Physiology and Pharmacology 30 (2026) 159-167
Clinical Research Article

Foot mental rotation deficits in relapsing-remitting multiple sclerosis and their relationship with cognitive function

Faezeh Esmaeili Ranjbar[1], Zahra Assadollahi[2], MohammadJavad RanjbarKarimi ShahamAbadi[3], Fatemeh Toyserkani[4], Zeinab Heidari[5], Fatemeh Ayoobi[6], Mostafa Hadavinejad[7], Mahdieh Azin[8*]

1. Molecular Medicine Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
2. Department of Epidemiology and Biostatistics, Health School, Occupational Environment Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
3. Immunology of Infectious Disease Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
4. Student Research Committee, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
5. Vice President of Health, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
6. Occupational Safety and Health Research Center, NICICO, World Safety Organization and Rafsanjan University of Medical Sciences, Rafsanjan, Iran
7. Department of Management, Faculty of Administrative Sciences & Economy, Vali-e-Asr University, Rafsanjan, Iran
8. Department of Physiology and Pharmacology, School of Medicine, Physiology-Pharmacology Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

ABSTRACT

Introduction: Mental rotation (MR) of body parts relies not only on visuospatial processing but also on motor imagery mechanisms involving premotor cortical areas. Therefore, impairment in MR tasks may reflect both cognitive and motor dysfunction. We studied whether there is an impairment in reaction time and response accuracy rate of foot mental rotation (FMR), Paced Auditory Serial Addition (PASAT) score, and walking time in individuals with relapsing-remitting multiple sclerosis (RRMS). The study also examined potential links between walking duration, FMR, and PASAT accuracy.

Methods: Basic procedures: 37 RRMS patients and 40 healthy subjects performed FMR tasks. Physical activity and auditory information processing were assessed by the Timed 25-Foot Walk (T25-FW) and PASAT tests.

Results: The average reaction time to stimuli of both legs and walking time in the RRMS group significantly increased compared with the control group. The mean PASAT score of the control group was significantly higher than that of the RRMS. There was no notable correlation between walking time and response accuracy rate in the FMR task. Meanwhile, there was a negative correlation between walking time and the number of correct responses in PASAT and a positive correlation between walking time and reaction time in FMR.

Conclusion: The present study demonstrates that RRMS patients exhibit significant impairments in both motor and cognitive performance compared with healthy subjects. These findings suggest that RRMS affects not only motor functions but also cognitive-motor integration processes such as MR. Also, rehabilitation, especially a combination of motor imagery exercises and physical therapy, may help walking improvement in RRMS.

Keywords:
Multiple sclerosis
Foot Mental Rotation
Motor imagery
Walking Time
Paced Auditory Serial Addition
Relapsing-remitting multiple sclerosis

* Corresponding author: Mahdieh Azin, m.azin@rums.ac.ir
Received 16 July 2025; Revised from 12 May 2026; Accepted 13 May 2026

Citation: Esmaeili Ranjbar F, Assadollahi Z, RanjbarKarimi ShahamAbadi MJ, Toyserkani F, Heidari Z, Ayoobi F, Hadavinejad M, Azin M. Foot mental rotation deficits in relapsing-remitting multiple sclerosis and their relationship with cognitive function. Physiology and Pharmacology 2026; 30: 159-167. http://dx.doi.org/10.22034/phypha.30.2.159

Introduction

Multiple sclerosis (MS) is a common autoimmune neurological disorder damaging the central nervous system (CNS) through demyelination and axonal degeneration, leading to cognitive, sensory, and motor dysfunction. (Matute-Blanch et al., 2018). In addition, approximately 43–65% of patients develop cognitive deficits, which may emerge in the early stages of the disease and, in some cases, precede motor impairment (Iezzoni et al., 2009; Rahn et al., 2012). In some patients, cognitive dysfunction is the first manifestation of the disease, even before severe motor symptoms appear (Amato et al., 2006; Ruggieri et al., 2003). MS is categorized into three subtypes: relapsing-remitting multiple sclerosis (RRMS), which is the most prevalent form, secondary progressive MS, and primary progressive MS (Tabrizi et al., 2014).

Reduced cognitive processing speed and episodic memory impairment are among the most common symptoms of MS symptoms (Benedict et al., 2020)/ Many patients struggle with multitasking due to impaired cognitive-motor integration when performing simultaneous mental and physical tasks (e.g., walking while thinking) (Wajda and Sosnoff 2015) Mental imagery is a neural process involving structures responsible for cognitive control and motor planning. It is identified as a dynamic process, in which a specific motor action is internally simulated without actual motor output (Duarte-Mendes et al., 2025). Patients in the early stages of MS show disease severity–dependent changes in mental imagery performance and associated brain activity (Biggio et al., 2026). Based on previous studies, imaging has shown that areas of the brain are involved in motor planning and execution (Lacourse et al., 2005; Saiote et al., 2016) 2005; Saiote et al., 2016. Mental rotation (MR), a measure of implicit motor imagery, involves visualizing how an object appears when rotated to new angles. It plays a key role in cognitive and behavioral processes (Bersier et al., 2025). MR of body parts or objects is commonly used to assess implicit motor imagery. In this task, participants identify left or right orientations of rotated images, which reveals unconscious spatial processing (Pierpaoli et al., 2020). Decision-making becomes more difficult as the stimulus orientation approaches the actual biomechanical limits of joint mobility, reflecting biomechanical constraints on MR (Azin et al., 2016b) . In normal persons, the decision time for determining foot position is equal to the expected time (Parsons 1987). However, due to neurobiological problems, structural and functional changes associated with aging, synchronization between imaging and actual executed movement may be disrupted (Daprati et al., 2010).

Cognitive dysfunction in MS impairs social and professional functioning, often emerging early and correlating with disease severity (Gómez-Melero et al., 2024). Early and accurate identification of cognitive dysfunction, followed by appropriate therapeutic interventions and rapid rehabilitation, may reduce the negative impact of cognitive deficits on patients' quality of life (Benedict et al., 2020; Gómez-Melero et al., 2024). However, compared with Parkinson's disease (Lambert et al., 2025)' and stroke (Lin et al., 2025), relatively few studies have investigated motor imagery ability and its therapeutic applications in patients with MS (Tacchino et al., 2018). Moreover, most previous studies in MS have focused on hand rotation tasks. Therefore, further research is needed to examine mental motor imagery in patients with RRMS using other assessments, such as foot mental rotation (FMR).

Therefore, the purpose of this study was to consider the ability of mental motor imagery by the FMR test in patients with RRMS and to evaluate its relationship with lower extremity motor function. Also, the relationship between MR ability and auditory processing speed, working memory, and walking speed was studied. We hypothesized that FMR performance would be significantly impaired in patients with RRMS and that these impairments would correlate with walking time and cognitive processing speed.

Materials and Methods

Participants

This study was conducted at Rafsanjan Non-Communicable Disease Research Center with ethical approval (IR.RUMS.REC.1397.218) from Rafsanjan University of Medical Sciences, following Helsinki Declaration guidelines. The purpose of this study was to consider the ability of mental motor imagery by the FMR test in patients with RRMS and to evaluate its relationship with lower extremity motor function. Also, the relationship between MR ability and auditory processing speed, working memory, and walking speed was studied.

All participants provided written informed consent. The sample size calculation is based on the following equations 1 (Eq1) and 2 (Eq2), the standard deviation was 547, and the minimum detectable effect is 175 (Azin et al., 2016a; Haghdoost 2009).

$$\text{Eq1.} \quad n= (Z^2 \times SD^2)/d^2$$

$$\text{Eq2.} \quad n= [(1.96)2\ (547.8)2] / (175)2 = 37$$

The study included 40 healthy individuals and 37 RRMS patients from Rafsanjan, Iran (2018–2019), recruited via call announcements from the MS Association and Special Patients Center. A neurologist confirmed the MS diagnosis using McDonald's criteria (Polman et al., 2011). Patients' motor function and disability were measured based on the Kurtzke Expanded Disability Status Scale (EDSS) (Kurtzke 1983).

Patients with an EDSS score higher than 3.5, recent relapse, other neurological diseases (stroke, seizures, etc.), a history of head trauma, chronic psychiatric disorder, severe visual impairment, and those receiving corticosteroids were excluded from this study. Normal participants who were homogeneous with patients in terms of gender, age, and level of education were invited to participate in this study; it should be noted that they were relatives of patients. All participants completed the experimental tasks in the following fixed order: 1- Timed 25-Foot Walk (T25-FW), 2- FMR task, and 3- PASAT. Short seated rest periods were provided between tasks. The experiment protocols were similar throughout the study.

Experiments

Walking assessment

The Multiple Sclerosis Functional Composite (MSFC) assesses MS-related impairment through three components. Its first component, the T25-FW test, evaluates lower limb motor function by timing a 25-foot (7.62 m) walk, providing a quantitative measure of leg performance (Fischer et al., 1999). During our study, the patient was guided to the end of a marked 25-foot path and instructed to walk 25 feet quickly and cautiously. The test was repeated immediately after completion, and the patient was asked to return to the route. Patients were permitted to use assistive devices; the maximum time for each test was 3 minutes.

Assessment of auditory processing speed and working memory

The Paced Auditory Serial Addition (PASAT), a key component of the MSFC, assesses cognitive function by evaluating auditory processing speed, working memory, and computational ability. The PASAT was provided on a tape recorder or compact disc (CD) to play single-digit numbers every 3 seconds, and the participants had to add each new number to the previous one. The test score was the number of right answers out of 60 possible in each test (Brenton et al., 2019).

Assessment of FMR

The FMR task was administered as a computerized behavioral paradigm to assess lower-limb motor imagery ability. The task was adapted from previous work (Rezaeinasab et al. 2020)images and line drawings of hand at different angles are shown to the subjects, and they are asked to choose which hand (left or right, and was conceptually similar to the hand MR test.

The images of the plantar and dorsal surfaces of the foot at various angles, ranging from 0 to 300 degrees, are captured. The angle increased by 60 degrees at every step of the test. In this way, the images are exhibited at 6 angles of 0, 60, 120, 180, 240, and 300 degrees.

Participants observed 72 randomly ordered images to minimize learning effects. Each trial began with a fixation cross (+) displayed at the center of the screen to direct the participant's gaze (visual angle = 5.7°). Participants were instructed to identify whether the image represented a left or right foot by pressing the corresponding arrow key. The software recorded reaction time and response accuracy. Reaction time (The time duration from stimulus presentation to correct response) and accuracy (% correct responses) were measured. The FMR task was designed based on our previous studies and is similar to the hand mental rotation test (Rezaeinasab et al., 2020).

Statistical analysis

Subjects' experimental data are presented as mean±SD, except for sex, which is shown as n (%). Normality of continuous variables was assessed using the Shapiro-Wilk test (preferred for sample sizes <50) supplemented by visual inspection of histograms and Q-Q plots. Parametric tests (independent samples t-test) were applied to normally distributed data, whereas non-para-

TABLE 1: The comparison of age and gender in MS and control group

group	Gender	
	female n (%)	Male n (%)
Control	30 (75.0)	10 (25.0)
RRMS	27 (73.0)	10 (27.0)
p-value	[a]0.839	

[a] Chi-square test

TABLE 2: Reaction Time and Response Accuracy Rate in MS and Control Groups

Dependent variable		Groups	Mean ± SD	p-value
walking time		Control group	4.56 ± 0.77	<0.001
		MS group	5.99 ± 1.86	
PASAT score		Control group	49.27 ± 6.78	
		MS group	44.18 ± 11.04	<0.05
Reaction time (milliseconds)	Left	Control group	1755.72 ± 366.30	<0.001
		MS group	2296.19 ± 544.40	
	Right	Control group	1576.10 ± 340.36	<0.001
		MS group	2184.90 ± 608.54	
	Mean of both hands	Control group	1660.66±337.98	<0.001
		MS group	2242.37±566.43	
Accuracy rate	Left	Control group	64.44 ± 19.93	0.961
		MS group	64.63 ± 16.81	
	Right	Control group	66.73 ± 17.96	0.371
		MS group	63.05 ± 17.79	
	Mean of both hands	Control group	65.58 ± 16.62	0.642
		MS group	63.84 ± 16.08	

metric tests (Mann-Whitney U test) were used when normality was violated or for non-normally distributed/ordinal data. Categorical variables were compared using the Pearson chi-square test. All statistical tests were two-tailed, and a p-value <0.05 was considered significant. Analyses were performed using SPSS version 18 (SPSS Inc., Chicago, IL, USA).

Results

40 healthy (control group) and 37 RRMS persons were included in this study; the homogeneity of the two groups was compared based on the variables of age, sex (p = 0.839), and level of education. As shown in Table 1, the two groups did not differ significantly in terms of these variables.

The results of the independent *t-test* showed that walking time in the control group (4.56 ± 0.77) was significantly lower compared to the RRMS group (5.99 ± 1.86) (p0.001>). (Table 2)

PASAT finding presented that the mean PASAT score of the control group was 49.27 ± 6.78, which was higher than the RRMS group (44.18±11.04), and this modification was statistically significant (p< 0.05) (Table 2).

Based on the results of the FMR test, the mean reaction time for the left foot and right foot in the control group was 1755.72± 366.3 and 1576.10±340.36, respectively, as these results for the RRMS group were 2296.19± 554.4 and 2184.9± 608.59, and differences between the control and RRMS groups in both right and left foot were significant (p<0.001). The mean reaction time averaged across both feet and all angles was 1660.66 ± 337.98 ms in the control group and 2242.37 ±

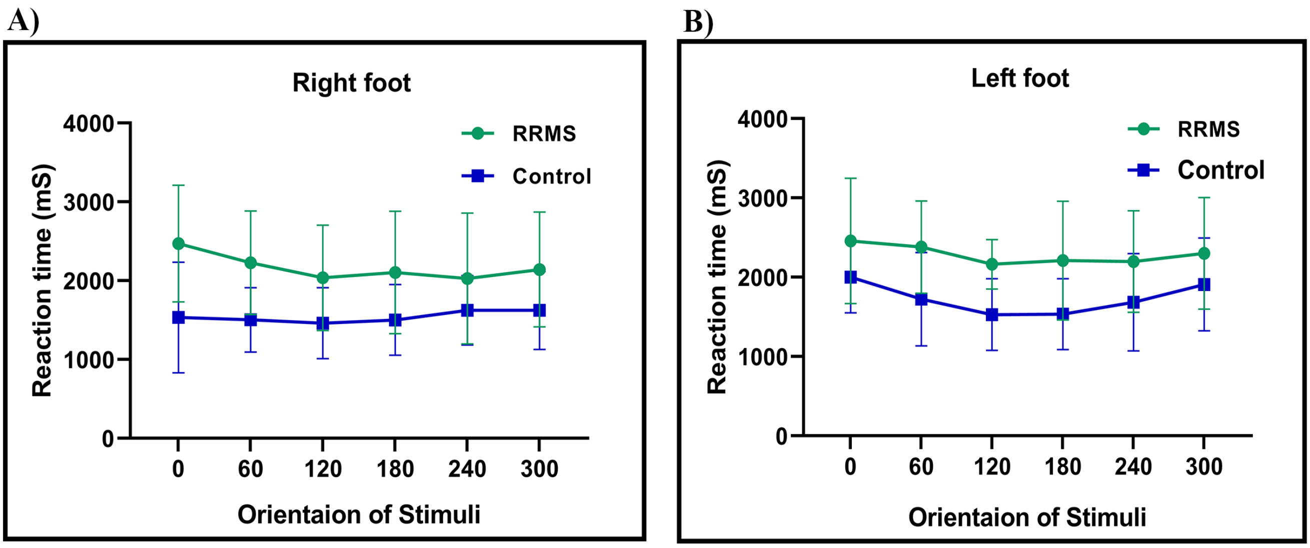

FIGURE 1. Reaction time (ms) is identified at different stimulus orientations in RRMS patients and healthy subjects. Graph A represents the reaction time for right foot stimuli. Graph B represents the reaction time for left foot stimuli. The error bar shows the standard error of the mean.

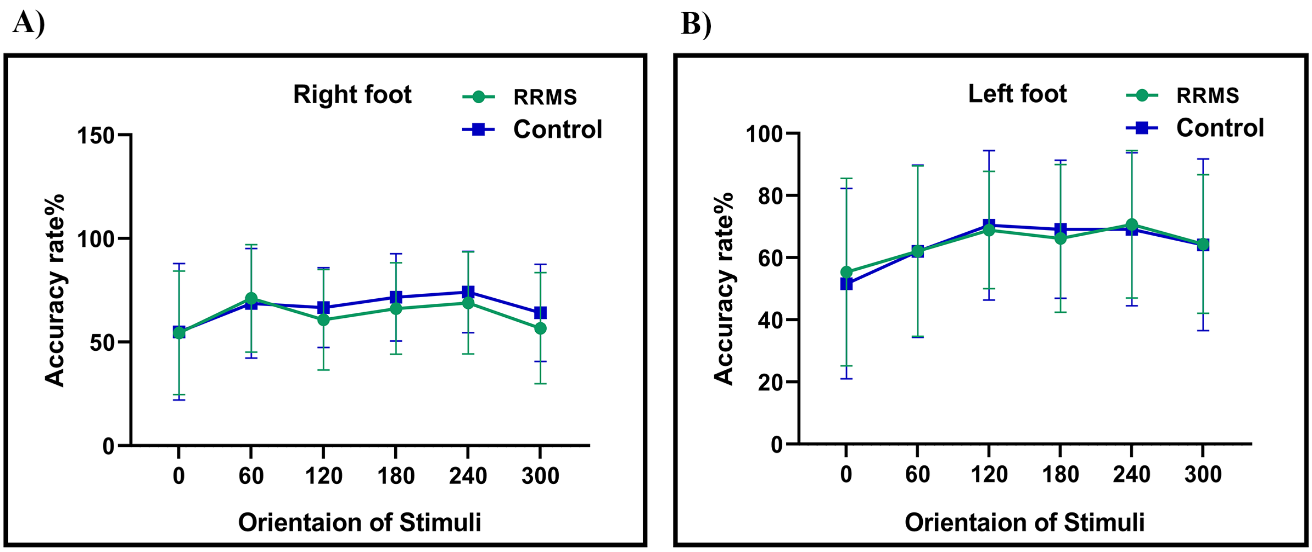

FIGURE 2. Accuracy rate (%) is identified at different stimulus orientations in RRMS patients and healthy subjects. Graph A represents accuracy rate for right foot stimuli. Graph B represents accuracy rate for left foot stimuli. The error bar shows standard error of the means.

566.43 ms in the RRMS group, with a statistically significant difference between groups ($p < 0.001$) (Table 2).

While reaction times differed significantly between groups, response accuracy (% correct) showed no significant differences. ($p > 0.05$). (Table 2)

Figure 1 compares the reaction time at different angles of 0, 60, 120, 180, 240, and 300 between the two groups of control and RRMS, with separation of the right and left foot. In general, as shown in Fig. 1, reaction times were higher in all angles and in both left and right legs in the RRMS group compared with the control group. The difference between the mean reaction time of the two groups was significant in all right and left leg angles ($p < 0.05$).

In order to compare the accuracy rate of responses at different angles of 0, 60, 120, 180, 240, 300 ˚C and independent of right and left foot between the two experimental groups (control and RRMS), Mann-Whitney and Independent *t* tests were used, respectively. The difference in mean response accuracy between the two groups was not significant in all right and left foot angles ($p > 0.05$) (Fig. 2).

In order to investigate the relationship between walking time and FMR and the number of correct answers in the PASAT test in two groups, Pearson correlation coefficients revealed a significant negative association between walking time and PASAT correct answers ($r = -0.31$, $p < 0.01$), indicating that longer walking times corresponded to poorer PASAT performance. Walking time was also positively correlated with reaction time ($r = 0.30$, $p < 0.01$). No significant correlations were found between PASAT correct answers and MR test variables (percentage correct: $r = 0.06$, $p > 0.72$; reaction time: $r = -0.06$, $p = 0.36$), nor between walking time and MR test percentage correct ($r = 0.09$, $p = 0.45$).

Discussion

This study aims to investigate the ability of MR by means of the FMR task in RRMS patients with mild disabilities, and to use the results of the study for cognitive disorder recognition, which can lead to movement disability. In addition, the results of this study can be used for new treatment methods of motor function improvement. We studied whether FMR was associated with gait disturbance in the T25-FW test and with cognitive dysfunction in the PASAT test in RRMS patients.

The present study provides converging evidence that implicit MR of the lower limbs, as assessed by the FMR task, is significantly impaired in individuals with RRMS, even in the context of relatively mild physical disability (EDSS ≤ 3.5). Specifically, RRMS patients demonstrated markedly prolonged reaction times during FMR, accompanied by slower walking speed and reduced cognitive performance on the PASAT, while maintaining response accuracy comparable to healthy controls. These findings contribute to a growing body of literature indicating that cognitive motor integration deficits emerge early in MS and may precede overt motor deterioration.

Based on our results, acquired from 37 RRMS patients and 40 normal people, the walking time of RRMS patients was significantly higher than that of normal individuals. The T25-FW is known as an excellent test to measure ambulation in MS patients (Kieseier and Pozzilli 2012). Research indicates that although walking time increases with age, disease type, disability, and disease duration, relapses are not correlated with an increase in walking time (Kalinowski et al. 2022).More over Mate et al., indicated that MS patients walked shorter distances in the 6-Minute walk test, and the walking speed of patients was slower than that of healthy subjects (Mate and Mayo 2020)mean number of steps at a brisk cadence or faster, and cumulative time per week spent walking at a brisk cadence or faster were regressed on 6MWT categories using quantile (median.

Our results demonstrated that RRMS patients have FMR impairments. Our results were consistent with a previous study, which indicated that reaction times to the foot and hand stimulus in MS patients are higher than those of healthy subjects (Azin et al. 2016a). Aligned with our study, another study was done by Tabrizi et al. Showed that responding to hand stimulation in MS patients is slower compared to healthy individuals (Tabrizi et al. 2014b). Prior research has demonstrated that MR plays a role in the process of planning movements (Johnson 1998). The deficiency in planning observed in patients with hemiparetic cerebral palsy can be attributed to impaired MR (Mutsaarts et al. 2006)predominantly on one side of the body. The question pursued here is whether HCP participants have the ability to anticipate the forthcoming perceptual-motor demands of the goal of an action sequence. Such anticipatory planning was necessary to successfully perform the tasks that were studied. In experiment I, HCP participants had to grasp a hexagonal knob with their unimpaired hand by choosing one of five possible grasping patterns (free choice. Hence, it is important to conduct more research to investigate the correlation between MR deficits and motor planning impairment in MS patients, because MR impairments in MS patients might potentially lead to difficulties in motor planning. (Baird et al. 2019)

Based on our results, the accuracy rate of FMR was the same in both groups (RRMS patients and healthy individuals), which is consistent with previous studies reporting no difference between MS patients and healthy subjects in terms of response accuracy rate to foot stimuli. (Azin et al. 2016a). Whereas, response accuracy rate to hand stimuli in MS patients is significantly reduced compared with healthy subjects and is associated with cognitive dysfunction rather than motor impairment. But a slower imagery duration is associated with a closer relationship with motor impairment (Heremans et al. 2012). A study demonstrated response accuracy rate to hand stimuli in mildly disabling RRMS patients was significantly impaired compared with healthy subjects, and reduced accuracy is associated with cognitive impairment (Tabrizi et al. 2014b). The difference between the present study and the Hermans and Tabrizi studies is that in these two studies, hand motor imagery was performed, but in the present study, FMR was assessed, and previous studies have shown that responding to the lower limbs imagery is more difficult than that of the upper limbs imagery in all healthy and MS patients. (Azin et al. 2016a). Also, in the Hermans study, there were people with severe MS, but in the present study, mildly disabling patients.

A key finding of this study is the positive and significant correlation between T25-FW and reaction time of FMR, indicating that individuals who walked more slowly also exhibited slower implicit motor imagery. This association supports the concept of shared neural resources for imagined and executed movement, as proposed by the motor simulation theory (Jeannerod 2001) and confirmed in neuroimaging studies demonstrating overlapping activation during real and imagined actions (Saiote et al., 2016). Similar to our results, Mulder et al., revealed that there is a significant correlation between vividness of the movement imagery questionnaire (VMIQ-S) test and reaction time and walking time in older individuals (Mulder et al., 2007). Similar to the present results, a previous study suggested that impaired information processing speed in RRMS patients leads to general slowness (mental processing and movement) even in the early stages of the disease (Azin et al., 2016b).

According to our results, the RRMS patients presented significantly fewer correct and more inaccurate responses on the PASAT than controls, which was compatible with Rosti et al. findings (Rosti et al., 2006). We confirmed a significant negative correlation between two variables, including walking time and the number of correct answers in PASAT. The inverse relationship between PASAT score and walking time reinforces the notion that gait in MS is not purely motoric but is strongly influenced by cognitive capacity, particularly executive control and attention (Motl et al., 2014).

Interestingly, PASAT performance was not significantly correlated with the reaction time of FMR. PASAT focuses on the speed of auditory information processing and working memory; some factors, such as IQ and math calculation ability, can have an effect on PASAT. while the MR tasks focus on visual processing speed and visuospatial ability (Tombaugh 2006)Probably due to the same reasons mentioned, in our study, there was no significant correlation between the PASAT score and the reaction time to the foot stimulus.

The sensitivity of the reaction time of FMR to minor impairment suggests that it may serve as an early behavioral marker of cognitive-motor dysfunction, potentially useful for monitoring disease progression or response to treatment. From a clinical perspective, the results emphasize the importance of including motor imagery assessment and training in the standard assessment and rehabilitation of RRMS patients.

Several limitations should be noted. First, the cross-sectional design precludes causal inferences about the temporal evolution of motor imagery deficits. Longitudinal studies are needed to determine whether FMR slowing predicts future gait decline or cognitive decline. Second, although the PASAT is a well-established measure, its reliance on mathematical skills may introduce confounding effects related to training or test anxiety. Finally, combining behavioral FMR measures with neuroimaging could shed light on the neural substrates underlying lower limb motor imagery deficits in RRMS.

Conclusion

To our knowledge, this is one of the first studies to assess FMR in mildly disabling RRMS patients and to correlate it with gait and cognitive performance simultaneously.

This study shows that FMR is selectively slowed in RRMS, indicating impairments in implicit motor imagery that are closely related to gait performance but are partially independent of auditory processing speed and working memory. These findings could strengthen the view that MS is characterized by early and pervasive impairments in cognitive-motor integration.

From a clinical perspective, these findings highlight the utility of FMR as a potential tool for assessing cognitive-motor impairments in RRMS. FMR assessment alongside standard motor assessments may provide a more comprehensive assessment of disease impact and progression. Future studies guide targeted rehabilitation interventions that combine cognitive training with physical therapy.

Acknowledgements

This study was supported by Rafsanjan university of medical sciences, with ethical code: IR.RUMS.REC.1397.218

Conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval and consent to participate

This study was approved by Rafsanjan university of medical sciences with ethical code: IR.RUMS.REC.1397.218. It was based on the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author(s) used ChatGPT and QuillBot in order to paraphrase.

References

Amato M P, Zipoli V, Portaccio E. Multiple sclerosis-related cognitive changes: a review of cross-sectional and longitudinal studies. Journal of the Neurological Sciences 2006; 245: 41-46. https://doi.org/10.1016/j.jns.2005.08.019

Azin M, Zangiabadi N, Iranmanesh F, Baneshi M R, Banihashem S. Effects of intermittent theta burst stimulation on manual dexterity and motor imagery in patients with multiple sclerosis: a quasi-experimental controlled study. Iranian Red Crescent Medical Journal 2016a; 18: e27056. https://doi.org/10.5812/ircmj.27056

Azin M, Zangiabadi N, Tabrizi Y M, Iranmanesh F, Baneshi M R. Deficiency in mental rotation of upper and lower-limbs in patients with multiple sclerosis and its relation with cognitive functions. Acta Medica Iranica 2016b: 510-517.

Benedict R H, Amato M P, DeLuca J, Geurts J J. Cognitive impairment in multiple sclerosis: clinical management, MRI, and therapeutic avenues. The Lancet Neurology 2020; 19: 860-871. https://doi.org/10.1016/S1474-4422(20)30277-5

Bersier N M, Fornari E, Rumiati R I, Ionta S. Cognitive traits shape the brain activity associated with mental rotation. Cerebral Cortex 2025; 35: bhaf069. https://doi.org/10.1093/cercor/bhaf069

Biggio M, Pedulla L, Albergoni A, Bellosta A, Tacchino A, Podda J, et al. Motor imagery training promotes motor learning and brain plasticity without fatigability in people with progressive multiple sclerosis. European Journal of Physical and Rehabilitation Medicine 2026; 61: 831. https://doi.org/10.23736/S1973-9087.25.09116-6

Brenton J N, Koshiya H, Woolbright E, Goldman M D. The multiple sclerosis functional composite and symbol digit modalities test as outcome measures in pediatric multiple sclerosis. Multiple Sclerosis Journal-Experimental, Translational and Clinical 2019; 5: 2055217319846141. https://doi.org/10.1177/2055217319846141

Daprati E, Nico D, Duval S, Lacquaniti F. Different motor imagery modes following brain damage. Cortex 2010; 46: 1016-1030. https://doi.org/10.1016/j.cortex.2009.08.002

Duarte-Mendes P, Ramalho A, Bertollo M, Neiva H P, Marinho D A. To move without moving: a perspective article on motor imagery. Frontiers in Psychology 2025; 16: 1697086. https://doi.org/10.3389/fpsyg.2025.1697086

Fischer J, Rudick R, Cutter G, Reingold S, Force N M S C O A T. The Multiple Sclerosis Functional Composite measure (MSFC): an integrated approach to MS clinical outcome assessment. Multiple Sclerosis Journal 1999; 5: 244-250. https://doi.org/10.1177/135245859900500409

Gómez-Melero S, Caballero-Villarraso J, Escribano B M, Galvao-Carmona A, Túnez I, Agüera-Morales E. Impact of cognitive impairment on quality of life in multiple sclerosis patients-a comprehensive review. Journal of Clinical Medicine 2024; 13: 3321. https://doi.org/10.3390/jcm13113321

Haghdoost A. Do you want to gain a profound insight into sample size and statistical power. Iranian Journal of Epidemiology 2009; 5: 57-63.

Iezzoni L I, Rao S R, Kinkel R P. Patterns of mobility aid use among working-age persons with multiple sclerosis living in the community in the United States. Disability and Health Journal 2009; 2: 67-76. https://doi.org/10.1016/j.dhjo.2008.12.001

Jeannerod M. Neural simulation of action: a unifying mechanism for motor cognition. Neuroimage 2001; 14: 103-109. https://doi.org/10.1006/nimg.2001.0832

Kurtzke J F. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 1983; 33: 1444. https://doi.org/10.1212/WNL.33.11.1444

Lacourse M G, Orr E L, Cramer S C, Cohen M J. Brain activation during execution and motor imagery of novel and skilled sequential hand movements. Neuroimage 2005; 27: 505-519. https://doi.org/10.1016/j.neuroimage.2005.04.025

Lambert K J, Singhal A, Leung A W. Parkinson's disease impairs the controllability of imagined action sequences. Experimental Brain Research 2025; 243: 120. https://doi.org/10.1007/s00221-025-07071-2

Lin D, Eaves D L, Franklin J D, Robinson J R, Binks J A, Emerson J R. Combined action observation and motor imagery practice for upper limb recovery following stroke: a systematic review and meta-analysis. Frontiers in Neurology 2025; 16: 1567421. https://doi.org/10.3389/fneur.2025.1567421

Matute-Blanch C, Montalban X, Comabella M. Multiple sclerosis, and other demyelinating and autoimmune inflammatory diseases of the central nervous system. Handbook of clinical neurology 2018; 146: 67-84. https://doi.org/10.1016/B978-0-12-804279-3.00005-8

Motl R W, Sosnoff J J, Dlugonski D, Pilutti L A, Klaren R, Sandroff B M. Walking and cognition, but not symptoms, correlate with dual task cost of walking in multiple sclerosis. Gait & posture 2014; 39: 870-874. https://doi.org/10.1016/j.gaitpost.2013.11.023

Mulder T, Hochstenbach J, Van Heuvelen M, Den Otter A. Motor imagery: the relation between age and imagery capacity. Human Movement Science 2007; 26: 203-211. https://doi.org/10.1016/j.humov.2007.01.001

Parsons L M. Imagined spatial transformations of one's hands and feet. Cognitive psychology 1987; 19: 178-241. https://doi.org/10.1016/0010-0285(87)90011-9

Pierpaoli C, Ferrante L, Foschi N, Lattanzi S, Sansonetti R, Polonara G, et al. Mental rotation ability: right or left hemisphere competence? what we can learn from callosotomized and psychotic patients. Symmetry 2020; 12: 1137. https://doi.org/10.3390/sym12071137

Polman C H, Reingold S C, Banwell B, Clanet M, Cohen J A, Filippi M, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Annals of Neurology 2011; 69: 292-302. https://doi.org/10.1002/ana.22366

Rahn K, Slusher B, Kaplin A. Cognitive impairment in multiple sclerosis: a forgotten disability remembered. Cerebrum 2012; 2012: 14.

Rezaeinasab M, Fotooh E M, Akbari C S, Shamsizadeh A, Assadollahi Z, Hasanshahi A, Azin M. Effect of tactile stimulation on hand mental rotation among young healthy adults: A randomized controlled trial. Archives of Neuroscience 2020; 7: e99078. https://doi.org/10.5812/ans.99078

Rosti E, Hämäläinen P, Koivisto K, Hokkanen L. The PASAT performance among patients with multiple sclerosis: analyses of responding patterns using different scoring methods. Multiple Sclerosis Journal 2006; 12: 586-593. https://doi.org/10.1177/1352458506070624

Ruggieri R, Palermo R, Vitello G, Gennuso M, Settipani N, Piccoli F. Cognitive impairment in patients suffering from relapsing-remitting multiple sclerosis with EDSS≤ 3.5. Acta Neurologica Scandinavica 2003; 108: 323-326. https://doi.org/10.1034/j.1600-0404.2003.00157.x

Saiote C, Tacchino A, Brichetto G, Roccatagliata L, Bommarito G, Cordano C, et al. Resting-state functional connectivity and motor imagery brain activation. Human Brain Mapping 2016; 37: 3847-3857. https://doi.org/10.1002/hbm.23280

Tabrizi Y M, Mazhari S, Nazari M A, Zangiabadi N, Sheibani V. Abnormalities of motor imagery and relationship with depressive symptoms in mildly disabling relapsing-remitting multiple sclerosis. Journal of Neurologic Physical Therapy 2014; 38: 111-118. https://doi.org/10.1097/NPT.0000000000000033

Tacchino A, Saiote C, Brichetto G, Bommarito G, Roccatagliata L, Cordano C, et al. Motor imagery as a function of disease severity in multiple sclerosis: an fMRI study. Frontiers in Human Neuroscience 2018; 11: 628. https://doi.org/10.3389/fnhum.2017.00628

Tombaugh T N. A comprehensive review of the paced auditory serial addition test (PASAT). Archives of Clinical Neuropsychology 2006; 21: 53-76. https://doi.org/10.1016/j.acn.2005.07.006

Wajda D A, Sosnoff J J. Cognitive-motor interference in multiple sclerosis: A systematic review of evidence, correlates, and consequences. BioMed Research International 2015; 2015: 720856. https://doi.org/10.1155/2015/720856