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RESEARCH ARTICLE

Determination of the Factors Related to Neuropsychological Competence in People with Multiple Sclerosis

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Abstract

Objective: Cognitive impairment occurs in 34-65% of persons with multiple sclerosis (pwMS). MS Neuropsychological Screening Questionnaire (MSNQ) is a self-report scale that measures neuropsychological competence and has the power to detect cognitive impairment. However, there are many other objective tests that can measure cognitive impairment. The aim of this study is to examine the relationship between neuropsychological competence and anxiety, depression, cognitive functions, fatigue, quality of life, disease duration and disability level in pwMS.

Materials and Methods: Six hundred and forty-eight pwMS (n=479 female) were enrolled in this study. PwMS with a score of 23 and above on the MSNQ were considered positive for neuropsychological competence impairment test, while pwMS with a score below 23 in MSNQ were considered negative. Disability was assessed using the Expanded Disability Status Scale (EDSS), quality of life with EuroQol 5-Dimensions (EQ-5-D), cognitive functions with the Brief International Cognitive Assessment in Multiple Sclerosis, fatigue with the brief Modified Fatigue Impact Scale, and anxiety and depression levels with The Hospital Anxiety and Depression Scale.

Results: Positive MSNQ was detected in 264 (41%) pwMS, which means worse neuropsychological competence. A statistically significant difference was found between pwMS with positive MSNQ and pwMS with negative MSNQ in terms of age, education, gender, EDSS, fatigue, quality of life, anxiety and depression levels, and cognitive functions. While increasing anxiety level was considered a risk factor for positive MSNQ, each additional increase in the usual activities subscore of the EQ-5D was found to be related to the decrease in the odds of having positive MSNQ.

Conclusion: In this study, it was found that pwMS with positive MSNQ had worse cognitive functions, had higher fatigue levels, were unemployed, and had higher levels of depression and anxiety. Also, the dependence and anxiety level of the pwMS should be considered during cognitive rehabilitation.

Keywords: Depression, multiple sclerosis, neuropsychological competence, quality of life

Introduction

Multiple sclerosis (MS) is the most common chronic inflammatory disease of the central nervous system (CNS), affecting more than 2 million people worldwide (1). The condition is characterized by effects on the brain and the spinal cord. Since MS can affect any part of the CNS, its symptoms may be associated with motor, gait, sensory, visual, bowel/bladder, and/or cognitive impairments. However, cognitive impairment is more insidious and can be destructive if not assessed (2). Cognitive impairment could range from 34% to 65%, depending on the research design in people with MS (pwMS) (3). Cognitive impairment leads to problems such as vocational disability and deterioration in the quality of life (4). Early diagnosis and follow-up on cognitive impairments in MS are also important in helping patients' psychosocial adjustment. Neuropsychological tests were developed to identify neuropsychological disorders and their severity. These tests are also used to assess decline in neuropsychological competence, which is defined as the efficacy of brain functioning after brain injury.

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Neuropsychological testing can be used to monitor patients during treatment (5). The availability of neuropsychological tests has increased significantly over the past decade. Cognitive impairment is measured in pwMS based on a broad range of tests. However, these measurement methods can take time. For this reason, the MS Neuropsychological Screening Questionnaire (MSNQ) has been recommended as a rapid screening test for neuropsychological evaluation (4,6). A score of 23 and above on pwMS is considered positive for this test, an indication of impaired neuropsychological function, while a pwMS score of below 23 indicates negative results (4). With 23 as the cut-off value in pwMS for the MSNQ, 74% of patients were correctly classified as affected compared to the healthy population.

To improve patients' functionality and quality of life in daily and vocational life, it is important not only to determine their neuropsychological competence, but also to determine the factors associated with the neuropsychological competence. Therefore, this study aims to examine the relationship between neuropsychological competence and anxiety, depression, cognitive functions, fatigue, quality of life, disease duration, and disability level in pwMS.

Materials and Methods

Study Design

This cross-sectional study was conducted at the MS Clinic of Dokuz Eylul University, Izmir, Turkey. This study was approved by the Non-Invasive Research Ethics Board of Dokuz Eylul University (protocol number: 7368-GOA and approval number 2022/39-04). All participants were required to complete the informed consent form.

Participants

Participants with a confirmed diagnosis of MS according to 2017 McDonald criteria and aged between 18 and 65 were included in the study. Patients having neurological disorders other than MS and those with cognitive impairments that made them unable to engage in tests and/or complete questionnaires were excluded.

Outcome Measures

Demographic (gender, age, education level, marital status) and clinical data (disease course, disease duration) of pwMS were obtained by interviewing and based on medical records.

The Kurtzke Expanded Disability Status Scale (EDSS) is used widely to evaluate disability levels in pwMS (7). It consists of seven functional systems (pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, mental) and the ambulatory system (8). Based on the patient's neurologic examination, each of these functional systems is scored between 0 and 10. 0 indicates routine neurological examination, and 10 indicates MS-related death.

MSNQ-Patient Version (MSNQ-P) is a self-report scale consisting of 15 questions reflecting neuropsychological competence in the performance of activities of daily living. Responses are scored between 0 and 4 (5). A maximum of 60 points can be obtained from this scale, and higher scores mean deteriorated neuropsychological competence. MSNQ scores were considered positive if self-report scores were greater than 23 (9).

The Hospital Anxiety and Depression Scale (HAD) was developed by Zigmond and Snaith (10) in 1983 to assess clinical anxiety and depression. This scale has also been shown to be a valid measure of the severity of mood disorders. It consists of 14 questions, seven of which measure anxiety while the other seven measure depression (10). The Turkish version of the scale was validated (11).

EuroQol 5-Dimensions (EQ-5D) developed by the European Quality of Life Group to measure health-related quality of life. The EQ-5D scale consists of five sub-dimensions; mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (12).

The brief MFIS is a fatigue scale frequently used in clinical and experimental studies (13). The scale consists of a total of 5 questions aimed at evaluating the cognitive, physical and psychosocial aspect of the perceived fatigue. Each item is scored between 0 and 4, and a low score indicates a low degree of fatigue (14).

The Brief International Cognitive Assessment in Multiple Sclerosis (BICAMS) is a time-consuming measurement method developed for cognitive assessment in MS that does not require special evaluator training or equipment. BICAMS consists of Symbol Digit Modalities Test, California Verbal Learning Test (CVLT), and Brief Visuospatial Memory Tests (BVMT) (15). The validation study on Turkish pwMS was performed by Ozakbas et al. (16).

Sample Size

In a study examining the relationship between factors such as depression, pain, age, gender, disability level, and neuropsychological competence, the adjusted R-square value of the regression model was reported to be 0.13 (17). With these data, the effect size of the model in the study was calculated to be 0.15. In this context, the smallest sample size for the study was calculated as 107 with effect size =0.15, power =95%, while the error probability was determined to be 0.05 using G*Power (version 3.1) software.

Statistical Analysis

The normal data distribution was checked using the Kolmogorov-Smirnov test and histograms. Descriptive analyses were presented namely, the median and interquartile range for continuous variables and percentages for categorical variables.

The difference between pwMS with positive MSNQ and pwMS with negative MSNQ was measured by the Mann-Whitney U test. Binary logistic regression was used to determine the related factors with positive MSNQ. Statistical significance was set at $p<0.05$. Data were analyzed using IBM SPSS Statistics software (Version 25.0. Armonk, NY: IBM Corp.).

Results

Six hundred and forty-eight pwMS (n=479 female) were enrolled in this study. Positive MSNQ was detected in 264 (41%) pwMS. PwMS with positive MSNQ were older in age and had higher disability levels compared with pwMS with negative MSNQ. Between-group differences were also observed to be influenced by gender, education level, employment status, and marital status. The demographic and clinical differences between pwMS with positive MSNQ and pwMS with negative MSNQ are given in Table 1.

Table 2 shows differences between pwMS with positive MSNQ and pwMS with negative MSNQ in terms of EQ-5D subscales, MFIS subscales, BICAMS subscales, and HAD anxiety and depression subscales. There was a statistically significant difference between these two groups across all the variables. PwMS with positive MSNQ has worse cognitive performance and quality of life and higher fatigue, anxiety, and depression score than pwMS with negative MSNQ.

Table 3 presents the results of the binary logistic regression models to determine the contribution of fatigue, quality of life, depression and anxiety, and cognitive function on affected neuropsychological competence in pwMS. From binary logistic regression, increasing anxiety level was found to be a risk factor for positive MSNQ. However, each additional increase in the usual activities subscore of the EQ-5D is related to a decrease in the odds of having positive MSNQ.

Discussion

The primary finding of this study is that neuropsychological competence could be related to anxiety level and the usual activities subscore of the quality of life. Moreover, except for disease course and duration, all variables were found to be different between groups. PwMS with positive MSNQ have a worse score in patient-reported outcomes, worse cognitive functions, and a higher disability level than pwMS with negative MSNQ.

Table 1. Demographic and clinical characteristics of the participants

		pwMS with positive MSNQ (n=264)	pwMS with negative MSNQ (n=384)	p-value
Age (years) median (IR)		36.00 (30.0; 45.0)	34.00 (27.0; 42.0)	0.002*
Gender (n, %)	**Female**	208, 78.8%	271, 70.6%	0.019*
	Male	56, %21.2	113, 29.4%	
Disease duration (years) median (IR)		5.68 (1.82; 11.40)	4.84 (1.02; 10.13)	0.055
Disease course (n, %)	**Relapsing-remitting MS**	260, 98.5%	379, 98.7%	0.667
	Secondary progressive MS	3, 1.1%	5, 1.3%	
	Primary progressive MS	1, 0.4%	0, 0.0%	
EDSS median (IR) (range between 0-10)		1.50 (0.0; 2.0)	1.0 (0.0; 1.50)	<0.001*
Education level (n, %)	**Elementary school**	72, 27.3%	63, 16.4%	0.001*
	High school	82, 31.1%	117, 30.5%	
	University	107, 40.5%	204, 53.1%	
Employment status (n, %)	**Employment**	108, 41.2%	200, 52.2%	0.003*
	Unemployment	115, 43.9%	118, 30.8%	
	Retired	20, 7.6%	24, 6.3%	
	Student	19, %7.3	41, 10.7%	
Marital status (n, %)	**Single**	66, 25.0%	148, 38.6%	0.001*
	Married	180, 68.2%	213, 55.6%	
	Divorced	18, 6.8%	22, 5.7%	

*p<0.05, IR: Interquartile range, pwMS: People with multiple sclerosis, MSNQ: Multiple Sclerosis Neuropsychological Questionnaire, EDSS: Expanded Disability Status Scale

Table 2. Differences in pwMS with positive MSNQ and pwMS with negative MSNQ in terms of EQ-5D subscales, MFIS subscales, BICAMS subscales, and HAD anxiety and depression subscales

	pwMS with positive MSNQ (n=264)	pwMS with negative MSNQ (n=384)	p-value
Brief-MFIS total	11.0 (7.0; 14.0)	3 (1.0; 6.0)	<0.001*
Brief-MFIS physical score	4.0 (3.0; 6.0)	1.0 (0.0; 3.0)	<0.001*
Brief-MFIS cognitive score	4.0 (3.0; 6.0)	1.0 (0.0; 3.0)	<0.001*
Brief-MFIS psychosocial score	2.0 (1.0; 3.0)	0.0 (0.0; 1.0)	<0.001*
EQ-5D-mobility	15.0 (6.9; 93.1)	93.1 (79.1; 93.4)	<0.001*
EQ-5D-self care	98.7 (6.8; 98.8)	98.7 (98.0; 98.8)	<0.001*
EQ-5D-usual activities	10.9 (6.6; 91.2)	91.2 (84.1; 92.8)	<0.001*
EQ-5D-pain-discomfort	22.0 (15.4; 64.3)	68.3 (22.0; 83.4)	<0.001*
EQ-5D-anxiety-depression	19.0 (12.6; 22.8)	72.2 (17.3; 82.0)	<0.001*
EQ-5D-visual analog scale	70.0 (60.0; 80.0)	90.0 (70.0; 90.0)	<0.001*
HADS-A	9.0 (6.0; 13.0)	5.0 (2.0; 7.0)	<0.001*
HADS-D	8.0 (5.0; 10.0)	3.0 (1.0; 6.0)	<0.001*
SDMT	45.0 (35.0; 54.0)	51.5 (42.0; 60.0)	<0.001*
CVLT-II	49.0 (39.0; 57.0)	51.0 (43.0; 61.0)	<0.001*
BVMT	24.0 (19.0; 28.0)	26.0 (22.0; 31.0)	<0.001*

*p<0.05, MSNQ: Multiple Sclerosis Neuropsychological Questionnaire, MFIS: Modified Fatigue Impact Scale, HADS-A: Hospital Anxiety and Depression Scale-Anxiety, HADS-D: Hospital Anxiety and Depression Scale-Depression, SDMT: Symbol Digit Modalities Test, CVLT: California Verbal Learning Test, BVMT: Brief Visuospatial Memory Tests, pwMS: People with multiple sclerosis, BICAMS: Brief International Cognitive Assessment farms

Table 3. Estimates of binary logistic regression for having positive MSNQ

Risk factors	OR	95% CI	p-value
Brief-MFIS total	1.202	0.951-1.520	0.124
Brief-MFIS physical score	0.842	0.622-1.142	0.269
Brief-MFIS cognitive score	1.183	0.891-1.572	0.245
Brief-MFIS psychosocial score	1.014	0.846-1.215	0.881
EQ-5D-mobility	0.999	0.992-1.005	0.731
EQ-5D-self care	0.995	0.987-1.003	0.237
EQ-5D-usual activities	0.992	0.986-0.999	0.017*
EQ-5D-pain-discomfort	1.000	0.992-1.008	0.947
EQ-5D-anxiety-depression	0.996	0.988-1.004	0.289
EQ-5D-visual analog scale	0.992	0.977-1.007	0.288
HADS-D	1.053	0.975-1.137	0.191
HADS-A	1.098	1.027-1.175	0.006*
SDMT	0.979	0.957-1.002	0.074
CVLT II	0.999	0.977-1.023	0.955
BVMT	0.992	0.946-1.041	0.793
Hosmer and Lemeshow test		11.547	
Sig.		0.173	
Nagelkerke R2		0.531 (53.1%)	

*p<0.05, MSNQ: Multiple Sclerosis Neuropsychological Questionnaire, MFIS: Modified Fatigue Impact Scale, HADS-A: Hospital Anxiety and Depression Scale-Anxiety, HADS-D: Hospital Anxiety and Depression Scale-Depression, SDMT: Symbol Digit Modalities Test, CVLT: California Verbal Learning Test, BVMT: Brief Visuospatial Memory Tests, CI: Confidence interval, OR: Odds ratio

Fenu et al. (18) investigated the relationship between cognitive functions and daily activities in pwMS from both the patient and the caregivers' perspective. The authors showed a significant correlation between the performance of daily activities and cognitive impairment. It should be highlighted that the correlation coefficient was higher in caregiver perception (18). Similarly, we found that increasing independence in usual activities decreased the risk of neuropsychological competence. However, there is an informant report version of the MSNQ questionnaire that was not applied in the present study. For future studies, using the two versions of the MSNQ could be more informative.

Akbar et al. (19) examined the role of anxiety on self-reported measures of cognitive functions in pwMS. They reported that the anxiety level negatively affects perceptions reported in self-cognitive assessment of the pwMS (19). Our study showed that increased anxiety level is one of the risk factors for positive MSNQ. Therefore, the cognitive rehabilitation process for pwMS should consider the dependence and anxiety levels.

Although it is accepted that an increase in MSNQ score can be due to depression, many studies show that perceived cognitive difficulties are correlated with decreased employment and job performance, decreased health-related quality of life and increased subjective cognitive complaints (20,21). Likewise, the results of this study show that unemployment is higher among pwMS with positive MSNQ than among pwMS with negative MSNQ. Also, the quality of life and depression levels are shown to be worse among the pwMS with positive MSNQ than among those with negative MSNQ negative.

While there is no difference between the two groups in terms of disease duration and disease course, the higher EDSS in MSNQ-positive patients was statistically significant and was not consistent with the lack of a relationship between EDSS and MSNQ in a few studies (20,21). The difference between these findings and our study is that in the present study, the EDSS interval is relatively narrow and any slight increase has significant impacts on the measurement.

Our study found that pwMS with MSNQ positive had worse cognitive functions, had higher fatigue levels, were more likely to be unemployed, and had higher levels of depression and anxiety. This finding is consistent with studies showing that working capacity in pwMS is affected by the combination of these factors (22).

Study Limitations

The most important limitation of this study is the low EDSS level. However, it has been shown that pwMS have low neuropsychological competence even in cases where the EDSS is low.

Conclusion

This study showed that worse neuropsychological competence could be seen even at low EDSS levels. It has been shown that there is a correlation between employment statuses, quality of life, fatigue, depression, anxiety, and cognitive impairment affect neuropsychological competence in pwMS, affecting daily life functionality negatively. Also, the dependence and anxiety level of the pwMS should be considered during cognitive rehabilitation.

Ethics

Ethics Committee Approval: This study was approved by the Non-Invasive Research Ethics Board of Dokuz Eylul University (protocol number: 7368-GOA and approval number 2022/39-04).

Informed Consent: All participants were required to complete the informed consent form.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.O., Concept: O.S., H.K., S.O., Design: O.S., H.K., S.O., Data Collection or Processing: O.S., H.K., S.O., Analysis or Interpretation: O.S., H.K., S.O., Literature Search: O.S., H.K., S.O., Writing: O.S., H.K., S.O.

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