Ayşe Hazal DÜNDAR

Memory Functionality and Mental Health in Multiple Sclerosis[1]

Multipl Sklerozda Bellek İşlevselliği ve Ruh Sağlığı

Ayşe Hazal DÜNDAR[2]

ARTICLE INFO	ABSTRACT
	The aim of the study is to evaluate the memory functions and symptoms of mental disorders in patients diagnosed with Multiple Sclerosis and to compare them with healthy individuals. 100 individuals diagnosed with Multiple Sclerosis and 60 individuals not diagnosed with Multiple Sclerosis voluntarily participated in the study. In order to evaluate the memory functions of individuals, the Selective Recall Test, 10/36 Spatial Recall Test and Digit SpanTest tasks were applied. The Depression, Anxiety and Stress Scale-21 was used to evaluate the symptoms of mental disorders. As a result of the cognitive evaluation, it was found that individuals diagnosed with Multiple Sclerosis scored lower in all sub-scores of the Selective Recall Test, 10/36 Spatial Recall Test and Digit Span Tests compared to the control group, and this difference was statistically significant. In the evaluation of mental health, the group diagnosed with Multiple Sclerosis had higher depression, anxiety and stress levels compared to the control group, and there was a statistically significant difference between the two groups. It was found that being diagnosed with Multiple Sclerosis was associated with poor memory performance and higher symptoms of mental disorders. The findings of the study support the findings of the studies conducted in the field.

MAKALE BİLGİSİ	ÖZET
	Çalışmanın amacı, Multipl Skleroz tanısı alan hastaların bellek işlevselliğinin ve ruhsal bozukluk semptomlarının değerlendirilmesi ve sağlıklı bireyler ile karşılaştırılmasıdır. Araştırmaya 100 MS'li birey ve 60 Multipl Skleroz tanısı almayan sağlıklı birey gönüllü olarak katılmıştır. Bireylerin bellek işlevlerinin değerlendirilmesi amacıyla Seçici Hatırlama Testi, 10/36 Uzamsal Bellek Testi ve Sayı Dizisi Testi görevleri uygulanmıştır. Ruhsal bozukluk semptomlarının değerlendirilmesi amacıyla ise Depresyon, Anksiyete, Stres Ölçeği-21 kullanılmıştır. Yapılan bilişsel değerlendirme sonucu, Multipl Skleroz tanısı alan bireylerin Seçici Hatırlama Testi, 10/36 Uzamsal Bellek Testi ve Sayı Dizisi testlerinin tüm alt puanlamalarından kontrol grubuna göre daha düşük puan aldığı ve bu farkın istatistiksel olarak

Memory Functionality and Mental Health in Multiple Sclerosis

1. Introduction

Multiple Sclerosis (MS) is an autoimmune central nervous system disease characterised by demyelination and axon damage, causing symptoms in many different areas and levels (Oh et al., 2018). MS is a disease with multiple symptoms. Symptoms vary according to the location and amount of lesions present and the level of damage. In the early stages of the disease, sensory symptoms have been reported in 85% of patients and fatigue in 81% (Kister et al., 2013). In addition to these symptoms, complaints in many areas such as blurred or double vision, dizziness, imbalance, tremor, muscle weakness and numbness, and pain may occur.

Although physical dysfunctions are observed in individuals with MS, difficulties are also observed in cognitive processes. When the cognitive functionality of individuals with different types of MS is evaluated, cognitive performance decreases at different levels and in different areas of functionality in approximately 40-60% of individuals with MS (Rao et al., 1991). Cognitive dysfunctions show themselves prominently in the advanced stages of the disease. However, studies have revealed that impairments in this area are also observed in the clinically isolated syndrome (CIS) stage, when the first clinical findings of the disease are observed (Chiaravalloti & DeLuca, 2008; Glanz et al., 2007). In a study conducted by Tettenborn and colleagues in 2014, in which 78 individuals with RRMS participated, it was reported that cognitive impairment was observed in 44.87% of individuals with RRMS (Tettenborn et al., 2014). In another study conducted by Campbell and colleagues (2016), individuals with RRMS and SPMS, this rate was shown to be 64.5%, and in a study conducted by Romero and colleagues (2015), the rate was shown to be 44.32%. The results of a study conducted with a Turkish sample and evaluating cognitive functioning in individuals with MS were analysed. In this study conducted by Bilge and colleagues (2013), it was reported that cognitive impairment was observed in 41.7% of individuals with MS. In a similar study involving individuals with RRMS, 51 individuals with RRMS were included and cognitive impairment was reported in 41.18% of the participants (Keklikoğlu et al., 2010; Topçular et al., 2012).

In summary, it is seen that cognitive functions are affected in individuals diagnosed with MS. Related studies support that the affected cognitive areas are memory, attention, executive functions and information processing speed (Migliore et al., 2017).

Complaints in individuals with MS are often accompanied by symptoms of mental disorders. Depression and anxiety are the leading psychiatric disorders seen in individuals with MS. A study revealed that the rate of depression in individuals with MS was 40% (Chwastiak et al., 2002). Another study reported a point prevalence of depression in individuals with MS of 20-50% and a lifetime prevalence of 50% (Giardono, 2011). All these findings obtained from studies support the existence of a strong relationship between MS and depressive symptoms (Chwastiak et al., 2002; Patten et al., 2003). In the meta-analysis conducted by Boeschoten and colleagues (Boeschoten et al., 2017), 58 studies were evaluated and thus, data of 87.756 individuals with MS were analysed. The findings of the study revealed that the rate of depression in patients was 30.5%. Another mental disorder analysed in this study was anxiety disorder. Like depression, anxiety symptoms are one of the most common complaints in MS patients. In studies, the prevalence of anxiety disorder in MS patients is known to be approximately 20-40% (Giardono, 2011). In the meta-analysis study of Boeschoten and

colleagues this rate was 21.1% (Boeschoten et al., 2017). When the studies conducted in the Turkish sample were analysed, it was reported that the prevalence of depression was 32% and the prevalence of anxiety was 74% in one study (Şen et al., 2015). In another study, 13 of 23 individuals diagnosed with MS had moderate-high level depressive symptoms and 16 had moderate-high level anxiety symptoms (Emre et al., 2003). All these findings support that depression and anxiety symptoms observed in individuals with MS are significantly higher compared with individuals without MS.

The aim of the study was to evaluate the memory functioning and mental disorder symptom level of individuals with MS and to compare them with individuals without MS.

2. Methods

2.1. Study design and participant

100 volunteer patients who met the inclusion criteria among the patients who applied to the Multiple Sclerosis Polyclinic of Dokuz Eylül University Faculty of Medicine, Department of Neurology, were included in the study. The inclusion criteria of the sample included in the patient group were to be older than 18 years of age, to have been diagnosed with MS according to McDonald 2017 criteria (Thompson et al., 2018), not to be in an attack period, and not to have used steroids in the last 1 month before the test. In the healthy sample group, which included individuals who were not diagnosed with MS, 60 volunteer individuals were included. Exclusion criteria were determined for individuals included in both groups. These are having a diagnosis of psychosis, being illiterate, having a diagnosis of substance and alcohol use disorder. The ethics committee approval of the study was granted by Dokuz Eylül University Non-Interventional Research Ethics Committee (Date: 15.11.2018/Decision No: 2018/29-05). All individuals who voluntarily agreed to participate in the study were informed about the study and all participants were read and signed an informed consent document.

2.2. Data collection tools

2.2.1. Socio-demographic and clinical information form

A form created by the researchers was used to obtain socio-demographic information such as age, marital status, gender, employment status and clinical information on the presence of chronic disease, medication use, MS type, duration and disability status of the participants.

2.2.2. Selective reminding test (SRT)

The test, which is used to evaluate verbal learning, long-term memory, recall and executive functions, consists of 12 words. The individuals are asked to recall 15 minutes after the applications in order to evaluate their long-term memory performance and are evaluated. The Selective Recall Test offers three types of scores. These score types are Long Term Storage (SRT-LTS), Consistent Long-Term Recall (SRT-CLTS) and Delayed Recall (SRT-DR) (Ehrenreich, 1995). Selective Reminding Test is included in the Brief Repeatable Battery Of Neuropsychological Tests (BRB-N), a neuropsychological test battery widely used to evaluate cognitive status in individuals with MS. BRB-N is a neuropsychological test battery with high specificity (94%) and sensitivity (71%).

2.2.3. 10/36 spatial memory test (SPART)

The test, which aims to evaluate visual-spatial learning, immediate recall and recall performance, was designed as a checkerboard consisting of 6x6 squares. Participants are expected to learn the locations of 10 tokens placed in the sample table and then recall them instantaneously and with a delay. The test is evaluated with two types of scoring. The score type that evaluates immediate recall is SPART-TL and SPART-DR, which presents the long-

term memory performance of individuals (Boringa et al., 2001). This test is included in the Brief Repeatable Battery of Neuropsychological Tests (BRB-N).

2.2.4. Digit span test (DST)

The Digit Span Test, one of the tests of the Wechsler Memory Battery, aims to evaluate auditory attention, short-term memory and working memory performance. The test consists of two different subtests, seven pairs of forward and seven pairs of backward number sequences. These are the Digit Span Forward (DSF) and Digit Span Backward (DSB) subtests.

2.2.5. Depression, anxiety, stress scale-21 (DASS-21)

The Turkish adaptation of the scale developed by Lovibond and Lovibond (Lovibond and Lovibond, 1995) was conducted by Sarıçam (Sarıçam, 2018). The Turkish adaptation study of the scale consisting of 21 items and 3 factors was conducted in both clinical and normal samples. As a result of reliability analyses, the reliability coefficient of the scale was 0.85 for depression sub-factor, .80 for anxiety sub-factor and .77 for stress sub-factor.

2.3. Statistical evaluation

The data were analysed using SPSS 21 statistical software. Prior to the analysis, the data of the study were examined in terms of missing values and the assumptions of normal distribution and were included in the analysis with the necessary tests depending on these results. Pearson correlation analysis was used to evaluate the relationships between variables, and Chi-square and independent groups T-test were applied to examine the differences between groups.

3. Results

The data of 100 individuals with MS (68 females, 32 males) and 60 individuals without MS (36 females, 24 males) were included in the analysis. The mean age of the individuals with MS was 40.79 ± 12.17 years and the mean age of the individuals without MS was 38.52 ± 13.67 years. There was no statistically significant difference between the education levels of the participants in both groups ($p= 0.99$). When the marital status of the participants was evaluated, 58% of the individuals with MS were married, 42% were single; 51.7% of the control group were married, 48.3% were single.

Diagnostic categories of the patient group were analysed. In the patient group, 81% were diagnosed with RRMS, 10% with SPMS, 3% with PPMS and 1% with CIS. The mean Expanded Disability Status Scale (EDSS) score of the patients was 2.47 and the mean disease duration was 12.5 ± 2.2. Socio-demographic and clinical information of the participants are given in Table 1.

Table 1. Sociodemographic and Clinical Information

	Patient (n=100)	Non-Patient (n=60)	t/X^2	p
Gender Female Male	68 (%68) 32 (%32)	36 (%60) 24 (%40)	1.06	0.30
Education Status Primary school Middle school High school University	16 (%16) 14 (%14) 26 (%26) 44 (%44)	9 (%15) 8 (%13.3) 17 (%28.3) 26 (%43.3)	0.12	0.99
Age (year)	40.79 (SD=12.17)	38.52 (SD=13.67)	-1.09	0.28
Marital Status Married Single	58 (%58) 42 (%42)	31 (%51.7) 29 (%48.3)		
Employment Status				

Not working	55 (%55)	12 (%20)		
Working	41 (%41)	37 (%61.7)		
Student	4 (%4)	11 (%18.3)		
MS Type				
RRMS	81 (%81)			
SPMS	10 (%10)			
PPMS	3 (%3)			
CIS	1 (%1)			
EDSS Mean	2.47 (SD=2.20)			
Duration of Illness (Year)	12.47 (SD=9.16)			

The normality distribution of the data was examined, and it was determined that the data obtained showed normal distribution. Therefore, the difference between the groups was analysed by Independent Groups T Test.

Memory functioning of the individuals was evaluated with three different tests and memory performance scores were compared between the two groups (Table 2). It was found that the performance scores of individuals with MS were significantly lower than those of individuals without MS in each score type of memory functionality.

Table 2. Cognitive Assessment Results

	Patient (n=100)		Non Patient (n=60)			
	Mean	**SD**	**Mean**	**SD**	**t**	**p**
SRT						
SRT-LTS	32.00	15.26	46.80	14.06	6.12**	.000
SRT-CLTS	20.68	14.54	39.60	16.86	7.50**	.000
SRT-DR	6.28	2.64	8.58	2.45	5.49**	.000
SPART						
SPART-TL	14.38	4.86	19.07	5.57	5.59**	.000
SPART-DR	4.85	2.05	6.93	2.54	5.39**	.000
DST						
DSF	12.03	3.85	14.28	4.60	3.33**	.001
DSB	1136	3.86	13.90	4.84	3.64**	.000

DSB: Digit Span Backward; DSF: Digit Span Forward; DST: Digit Span Test; SPART: 10/36 Spatial Memory Test; SPART-DR: long-term memory performance; SPART-TL: immediate recall; SRT: Selective Reminding Test; SRT-CLTS: Consistent Long-Term Recall; SRT-DR: Delayed Recall; SRT-LTS: Long Term Storage
**p<.001

Depression, anxiety and stress levels of the participants were evaluated with the Depression Anxiety Stress Scale-21. As a result of the analyses, it was found that the stress, depression and anxiety levels of individuals with MS were significantly higher compared to the control group without MS (Table 3).

Table 3. Intergroup Scores of DASS-21 Scores

	Patient (n=100)		Non-Patient (n=60)			
	Mean	**SD**	**Mean**	**SD**	**t**	**p**
Depression	5.52	4.42	3.75	3.14	2.72**	.007
Anxiety	4.93	3.43	2.93	2.38	3.97**	.000
Stress	7.81	4.20	5.05	3.27	4.64**	.000

**p<0.01

DASS-21 scores of the individuals were also evaluated according to various levels of depression and anxiety sub-dimensions. Accordingly, 76% of individuals with MS showed normal, 16% mild, 7% moderate and 1% severe anxiety symptoms. In individuals without MS,

96.7% showed normal level anxiety symptoms and only 3.3% showed mild level anxiety symptoms. Similar results were observed when the scores of the depression sub-dimension were analysed. It was observed that 83% of individuals with MS showed normal, 11% mild and 6% moderate anxiety symptoms. When the scores of the control group without MS were analysed, it was observed that 95% of the individuals showed normal, 3.3% mild and 1.7% moderate depressive symptoms.

4. Discussion

MS is a multi-symptomatic disease in which cognitive dysfunction and symptoms of mental disorders can be observed in addition to physical symptoms (Boeschoten et al., 2017; Giardono, 2011; Kister et al., 2013; Rao et al., 1991). This study aimed to evaluate memory functionality, depression, anxiety and stress levels in individuals with MS. For this purpose, memory performance and mental disorder symptom level of 100 individuals with MS and 60 healthy individuals were evaluated.

Related studies show that impairments in immediate and delayed visual and verbal memory, information processing speed, working memory, attention and executive functions frequently occur in individuals with MS (Amato et al., 2013; Benedict et al., 2006; Rao et al., 1991). In the study conducted by Migliore and colleagues (2017), cognitive functions were evaluated with the MACFIMS test battery and conducted with individuals with RRMS. It was shown that 51% of the participants had involvement in verbal, visual and working memory areas (Migliore et al., 2017). Another study evaluated the cognitive functions of individuals with MS and healthy individuals. It was observed that the Selective Recall Test and 10/36 Spatial Memory Test scores of individuals with MS were significantly lower compared to healthy individuals (Sepulcre et al., 2016).

Amato and colleagues (2010) reported that individuals with RRMS scored statistically significantly lower on the Selective Recall and 10/36 Spatial Memory Test than healthy individuals (Amato et al., 2010). Borghi and colleagues (2016) compared the cognitive functions of individuals with RRMS and PPMS with healthy individuals. Cognitive functions were evaluated with the Selective Recall Test and 10/36 Spatial Memory Test, as well as PASAT (Paced Auditory Serial Addition Test) and SDMT (Symbol Digit Modalities Test). It was observed that individuals with MS had lower scores compared to healthy individuals and this difference was statistically significant (Borghi et al., 2016). Similar results were obtained in another study conducted by López-Góngora and colleagues (2015). Individuals with MS had lower scores on the Selective Recall Test and 10/36 Spatial Memory Test compared to healthy controls, and this difference was statistically significant (López-Góngora et al., 2015).

In this study, Selective Recall Test, 10/36 Spatial Memory Test and Digit Span Test were administered to compare memory functioning between the groups. The test scores obtained by the two groups were compared. It was observed that the test scores of the patient group were lower than those of the control group and this difference was statistically significant. This finding shows that verbal, visual and working memory performance of individuals with MS is lower than that of healthy individuals, and it also reveals that there are impairments in immediate and delayed recall processes. This finding is consistent with the literature.

The DASS-21 was used to evaluate the level of mental disorder symptoms, which was another aim of the study. When the scores belonging to the sub-dimensions of the scale were compared, it was seen that the depression, anxiety and stress levels of the patient group were higher than the healthy group and this difference was statistically significant. This finding supports the results of the studies in the literature. Studies show that depression and anxiety levels in individuals with MS are higher than the general population. The worldwide prevalence rate of depressive disorders is 3.76% and the rate of those diagnosed with anxiety disorders is reported

as 4.05% (GBD, 2019). Findings regarding the presence of depression in individuals with MS vary between 20 and 50% for point prevalence (Boeschoten et al., 2017; Chwastiak et al., 2002; Giardono, 2011; Şen et al., 2015). In studies evaluating anxiety symptoms in individuals with MS, point prevalence rates ranged between 14% and 74% (Giardono, 2011; Şen et al., 2015). Although the prevalence rates of depression and anxiety show a wide range, the results of many studies show that the level of depression and anxiety in individuals with MS is higher than the general population.

The study has some limitations. Considering the type of MS, there is no heterogeneous distribution. A large part of the sample consists of patients diagnosed with RRMS. This limitation weakens the generalisability of the results. The use of cross-sectional method in the study causes that the measurements were not repeated at different times. Repeated measurements with a larger and heterogeneous sample may be recommended for future studies. Having a control group in the study enabled the comparison of cognitive functioning and mental disorder symptom level. At the same time, the fact that many areas of memory, including verbal, visual, working memory, and immediate and delayed memory, were included in the study provides a comprehensive evaluation. The study allows different domains of mental disorder symptoms such as anxiety, depression and stress to be addressed and the measurement tool to identify different levels of psychopathology. This not only shows that symptoms of mental disorders are higher in individuals with MS, but also provides information on the levels and extent of this difference. The study shows that functioning in different memory domains is lower in individuals with MS compared to healthy individuals, and that symptoms of mental disorders are higher in individuals with MS.

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