācīts personāls. Tāpēc ekspertu komiteja ir ieteikusi īsu starptautisko kognitīvo funkciju novērtēšanu multiplās sklerozes pacientiem (*Brief International Cognitive Assessment for Multiple Sclerosis,* BICAMS), kas ir piemērota lietošanai multiplās sklerozes centros. Mūsu pētījumā tika lietoti testi *Symbol Digit Modalities Test* (SDMT) un *Brief Visuospatial Memory Test* (BVMT) — iegūtie rezultāti tika salīdzināti ar atbilstošo testu rezultātiem pēc literatūras datiem. Diemžēl mēs nevarējām izmantot *California Verbal Learning Test – Second Edition* (CVLT2) sakarā ar to, ka tests nav validēts, kā arī augstu izmaksu dēļ. Mūsu iegūtie dati liecina, ka kognitīvo funkciju īsu novērtējumu MS pacientiem var pielietot arī MS centros, kur nav pieejams speciāli apmācīts neiropsihologs — SDMT un BVMTR T1-3 testi ir viegli un ātri veicami. Lai Latvijā varētu pilnībā izmantot BICAMS, nepieciešams veikt CVLT2 tulkošanu un validēšanu. Šo iemeslu dēļ dotajā pētījumā CVLT2 skala netika izmantota, skalas tulkošana un validēšana ir ilgs un darbietilpīgs process, kā arī skalas licences iegūšana ir finansiāli dārga. Mūsu pētījumā verificēti prevalējoši zemi testu rezultāti MS pacientiem pēc SDMT, bet vairumam MS slimnieku BVMT rezultāti bijuši normas robežās vai uz normas apakšējās robežas. Novērots, ka kognitīvo traucējumu attīstība nav ciešā saistībā ar nespējas pakāpi pēc EDSS.