

Work status and cognitive performance in patients with relapsing remitting multiple sclerosis

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Resumen

La discapacidad física y el curso de la enfermedad son fuertes predictores del estatus laboral en los pacientes con Esclerosis Múltiple (EM). Sin embargo, la cognición no tiene el mismo grado de evidencia. Este estudio plantea el objetivo de investigar la relación entre la situación laboral y el rendimiento cognitivo en la EM.

Se recogieron los datos de 61 pacientes con EM de curso recurrente-remitente (EMRR) que fueron a atenderse en un hospital público entre abril de 2014 y abril de 2015. El 29.5% estaban desempleados, el 54.1% estaban empleados y el 10.4% eran estudiantes o amas de casa. Se im-

plementaron como test neuropsicológicos la Bateria Neuropsicológica Breve para Esclerosis Múltiple y el test Símbolo-Dígito. Además se administraron la Escala de Estatus de Discapacidad Expandida y el Inventario de Depresión de Beck II. La evaluación se realizó de forma individual en dos sesiones, una con el neurólogo y otra con el neuropsicólogo en un consultorio privado.

Las diferencias no fueron significativas en edad y años de instrucción entre los pacientes con y sin empleo. En cambio, los pacientes desempleados tenían un puntaje más bajo en el Símbolo-Dígito, así como la Escala de Estatus de Discapacidad Expandida y un Inventario de

Depresión de Beck más altos que aquellos con trabajos.

Los pacientes con EMRR que estaban desempleados tenían un peor desempeño en la velocidad de procesamiento de la información, más depresión y discapacidad física que aquellos que conservan sus trabajos.

Palabras clave: Esclerosis múltiple; Cognición; Discapacidad; Desempleo; Atención.

Abstract

Employment is a very important aspect of a person's life, and that is why any health-related factor that can interfere in such activity must be identified. The reality of a Latin American country is different and should be approached as a separate object of study. Many factors that contribute to a patient losing the job can be identified in time in order to be reversed or compensated. Thus, identifying the vulnerability profile of the patients with multiple sclerosis (MS) who are at risk of losing their jobs is an important task for researchers. Physical disability and disease course are both strong predictors of work status in MS patients, however, cognition and affective variables do not have the same degree of evidence. This study raises the aim of investigating the relationship between employment status and cognitive performance in MS. With this knowledge, it would be possible to design a neuropsychological rehabilitation plan for patients, which focuses on compensating and recovering from cognitive impairment, as well as on serving as orientation for the person who is at risk of losing their job.

A group difference design was used. The sample units were selected through a non-probability accidental sampling. We collected the data of 61 patients with relapsing-remitting MS (RRMS) who had attended consultation between April 2014 and April 2015, in a public hospital. 29.5% were unemployed; 54.1% were employed; and 10.4% were students or housewives. The Brief Repeatable Battery of Neuropsychology Tests adapted for Argentine population;

Symbol Digit Modalities Test (SDMT), Expanded Disability Status Scale (EDSS) and Beck Depression Inventory-II (BDI-II), were administered individually in two sessions, one with a neurologist and one with the neuropsychologist in a private consulting room.

Age and years of instruction differences between patients with and without employment were not significant. There were 60.8% of patients with cognitive impairment. Among them, 38.7% were unemployed. The relationship between cognitive deterioration and work status was not significant, $\chi^2 = .404$, $df = 1$, $p = .371$.

When comparing the groups in the cognitive battery, a meaningful difference in cognitive performance was observed between the subjects who had a job with those who were unemployed in SDMT ($t = -2.421$, $df = 49$, $p = .019$); performance being higher among the former. No other cognitive score showed significant results. Unemployed patients had higher EDSS and depression, than those with jobs. The cognitive tests administered, together with the BDI-II and EDSS, were included in the binary logistic regression analysis. The second model retained the SDMT and the BDI-II; both tests were able to correctly classify almost 80% of the cases. Also, both SDMT ($\beta = .080$, $p = .014$) and BDI-II ($\beta = -.098$, $p = .022$) shown significant effects on work status.

This study is one of the first attempts in Argentina to analyze the possible determinants of unemployment, which is extremely important in the context of a lack of determining literature about the issue in Latin America. According to results, patients with RRMS who are unemployed have worse performance in speed of information processing, more depression and physical disability than those who retain their jobs. Results are in line with previous studies, although in the present research a cognitive variable showed a greater negative influence on employment status over motor difficulties or physical disability. Clinicians would be able to identify patients whose profile shows a higher tendency towards work life decline, so that they can receive early treatment and delay that progression. It is suggested the realization of a multicentric Latin American study, blind to the pa-

tients labor status, with the aim of broadening the results by improving the study methodology. Key words: Multiple sclerosis; Cognition; Disability evaluation; Unemployment; Attention.

Introduction

Employment is a very important aspect of a person's life, and that is why any health-related factor that can interfere in such activity must be identified. Numerous studies in the USA and Europe address this issue in patients with Multiple Sclerosis (MS) (Kordovski et al., 2015; Raggi et al., 2016; Wicks et al., 2016). The reality of Latin-American is different and should be approached as a separate object of study; however, there is a great lack of studies on the subject in this geographic area.

Unemployment is frequent among patients who are afflicted with MS, literature reports a rate of 40 to 60% (Cores et al., 2014). Studies have explored the variables associated with the work status of patients with MS, showing that physical disability, fatigue, and the progress of the disease have a direct impact on the patients' work status (Honarmand et al., 2011; Salter et al., 2010; Smith et al., 2005). However, variables such as gender, age, cognition, depression and disease duration do not present the same level of evidence. As regards the cognitive aspect, the executive functions (Morrow et al., 2010; Morse et al., 2013) and the information processing speed (Benedict et al., 2006) seem to be connected with unemployment or other occupational disorders, although there are also some studies that found a connection with episodic memory (Glad et al., 2011; Goverover et al., 2007). In addition, studies have proved that the factors that impact on the work status interact with each other. For example, having some grade of cognitive impairment (as reported by the patient) increases the negative effect that motor disabilities have on the patient's work life (Johnson et al., 2009).

Losing the job generates frustration and low esteem, which in turn affects the patient's mental health (Krokavcova et al., 2012) and quality of life (Kikuchi et al., 2013; Patti et al., 2007; Pluta-Fuerst et al., 2011). Nevertheless, many factors that contribute to a patient losing the job can be identified in time in order to be reversed or compensated (Rumrill et al., 2004). Thus, identifying the vulnerability profile of the patients with MS who are at risk of losing their jobs is an important task for researchers.

The aim of the present study is to explore the relationship between cognitive performance and work status in patients with MS. It is important to be able to discern the effect that each cognitive variable has on the daily life of subjects with MS, and especially on their performance at work. With this knowledge, it would be possible to design a neuropsychological rehabilitation plan for patients, which focuses on compensating and recovering from cognitive impairment, as well as on serving as orientation for the person who is at risk of losing their job.

Materials and methods

Design

A group difference design was used. The sample units were selected through a non-probability accidental sampling. All participants who met inclusion and exclusion criteria were asked to participate in the study.

Subjects

Patients with relapsing-remitting multiple sclerosis (RRMS) who had attended consultation between April 2014 and April 2015, in a public hospital were recruited.

Inclusion criteria: being more than 18 years-old, having a diagnosis of RRMS as

per McDonald's criteria (Polman et al., 2011), being in remitting period for over 4 weeks before assessment, and being under immunomodulatory therapy. Exclusion criteria: having a history of brain injury, history of drug abuse, motor disability in the upper limbs, visual or auditory impairment that prevents the normal execution of the neuropsychological tests; being under corticoid treatment, having a diagnosis of major depressive disorder, bipolar disorder, schizophrenia, euphoria, pathological laughing and crying, brain injury on brain magnetic resonance imaging not due to MS.

The study was approved by the Institutional Review Board. All participants signed informed consents.

Instruments

The Brief Repeatable Battery of Neuropsychology Tests (BRB-N) was administered, as adapted for Argentina (Cáceres et al., 2011). The BRB-N includes the following tests:

1. The Selective Reminding Test (SRT), which measures consistent long-term recall (LTR) and long-term storage (LTS) by displaying a list of twelve words and asking the subjects to retrieve them along five learning trials and a delayed recall.

2. The 7/24 Spatial Recall Test, which assesses visual learning and recall by displaying a pattern of seven checkers on a 6x6 checkerboard during ten seconds, and executing delayed recall.

3. The Paced Auditory Serial Addition Task (PASAT), which evaluates sustained attention by presenting numbers every three (PASAT-3'') or every two seconds (PASAT-2'') and asking the patient to add the number they hear to the one they heard immediately before.

4. The Word List Generation Test (WLG), which measures the subjects' verbal fluency as they spontaneously produce

words that begin with letters F, A and S during 60 seconds.

5. The Symbol Digit Modalities Test (SDMT) (Smith, 1982; Vanotti et al., 2015), which measures information processing speed by asking the subject to link symbols with numbers during 90 seconds. The latter is an additional task not originally included in the BRB-N. The oral version was used.

As a measure of disability, the Expanded Disability Status Scale (EDSS) (Kurtzke, 1983) was administered, and Beck Depression Inventory-II (BDI-II) was used for assessing depression (Brenlla et al., 2006).

Cognitive impairment was defined as two tests from different areas (attention, verbal memory, visual memory, information processing speed and verbal fluency), below the fifth percentile with respect to normative data (Cáceres et al., 2011; Vanotti et al., 2015).

Work status was surveyed through a semi-structured interview designed by the authors. Two values were created for this variable: the subjects who did not have a stable job for the last year were considered unemployed; the subjects with full-time jobs or part-time jobs for the last year were considered employed. Housewives and students were excluded from the analysis.

Statistical analysis

The following analysis was performed in the study: Student's *t*-test for independent samples for comparisons between employed and unemployed patients (Work status is the independent variable) in demographic, clinical and cognitive variable (dependent variables); and a stepwise binary logistic regression, forward selection (conditional) in order to determine predictors of Work status, a variable that has two values. The level of significance was established at .05. The Statistical Package for Social Sciences software, 19 version, was used.

Results

Sixty one EMRR patients were recruited, 63.9% of them were women. At the time of evaluation, 54.1% of the subjects had a full-time or part-time job, 29.5% were unemployed and 16.4% were either housewives or students. Henceforth, data from the employed and unemployed are presented.

Between these two groups, differences in age were not significant ($t = -.115$, $df = 49$, $p = .909$), neither were in years of instruction ($t = 1.931$, $df = 49$, $p = .061$), although there is a tendency of significance, nor in years of disease duration ($t = 1.106$, $df = 49$, $p = .251$). Unemployed subjects had a higher EDSS ($t = -2.104$, $df = 49$, $p = .041$), and BDI-II, ($t = -2.497$, $df = 49$, $p = .016$) than those who had a stable job. Data are shown in Table 1.

There were 60.8% of patients with cognitive impairment. Among them, 38.7% were unemployed. The relationship between cognitive deterioration and work status was not significant, $\chi^2 = .404$, $df = 1$, $p = .371$.

When comparing the groups in the cognitive battery, a meaningful difference in cognitive performance was observed between the subjects who had a job with those who were unemployed in SDMT ($t = -2.421$, $df = 49$, $p = .019$); performance being higher among the former. No other cognitive score showed significant results. Data are shown in Table 2.

The cognitive tests administered, together with the BDI-II and EDSS, were included in the binary logistic regression analysis. The second model retained the SDMT and the BDI-II; both tests were able to correctly classify almost 80% of the cases. Also, both SDMT ($\beta = .080$, $p = .014$) and BDI-II ($\beta = -.098$, $p = .022$) shown significant effects on work status.

Discussion

The studies that have attempted to identify predictors of work status in subjects with MS differ with each other regarding certain variables -such as the number of subjects evaluated and the type of neuropsychological assessment implemented (screening/comprehensive; subjective/objective)-, as well as regarding the tests administered (in the case of longitudinal tests, for example, in the number of years during which patients were evaluated). This lack of homogeneity among studies makes it difficult to extract general conclusions. Nevertheless, motor disability, fatigue and other factors such as depression and anxiety have been shown to be connected with unemployment (Cores et al., 2014). There is not enough evidence to claim that variables such as gender, cognition and personality have similar effects. On the other hand, there are variables that have not been taken into account in the analysis, such as: job characteristics, discrimination at work, labour laws, behaviour of the employer and co-workers, and transportation to and from the workplace (Grønning et al., 1990; Messmer Uccelli et al., 2009).

The results of this study show that an important percentage of patients with RRMS (29.5%) are currently unemployed, although it is less than reported in other previous studies, in which that percentage varies from 40-60% (Benedict et al., 2004; Busche et al., 2003; Johnson et al., 2009; Krokavcova et al., 2012; O'Connor et al., 2005; Roessler et al., 2004; Smith et al., 2005; Strober et al., 2012). This may be due, in part, to the fact that in most of the studies, the sample is composed of subjects with MS of the secondary and primary progressive type, in which cases a higher disability and a higher decline in work life can be found (Busche et al., 2003; Glad et al., 2011; Morrow et al., 2010; Salter et al., 2010; Strober et al., 2012). A bigger sample is needed to carry out an epidemiological study that determines

the unemployment percentage among subjects with MS present in a Latin American country. Nevertheless, this study is one of the first attempts in Argentina to analyze the possible determinants of unemployment, which is extremely important in the context of a lack of determining literature about the issue in Latin America.

Unemployed subjects with RRMS performed worse in information processing speed, and they had higher levels of depression and motor disability than those who had a job.

The results highlight the need for the clinical neurologist to plan specific cognitive screening-neuropsychological assessment for patients with MS and to consider cognitive stimulation as a component of the usual treatment of their patients with the aim of preventing job loss.

Among these subjects, motor disability is a clear factor of unemployment (Honarmand et al., 2011; Krokavcova et al., 2012; Messmer Uccelli et al., 2009; Roessler et al., 2004; Smith et al., 2005; Strober et al., 2012; Johnson et al., 2009). In the present research, however, depression and information processing speed were the strongest predictors of work status, over motor disability measured by EDSS. Depression is very common in MS, affecting more than 50% of the patients, but its connection with occupational disorders is not evident. Smith and Arnett (2005) have found that there is a higher depression rate among people who have a job; they argue that the effort to try to keep the job generates stress in subjects with MS. In addition, the direction of this connection is not clear, because at first, it can be intuitively assumed that depression

generates unemployment, when there is also the case that unemployment can cause depression (Honarmand et al., 2011).

Regarding the relationship between unemployment and cognition, other studies used different cognitive batteries but some included the SDMT to value information processing speed and they also found that the SDMT differentiated patients with and without employment, (Honarmand et al., 2011; Morrow et al., 2010), in agreement with present results.

As for the limitations of this study, it can be mentioned that the sample was somewhat small and that the cognitive assessment was not carried out by an examiner blind to the work status of the subject. Finally, future studies should be able to overcome these limitations and analyze the interaction between the variables that impact on the work status of subjects with MS. There are also adverse working events such as accidents in the work place that occur in MS (Incerti et al., 2017), these negative work events may precede job loss, so clinical factors related to them, should be studied (Frndak et al., 2015). Clinicians would be able to identify patients whose cognitive profile shows a higher tendency towards work life decline, so that they can receive early treatment and delay that progression. It is worth mentioning that the economic situation of the country must be taken into account, since it can affect unemployment rates and other work life difficulties, this is why local studies on the matter are needed. In sum, it is suggested the realization of a multicentric Latin American study, blind to the patients labor status, with the aim of broadening the results by improving the study methodology.

Table 1
Demographic and clinical data, comparison between employed and unemployed patients

	Work status		<i>t</i>	<i>df</i>	<i>p</i>	<i>d</i>
	Employed patients <i>n</i> = 33	Unemployed <i>n</i> = 18				
Age	40.42 (11.3)	40.83 (13.6)	-.115	49	.909	0
Years of instruction	13.18 (2.8)	11.56 (2.8)	1.931	49	.061	1
EDSS	2.81 (1.6)	3.75 (2)	-2.104	49	.041	-.6
Years of disease duration	11.51 (9.5)	8.57 (6.6)	1.106	49	.251	.3
BDI-II	10.7 (7.7)	16.8 (9.6)	-2.497	49	.016	-.7

Note:

EDSS: Expanded Disability Status Scale

BDI-II: Beck Depression Inventory

Table 2
Cognitive performance in employed and unemployed patients

Test	Subtest	Work Status		<i>t</i>	<i>g^l</i>	<i>p</i>	<i>d</i>
		Employed patients	Unemployed				
SRT	LTS	38.15 (14.7)	35.44 (11.6)	-.672	49	.505	.2
	LTR	25.15 (15.1)	27.39 (13.6)	.521	49	.605	-.1
	Delayed recall	6.75 (2.5)	6.89 (2.4)	.175	49	.861	0
7/24	Total	27.03 (6.7)	27 (6.8)	-.015	49	.988	0
Visuo-spatial	Delayed recall	4.97 (1.7)	5 (1.8)	.059	49	.953	-.1
PASAT-3		37.35 (18.1)	30.11 (16)	-1.417	49	.163	.4
PASAT-2		25.82 (16.2)	21.12 (15.8)	-.976	48	.334	.2
WLG		28.97 (6.7)	28.89 (7.2)	-.040	49	.968	0
SDMT		43.27 (13)	34.39 (11.4)	-2.421	49	.019	.7

Note:

SRT: Selective Reminding Test
LTS: Long Term Storage
LTR: Long Term Reminding

PASAT: Paced Auditory Serial Addition Test
WLG: Word List Generation
SDMT: Symbol Digit Modalities Test

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