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ASSESSMENT OF COGNITIVE CHANGES IN MULTIPLE SCLEROSIS WITH THE COMPUTERIZED DIRECT AND INVERSE CONVERSION TEST

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Резюме: *с помощью оригинальной методики компьютерного тестирования были изучены когнитивные изменения при разных типах течения рассеянного склероза (РС). Были выделены характеристики когниций, связанные и не связанные с тяжестью клинических проявлений РС, и выявлены специфические особенности когнитивных изменений у пациентов с релапсирующе-ремиттирующим и вторично-прогрессирующим типами течения РС.*

Resume: *cognitive changes in different types of the course of multiple sclerosis (MS) were investigated by means of an original method of a computerized testing. Cognition characteristics, which were associated and non-associated with a severity level of MS clinical manifestation, were determined. Specific peculiarities of cognitive changes in patients with relapsing-remitting and secondary progressive types of MS course were found out.*

Relevance. Cognitive impairments (CIs) are common in multiple sclerosis (MS) with prevalence rates ranging from 45 % up to 70 % and, due to a relevant role of these impairments in MS, neuropsychological assessment in routine clinical practice is needed [1]. CIs in MS cover recent memory, sustained attention, verbal fluency, conceptual reasoning, visuospatial perception [2], are present at all stages of the disease and limit work and social activities [3; 4]. The most commonly used neuropsychological test to measure the status of a large number of cognitive domains is the Symbol Digit Modalities Test (SDMT) [5; 6]. However, as the SDMT is done either voice or written, its performance is influenced by manual motor skill or writing difficulties, speech disturbances, and dyslexia. To avoid these problems, the computerized Direct and Inverse Conversion Test (DICT) was developed.

Purpose: To investigate cognitive changes in MS using a testing of encoding in the direct order (Letter Digit (LD)) and the reverse order (Digit Letter (DL)) tasks with DICT.

Objectives: 1. To assess and compare the simple reaction time (SRT) and the motor reaction time (MRT) in examined groups; 2. To assess the efficiency and resultativity of performance of the LD and DL tasks; 3. To investigate the connection between the Expanded Disability Status Scale (EDSS) score and cognitive changes; 4. To assess the efficiency of the computerized DICT testing in MS.

Material and research methods. 14 patients with a relapsing-remitting MS (RRMS) (mean age 36.25±1.23 years old) and 6 patients with a secondary progressive MS (SPMS) (mean age 30.50±2.84 years old) ($p < 0,05$) were examined. The control group (CG) included 20 persons (mean age 33.60±5.50 years old) with parameters which did not differ from the patients with RRMS and SPMS. The disability level according to the EDSS was 2 points higher in the SPMS-group as compared with RRMS-group (3.31±0.29 vs. 5.33±0.56; $p < 0,001$). Spot Hunt Test (SHT) and DICT, that were part of the POTesMANU cSACCAS app [7], were used for the cognitive testing. DICT is SDMT similar test, in DICT firstly 45 letters in 3 sets (15 in each) should be encoded into digits (LD task), and after that 45 digits

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in 3 sets should be encoded into letters vice versa (DL task). Spot Hunt Test consisted of SRT and MRT assessments and was performed before and after DICT. The test device was equipped with a 10.1' capacitive touch screen with a resolution of 160 ppi and a 4:3 aspect ratio. It was based on the Google Android 8.1 Oreo.

Research results and their discussion. In each group, the SRT and MRT parameters did not differ at the beginning and end of the test (Table 1), indicating that fatigue did not formed as result of the testing. A comparison of these parameters between the groups showed that the SRT at the beginning and at the end of testing was greater as compared with CG: for patients with RRMS by 19 % and 27 %, respectively, and for patients with SPMS by 77 % and 65 %, respectively ($p < 0,01$). MRT at the beginning and at the end of testing was also greater as compared with CG: for patients with RRMS by 15 % and 14 %, respectively, and for patients with SPMS by 32 % and 36 %, respectively, ($p < 0,05$).

Table 1 - Parameters of performance of the Spot Hunt Test

Group	Opening		Final	
	SRT, s	MRT, s	SRT, s	MRT, s
CG (n=20)	0,53±0,05[1]	12,32±1,02[2]	0,52±0,04[3]	11,74±0,99[4]
RRMS (n=14)	0,63±0,05	14,15±0,92[5]	0,66±0,05[6]	13,38±0,62[7]
SPMS (n=6)	0,94±0,17	16,22±0,96	0,86±0,09	16,01±1,25

[1]p=0,005; [2]p=0,02; [3]p=0,001; [4]p=0,01 – as compared with SPMS patients;
[5]p=0,05; [6]p=0,033; [7]p=0,037 – as compared with RRMS patients

As compared with CG, in the LD task during 90 s, patients with RRMS encoded correctly a lower number of symbols by 25 % ($p < 0,01$), whereas patients with SPMS by 55 % ($p < 0,001$) (Table 2). As compared with CG, in the DL task during 90 s, patients with RRMS encoded correctly a lower number of symols by 31 % ($p < 0,01$), whereas patients with SPMS by 53 % ($p < 0,001$) (Table 2).

In both tasks, during 90 s patients with SPMS encoded one-third less symbols than patients with RRMS ($p < 0,001$). For all groups, there was a decrease in the number of correctly encoded symbols during 90 s in the DL tasks: control group – by 17 %, patients with RRMS - by 9 %, patients with RRMS - by 20 % (Table 2).

Table 2 - Parameters of DICT performance

Group	The correct answers during 90 s		Total time for 45 symbols, s	
	DICT LD	DICT DL	DICT LD	DICT DL
CG (n=20)	34,60±2,74[1]	28,70±1,84[1]	119,78±10,87[1]	134,57±8,84[1]
RRMS (n=14)	23,81±1,73[2]	21,63±1,77[2]	158,03±9,01[2]	173,96±12,05[2]
SPMS (n=6)	16,33±3,43[3]	13,00±2,00[4]	230,86±27,88[5]	253,03±9,44[5]

[1]p < 0,001 – as compared with SPMS patients;
[2]p < 0,001 – as compared with SPMS patients;
[3]p < 0,03; [4]p=0,002; [5]p < 0,01 – as compared with RRMS patients

An analysis of correlation between the number of correctly encoded pairs during 90 s in LD task and DL tasks with the EDSS score found out a strong feedback (r_S=-0,52 and r_S=-0,64, respectively), that indicates a decrease in the quality and speed of encoding with increasing of clinical manifestations of the disease. The encoding time for 45 symbols separately in LD and DL tasks also correlated with the EDSS score (r_S=0,64 and r_S=0,71, respectively). These relationships suggested a slowing of the encoding because of severity of MS symptoms.

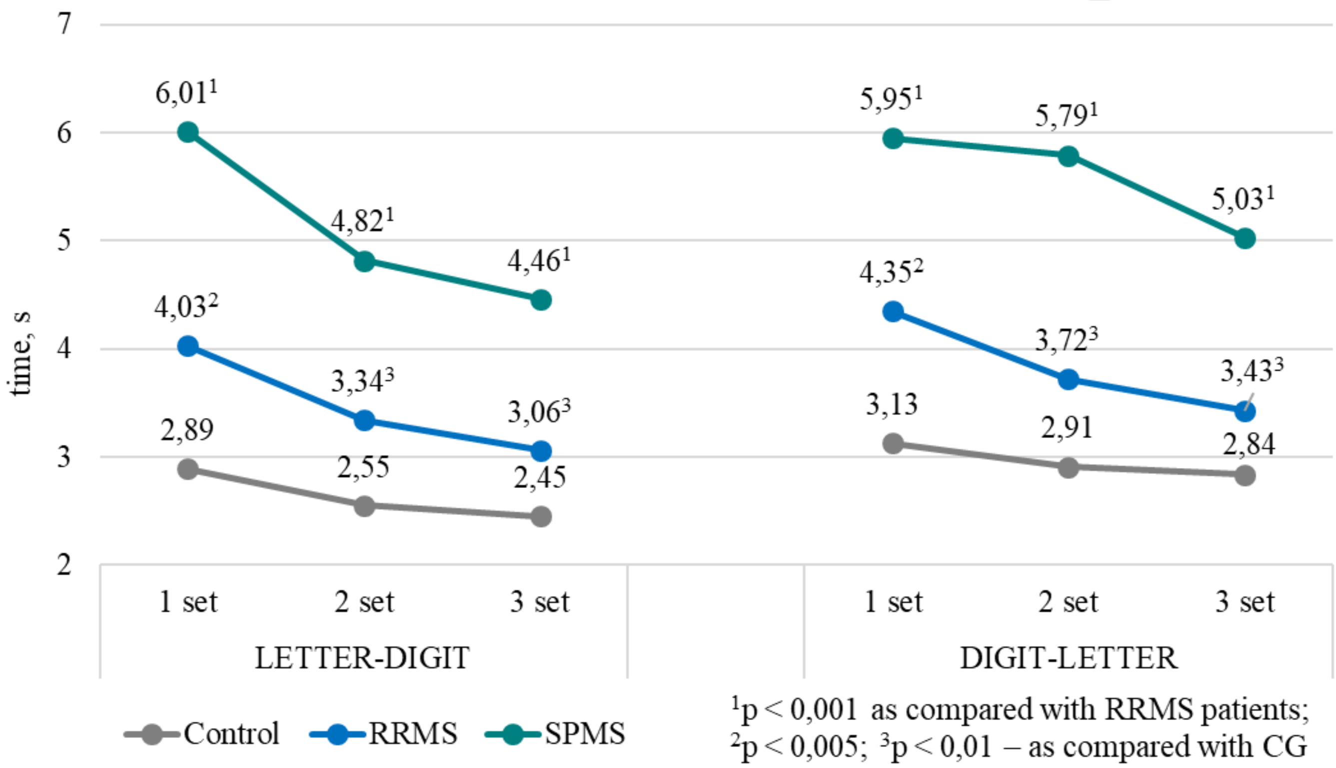

Fig. 1 - The profiles of changes of time to encode a single symbol in LD task and DL tasks

An analysis of results of the LD task performance revealed for all groups in 3 sets a similar profile of descending of the function of time required to encode a single symbol (Fig. 1). When completing the 2nd set, as compared with completing of the 1st one, the time to encode a single symbol was decreased: in CG – by 12 %, in patients with RRMS – by 17 %, in patients with SPMS – by 20 %. When completing the 3rd set, as compared with completing of the 2nd one, the time to encode a single symbol was decreased: in CG – by 4 %, in patients with RRMS – by 8 %, in patients with SPMS – by 7,5 %.

During the performance of the DL tasks, only CG and patients with RRMS had a similar profile of descending of the function of time required to encode a single symbol (Fig. 1), and a decrease of time required to encode a single symbol was observed: in the 2nd row – by 7 % and 14,5 %, respectively, in the 3rd row – by 2,5 % and 8 %, respectively. In patients with SPMS an encoding profile differed from that one in CG and patients with RRMS due to problems with switching to perform other conditions and due to deceleration of learning of key values and encoding keys, that reflected in a significant reduction of time required to encode a single symbol in completing the 2nd and 3rd sets (3 % vs. 13 %).

For both type of the MS course, at the end of each task there was a reduction of the difference between CG and patients by encoding rate. When completing the 3rd set compared to the 1st set in LD task and DL tasks, the difference in the time required to encode a single symbol between CG and patients with RRMS was decreased from 39,5 % to 25 %, and from 39 % to 17,5 %, respectively; between CG and patients with SPMS it was decreased from 108 % to 82 %, and from 90 % to 77 %, respectively.

A set-by-set analysis of encoding mistake profiles found out a significant difference inside each group between LD and DL tasks. In the LD task, the mistake profiles of CG and patients with SPMS were almost identical (Fig. 2). In patients with RRMS, a straight-line 2-fold reduction of the number of mistakes from the 1st to the 3rd sets was observed, while the number of mistakes in the 3rd set was less than in the CG. In DL task, CG demonstrated a straight-line increase of the number of mistakes; in patients with RRMS this parameter was almost unchanged. Patients with SPMS had a prominently descending profile. In the 1st set they made mistakes 5 times more often than the CG and 2,5 times more often than patients with RRMS. In the 3rd set they had no mistakes.

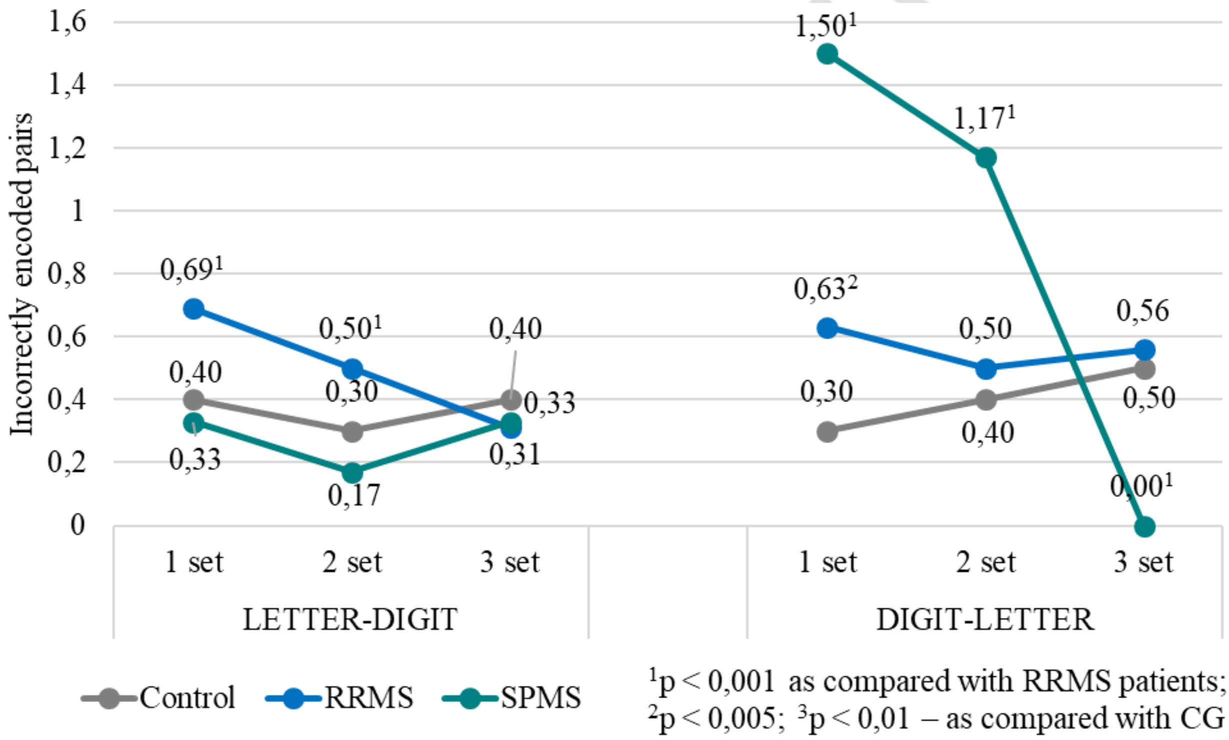

Fig. 2 - The profiles of set-by-set mistakes in LD task and DL tasks

The computerized testing with Spot Hunt Test and DICT allowed us to demonstrate that the difference in the speed of performance of attempts between the groups is connected to two different factors. Firstly, there was a significant difference between the groups in SMT and MRT, which was an integral component of encoding of each symbol. It is motor deficit that impairs the speed of information processing and leads to a distorted perception of cognitive abilities, especially for patients with SPMS. Secondly, a sharp contrast between SPMS patients and CG and RRMS patients on the profile of the time to encode a single symbol and the profile of mistakes in DL tasks indicated a decreasing of a cognitive flexibility and slowed switching when task conditions were changed to opposite ones. Thirdly, the difference between the speed of performance of the same in turn attempts in LD and DL tasks was connected to the increasing role of spatial memory in DL tasks. The encoding symbols are intuitively understandable ascending ordered from 1 to 9 on the LD-keyboard, whereas they have not a known order on the DL-keyboard. Most patients with SPMS and some patients with RRMS compensated their lack of spatial memory by double-looking for the needed symbol (firstly in the key and then on the keyboard). That was reflected as an increase of the encoding time for one pair.

The LD and DL profile of mistakes in CG reflected a decreased concentration. However, an average rate of mistakes decreased or remained constant between attempts both for SPMS and RRMS patients. Patients with SPMS were significantly different from patients with RRMS and CG regarding their profiles of the DL task performance parameters. On the one hand, the large number of mistakes in the 1st and 2nd sets along with a little acceleration of the 2nd set performance indicated problems with switching of attention and a slower learning of key values and encoding keys. On the other hand, an absence of mistakes in the 3rd set and a considerable coding time demonstrated patients` interest not to speed, but to quality of the task completion.

An analysis of the distribution of encoding mistakes in each row revealed fundamentally different patterns of mistakes and their reasons. Firstly, non-system mistakes (no more than 1-2 per set) due to decreased concentration were more frequently in CG, whereas system mistakes (4-6 per set) with even distribution across sets due to a reduced differentiation of mirror letters were more frequently in patients with a higher EDSS score. Secondly, the confusion of the key with the encoding row in CG were associated with the prevalence of speed, whereas in MS patients it was associated with inattention and working memory.

Conclusions: 1. The computerized testing with the Spot Hunt Test and DICT allows to identify individual performance components and to assess conditions of specific cognitive domains; 2. In patients with MS, EDSS score is associated with an increasing of time of the test performance and a decreasing of the amount of correctly encoded symbols during 90 s, but not with the number and density of mistakes both for LD and DL tasks; 3. A motor slowing (MRT) and SRT increasing contribute significantly to reduced speed and resultativity of the encoding test performance, especially in SPMS patients, and this should be taken into account to assess correctly the speed of information processing in MS; 4. SPMS patients have a lower level of switching of attention and problems with spatial memory, but they are more motivated to complete the task correctly than RRMS patients and CG.

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