

Original Article

Is Everything a Challenge for Multiple Sclerosis patients? Nonverbal Semantic Memory Performance in Iranian Relapsing-Remitting Multiple Sclerosis Patients

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Abstract

Objectives: The objective of the current study was to evaluate the nonverbal semantic memory performance of MS patients and compare it with their healthy counterparts. **Materials and methods:** In this study, 70 patients with definite relapsing-remitting multiple sclerosis (15 men and 55 women) and 70 healthy individuals of comparable demographics (age, gender, and education) from patients' relatives and family members were selected based on convenient sampling. The patients recruited for this study were divided into two groups based on their Montreal Cognitive Assessment (MoCA) scores. The first group of patients (MS1) with MoCA scores of 18-25, and the MoCA scores of the second group (MS2) ranged from 10 -17. All of the participants were right-handed, originally born in Mashhad, Iran, and native speakers of Persian. To assess the nonverbal semantic memory performance of the participants, the picture version of The Camel and Cactus Test (CCT) was selected and administered from the Cambridge Semantic Memory battery test. **Results:** The results revealed that there was no significant difference between the MS1 and the Healthy Controls group in living and man-made variables, while MS 2 performed significantly different compared to other groups in these variables. The results also showed that all three groups of participants performed significantly different from each other in reaction time variable. **Conclusion:** The findings showed that cognitive impairment in multiple sclerosis patients did not affect their nonverbal semantic memory performance, however, it had an impact on their reaction time.

Keywords: nonverbal information; semantic memory; Multiple sclerosis; Iran

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Introduction

Multiple Sclerosis (MS) is a neurological disorder which affects Central Nervous System (CNS) and leads to demyelination and neurodegeneration through disease progression^{1, 2}. One of the most common deficits in Multiple Sclerosis (MS) is cognitive impairment and might be manifested even in the early phase of the disease^{3, 4}. This disability affects the speed of information processing, attention, executive function and long-term memory

performance of 40 to 65% of MS patients^{5,6, 7}.

Long-term memory is classified into two systems: declarative and procedural memory. Declarative memory is further divided into semantic and episodic memory⁸. Semantic memory, contrary to episodic memory, is a mental lexicon organized hierarchically and contains the individual's general acquired knowledge about the world and concepts of words and pictures that are not time- or place-oriented⁹. Semantic memory plays an essential role in human's

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cognition such as social communication, reasoning, judgment, distinguishing fact from fiction, and language^{10, 11}; for instance, it might not affect the action of sitting but would involve the recognition of a familiar chair a person used to sit on. Therefore, dysfunction of semantic memory would adversely affect individuals' social and personal life.

Studies have been carried out regarding semantic memory impairment in Schizophrenia¹², Obsessive-Compulsive disorder¹³, amnesic mild cognitive impairment¹⁴, and Multiple Sclerosis^{15,16,17}. In contrast to verbal semantic memory, according to the literature, very few studies have evaluated nonverbal semantic memory in neurodegenerative diseases¹⁸, semantic dementia¹⁹, and aphasia²⁰. Despite the authors' attempts, no previous study addressing this issue in Multiple Sclerosis patients were found. Therefore, the purpose of the current study is to investigate the nonverbal semantic memory performance of Iranian relapsing-remitting Multiple Sclerosis patients.

Materials and methods:

Participants

In this cross-sectional study, 70 patients (15men and 55women) from those referred to a private neurology clinic in Mashhad, Iran, and 70 healthy individuals of comparable demographics (age, gender, and education) from patients' relatives and family members were selected based on convenient sampling. All patients were diagnosed with definite relapsing-remitting multiple sclerosis, total disease duration ranged from 1 year to 14 years, according to McDonald's diagnostic criteria. The patients were aged 18 to 65 years old, their formal educational background ranged from high school diploma to master's degree in different fields of study and their Expanded Disability Status Scale (EDSS) scores was < 6. The patients recruited for this study were divided into two groups (MS1& MS2) according to their Montreal Cognitive Assessment (MoCA) scores, cut off score ≥ 26 . The reason for this type of categorization was that the first group of patients (N=35), with MoCA scores of 18-25, were still fully ambulatory, self-sufficient, their EDSS scores were normally ranged from 0-2.5, and had mild cognitive impairment, while the MoCA scores of the second group (N=35), ranged from 10 -17, had disabilities that impeded their daily activities, their EDSS scores were ranged from 3- 5.5 and had moderate cognitive decline due to the disease progression. All of the

participants were right-handed, originally born in Mashhad, Iran, and native speakers of Persian. The participants would be excluded from the research if they had a history of drug and/or alcohol abuse, other neurological disorders, brain surgery, psychiatric disorder, and uncorrected visual or auditory problems and/or systematic diseases such as diabetes and hypertension.

Cognitive and Memory Scale

The Montreal Cognitive Assessment (MoCA) test was used to screen the participants' cognitive performance and this was done based on the superiority of MoCA as compared to MMSE for measuring cognitive function in individuals with MS. MoCA is a brief, stand-alone screening measure for cognitive impairments created by Dr. Naserddin et al. in 2000 and evaluates language, visuospatial skill, naming, orientations, memory and attention²¹. The cutoff score for this test is ≥ 26 , and those who received lower scores are regarded as cognitively impaired. To assess the nonverbal semantic memory performance of the participants, the picture version of The Camel and Cactus Test (CCT) was selected and administered from the Cambridge Semantic Memory battery test²². This test is an improved and difficult form of the Palm and Pyramid Trees test (PPT)²³ and evaluates the participant's ability to figure out the semantic associations between a target picture on the top of the page and the other four pictures from the same category in the bottom. The CCT comprised of 64 pictures which shows 32 living (domestic and foreign animal, fruits, birds) and 32 man-made (large and small household items, vehicles, tools) items. This test is easy to administer, and more scrutinizing in evaluating mild semantic memory²⁴.

Procedure

The present study was carried out according to the Declaration of Helsinki and the ethical rules of the National Public Health Institute. This research was approved by the Health Research Ethics Community of Ferdowsi University of Mashhad under the code: IR.MUM.FUM.REC.1397.034. The written informed consent was obtained from all the participants prior to the study. At first, the participants' cognitive function was evaluated through the MoCA. Then, the participants were instructed to perform the CCT test. Prior to starting the real test, participants were presented with some examples for understanding the rules. They were given the pictures and asked to see

whether they could find the relationship between the stimuli and the target picture. The participants would be reinforced, without providing a clue to conduct the test, even if they could not find the connection between the pictures. The participants' answers and their reaction times were recorded and calculated for the assessment.

Results:

The Kolmogorov-Smirnov Test showed that the data were normally distributed ($P > 0.05$). Demographic and clinical characteristics of 140 participants are presented in table 1.

As table 1 shows, there is no significant difference between the three groups of participants in age and years of education ($P > 0.5$). Furthermore, there was no significant difference between the two groups of patients in total years of disease duration ($P > 0.5$). The Tukey post hoc test showed that the lowest performance in MoCA test, significantly belonged to the patient group with higher EDSS score (moderate), the next rank belonged to the patient group with lower EDSS ratings (mild), while the highest scores received by the healthy controls. Mean and standard deviation of all participants' performance in all variables of the test are presented in table 2.

The results shown in table 2 were as follows: (1) both HC (7.89) and MS1(7.75) performed similarly in living variable, while MS 2 had the lowest score (6.54). In man-made variable, the poor performance belonged to the MS2 (6.06), but both HC (7.86) and MS1 (7.74) had resembling performance. Nonetheless, in reaction time variable, HC (8.13) had the fastest performance and the next group was MS 1 (13.69), while the MS 2 (25.77) had the longest performance. One way ANOVA was run to

Table 2: Mean & standard deviation of participants' performance in Living, Man-made, & reaction time

Variables	Groups	N	Mean	Std. Deviation
Living	HC*	70	7.89	0.31
	MS 1*	35	7.75	0.40
	MS 2*	35	6.54	0.70
Man-made	Control	70	7.86	0.36
	MS 1	35	7.74	0.45
	MS 2	35	6.06	0.70
Reaction time	Control	70	8.13	1.61
	MS 1	35	13.69	1.88
	MS 2	35	25.77	4.31

*HC: healthy control, MS1: MS group with mild cognitive impairment, MS2: MS group with mild cognitive difficulty

evaluate the probable difference between groups in all variables. The results are shown in table 3.

The results in table 3 revealed that all three groups of participant (HC, MS1, MS2) performed significantly different from each other in living, man-made, and reaction time variables ($P=0.000 < 0.05$). Therefore, the Tukey post hoc test was run to determine which groups act significantly different in these three variables. The results of the post hoc Tukey test are displayed in table 4. As shown in table 4, there was no significant difference between HC and MS1 in living ($P= 0.309 > 0.05$) and man-made ($P= 0.429 > 0.05$) variables, while MS2 performed significantly different ($P=0.000 < 0.05$) from the others in these variables. However, there was a significant difference between all three groups of participants in reaction time variable ($P=0.000 < 0.05$). In other words, the MS2 had the worst performance, while the HC and MS1 performed respectively better compared to MS2 in this variable. The results are best shown in Figure 1.

Discussion and conclusion:

The objective of the current study was to evaluate the nonverbal semantic memory performance of MS patients and compare it with their healthy counterparts. This makes the results of the present research unique and interesting. The results of this study revealed that there was no significant

Table 1: Demographic and clinical characteristics

	Healthy control group (N=70)	MS 1 (N=35)	MS 2 (N=35)	F-value	P-value
Age (M(SD))	(41.5 (11.55))	(38.57 (11.85))	(42 (10.42))	0.996	0.371
Gender Male(%)	21.42%	20%	22.85%		
Female(%)	78.57%	80%	77.14%	-----	-----
Years of formal education (M(SD))	(14.45 (2.15))	(14.85 (2.13))	(14.11 (2.11))	1.057	0.350
Total disease duration [years] (M(SD))	-----	(6.11(3.34))	(5.74(3.26))	-----	0.640
EDSS (M(SD))	-----	(2.05 (3.60))	(3.68 (0.65))	-----	0.010
MoCA(M(SD))	(29.8 (0.46))	(21.6(2.21))	(15.6 (1.03))	1577.5	0.000

Table 3: ANOVA results of total correct answers, total correct names & errors in 3 groups of participants

Variables	Groups	Sum of Squares	Df	Mean Square	F-value	P-value
Living	Between groups	45.304	2	22.652	108.046	.000
	Within groups	28.722	137	.210		
Man-made	Between groups	81.193	2	40.597	172.510	.000
	Within groups	32.240	137	.235		
Reaction time	Between groups	7265.729	2	3632.864	536.573	.000
	Within groups	927.557	137	6.770		

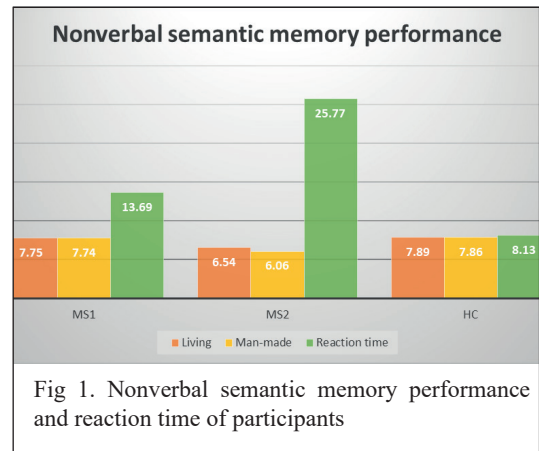


Fig 1. Nonverbal semantic memory performance and reaction time of participants

difference between MS1 (EDSS= 0-2.5) and HC group in the living variable, while MS 2 (3- 5.5) performed significantly different as compared to MS1 and HC groups in this variable. It is important to bear in mind that although MS1 performance in nonverbal semantic memory was not significantly different from HC, their mean scores in both living and man-made variables were lower as compared to their healthy counterparts. This indicates that they might have an impaired nonverbal semantic memory, but it is not significant. So far, no research has evaluated the nonverbal semantic memory performance in MS patients, however, these findings broadly supports the work of other studies^{25,26} which claimed that with disease progression, the cognitive decline became more evident and had an adverse impact on semantic memory. Additionally, the grey matter cortical thinning²⁷ and hippocampus atrophy in grey matter²⁸ would lead to memory dysfunction. In this regard, a research was conducted by Bozeat²⁹ investigating the nonverbal semantic dysfunction in individuals with semantic dementia (SD) and the

result of his study showed that nonverbal semantic performance of SD patients was significantly poor as compared to controls which is due to comprehension deficit. Nevertheless, the results of Lambon Ralph and Howard's³⁰ study indicated that even with impaired semantic memory, patients' comprehension would be better when the stimuli of a test were pictures rather words. This might explain why MS1 performance was similar to HC on this test.

Another finding of this study was that there was a significant difference between MS 2 and the other two groups (MS1 and HC) in the man-made variable; however, no significant difference was found between MS1 and HC in this variable. It seems possible that this result might be due to the cerebral cortex deficits and its impact on visual cortex and processing sensory information caused by demyelination and neurodegeneration in MS^{31,32}. Moreover, the results showed that the MS2 performance in the living variable was better than the man-made variable. This result is in line with the study of Ikeda³³ and Rogers³⁴ which claimed that at the basic levels of semantic association, living things might have more common features than nonliving objects; therefore, perception, recognition, and distinguishing a man-made picture might become difficult for MS patients with moderate cognitive impairment.

Perhaps the most interesting finding to emerge from the analysis was that all three groups of participant performed significantly different from each other in reaction time variable. MS 2 received the lowest score as compared to MS1 in this variable. This finding confirms that the reaction time is associated with information processing speed

Table 4: Multiple Comparisons groups, Tukey HSD

Variable	Group 1	Group 2	Mean Difference (1-2)	Std. Error	P-value
Living	Control	MS 1	0.14	0.09	.309
		MS 2	1.35*	0.09	.000
Man-made	Control	MS 1	0.13	0.10	.429
		MS 2	1.80*	0.10	.000
Reaction time	Control	MS 1	-5.56*	0.54	.000
		MS 2	-17.64*	0.54	.000

*P< 0.05

and is consistent with that of Deluca³⁵ who believed that deficit in this skill would adversely impact other cognitive functions such as decision making. Decision making in this test is very important and puts more demands on semantic memory as it evaluates the semantic association via decisional components. Therefore, due to the higher cognitive impairment in MS2, their performance took longer as compared to MS1. This result is in accord with the study of Reicker³⁶ indicating that choice tasks are more difficult and hence, this increases the reaction time as compared to simple tasks.

The lack of progressive types of MS patients in the sample adds further caution regarding the generalizability of these findings. Notwithstanding the limitation, this study has several strengths: (1) findings of the research showed that multiple sclerosis could not affect the nonverbal performance in semantic memory in the early phase of the disease and semantic association knowledge of MS patients

with mild cognitive impairment; therefore, further studies need to be carried out to validate these findings in the early phase of MS, (2) with the progression of MS, the patient would experience evident cognitive decline even in comprehending tasks with no words or sentences, and (3) regardless of the disease phase, multiple sclerosis significantly impacts the reaction time. This is a remarkable result because MS patients might not have an impaired nonverbal semantic memory, however, their reaction time is significantly longer as compared to their healthy counterparts. Therefore, the findings of this research provide insights for clinicians and rehabilitation service providers to regard reaction time of MS patients in their assessments and treatments since it would directly affect the social and personal life of this population. It is recommended that further research be undertaken regarding the nonverbal semantic memory performance in MS progressive type.

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