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Examination of High-Level Language Skills in 2 Phases of Multiple Sclerosis (Relapsing-Remitting & Secondary Progressive) in Comparison With Healthy Counterparts

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Abstract

Background: Language skills compromised after neurological damage, such as multiple sclerosis (MS), significantly impacting patients' quality of life. MS impairs high-level language functioning. Despite existing research, no studies have examined high-level language functions during different phases of the disease. This is crucial for a better understanding of the linguistic profiles of affected patients.

Methods: This descriptive-analytical study included 25 patients with RRMS, 27 patients with SPMS, and 30 healthy individuals (age range, 22-57 years). They were selected based on convenience sampling. All participants were sampled using the Persian version of the high-level language skills assessment test. The Kruskal-Wallis test was used to compare the performance of the 3 groups, and the Bonferroni test was employed to make pairwise comparisons between groups.

Results: The Kruskal-Wallis test revealed significant differences in the total score and all subtest scores ($P \leq 0.05$), except for the ambiguous sentence comprehension subtest ($P \geq 0.05$). The Bonferroni test revealed a significant difference in the total score and all subtest scores ($P \leq 0.05$) between healthy individuals and those with SPMS & RRMS, except for the ambiguous sentence comprehension subtest ($P \leq 0.05$). Also, no significant differences were found in the total score and all subtest scores between the SPMS and RRMS patients ($P \geq 0.05$).

Conclusion: The results of the present study showed that the high-level language functions were weaker in MS patients compared to healthy individuals. However, no significant difference was found between the RRMS and SPMS patients.

Keywords: Multiple Sclerosis, Relapsing-Remitting, Chronic Progressive, Language Tests

Conflicts of Interest: None declared
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Introduction

Multiple sclerosis (MS) affects the central nervous system (CNS) and is characterized by demyelination, axonal damage, and progressive neurological impairment. It often emerges in early adulthood and is more prevalent in wom-

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↑What is "already known" in this topic:
High-level language disorders can occur in multiple sclerosis (MS). Therefore, it is essential for the healthcare system to recognize potential language disorders in MS and to refer patients for timely evaluation and treatment. Studies conducted so far have only focused on examining the presence or absence of high-level language skills impairment in MS without considering the effects of different MS types.

→What this article adds:
The high-level language functions were weaker in MS patients compared with healthy individuals. Also, no significant difference was found between the relapsing-remitting MS (RRMS) and secondary progressive MS (SPMS) patients. The lack of difference between the 2 disease patterns may be related to cognitive skills and the duration of the disease.

en than in men (1, 2). Based on the progression rate, the disease is classified into 4 clinical types: relapsing-remitting (RR), primary progressive (PP), secondary progressive (SP), and relapsing-progressive (RP). Among these, relapsing-remitting MS (RRMS) is one of the most common types, accounting for 85% to 90% of cases (3). The secondary progressive MS (SPMS) is further divided into primary and secondary progressive forms. Primary Progressive MS (PPMS) is observed in 9% of patients and worsens over time (4, 5). SPMS is observed in 31% of patients who initially have RRMS but later progress to the SP phase (3).The prevalence of this disease has increased in the past 2 decades (6), and according to the literature, its prevalence in Iran is 100 per 100,000 (7). Symptoms and signs resulting from damage to the pyramidal system, brain, and brainstem include spasticity, weakness, ataxia, tremors, language skill impairment, swallowing difficulty, voice changes, and even alterations in sensation and behavior (6).

Language disorders have been increasingly recognized as one of the clinical manifestations of MS, as diminished language abilities can restrict participation in daily activities—including occupational, social, and educational domains (8). Studies indicate that MS patients experience such language impairments. Derek et al (2000) conducted a study on language functions, focusing particularly on naming and verbal fluency, involving MS patients compared to healthy individuals who spoke Spanish. They concluded that language function was impaired in MS patients, and naming errors in MS patients were more semantic. Moreover, they found a correlation between the error rate and the mean number of words produced in the verbal fluency test (9). Arrondo et al (2009) examined speech samples of MS patients and compared them with those of healthy peers and concluded that MS patients have difficulties in language construction (10). Ebrahimipour et al (2008) examined verbal fluency performance in Persian-speaking patients with RRMS and compared them with a healthy control group. They concluded that the average performance of these individuals was lower in the verbal fluency test compared with the control group (11). Jamalpour et al (2013) compared grammatical skills in Persian-speaking MS patients with healthy individuals and concluded that grammatical skills in MS patients differ significantly from healthy individuals (12). Rahimifar et al (2016) compared the skill of repeating long sentences and some grammatical skills in MS patients with healthy individuals and concluded that the skill of repeating long sentences and some grammatical skills in MS patients differ significantly from healthy individuals (13). Laakso et al (2000) investigated high-level language skills in female MS patients and a similar control group and showed that the mean score in MS patients decreased compared with the control group (14). Stefani Renauld et al (2016) in a review article examined cognitive disorders in MS patients and concluded that it is expected that high-level language skills are affected (15). In short, according to studies MS patients experience language impairments such as naming difficulties (7, 8, 10, 16, 17), semantic errors, paraphasias during naming (8), semantic paraphasia (17), verbal fluency problems(10, 17-19), deficits in syntactic skills (eg, reduced maximum sentence length and word count) (10, 12), and impairment in high-level language skills (10, 14, 18).

High-level language skills encompass multiple linguistic areas and cognitive processes (18). These skills may predict progressive brain damage (19, 20). High-level language skills include understanding ambiguous sentences, expressing and interpreting metaphors and proverbs, drawing inferences, sentence construction, repeating long sentences, naming famous individuals, defining words, comprehension of complex grammatical sentences, and recognizing similarities and differences (14). However, these skills have not been thoroughly investigated across various types of MS; they have only been studied in patients with progressive MS (21). Approximately 75% of MS patients report experiencing language disorders. Decreased language skills in MS patients can lead to limited participation in daily activities that require exchanging information and ideas (17, 22). Limited communicative participation can lead to social disengagement, job loss, despair, loss of independence, increased caregiver burden, and reduced participation in daily activities (23). Language disorder may also affect access to medical services and necessary interventions, as patients may have difficulty understanding physicians and following medical instructions (8).

Language disorders can occur in those with MS regardless of clinical features and demographic characteristics. Therefore, it is essential for the healthcare system to recognize potential language disorders in MS patients and to refer patients to speech-language therapists for timely evaluation and treatment (8). Studies conducted to date have only focused on examining the presence or absence of high-level language skills impairment in MS patients (11, 24) without considering the effects of different MS types. Thus, comparing high-level language proficiency across various MS types and aiding in the early detection of language abnormalities can be a useful first step.

In the healthcare system, early diagnosis and intervention are essential for enhancing quality of life. Given the rising prevalence of MS among Persian-speaking people in Iran and the lack of accurate tests of language proficiency across various forms of the disease, this study sought to compare high-level language proficiency in the 2 phases of MS (RR & SP) to that of healthy people.

This study aims to guide neurologists and speech-language pathologists in the early detection, evaluation, and prediction of high-level language impairments. It also aims to help them develop suitable treatment plans to improve the quality of life for these patients. In addition, by defining the impact of various forms of MS on language functions, this research aids speech and language pathologists.

Methods

This is a descriptive-analytical study. The ethics committee of Ahvas Jundishapour University of Medical Sciences approved the study (ethics code: IR.AJUMS.REC.1398.963).

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Participants

In this study, there were 3 groups—including 25 patients with RRMS, 27 patients with SPMS from the MS Society of Khuzestan Province, and 30 healthy individuals aged 22 to 58 years. All patients received a definitive diagnosis of MS & its type by a neurologist.

Inclusion Criteria

Patients' Group

The maximum age of 75 years

Patients with no other neurological problems except for MS (confirmed by neurological diagnosis)

Patients who were native Persian speakers

Those with a minimum secondary school education

Those with no uncorrected visual and hearing impairments

Those with a minimum score of 22 in the Mini-Mental State Examination test (MMSE)

Control Group

Persian speakers with no history of MS or other neurological disorders who were matched in age, education level, and sex with the patients were selected.

Exclusion Criteria

Patient Group

- Individuals with hearing and visual problems
- Individuals with a history of language disorders for reasons other than MS
- Individuals with other neurological diseases such as Parkinson's, amyotrophic lateral sclerosis (ALS), or Alzheimer's disease, et cetera.

Control group

- Individuals with a history of language disorders.
- Individuals with neurological diseases such as MS, Parkinson's, amyotrophic lateral sclerosis (ALS), or Alzheimer's disease, et cetera

Tools and Procedures

1. Personal Information Questionnaire: This questionnaire collected data on age, sex, employment status, education level, disease type, duration of illness, Expanded Disability Status Scale (EDSS) score, mobility status, comorbidities, and medications taken.

2. Persian version of the Behavioral and Emotional Screening System (BESS) test (21): The Persian version of the BESS test was developed in 2019 and its validity and reliability were determined (internal consistency of the Persian version of the test in MS patients was 0.94, and the intraclass correlation coefficient (ICC) was 0.96, with $P < 0.001$). The test consists of 7 sections as follows: (1) repeating long sentences; (2) sentence construction; (3) inference; (4) comprehension of complex grammatical sentences; (5) comprehension of ambiguous sentences (syntactic and semantic); (6) proverbs; and (7) word definitions. There are 10 items in each subtest. A 3-point (0–3) scale was used to score each item in each subtest; the results ranged from 0 to 30 for each subtest and from 0 to 210 for the total score (21).

To assess high-level language skills, the Persian version of the BESS test (21) was utilized in MS patients. MS patients were separately provided with instructions on how to respond to the questions according to the test guidelines before administering the tests. The examiner presented relevant explanations for each subtest to the patient and 1 or 2 practice items were provided at the beginning of each subtest to familiarize the patient with the test. If they did not respond appropriately after the explanations and practice, instructions were repeated, and self-correction was allowed within a limited time frame. Individual exams were administered in a well-lit, peaceful space with few distractions. To lessen the impact of MS patients' weariness on test outcomes, the tests were administered outside of times when they were most tired. Time was set aside for relaxation periods halfway through each section if needed.

Statistical Analysis

The research data were analyzed using SPSS Version 22 (IBM Corp). The normal distribution of data was assessed using the Kolmogorov-Smirnov test. The normality test results showed that the data did not follow a normal distribution among the 3 groups. Consequently, the nonparametric Kruskal-Wallis test was employed to compare the subtest and total scores for the high-level language skills (BESS). In addition, pairwise comparisons were conducted using the Bonferroni post-hoc test. The significance level was set at $P \leq 0.05$.

Results

The present study aimed to investigate high-level language skills in patients with different patterns of MS compared with healthy controls. The mean (SD) age of healthy people who willingly participated was 39.10 ±12.24 years, the mean (SD) age of RRMS patients was 35.76 ± 7.63 years, and the mean (SD) age of SPMS patients was 40.51 ±10.33 years (Table 1).

The descriptive statistics in Table 2 summarize the mean and standard deviation for each of the 7 subtests, as well as the overall score across the 3 groups.

Table 1. Demographic Information of the Participants

Variable		[a]RRMS	[b]SPMS	[c]HI
Age, years	Mean ± SD	35.76±7.63	40.51±10.33	39.10±12.24
Sex Distribution, frequency	Male	3 (12%)	9 (33%)	9 (30%)
	Female	22 (88%)	18 (67%)	21 (70%)
	Total	25 (100%)	27 (100%)	30 (100%)

[a] Relapsing-remitting MS, [b]Secondary Progressive MS, [c]Healthy individuals

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Table 2. Descriptive Statistics & Comparison of the Mean Scores of the Subtests and the Total Score of the High-Level Language Test in 3 Groups Using the Kruskal-Wallis test

Subtests	Groups	Mean ± SD	*P* Value
Repetition of long sentences	[a]RRMS	16.79±6.71	0.001
	[b]SPMS	14.28±6.84	
	[c]HI	20.50±5.56	
Sentence recreation	RRMS	14.12±6.33	<0.001
	SPMS	9.00±6.96	
	HI	18.13±6.50	
Making inferences	RRMS	11.75±5.32	<0.001
	SPMS	11.25±4.83	
	HI	16.76±5.48	
Comprehension of logico-grammatical sentences	RRMS	15.91±5.46	0.001
	SPMS	17.57±6.98	
	HI	21.86±5.33	
Comprehension of syntactically and semantically ambiguous sentences	RRMS	14.50±8.31	0. 25
	SPMS	12.53±8.45	
	HI	16.53±7.40	
Metaphor comprehension	RRMS	8.62±7.28	0.001
	SPMS	10.39±6.82	
	HI	13.80±3.80	
Word definition	RRMS	10.00±8.48	<0.001
	SPMS	13.75±10.01	
	HI	21.26±4.82	
Total score	RRMS	91.08±34.70	<0.001
	SPMS	89.07±39.44	
	HI	124.40±34.97	

[a] Relapsing-remitting MS
[b] Secondary Progressive MS
[c] Healthy individuals

Nonparametric Kruskal-Wallis test results indicated a significant difference ($P \leq 0.05$) in the total score and all subtests except for comprehension of syntactically and semantically ambiguous sentences among the 3 groups (RRMS patients, SPMS patients, and healthy individuals) (Table 2).

Pairwise comparisons using the Bonferroni test in the repetition of long sentences subtest revealed a significant difference ($P \leq 0.05$) between healthy individuals and the SPMS & RRMS. However, no significant differences were found between the SPMS and RRMS ($P \geq 0.05$). The same was true for the subtests of sentence recreation making inferences and comprehension of logico-grammatical sentences, metaphor comprehension, word definition, and the total score of the BESS test.

There was no significant difference among healthy individuals with the SPMS & with RRMS in the comprehension of syntactically and semantically ambiguous sentences subtest ($P \geq 0.05$). Also, no significant differences were found between the SPMS and RRMS groups ($P \geq 0.05$) (Table 3).

Discussion

This study aimed to examine high-level language skills in 2 phases of MS (RR & SP) in comparison with healthy controls. The 3 study groups (RRMS, SPMS, and healthy individuals) demonstrated a statistically significant difference in the total score and all its subtests except for the comprehension of syntactically and semantically ambiguous sentences subtest. These results are consistent with those of the following studies: Lethlean et al (1997), Laakso et al (2000), Stefani Renauld et al (2016), Beatty and Monson (1989), Kujala et al (1996), Friend et al (1999), Arrondo et al (2009), Derek et al (2000), Ebrahimipour et al (2008), Jamalpour et al (2013), and Rahimifar et al (2016) (9-15, 18, 24-26).The results of this study indicated that the healthy group had the highest mean scores in high-level language skills. On the other hand, the healthy group performed the best, while the patient group did not.

The neuropathology of MS indicates damage to the brain's subcortical structures (27). Recent studies, along with advancements in brain imaging, demonstrate that subcortical structures are critical components of neural circuits that regulate language and cognitive functions and become active during language tasks (27, 28). Therefore, according to the conducted research, language is impaired in MS patients (10). Another issue suggesting the likelihood of language deficits in MS patients is the presence of cognitive impairments—including problems with long-term and working memory, attention deficits, executive function impairments, and reduced information processing speed in these patients—as cognitive skills are related to language abilities (29-31). In MS patients, high-level language skills are compromised due to decreased myelination and damage to subcortical pathways. Moreover, the disconnection between cortical regions and subcortical areas is a probable cause of high-level language skill deficits in MS patients (18).

Another finding of the present study, which aimed at pairwise comparisons of the groups, indicates that when comparing the mean overall high-level language skill scores and all subtests—except for the comprehension of syntactically and semantically ambiguous sentences subtest—the differences between the healthy group and the RRMS and SPMS groups were significant. The results of the pairwise group comparisons show that when comparing the mean overall high-level language skill scores and

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Table 3. Paired Comparison of the Mean Scores of the Subtests and the Total Score of the High-Level Language Test Using the Bonferroni Test

Subtests	Groups		*P* Value
Repetition of long sentences	[a]RRMS	SPMS	0.248
	[b]SPMS	[c]HI	<0.001
	RRMS	HI	0.024
Sentence recreation	RRMS	SPMS	0.110
	SPMS	HI	<0.001
	RRMS	HI	0.046
Making inferences	RRMS	SPMS	0.800
	SPMS	HI	<0.001
	RRMS	HI	0.002
Comprehension of logico-grammatical sentences	RRMS	SPMS	0.310
	SPMS	HI	0.001
	RRMS	HI	0.011
Comprehension of syntactically and semantically ambiguous sentences	RRMS	SPMS	1.000
	SPMS	HI	0.180
	RRMS	HI	1.000
Metaphor comprehension	RRMS	SPMS	0.290
	SPMS	HI	<0.001
	RRMS	HI	0.008
Word definition	RRMS	SPMS	0.090
	SPMS	HI	<0.001
	RRMS	HI	0.003
Total score	RRMS	SPMS	0.990
	SPMS	HI	<0.001
	RRMS	HI	<0.001

[a] Relapsing-remitting MS
[b] Secondary Progressive MS
[c] Healthy individuals

all subtests, the differences between the RRMS group and the SPMS group were not significant. Katerina Ntosko et al (2018) conducted a study examining the severity of language and cognitive impairments in RRMS and SPMS, comparing them to healthy controls. They used a flexible, comprehensive neuropsychological-language battery test and found that MS patients, regardless of their clinical subtype, exhibited cognitive impairments compared with healthy participants. The study also found that while the general pattern of relative stability in deficits persists, these impairments get worse when moving from RRMS to SPMS (31).

Martzoukou Maria et al (2024) examined language and cognitive skills in 2 groups: RRMS and SPMS. Their study found that language and cognitive functions were weaker in MS patients compared with healthy individuals, but no significant difference was observed between the performance of RRMS and SPMS patients (32). Fyndanis et al (2024) studied morphosyntactic skills in the RRMS and SPMS groups, and no significant performance differences were found between the 2 patient groups (33). The main difference between the present study and others lies in the type of language skill investigated. Here, we focused on high-level language skills, which involve multiple expressive and receptive tasks that impact various linguistic and cognitive processing areas (18). Another difference is that the participants in this study were Persian speakers. According to Fyndanis et al (2024) (33), the lack of difference between the 2 disease patterns might be related to the duration of the disease and cognitive functions—including working memory, processing speed, attention, and executive functions. Approximately 65% of MS patients experience cognitive issues (34), and according to Kalkan & Kurt (2024), cognitive deficits in RRMS patients appear after the seventh year of disease onset (35), while in progressive MS patients, they emerge after many years of disease progression (36). In the present study, the lack of difference between the 2 disease patterns may also be due to the fact that only MS patients with an MMSE score >22 were included, and the duration of the disease was not considered.

In the present study, no statistically significant difference was observed between the healthy group and patients in the comprehension of syntactically and semantically ambiguous sentences subtest. This lack of difference may be due to the subtest's reliance on cognitive skills—particularly executive functions and working memory (37). In this study, only patients with MMSE scores >22 (within the normal range) were included. However, the mean score for this subtest in the healthy group was higher than that in both the RRMS and SPMS groups, which suggests poorer performance in patients compared with healthy individuals in terms of clinical performance.

Limitations

Limitations of the present study include the exclusion of PPMS and RPMS patients and the lack of consideration of disease duration. Therefore, it is recommended that future studies include these 2 disease types and investigate the duration of disease onset. Furthermore, in the present study, the MMSE test was used as a condition for assessing patients' cognitive functions. It is suggested that future research explore the relationship between language functions in different disease patterns and their connection to cognitive performance.

Conclusion

The results of the present study showed that the overall score for high-level language functions and all subtests, except for comprehension of syntactically and semantical-

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ly ambiguous sentences, was weaker in MS patients compared with healthy individuals. However, no significant difference was found between the RRMS and SPMS patients. The lack of difference between the 2 disease patterns may be related to cognitive skills and the duration of the disease, which warrants further investigation.

Authors' Contributions

Concepts: Parvaneh Rahimifar, Majid Soltani

Design: Parvaneh Rahimifar, Majid Soltani

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Manuscript editing: Parvaneh Rahimifar, Majid Soltani, Rezvan Isazadeh.

Ethical Considerations

The study was conducted and complied with the guidelines for human subject studies. In this study, participants were informed about the study and signed a written consent.

Acknowledgment

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Conflict of Interests

The authors declare that they have no competing interests.

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