VISUO-SPATIAL MEMORY EVALUATION OF SUBJECTS WITH RECENTLY-DIAGNOSED MULTIPLE SCLEROSIS. COMPARISON BETWEEN TWO TESTS

AVALIAÇÃO DA MEMÓRIA VISUAL-ESPACIAL DE INDIVÍDUOS COM ESCLEROSE MÚLTIPLA RECÉM-DIAGNOSTICADOS. COMPARAÇÃO ENTRE DOIS TESTES

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ABSTRACT
Objective: It has been claimed that the Brief Visuospatial Memory Test-Revised (BVMTR) is more sensitive than the 7/24 Spatial Recall Test, the aim of this research is to compare the tests qualitatively and quantitatively. Methods: the tests were administered to a group of 100 subjects who had had relapsing-remitting multiple sclerosis for less than five years, and to another group of 45 healthy participants. Results: both tests showed significant differences between groups, $p < .05$, healthy participants obtained the highest performance rate. BVMTR had the highest effect size, with 1.8 total score. A binary logistic regression analysis for the cases and controls variable (Diagnosis Status) retained only the delayed recall score of BVMT-R, explaining 33% of the variance, with an adequate prediction of 77.9% of the cases. Conclusions: results show that the BVMTR is more sensitive, but each test's specific characteristics need to be pondered during the neuropsychological practice, when examining cases in particular. This is the first study to compare the two most popular visual memory tests for recently-diagnosed relapsing-remitting multiple sclerosis subjects.

Keywords: Memory; Neuropsychological tests; Multiple sclerosis; Neuropsychology.

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RESUMO
Objetivo: Foi alegado que o Brief Visuospatial Memory Test-Revised (BVMTR) é mais sensível do que o Spatial Lembre Teste 7/24. O objetivo desta pesquisa é comparar os testes qualitativa e quantitativamente. Métodos: os testes foram administrados a um grupo de 100 indivíduos que tiveram esclerose múltipla remitente-recorrente por menos de cinco anos, e outro grupo de 45 participantes saudáveis. Resultados: ambos os testes mostraram diferenças significativas entre os grupos, p <0,05, participantes saudáveis que têm a taxa de desempenho mais alto. BVMTR tinha o tamanho maior efeito, com 1,8 pontuação total. A análise de regressão logística binária para os casos e controles variável (Status Diagnosis) manteve apenas a pontuação recordação tardia de BVMT-R, explicando 33% da variância, com uma previsão adequado de 77,9% dos casos. Conclusões: os resultados mostram que o BVMTR é mais sensível, mas as características específicas de cada teste precisa ser ponderado durante a prática neuropsicológica, ao examinar os casos em particular. Este é o primeiro estudo para comparar os dois testes de memória visual mais populares para esclerose múltipla temas reincidente-remitente recém-diagnosticados.

Palavras-chave: Memória; Testes neuropsicológicos; Esclerose múltipla; Neuropsicologia.

INTRODUCTION

The prevalence of multiple sclerosis (MS) in Argentina is 14 to 19.8 per 100000 inhabitants, considering data from Buenos Aires city [1]. Cognitive impairment is common in subjects with MS. In Argentina, a prevalence of 43.2% has been confirmed by the RECONEM study [2]. The cognitive areas most frequently affected are attention and processing speed [3], retrospective episodic memory [4], and executive function [5,6].

Among episodic memory, visual memory is one of the most affected functions, but has been given little consideration in research. Studies have shown that subjects need more learning trials in order to acquire new visual information [7]. Visual memory impairment affects instrumental activities of daily life, such as driving [8]. As observed in neuroimaging, that impairment has been associated with glutamate concentration in the hippocampus [9], atrophy of the corpus callosum [10], lesion volume [11,12] and cortical volume [13].

Visual memory is frequently assessed through the 7/24 Spatial Recall Test (7/24 SRT) and the Brief Visuospatial Memory Test – Revised (BVMT-R). The 7/24 SRT was invented by Barbizet [14] and was called 10/36 Spatial Recall Test (10/36 SRT) and then was modified by Rao [15] by reducing the number of items to recall. The revised BVMTR was developed by Benedict [16] when he enriched the scoring point of the test.

Each of them belongs to two different batteries for neuropsychological testing of subjects with MS. 7/24 SRT is part of Rao's Battery for Neuropsychological Screening [15], whereas BVMT-R is part of MACFIMS: Minimal Assessment of Cognitive Function in Multiple Sclerosis [17]. Both 7/24 SRT [18] and BVMT-R [19] have shown construct validity.

There is currently not enough data to determine which of the two is the most suitable test to administer as part of a neuropsychological battery for subjects with MS. Strober et al. [20] have compared the differentiation capacity of these techniques and found that BVMT-R is more sensitive than a version of 10/36 SRT, in which the visual patters to remember are more complex. The difference between subjects with MS (N = 65) and healthy controls (N = 46) has produced Cohen's *d* effect sizes of 0.8 and 0.9 for BVMT-R, and 0.5 and 0.3 for version 10/36. In 2001, a panel of experts chose BVMT-R as the visual memory test for subjects with MS [21]; one of the reasons was that it has six different forms that contribute to the cognitive monitoring of the subject. Since the 10/36 SRT is different to 7/24 SRT, there is no evidence that the BVMTR is superior to 7/24 SRT in the assessment of patients with MS.

After a qualitative comparison between both tests, the following characteristics were observed: For 7/24 SRT: It evaluates learning through five consecutive trials. The level of motor disability of the upper limbs is low and can be avoided by telling the examinee to indicate were the pieces go on the board, with a minor modification of the instructions, be dismissed entirely, thus avoiding motor bias. Scoring is simple: it counts how many pieces have been placed correctly. It comes in two alternative versions. It does not have a visual memory recognition instance. For BVMT-R, on the other hand: It consists of only three learning trials. Motor level involvement of the upper limbs is relatively high and cannot be dismissed, since the subject is required to draw pictures. Scoring is more complete: not only does it evaluate the correct placing of the piece but also the quality of the drawing in relation to the model. There is a scoring manual that has to be properly studied by the examiner for that purpose. It consists of six different forms. It can evaluate the recognition phase, which helps determine if the subject has learned the figures, even if they cannot remember them at will.

Both tests require a similar total administration time and include a learning phase and a delayed recall phase.

The aim of the present study is to compare two visual memory tests that are widely in neuropsychology, in their capacity to differentiate patients with recently-diagnosed MS in Latin America from controls.

METHODS

SUBJECTS

Presented here are results obtained in the observation stage of a multi-center study. In this study, data from a group of 100 subjects diagnosed with relapsing-remitting MS (RRMS) is analyzed together with those of a control group of 45 healthy participants. In the first group, 69% were women, the average age was 34.79 years-old, and SD = 9.42 (Range = 18-56). In the second group, 60% were women, the average age was 32.36 years-old, and SD = 10.5 (Range = 19-58). Inclusion criteria for subjects with RRMS were: confirmed diagnosis of MS of the relapsing-remitting clinical type as defined by McDonald's criteria [22]; ≥ 18 years old; 1 to 5 years of disease affliction; Undergoing disease-modifying therapies treatment for at least 3 months; not being in a relapsing phase or under corticosteroid therapy 2 months before or during the evaluation; absence of any other neurological or psychiatric illness.

Enrollment started February 2010 and closed October 2010. The study was approved by each center’s local Ethics Committee. All participants signed an informed consent, as per the recommendations of the Helsinki Declaration.

Inclusion criteria for control group were: ≥ 18 years old; more or 7 years of formal schooling. Exclusion criteria for the control group were: a history of neurological illness; head trauma; alcohol or drug abuse.

OUTCOMES MEASURES

The 7/24 SRT displays a 7-point figure on a 6x4 board (Design 1) during 10 seconds, after which the subject must reproduce the design on an empty board, with some pieces. This is repeated five times. Then, as an interference, a different figure is displayed on another board (Design 2), and immediately afterwards the subject is asked to draw Design 1 again. After a 20-minute interval, the subject is asked to draw Design 1 one more time. Then, the total number of pieces placed correctly is counted.

The Brief Visuospatial Memory Test – Revised comprises six alternative and equivalent forms (forms 1 to 6). Form 1 was the one used in this study. Each form consists of six geometric figures printed on a 2x3 array on a separate page of the Recall Stimulus Booklet, and twelve recognition items, each printed on a separate page in the Recognition Stimulus Booklet. A Manual is required for precise scoring and interpretation, but it is not necessary to have it during the administration of the test. The six abstract figures are displayed during 10 seconds and then hidden, after which the subject is asked to draw them on a paper with a pencil. Each drawing receives a score of 0 to 2 points, representing location and accuracy. Total score thus ranges from 0 to 12. The primary outcome measure is the total number of points earned over the three learning trials.

In both tests, the total scores for trials and delayed recalls were taken into account.

STATISTICAL ANALYSIS

In order to compare both tests, a Student's t test was used for independent samples. Also, a step-by-step binary logistic regression analysis was used to assess a model for predicting the Diagnosis Status variable. Alpha level was set at .05.

RESULTS

As regards age or years of schooling, there were not significant differences between the groups, neither in gender distribution, $X^2 = 1.124$, $df = 1$, $p = .192$. The tests showed other marked differences between the groups, $p < .05$. Healthy controls had the higher performance rate, with the exception of 7/24 SRT total score, which presented a tendency towards significance. The effect size measured by Cohen's *d* was 0.4 for 7/24 SRT total score, 1 for 7/24 SRT delayed recall, 1.1 for BVMT-R delayed recall, and 1.8 for BVMT-R total score. The last score showed the highest effect size in the differentiation between subjects and controls as regards visual memory. Data is shown in Table 1.

Table 1 - Comparisons between groups on demographic, clinical and cognitive characteristics

	MS Mean (SD) N = 110	Control group Mean (SD) N = 48	*t*	*gl*	*p*	Cohen's *d*
Age	34.79 (9.42)	32.36 (10.5)	1.38	143	.167	0.2
Years of schooling	14.97 (2.99)	14.07 (3.65)	1.56	143	.120	0
7/24 SRT Total	28.55 (5.86)	30.6 (5.59)	-2.47	155	.050	0.4
7/24 SRT Delayed	5.78 (1.6)	6.31 (1.16)	-2.97	131	.027	1
BVMT-R Total	19.09 (7.29)	26.27 (5.94)	-6.29	155	.000	1.1
BVMT-R Delayed	7.28 (2.51)	10.29 (1.47)	-9.8	145	.000	1.8

Note: SD: standard deviation; 7/24 SRT: 7/24Spacial Recall Test; BVMT-R: Brief Visuoespacial Memory Test-Revised.

When entering the four variables of visual memory, a binary logistic regression for the Cases and Controls variable (Diagnosis Status), retained only the delayed recall score of BVMT-R, explaining 33% of the variance, with an adequate prediction of 77.9% of the cases. 83 of 100 subjects with RRMS and 30 of 45 healthy participants were classified correctly. Data is shown in Table 2.

Table 2 - Binary logistics regression. BVMT-R predicts diagnosis status

	Model	β	Wald	Cox and Snell $R2$	Exp(β)	p
Step 1 BVMT-R Delayed recall	$X^2 = 58.1$, $gl = 1$, $p < 0.001$	.853	31.16	0.330	2.348	.000

Note: BVMT-R: Brief Visuoespacial Memory Test-Revised.

DISCUSSION

The results allow us to claim that both tests detect differences between subjects who have had RRMS for 5 or less years, and healthy participants. However, differences between 7/24 SRT and BVMT-R were evidenced. The delayed recall score in BVMT-R shows the highest effect size and an adequate level of sensitivity, and properly discriminates between subjects with MS and healthy controls. In addition, that score was the best predictor of the Diagnosis Status variable, when all visual memory variables of both tests were entered in a regression analysis. These results are in concordance with a previous study by Strober et al. [20], where it was found that BVMT-R is more sensitive than 10/36 SRT. Furthermore, they extend the conclusions of that previous study, being as it is the first investigation to compare the two most used visual memory tests for recently-diagnosed RRMS subjects.
According to the analysis presented here, BVMT-R appears to be the most sensitive test for discriminating between subjects and controls. However, in some cases in the clinical assessment practice, it is also necessary to ponder other characteristics of the tests, such as the requirement of motor ability of the upper limbs and the complexity of the score, instances in which 7/24 SRT seems to be more appropriate. One of the advantages of 7/24 SRT is that it has the possibility to adapt to motor ability alterations of the subjects' upper limbs, something that is quite common among subjects with MS.

On the other hand, one of its limitations is that neuropsychologists in charge of scoring performance during the test were not blind to the Diagnosis Status variable of the participants. That would have increased the reliability of the study's results. In spite of that, results show that the two tests most frequently used for assessing visual memory of subjects with MS present different quantitative and qualitative characteristics. In the neuropsychological practice, it is important to consider each case in particular, so as to decide which of the visual memory tests is more convenient for a comprehensive assessment of cognitive abilities in subjects with MS.

REFERENCES

[1] Cristiano E, Patrucco L, Rojas JI, Cáceres F, Carrá A, Correale J, et al. Prevalence of multiple sclerosis in Buenos Aires, Argentina using the capture-recapture method. Eur J Neurol. 2009;16(2):183-187.

[2] Cáceres F, Vanotti S, Rao S, the RECONEM Workgroup. Epidemiological characteristics of cognitive impairment of multiple sclerosis patients in a Latin American country. J Clin Exp Neuropsyc. 2011;First:1–5.

[3] Denney DR, Lynch SG, Parmenter BA, Horne N. Cognitive Impairment in Relapsing and Primary Progressive Multiple Sclerosis: Mostly a matter of speed. J Int Neuropsychol Soc. 2004;10:948-956.

[4] Lafosse JM, Mitchell SM, Corboy JR, Filley C. M. The nature of verbal memory impairment in multiple sclerosis: a list-learning and meta-analytic study. J Int Neuropsychol Soc. 2013;19(9):995-1008.

[5] Arnett PA, Rao SM, Grafman J, Bernardin L, Luchetta T, Binder JR, et al. Executive functions in multiple sclerosis: an analysis of temporal ordering, semantic encoding and planning abilities. Neuropsychology 1997;11:535-544.

[6] Farez MF, Crivelli L, Leiguarda R, Correale J. Decision-making impairment in patients with multiple sclerosis: a case–control study. BMJ Open 2014;4. e004918.

[7] Gaudino EA, Chiaravalloti ND, DeLuca J, Diamond BJ.
A comparison of memory performance in relapsing- remitting, primary progressive and secondary progressive, multiple sclerosis. Neuropsy Neuropsy Be 2001;14(1):32-44.

[8] Schultheis MT, Weisser V, Ang J, Elovic E, Nead R, Sestito N, et al. Examining the relationship between cognition and driving performance in multiple sclerosis. Arch Phys Med Rehab 2010;91(3):465-473.

[9] Muhlert N, Atzori M, De Vita E, Thomas DL, Samson RS, Wheeler-Kingshott C, et al. Memory in multiple sclerosis is linked to glutamate concentration in grey matter regions. J Neurol Neurosur Psych 2014;85(8):833-839.

[10] Sánchez MP, Nieto A, Barroso J, Martín V, Hernández MA. Brain atrophy as a marker of cognitive impairment in mildly disabling relapsing-remitting multiple sclerosis. Eur J Neurol 2008;5(10):1091-1099.

[11] Amato MP, Portaccio E, Goretti B, Zipoli V, Iudice A, Della Pina D, et al. Relevance of cognitive deterioration in early relapsing–remitting MS: a 3-year follow-up study. Mult Scler 2010;16(12):1474–1482.

[12] Benedict RHB, Ramasamy D, Munschauer F, Weinstock-Guttman B, Zivadinov R. Memory impairment in multiple sclerosis: correlation with deep gray matter and mesial temporal atrophy. J Neurol Neurosur Psych 2009;80(2):201-206.

[13] Calabrese M, Agosta F, Rinaldi F, Mattisi I, Grossi P, Favaretto A, et al. Cortical lesions and atrophy associated with cognitive impairment in relapsing-remitting multiple sclerosis. Arch Neurol 2009;66(9);1144-1150.

[14] Barbizet J, Cany E. Clinical and psychometric study of a patient with memory disturbances. Int J Neurol 1968;7:44–54.

[15] Rao SM, Leo GJ, Bernardin L, Unverzagt F. Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. Neurology 1991;41:685-691.

[16] Benedict R. Brief Visuospatial Memory Test-Revised: Professional manual. Lutz, FL: Psychological Assessment Resources, Inc; 1997.

[17] Benedict RHB, 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 Neuropsych Soc 2006;12:549–558.

[18] Gontkovsky ST, Vickery CD, Beatty WW. Construct validity of the 7/24 spatial recall test. App Neuropsychol 2004;1(2):75-84.

[19] Kane KD, Yochim BP. Construct Validity and Extended Normative Data for Older Adults for the Brief Visuospatial Memory Test Revised. Am J Alzheimers Dis 2014;29;(7):606-606.

[20] Strober L, Englert J, Munschauer F, Weinstock-Guttman B, Rao S, Benedict RHB. Sensitivity of conventional memory tests in multiple sclerosis: comparing the Rao Brief Repeatable Neuropsychological Battery and the Minimal Assessment of Cognitive Function in MS. Mult Scler 2009;15:1077–1084.

[21] Benedict RHB, Fischer JS, Archibald CJ, Arnett PA, Beatty WW, Bobholz J, et al. (2002). Minimal Neuropsychological Assessment of MS Patients: A Consensus Approach. Clin Neuropsychol 2001;16(3)381–397.

[22] 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.