Revista Chilena de Fonoaudiología 21 (2022), 1-7
https://revfono.uchile.cl/
ISSN 0719-4692

Original Article

Exploratory Study for the Validation of the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) in the Population with Relapsing Remitting Multiple Sclerosis of the San Juan de Dios Hospital in Santiago, Chile

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ABSTRACT

The cognitive assessment of individuals with Multiple Sclerosis (MS) is a fundamental aspect of the process of intervention, because of the high prevalence of cognitive impairment associated with this condition. At present, it is recommended to carry out cognitive assessment through BICAMS (Brief International Cognitive Assessment for MS), a test battery specifically developed to evaluate individuals with MS. However, this battery has not yet been validated in Chile.
The present study aims at determining the impact of clinical factors (months of progression of the condition and level of impairment) and individual factors (sex, age, and education level) on the cognitive measures of BICAMS, to obtain accurate and relevant information for future validation processes. The sample consisted of 38 participants with Relapsing Remitting Multiple Sclerosis (RRMS). The results show that only age and sex significantly impact cognitive performance on all three BICAMS subtests. Therefore, when validating this test battery for Chilean individuals in the future, both age and sex should be included and/or controlled for.

Keywords:
Multiple Sclerosis; Cognition; Memory; Neuropsychological Test; Cognitive Dysfunction

Estudio exploratorio para la validación de la Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) en la población con Esclerosis Múltiple Remitente Recurrente del Hospital San Juan de Dios en Santiago de Chile

RESUMEN

La evaluación cognitiva en personas adultas con esclerosis múltiple (EM) es un área fundamental a tener en cuenta en el proceso de intervención, debido a la alta prevalencia de deterioro cognitivo. En la actualidad, se ha recomendado la evaluación cognitiva por medio de la BICAMS (del inglés Brief International Cognitive Assessment for MS), que es una batería específica para evaluar a personas con EM, pero que no cuenta con validación en nuestro país.
El presente estudio tiene como objetivo identificar el impacto de algunos factores clínicos (meses de evolución de la enfermedad y nivel de discapacidad) y personales (sexo, años de escolaridad y edad) que influyen en las medidas cognitivas de la BICAMS, a fin de contar con información relevante y precisa en un futuro proceso de validación. La muestra estuvo constituida por 38 personas con Esclerosis Múltiple Remitente Recurrente (EMRR). Los resultados mostraron que de los cinco factores clínicos observados, solo edad y sexo influyeron de manera significativa sobre los puntajes de las tres pruebas de la BICAMS. Por lo tanto, la validación de esta batería para la población chilena debiera incluir y/o controlar ambas variables de edad y sexo.

Palabras clave:
Esclerosis Múltiple; Cognición; Memoria; Pruebas Neuropsicológicas; Deterioro Cognitivo

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Received: 13-09-2021
Accepted: 11-10-2022
Published: 18-10-2022

https://doi.org/10.5354/0719-4692.2022.64813

INTRODUCTION

Multiple Sclerosis (MS) is an inflammatory demyelinating disease that affects the central nervous system in a multifocal manner. Its clinical presentation is very heterogeneous in terms of symptomatology (Sawcer et al., 2014), and it usually affects young and working people. Although its etiology has not been precisely determined to this day, it is known to be related to genetic (Lauer, 2010; Sawcer et al., 2014) and environmental factors (Inojosa et al., 2020). MS causes sensory, physical, mental, and cognitive disturbances that can result in different levels of impairment (Bravo-González & Álvarez-Roldán, 2019) that compromise social participation.

MS affects around 2.3 million people all over the world (Browne et al., 2014), with a prevalence of approximately 11.7 per 100,000 inhabitants in Chile (Chilean Ministry of Health [MINSAL], 2010). In our country, the average age of diagnostic confirmation is between 27 and 30 years old, with a higher prevalence in women, of 67% (Nogales-Gaete et al., 2014).

The course of MS is highly variable and the disease is categorized into different types, depending on its manifestations and degree of neurological compromise (Katz Sand, 2015). The most frequent form of presentation is Relapsing Remitting Multiple Sclerosis (RRMS), which represents approximately 80% of the cases (Rinker & Cross, 2007). Other types of MS are Primary Progressive MS, Secondary Progressive MS, and Clinical Isolated Syndrome (Lublin, 2014; Lublin et al., 2014). The damage to the cerebral hemispheres due to MS results in various degrees of cognitive impairment, which is observed in 45% to 60% of patients (Sehanovic et al., 2020). The cognitive profile of these individuals is characterized by a decrease in processing speed and a deterioration in episodic memory. In addition, they may show disturbances in executive functions, verbal fluency, and visuospatial abilities (Sumowski et al., 2018).

The decline in cognitive functions helps predict the progress and prognosis of the disease (Sehanovic et al., 2020). Therefore, it is critical to assess cognitive functions and monitor them over time, in order to reduce the repercussions of MS on the quality of life. Additionally, assessments and follow-ups allow for designing comprehensive treatment plans that focus on personalized activities based on the abilities of each individual (Sistiaga et al., 2014).

There is evidence recommending early assessment of cognitive functions, in order to provide people with MS and their families with adequate care (Kalb et al., 2018). However, comprehensive neuropsychological evaluations are not only costly but also require to be performed by qualified staff. Despite the importance of these assessments, not all healthcare centers have the necessary and adequate resources and staff (Langdon et al., 2012). This occurs at a national level in Chile as well.

The current clinical guide for MS, in force since 2010, guarantees the following benefits: 1) diagnostic confirmation, 2) pharmacological treatment, 3) access to rehabilitation and symptomatic treatment (for fatigue, spasticity, and ataxia, among others), 4) treatment of MS flare-ups, and 5) annual MRIs.

Among the guide's recommendations for assessment, it is suggested to use validated instruments, specifically mentioning Barthel and EDSS (Expanded Disability Status Scale). However, the same guide asserts:

> "Nonetheless, given that none (Barthel or EDSS) provide adequate information regarding cognitive impairment, and that this usually occurs in early stages of the disease with little correlation with motor impairment, time, or type of disease course, and that it is not always perceived by the person or their environment, cognitive compromise should be evaluated using specific tests" (MINSAL, 2010, p. 22).

On the other hand, traditional cognitive screening tests such as Mini-Mental (Folstein et al., 1975) are not sufficient to detect cognitive dysfunctions in people with MS. Because of this, various test batteries have been developed that have proven to be valid and reliable (Kalb et al., 2018).

Among the most widely used test batteries for the assessment of people with MS are: 1) Rao's Battery or Brief Repeatable Battery of Neuropsychological Tests, 2) Minimal Assessment of Cognitive Function in Multiple Sclerosis or MACFIMS, and 3) Brief International Cognitive Assessment for Multiple Sclerosis or BICAMS (Macías Islas & Ciampi., 2019). However, none of these test batteries has been adapted or validated for the Chilean population. BICAMS has the advantage that it can be applied by any health professional who works with people with MS and has received training in its use. Furthermore, it does not require expert knowledge of neuropsychology (Langdon et al., 2012). The application time is short, taking on average approximately 15 minutes (Langdon et al., 2012).

BICAMS measures the most affected cognitive functions in people with MS, and it consists of 3 subtests that should be applied consecutively, in the following order: (i) SDMT (Symbol Digit Modalities Test), (ii) CVLT-II (The California Verbal Learning Test II), and iii) BVMT-R (Brief Visuospatial Memory Test-Revised).

Different studies carried out on each subtest show that these are sensitive to sociodemographic factors (age and education level), physical symptoms of the disease, neurological disorders different than MS, and some medications (Langdon et al., 2012). This is related to cognitive impairment and is associated with factors such as type of MS, degree of disability, duration of the disease, level of physical activity, depression (Artemiadis et al., 2020), age, type of occupation, among others (Giedraitienė et al., 2015).

A study in Spanish, carried out in Argentina, examines the relationship between the cognitive performance of people with MS and some demographic and personal characteristics, with the purpose of obtaining relevant information for the validation of this instrument (Vanotti et al., 2018). Variables such as disease progression and employment status of the individual with MS were found to impact their score in the BICAMS. The variables of age, depression, and duration of the disease were found to be less significant. No relationship was found between cognitive performance and the variables of sex and age.

In summary, both the literature and the recommendations found in the Ministry's clinical guide for MS in Chile show the importance of assessment and monitoring of cognitive abilities in people with MS. However, as mentioned before, there are no instruments adapted to or validated for the Chilean population. In addition, to our knowledge, there are no previous studies that measure the impact of demographic and/or personal factors on cognitive performance. Therefore, the objective of this study is to determine which variables should be considered significant for the validation of BICAMS in the Chilean population. Specifically, the aim is to establish the possible impact on cognitive performance (measured using the BICAMS test) of the following variables: age, education level, sex, months since diagnosis of the disease, and level of impairment.

METHOD

Design

This is a quantitative, non-experimental, and cross-sectional study.

Participants

Recruitment and Selection

The participants in this study were selected by convenience sampling, from the population of people with MS in the Adult Neurology Service of the San Juan de Dios Hospital. All the participants had a diagnostic confirmation of MS. The inclusion criteria were: 1) to have been diagnosed with RRMS by a neurologist, 2) to be Chilean Spanish speakers over the age of 18 years, and 3) to have been neurologically stable for at least four weeks before the assessment (no clinical flare-ups during that period).

The exclusion criteria were: 1) having a neurological or psychiatric diagnosis different than MS, specifically depression (monitored using Beck's Depression Inventory, and accepting scores lower than 13 points) (Valdés et al., 2017), 2) having uncorrected visual and/or hearing problems, 3) having a history of learning disabilities, and 4) substance consumption.

No criterion was applied regarding the participants' education level, which made it possible to observe more realistically the influence of this variable, thus avoiding its impact on the assessment since the test does not require people to know how to read and/or write.

Sample

Initially, 48 people were recruited. Each participant voluntarily signed an informed consent approved by the Ethics Committee of the Faculty of Medicine of the University of Chile. In addition, this study was approved by the ethics committees of the San Juan de Dios hospital and the Faculty of Medicine of the University of Chile.

After applying the inclusion and exclusion criteria, the final sample consisted of 39 subjects. The demographic and clinical characteristics of the participants are presented in Table 1.

Table 1. Demographic and Clinical Characteristics of the Participants.

Variable	Participants (n = 39)
Age	37.7 (SD = 11.9; range) Age range between 18 and 65 years
Sex	
Female	n = 26 (66.6%)
Male	n = 13 (33.3%)
Education Level	13.3 (SD = 3.2; range) Range of education level in years, between 0 and 21 years
< 12 years	n = 3 (7.6%)
≥ 12 years	n = 36 (92.4%)
Months since Diagnostic Confirmation	51 (SD = 29.8; range) Range for diagnostic confirmation between 0 and 156 months

Procedures

Before applying the test battery, the clinical records of the patients with MS were reviewed in order to select the participants who met the inclusion criteria. Subsequently, a bespoke clinical interview was carried out, including questions around the following topics: onset of disease symptoms, date of diagnostic confirmation, current pharmacological treatment, presence of clinical flare-ups, hospitalizations due to flare-ups, presence or absence of secondary effects after flare-ups, use of technical aids, learning difficulties or language disorders in childhood, and prior speech therapy interventions.

Finally, the Spanish version of BICAMS was applied (Vanotti et al., 2016). The assessments took place between April 2019 and June 2021. The sequence recommended in the instrument's manual was followed: SDMT, CVLT-II, and finally BVMT-R.

(i) SDMT (Symbol Digit Modalities Test) is a test that evaluates attention span, information processing, and working memory (Smith, 2000). It is an adapted version that includes nine symbols, each one representing a single digit. The digits are found in a table at the beginning of the test for guidance, and the task consists in matching a number with a digit. Information processing speed is evaluated in 90 seconds.

(ii) CVLT-II (The California Verbal Learning Test II) (Delis et al., 2000) is an auditory/verbal learning test in which the examiner reads a list of 16 words. The patient must listen to the list, and subsequently, repeat as many words as possible. The order of repetition is irrelevant, and the process of reading and repetition of the stimuli is performed five times.

(iii) BVMT-R (Brief Visuospatial Memory Test-Revised) (Benedict, 1997) is a test that measures visuospatial memory using 6 abstract figures shown to the patient for 10 seconds. The task consists in remembering the images and then drawing them on a blank sheet, being scored based on the recall and position of the figure. This task is performed three times.

Results Analysis

The data were recorded and systematized using a spreadsheet, with the names of the participants encoded to preserve their anonymity. The date of assessment and application of the BICAMS test battery was logged. The results obtained for each participant and the demographic and personal data relevant to the study were also recorded. Statistical analyzes were performed using software R (R Core Team, 2022).

The first step consisted in obtaining the bivariate correlations (Pearson's test) between the variables selected for the study. Subsequently, and based on the magnitude of the correlation between the variables of interest and the BICAMS test scores, the variables that showed a minimum level of correlation (medium effect size, as specified by Cohen [1992]) were selected to use as predictors of the cognitive abilities measured in multiple regression models. No p-values were reported for the correlations, as these were adjusted based on the absolute value of the coefficients. For the regression tests, the p-values of the coefficients are presented, as well as the value of f2 as a measure of effect size (the increase in the explained variance of each model against an empty model).

RESULTS

Table 2 provides the correlation coefficients for the variables of interest. Here it can be observed that the variable of age shows significant correlation levels with the selected BICAMS subtests: the lowest value is -0.3, which represents a medium effect size. In contrast, education level, months since diagnostic confirmation, and the EDSS scale do not show a significant correlation with either of the three BICAMS subtests, with the highest coefficient being -0.15 and the majority of the values being close to zero.

Table 2. Pearson Correlation Coefficient (r).

	SDMT	BVMT-R	CVLT-II
Age	-0.46	-0.66	-0.3
Education Level	0.05	0.08	0.06
EDSS	-0.07	0.06	-0.13
Months since Diagnosis	-0.04	-0.15	0.01

Once the significance of the correlation between the age variable and the BICAMS subtests was established, its effect was modeled. For this, regression analyzes were used, together with the sex variable (excluded from the previous analyzes due to its categorical nature). Three regression analyzes were performed, with the scores of each subtest as the dependent variable. The three models met the usual assumptions of multiple regression (homoscedasticity and linearity). In addition, the possible presence of influential cases that could bias the value of the predictors' coefficients was checked. Based on this analysis, one

participant whose Cook's distance values were consistently high for all three models was removed from the sample. Therefore, the final sample for the regression analyses consisted of 38 participants.

Table 3 shows the results of the regressions carried out on the three dependent variables of interest, with "age" and "sex" as predictors.

As can be observed, both "sex" and "age" significantly predict the three dependent variables: SMDT, BVMT-R, and CVLT-II. It is noteworthy that, in all the models, the results for the sex variable reveal a higher expected score for the female participants. Given the small number of predictors, the R2 values of the three models show significant explained variances, especially in the case of the BVMT-R subtest.

Table 3. Regressions between predictors and variables of interest.

	SDMT			
	b	se	t	p
Sex	-14.81	4.04	-3.66	< .001
Age	-0.69	0.16	-4.33	< .001
R^2	0.42			
f^2	0.72			
	BVMTR			
	b	se	t	p
Sex	-2.12	1.12	-3.09	0.004
Age	-0.19	0.03	-6.86	< .001
R^2	0.57			
f^2	1.32			
	CVLT-II			
	B	se	t	p
Sex	-14.83	3.39	-4.37	< .001
Age	-0.45	0.13	-3.68	< .001
R^2	0.44			
f^2	0.79			

DISCUSSION

The aim of this research was to determine the factors that influence the scores of the cognitive subtests of the BICAMS test battery. For this purpose, two validation studies on this test were reviewed, one carried out in Lithuania and the other in Greece.

The Lithuanian study shows that the variables of age, education level, and level of impairment have an impact on performance (Giedraitienė et al., 2015). On its part, the research performed in Greece reveals a relationship between education level and cognitive reserve, a factor that would help reduce the presence of detectable cognitive impairment in cognitive screening tests (Artemiadis et al., 2020).

The evidence that has been exposed together with the information used to determine the norm and validity of the BICAMS in other countries, allows us to propose that the selected factors would have an impact on the scores of this test battery. Nonetheless, this influence is only observed in the variables "age" and "sex".

The regression analyzes show that both variables have a significant influence on the BICAMS subtests. A greater effect is found on the BVMT-R subtest, which assesses visuospatial memory, with lower expected performance for men compared to women (Beatty & Aupperle, 2002). This difference in performance according to sex is observed in a previous study, where at the moment of assessing visuospatial skills using verbal and non-verbal memory tests (Mini-Mental and Wisconsin Card Sorting Test), it was found that men scored lower than women in all cognitive tasks. This phenomenon was particularly pronounced for memory and visuospatial abilities, which are the functions measured by the BVMT-R (Beatty & Aupperle, 2002).

In summary, regarding the variable of sex, the results show that male participants achieve lower global scores in the cognitive tests of the BICAMS battery, therefore, they would be at a greater risk of experiencing cognitive decline due to MS. Concerning the variable of age, there is a greater probability of developing cognitive deterioration over the years, a phenomenon already described in the validation study carried out in Argentina (Vanotti et al., 2018).

The results of this research may be biased since the sample size is not representative of the total population of people diagnosed with MS in Chile. Furthermore, the assessments were carried out solely on patients undergoing medical treatment in San Juan de Dios Hospital. Nevertheless, this study can be considered as a first approach to the implementation of the BICAMS test for the assessment of cognitive functions in people diagnosed with MS. Therefore, it is suggested that in the future the sample size is increased for the validation of this instrument, in order to use it in different healthcare centers where people with MS receive treatment.

In addition, it becomes necessary for future validation processes to include measurements for fatigue, which is considered by the

literature to be an influential factor for cognitive performance and, consequently, impacts BICAMS scores (Langdon et al., 2012).

Lastly, having an instrument such as the BICAMS test battery allows for early diagnosis and monitoring of cognitive disturbances objectively and efficiently. This is critical in order to implement adequate multidisciplinary interventions since this instrument can be applied by any health professional who has received proper training. Moreover, the BICAMS test battery can be adapted to the needs and capacities of people with MS, thus contributing to a better quality of life for this population.

CONCLUSION

This research allowed us to determine the direct influence that the variables "age" and "sex" have on performance in the BICAMS cognitive tests. An inverse correlation was found between age and performance in the subtests, meaning that the older the person with RRMS, the lower the scores obtained. Regarding sex, it is revealed that men have a lower performance in cognitive tests than women. The cognitive subtest that showed the greatest difference between men and women was the BVMT-R, which measures visuospatial memory.

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