



# Egocentric mental rotation in individuals with multiple sclerosis: relationship with disability and cognitive parameters

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## Abstract

**Background** This study aims to examine whether egocentric-based mental rotation is affected in individuals with Multiple Sclerosis (MS) and to analyze its relationship with disability, functional system scores (FSS), and cognitive parameters.

**Methods** The study involved 57 right-dominant individuals with MS and 40 right dominant healthy subjects. Disability was assessed using the Neurostatus-Expanded Disability Status Scale (Neurostatus-EDSS). Participants' performance on mental rotation tasks was evaluated with the Recognise Hand App™, Recognise Foot App™, measuring reaction times (seconds) and accuracy (%) for hand and foot stimuli. Cognitive functioning was assessed using the Brief International Cognitive Assessment for MS (BICAMS).

**Results** MS patients exhibited lower performance in right hand mental rotation reaction time ( $p=0.042$ ), right hand accuracy percentage ( $p<0.001$ ), right foot accuracy percentage ( $p=0.035$ ). Positive correlations were found between disease duration, EDSS total score, cerebellar FSS, bladder-bowel FSS, and ambulation scores with reaction times, while negative correlations were observed with accuracy percentages ( $p<0.05$ ). Additionally, a positive correlation was identified between accuracy percentages and BICAMS ( $p<0.05$ ).

**Conclusions** The study revealed substantial impairments in right-hand and right-foot performance in right dominant individuals with MS. Mental rotation abilities were found to be related to disease duration, higher EDSS and FSS scores, as well as cognitive functioning. Identifying the cognitive domains and functional systems associated with egocentric mental rotation will contribute to better understanding this underexplored area and developing potential treatment strategies to enhance functionality.

**Keywords** Cognition · Disability · Egocentric-based · Mental rotation · Multiple sclerosis

## Introduction

MS is a complex neurodegenerative disease affecting over two million people, characterized by demyelination, axonal loss, and gliosis in the central nervous system (CNS) [1, 2]. The prevalence of MS, which is steadily increasing

[3], manifests with a wide clinical spectrum, encompassing sensory and motor deficits, in addition to cognitive impairments [4].

Mental rotation is the cognitive process of imagining what an object would like if it were rotated [5]. This ability is essential in both daily activities (e.g. driving, reading maps, loading a dishwasher) and in technical domains (e.g. air traffic control, architecture) [6]. Studies have shown that MS exhibit impairments in mental rotation findings compared to health subjects (HS). It has been noted that these impairments are related to various cognitive tests [7–10].

Mental rotation is categorized into object-based and egocentric-based types [6]. In egocentric-based tasks, participants imagine the rotation of their own body or body parts to assess left-right or front-back orientations. They mentally alter their perspective while maintaining a constant relationship between the object and the environment. In contrast,

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object-based tasks involve mentally rotating objects relative to a fixed environmental position, keeping the observer's position unchanged. The key distinction between these types lies in whether the observer's position relative to the environment changes [11, 12].

The assessment of egocentric-based mental rotation typically involves the use of hand images. Although the number of studies on this topic involving individuals with MS is limited, the available literature predominantly evaluates egocentric mental rotation using drawings rather than real photographs [8–10]. To our knowledge, only the study by Gauman et al. used real photographs of hands and feet with Recognise Flash Cards™ and presented these images in a random order on a computer screen from four different perspectives: dorsal/palm, radial/ulnar or medial/lateral sides and four different rotations: 0, 90, 180 and 270 degrees [13]. This study assesses perspective selection in motor imagery. Additionally, the body rotation task scores of individuals with MS were assessed across four different sessions, and a significant increase was observed between sessions. However, it does not include a control group for comparing individuals with MS to HS.

We hypothesize that egocentric-based mental rotation tasks may be more closely related to functional impairments in individuals with MS than object-based tasks. Furthermore, we believe that real body photographs, as opposed to drawings, may provide a more accurate assessment of egocentric mental rotation. To our knowledge, this study is the first to compare egocentric mental rotation assessed with real photographs between people with MS and HS, and to use the MS-specific BICAMS battery while assessing the relationship between cognitive parameters and a mental rotation task composed of real photographs. In contrast to previous research, the aim of this study is an in-depth analysis of the relationship between mental rotation and disability.

## Methods

### Participants

This study included 57 individuals with MS who applied to the Department of Neurology at Hacettepe University Hospital between September 2022 and November 2023, along with 40 HS matched for age and gender. The study was approved by the Non-Interventional Clinical Research Ethics Committee of Hacettepe University (GO22/832). The participants provided informed consent to take part in the study.

Inclusion criteria for individuals with MS: being literate and aged between 18 and 54, having a definitive MS

diagnosis of MS from a neurologist [14], having no attacks in the last 3 months, scoring full points on the Right-Left Discrimination Test (RLD) [15], being right-handed according to the Edinburgh Handedness Inventory (EHI) [16], having no vision problems according to the Snellen Visual Acuity Test (Snellen VA) [17], scoring  $\geq 24$  on the Mini-Mental State Examination (MMSE) [18],  $< 8$  on the Hospital Anxiety and Depression Scale (HADS) [19], and  $< 4$  on the Fatigue Severity Scale [20].

Inclusion criteria for HS: being literate and aged between 18 and 54, scoring full points on the RLD, being right-handed according to the EHI, having no vision problems according to the Snellen VA, scoring on the MMSE  $\geq 24$ , and HADS  $< 8$ .

Exclusion criteria for all participants: having musculoskeletal, cardiovascular, pulmonary, or metabolic diseases; having a history of different neurological disorders, head trauma, or chronic psychiatric disorders; using psychiatric medications that affect attention or alertness levels; experiencing chronic pain lasting longer than 6 months; and having previously participated in a study examining mental rotation.

## Procedure

Inclusion criteria tests were conducted for both individuals with MS and HS. Individuals with MS meeting these criteria had their disability assessed using the Neurostatus-EDSS and cognitive status evaluated with the BICAMS battery. Subsequently, both groups underwent mental rotation tasks using the NOI Group™ Recognise Hand App™ and Recognise Foot App™. Participants were provided with an overview of the test content and instructions on interacting with the visuals prior to the test phase. The hand and foot tests were administered sequentially, with each test performed once. All assessments were conducted on the same day.

## Outcome measurements

*Demographic data:* A range of socio-demographic and clinical characteristics were collected from participants, including age, body mass index (BMI), education, employment, activities/hobbies, family history, medication use, disease duration, exacerbations.

*Disease duration:* Disease durations were calculated in years based on the year of disease onset and the date of testing. A five-year cut-off was set for disease duration, creating two MS groups: Group I ( $\leq 5$  years) and Group II ( $> 5$  years). This division allowed for the examination of whether

disease duration affected egocentric mental rotation findings [21].

**Disability assessment:** Neurostatus-EDSS assessments were conducted by a certified physiotherapist to evaluate neurological impairment in individuals with MS. EDSS, based on functional system evaluations (e.g., pyramidal, cerebellar, sensory), were also used to categorize participants into minimal ( $EDSS < 3$ ) and moderate-severe ( $EDSS \geq 3$ ) disability groups, facilitating the analysis of the effect of disability on egocentric mental rotation (<http://www.neurostatus.net/>) [22–24].

**Egocentric mental rotation assessment:** Egocentric mental rotation was assessed using the Recognise Mobile Applications™, which measure speed and accuracy in right-left discrimination. Developed by NOI Group™ (<https://www.noigroup.com/>), the app allows for adjustments in the number of images and viewing duration, with necessary permissions obtained. After a brief procedural introduction, participants completed hand and foot mental rotation tasks sequentially using the Recognise Hand™ and Recognise Foot™ apps, clicking to indicate whether the presented images were

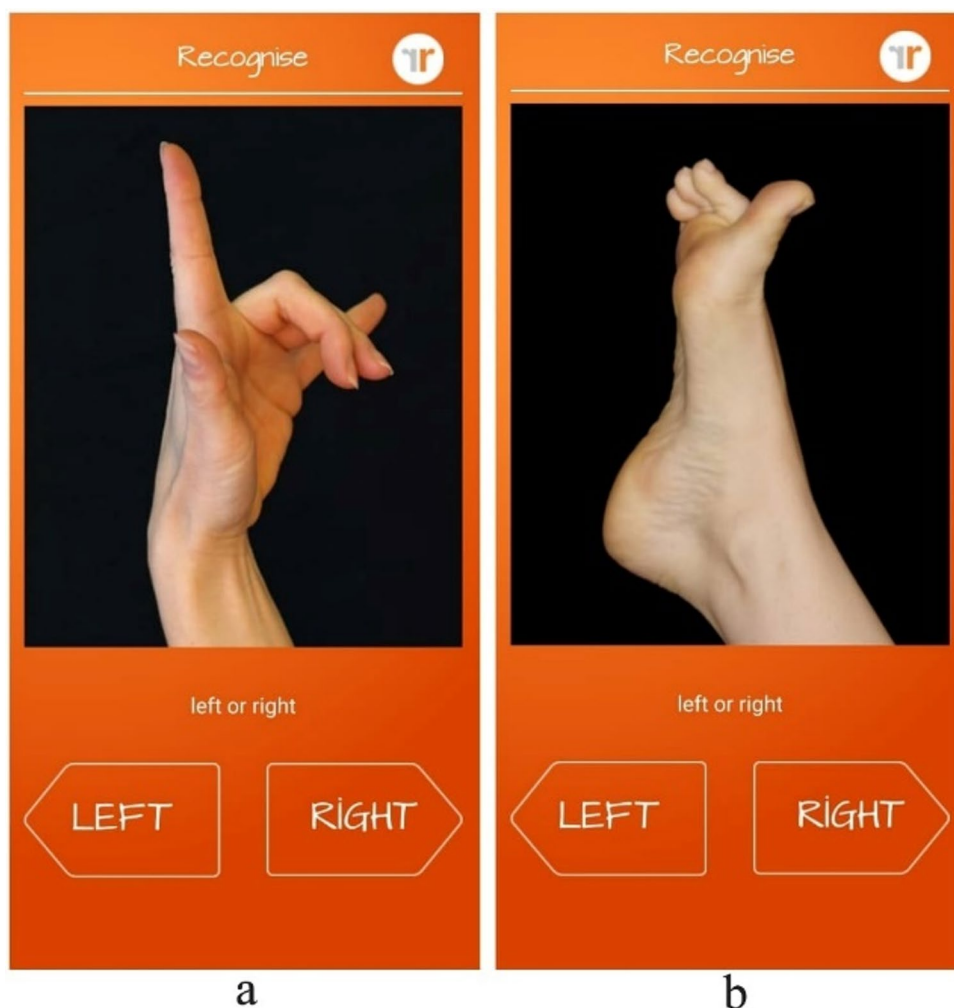
‘RIGHT’ or ‘LEFT.’ Each task involved 50 images (Fig. 1). Reaction times and accuracy percentages calculated by the app were recorded [25, 26].

**Cognitive assessment:** A cognitive assessment using BICAMS was conducted. The battery has three sub-tests: the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test-II (CVLT-II), and the Brief Visuospatial Memory Test-Revised (BVMT-R). The SDMT measures attention and processing speed, determined by the number of correct responses within 90 s. The CVLT-II evaluates verbal memory and learning ability, with the total score derived from five trials. The BVMT-R assesses visual memory, with the total score obtained from three learning trials [27, 28].

## Statistical analyses

Statistical analyses were performed using SPSS 23.0. Categorical variables were presented as counts (N) and percentages (%), and quantitative variables as mean  $\pm$  standard deviation ( $M \pm SD$ ) or median (min-max). The Chi-square

**Fig. 1** a: Recognise Hand App™, b: Recognise Foot App™



test was used for categorical variables. Normality was assessed, with normally distributed data analyzed by Independent Samples T-Test, and non-normally distributed data by Mann-Whitney U Test. Pearson Correlation was applied for parametric, and Spearman Correlation for non-parametric data. Correlation coefficients were interpreted as: 0.05–0.30 (low), 0.30–0.40 (low to moderate), 0.40–0.60 (moderate), 0.60–0.70 (good), 0.70–0.75 (very good), and 0.75–1.00 (excellent) [29].

Statistical significance was set at  $p=0.05$ . In our study, with a correlation coefficient of  $r=0.44$ , a post-hoc power analysis using G\*Power 3.1 ( $\alpha=0.05$ , two-tailed) showed 90% power. In addition to significance testing, effect sizes for between-group comparisons were calculated using Cohen's  $d$ , providing an estimate of the magnitude of observed differences. Effect sizes were interpreted as small ( $|d| = 0.2$ ), medium ( $|d| = 0.5$ ), and large ( $|d| = 0.8$ ) according to conventional thresholds.

## Results

**Demographic variables:** There were no significant differences between the two groups in terms of demographic variables ( $p>0.05$ ) (Table 1).

**Egocentric Mental Rotation:** Reaction times for the right hand and left foot were longer in individuals with MS compared to HS. However, only the reaction time for the right hand showed a statistically significant difference between the groups ( $p=0.042$ ). The percentages of accuracy were lower for the right hand, left hand, and right foot in individuals with MS compared to HS. Statistically significant differences were observed between the groups in the percentage of accuracy for the right hand ( $p<0.001$ ) and right foot ( $p=0.035$ ) (Table 2). In addition to these findings, effect size analyses revealed a small effect for right-hand reaction time ( $d = 0.44$ ) and a moderate effect for right-hand accuracy ( $d = -0.60$ ), and a small to moderate effect for right-foot accuracy ( $d = -0.47$ ). For left-hand and left-foot accuracy, effect sizes ranged from small to moderate ( $|d| = 0.41$ – $0.63$ ).

**Disease duration and egocentric mental rotation:** The median disease duration was 8 years, ranging from 0 to 27 years (Table 1). The reaction times and accuracy for mental rotation were similar for disease durations of less than or equal to five years and greater than five years (Table 3).

The correlations summarized in Table 4 indicate that right hand reaction time is positively associated with disease duration, EDSS, cerebellar function, bowel-bladder function, and ambulatory score. In contrast, right hand accuracy negatively correlates with EDSS and bowel-bladder function. Left hand accuracy shows negative correlations with

**Table 1** Participant characteristics

	Individuals with MS ( $N=57$ )	Healthy subjects ( $N=40$ )	$p$	Cohen's $d$
Age (years, $X\pm SS$ )	38.98 $\pm$ 10.64	39.65 $\pm$ 10.23	$p=0.755^b$	
BMI ( $\text{kg}/\text{m}^2$ , $X\pm SS$ )	25.38 $\pm$ 5.66	24.63 $\pm$ 3.83	$p=0.953^b$	
Gender (N, %)	39 (68.4)	29 (72.5)	$p=0.66^a$	
Female	18 (31.6)	11 (27.5)		
Male				
Education (N, %)	9 (15.8)	5 (12.5)	$p=0.073^a$	
Primary education	24 (42.1)	9 (22.5)		
Secondary education	24 (42.1)	26 (65.0)		
Post-secondary education				
Employment status (N, %)	21 (36.8)	21 (52.5)	$p=0.126^a$	
Employed	36 (63.2)	19 (47.5)		
Unemployed				
EDSS (median, min-max)	3 (1–7)	–		
Disease duration (years, median, min-max)	8 (0–27)	–		
MS type (N, %)	45 (78.9)	–		
RRMS	11 (19.3)			
SPMS	1 (1.8)			
PPMS				
SDMT (0–110) (median, min-max)	42 (9–74)	59.5 (29–86)	$<0.001^{b*}$	–1.27
CVLT-II (0–80) (median, min-max)	50 (28–75)	59 (29–78)	$0.005^{b*}$	–0.61
BVMT-R (0–36) (median, min-max)	25 (3–36)	32 (14–36)	$<0.001^{b*}$	–0.87

(N: number, cm: centimeter, kg: kilogram,  $\text{kg}/\text{m}^2$ : kilogram per square meter,  $X\pm SD$ : mean $\pm$ standard deviation, min: minimum, max: maximum, %: percentage, BMI: Body Mass Index, EDSS: Expanded Disability Status Scale, RRMS: Relapsing-Remitting Multiple Sclerosis, SPMS: Secondary Progressive Multiple Sclerosis, PPMS: Primary Progressive Multiple Sclerosis, SDMT: Symbol Digit Modalities Test, CVLT-II: California Verbal Learning Test-II, BVMT-R: Brief Visuospatial Memory Test-Revised,  $*p<0.05$ , Cohen's  $d$ : Effect size, a: Chi-square Test, b: Mann-Whitney U Test)

**Table 2** Comparison of mental rotation outcomes between individuals with MS and healthy subjects

	Individuals with MS ( <i>N</i> =57) median (min-max)	Healthy subjects ( <i>N</i> =40) median (min-max)	<i>p</i>	Cohen's <i>d</i>
Right hand reaction time (s)	2.10 (1.0–3.70)	1.80 (1.10–2.90)	<b>0.042<sup>a*</sup></b>	0.44
Right hand accuracy (%)	80.00 (24.00–100.00)	92.00 (48.00–100.00)	<b>&lt;0.001<sup>b*</sup></b>	–0.60
Left hand reaction time (s)	2.00 (0.80–3.20)	2.00 (1.10–3.10)	0.667 <sup>a</sup>	0.08
Left hand accuracy (%)	80.00 (20.00–100.00)	88.00 (56.00–100.00)	0.532 <sup>b</sup>	–0.63
Right foot reaction time (s)	1.50 (0.80–3.40)	1.50 (0.90–2.70)	0.423 <sup>b</sup>	–0.17
Right foot accuracy (%)	92.00 (56.00–100.00)	96.00 (56.00–100.00)	<b>0.035<sup>b*</sup></b>	–0.47
Left foot reaction time (s)	1.70 (0.50–2.50)	1.50 (0.90–2.50)	0.216 <sup>a</sup>	0.25
Left foot accuracy (%)	96.00 (24.00–100.00)	96.00 (64.00–100.00)	0.063 <sup>b</sup>	–0.41

(*N*: number, *s*: second, %: percentage, \**p*<0.05, Cohen's *d*: Effect size, a: Independent Samples T-Test, b: Mann-Whitney U Test)

**Table 3** Mental rotation outcomes based on disability and duration in individuals with MS

Individuals with MS ( <i>N</i> =57)	EDSS<3 ( <i>N</i> =27) median (min-max)	EDSS≥3 ( <i>N</i> =30) median (min-max)	<i>p</i>
Right hand reaction time (s)	1.80 (1.20–3.70)	2.20 (1.00–2.90)	<b>0.018<sup>b*</sup></b>
Right hand accuracy (%)	88.00 (60.00–100.00)	74.00 (24.00–100.00)	<b>0.004<sup>b*</sup></b>
Left hand reaction time (s)	1.90 (0.90–2.80)	2.05 (0.80–3.20)	0.231 <sup>a</sup>
Left hand accuracy (%)	88.00 (32.00–100.00)	68.00(20.00–100.00)	<b>0.006<sup>b*</sup></b>
Right foot reaction time (s)	1.50 (0.80–2.20)	1.60 (1.10–3.40)	0.050 <sup>b</sup>
Right foot accuracy (%)	92.00 (56.00–100.00)	92.00 (64.00–100.00)	0.254 <sup>b</sup>
Left foot reaction time (s)	1.70 (0.90–2.50)	1.60 (0.50–2.50)	0.729 <sup>a</sup>
Left foot accuracy (%)	96.00 (68.00–100.00)	92.00 (24.00–100.00)	<b>0.034<sup>b*</sup></b>
	Duration<5 years ( <i>N</i> =22) median (min-max)	Duration≥5 years ( <i>N</i> =35) median (min-max)	<i>p</i>
Right hand reaction time (s)	1.95 (1.20–3.70)	2.10 (1.00–2.90)	0.135
Right hand accuracy (%)	82.00 (24.00–96.00)	80.00 (32.00–100.00)	0.564
Left hand reaction time (s)	2.00 (0.90–2.50)	2.00 (0.80–3.20)	0.967
Left hand accuracy (%)	86.00 (20.00–100.00)	72.00 (32.00–100.00)	0.139
Right foot reaction time (s)	1.45 (0.80–2.70)	1.60 (0.90–3.40)	0.194
Right foot accuracy (%)	96.00 (56.00–100.00)	92.00 (64.00–100.00)	0.428
Left foot reaction time (s)	1.60 (0.90–2.50)	1.70 (0.50–2.50)	0.517 <sup>a</sup>
Left foot accuracy (%)	96.00 (68.00–100.00)	92.00 (24.00–100.00)	0.079

(*N*: number, *s*: second, %: percentage, EDSS: Expanded Disability Status Scale, \**p*<0.05 a: Independent Samples T-Test, b: Mann-Whitney U Test)

disease duration, EDSS, cerebellar function, and bowel-bladder function.

Additionally, right foot reaction time is positively correlated with disease duration, EDSS, bowel-bladder function, and ambulatory score, while right foot accuracy negatively correlates with cerebellar and bowel-bladder function. Left foot accuracy demonstrates negative correlations with cerebellar function, bowel-bladder function, and ambulatory score. No significant correlations were found for left hand and left foot reaction times with other parameters (Table 4).

Correlation analyses revealed that SDMT scores were negatively associated with reaction times and positively correlated with accuracy percentages across multiple limb conditions (*p*<0.001). CVLT II demonstrated moderate positive correlations with accuracy scores, particularly for lower limb tasks (*p*<0.01), while BVMT-R showed weaker yet significant associations with lower limb accuracy

(*p*<0.05) (Table 4). These findings indicate that processing speed, verbal memory, and visuospatial memory all contribute to egocentric mental rotation performance, with SDMT emerging as the most robust cognitive predictor.

## Discussion

This study examined the relationship between egocentric mental rotation and disability and cognitive parameters in people with MS. The findings indicate that individuals with MS perform worse in mental rotation tasks compared to HS, and these impairments are associated with disease duration, disability, functional systems, and cognitive function.

Literature indicates that the order of administration for hand and foot mental rotation tasks is frequently unspecified [13, 30]. A study assessing both hand and foot images found

**Table 4** The relationship between disease duration, EDSS, FSS, BICAMS, and mental rotation in individuals with MS

Individuals with MS (N = 57)	Right hand reaction time (s)		Right hand accuracy (%)		Left hand reaction time (s)		Left hand accuracy (%)		Right foot reaction time (s)		Right foot accuracy (%)		Left foot reaction time (s)		Left foot accuracy (%)	
	r/rho	p	r/rho	p	r/rho	p	r/rho	p	r/rho	p	r/rho	p	r/rho	p	r/rho	p
Disease duration	<b>0.356**</b>	0.171	-0.171	<b>0.276**</b>	<b>0.328*</b>	0.360	<b>0.276**</b>	<b>0.328*</b>	-0.095	0.182	-0.095	0.182	-0.260	0.051 <sup>b</sup>	-0.260	0.051 <sup>b</sup>
EDSS	<b>0.007<sup>b</sup></b>	0.204 <sup>b</sup>	0.204 <sup>b</sup>	<b>0.037<sup>b</sup></b>	<b>0.013<sup>b</sup></b>	0.788 <sup>b</sup>	<b>0.037<sup>b</sup></b>	<b>0.013<sup>b</sup></b>	-0.155	0.175 <sup>b</sup>	-0.155	0.175 <sup>b</sup>	-0.256	0.092	-0.256	0.092
Visual functions score	<b>0.414**</b>	<b>0.301*</b>	<b>0.301*</b>	<b>0.023<sup>b</sup></b>	<b>0.047<sup>b</sup></b>	0.136	<b>0.023<sup>b</sup></b>	<b>0.047<sup>b</sup></b>	0.249 <sup>b</sup>	0.498 <sup>b</sup>	0.249 <sup>b</sup>	0.498 <sup>b</sup>	0.055 <sup>b</sup>	0.092	0.055 <sup>b</sup>	0.092
Brainstem functions score	-0.012	0.932 <sup>b</sup>	0.261 <sup>b</sup>	0.044	0.044	0.044	0.044	0.044	-0.030	-0.020	-0.030	-0.020	-0.009	0.881 <sup>b</sup>	-0.009	0.881 <sup>b</sup>
Pyramidal function score	0.254	0.073 <sup>b</sup>	-0.239	0.747 <sup>b</sup>	0.747 <sup>b</sup>	0.074	0.747 <sup>b</sup>	0.747 <sup>b</sup>	0.826 <sup>b</sup>	0.880 <sup>b</sup>	0.826 <sup>b</sup>	0.880 <sup>b</sup>	0.948 <sup>b</sup>	0.000	0.948 <sup>b</sup>	0.000
Cerebellar functions score	0.057 <sup>b</sup>	0.073 <sup>b</sup>	0.073 <sup>b</sup>	-0.196	0.112	0.586 <sup>b</sup>	-0.196	0.112	-0.087	0.998 <sup>b</sup>	-0.087	0.998 <sup>b</sup>	-0.189	0.051	-0.189	0.051
Sensory functions score	0.210	0.117 <sup>b</sup>	-0.164	0.150 <sup>b</sup>	0.180	0.051	0.150 <sup>b</sup>	0.180	0.265 <sup>b</sup>	0.706 <sup>b</sup>	0.265 <sup>b</sup>	0.706 <sup>b</sup>	0.165 <sup>b</sup>	0.026	0.165 <sup>b</sup>	0.026
Bowel-bladder functions score	0.270*	0.042 <sup>b</sup>	0.042 <sup>b</sup>	-0.298*	0.044	-0.047	-0.298*	0.044	<b>0.028*</b>	-0.026	<b>0.028*</b>	-0.026	<b>0.004<sup>b</sup></b>	0.849 <sup>b</sup>	<b>0.004<sup>b</sup></b>	0.849 <sup>b</sup>
Cerebral functions score	0.171	0.205 <sup>b</sup>	-0.082	0.164	0.077	0.174	0.164	0.077	0.049	0.408 <sup>b</sup>	0.049	0.408 <sup>b</sup>	-0.009	0.946 <sup>b</sup>	-0.009	0.946 <sup>b</sup>
Ambulation score	<b>0.502**</b>	0.144 <sup>b</sup>	0.144 <sup>b</sup>	0.232	0.305*	0.221	0.232	0.305*	-0.175	0.157	-0.175	0.157	<b>0.325*</b>	0.014 <sup>b</sup>	<b>0.325*</b>	0.014 <sup>b</sup>
SDMT	<b>0.298*</b>	0.099 <sup>b</sup>	0.099 <sup>b</sup>	0.424**	<b>0.386**</b>	0.099 <sup>b</sup>	0.424**	<b>0.386**</b>	0.490**	0.226	0.490**	0.226	<b>0.521**</b>	0.091 <sup>a</sup>	<b>0.521**</b>	0.091 <sup>a</sup>
CVLT-II	<b>0.025<sup>a</sup></b>	0.241	0.241	0.185	<b>0.001<sup>b</sup></b>	0.394 <sup>a</sup>	0.185	<b>0.001<sup>b</sup></b>	< <b>0.001<sup>b</sup></b>	0.226	< <b>0.001<sup>b</sup></b>	0.226	< <b>0.001<sup>b</sup></b>	0.091 <sup>a</sup>	< <b>0.001<sup>b</sup></b>	0.091 <sup>a</sup>
BVMT-R	0.687 <sup>a</sup>	0.071 <sup>b</sup>	0.071 <sup>b</sup>	0.167 <sup>b</sup>	0.176 <sup>b</sup>	0.434 <sup>a</sup>	0.167 <sup>b</sup>	0.176 <sup>b</sup>	<b>0.375**</b>	-0.216	<b>0.375**</b>	-0.216	<b>0.342**</b>	0.107 <sup>a</sup>	<b>0.342**</b>	0.107 <sup>a</sup>
	-0.141	0.249	0.249	0.211	0.062	0.211	0.211	0.062	<b>0.282*</b>	-0.070	<b>0.282*</b>	-0.070	<b>0.305*</b>	0.606 <sup>b</sup>	<b>0.305*</b>	0.606 <sup>b</sup>
	0.296 <sup>b</sup>	0.062 <sup>b</sup>	0.062 <sup>b</sup>	0.115 <sup>b</sup>	0.648 <sup>b</sup>	0.062 <sup>b</sup>	0.115 <sup>b</sup>	0.648 <sup>b</sup>	<b>0.034<sup>b</sup></b>	0.606 <sup>b</sup>	<b>0.034<sup>b</sup></b>	0.606 <sup>b</sup>	<b>0.021<sup>b</sup></b>	0.606 <sup>b</sup>	<b>0.021<sup>b</sup></b>	0.606 <sup>b</sup>

(N: number, s:second, %:percentage, EDSS: Expanded Disability Status Scale, SDMT: Symbol Digit Modalities Test, CVLT-II: California Verbal Learning Test-II, BVMT-R: Brief Visuospatial Memory Test Revised r/rho: Pearson/Spearman Correlation Coefficient, \*: p<0,05 a: Pearson Correlation Test, b: Spearman Correlation Test)

that participants were more familiar with hand images, leading to quicker responses in hand mental rotation tasks [30]. In our study, however, response times for hand mental rotation tasks exceeded those for foot tasks. This discrepancy may stem from the order of test administration, or the greater dexterity required for hand tasks. While the thumb served as a reference for hand identification, the malleoli provided additional visual cues for foot identification, potentially favoring performance in the foot task.

In previous studies involving individuals with MS, mental rotation tasks utilized images of the palmar or dorsal surfaces of the hand and foot [10], presented at increasing angles from 0° to 300° [8–10, 13, 31]. In our study, however, we presented randomly sequenced images of hands and feet at increasing angles, which not only included the palmar and dorsal surfaces but also depicted flexion, adduction, and abduction movements of the fingers. Therefore, we believe that the mental rotation tasks used in our study were more challenging than those in existing literature.

Studies on three-dimensional block images and hand mental rotation in individuals with MS indicate that they exhibit longer reaction times and lower accuracy rates compared to HS [7–10, 31]. Although detailed outcomes regarding right- or left-sided performance are limited, one study noted that reaction times for individuals with MS significantly increased as the rotation angle from the upright position (0°) increased, with left-hand stimuli resulting in slower reaction times than right-hand stimuli compared to HS [31]. In our study, individuals with MS demonstrated lower performance in right-hand reaction time, right-hand accuracy, and right-foot accuracy compared to HS. These contradictory results necessitate clarification, particularly independent of the affected side. The complexity of MS-related impairments poses a significant challenge; for example, an individual with pronounced impairment in the right upper extremity may show greater dysfunction in the left lower extremity. When assessing which side is more affected, it is essential to consider the involved system. For example, pyramidal involvement may be more pronounced on the right, whereas cerebellar involvement may be more pronounced on the left. These intricate scenarios warrant further investigation to address these issues.

The lack of mental rotation studies in the literature that differentiate based on disease duration has made it challenging to compare our results. In our study, MS population were split into two groups based on disease duration. Increased reaction times and decreased accuracy were associated with longer disease duration. The unequal sample sizes may account for the lack of statistical significance.

In studies on mental rotation in MS, participants have generally been included based on EDSS < 3.5 or ≤ 3.5 [7, 10, 31]. Steiger's thesis found no association between EDSS and

mental rotation of three-dimensional figures [30]. Similarly, Heremans et al. reported no significant relationship between EDSS (from 3 to 7.5), MS type, disease duration, and motor imagery tests in hand mental rotation [8]. However, in our study, higher EDSS were linked to longer reaction times and significant differences in upper extremity assessments. Higher EDSS were also associated with decreased accuracy rates. This may be due to participants better recognizing foot images compared to hand tasks, suggesting that foot rotation results could be independent of disability. While larger samples are needed for definitive conclusions, current data suggest egocentric mental rotation deficits become more pronounced with upper extremity impairment. The lack of correlations in previous studies may be due to differences in mental rotation tasks.

When examining the relationship between FSS and mental rotation in our study, we found correlations between higher cerebellar function, bladder-bowel function, and ambulation scores with certain mental rotation parameters. The differences observed in FSS in our study may be due to the egocentric nature of the selected mental rotation task, indicating the need for further research to better understand the underlying relationships.

While cerebellar pathology in MS is commonly associated with motor symptoms, the cerebellum is also strongly connected to brain regions involved in cognitive functions [32]. Our mental rotation task may have engaged these cognitive processes. We speculate that existing tremor or ataxia symptoms in these individuals may have influenced the correlation between the cerebellar function score and the prolonged reaction time for the right hand. Similarly, the observed decrease in accuracy rates may also be related to these factors.

Previous studies have demonstrated that bowel dysfunction in individuals with MS is associated with spinal cord damage and impaired gait [33, 34]. Moreover, the link between bowel dysfunction and increased disability levels is attributed to limitations in mobility [35]. Interestingly, in our study, the bowel and bladder system score emerged as the functional system score most strongly correlated with mental rotation findings, supporting previous research. The relationship between mental rotation and bladder-bowel functions may be attributed to spinal cord involvement and associated proprioceptive losses, as well as neurodegenerative processes. However, since no previous study has demonstrated a direct association between spinal cord involvement and mental rotation, we recommend further investigation in future studies.

Participants in our study were selected based on the MMSE, a global cognitive assessment tool, while the BICAMS battery assessed cognitive impairment's impact on mental rotation in individuals with MS. Although MS

participants scored lower than healthy controls, their scores remained above cut-off values, indicating no significant cognitive impairment [36]. Previous research has demonstrated that cognitive tests such as the SDMT, BVMT-R, Line Orientation Judgment, and Paced Auditory Serial Addition Test are associated with mental rotation performance in MS [7, 9, 10, 31], and our findings are consistent with these results. Specifically, reduced scores on cognitive tests were linked to decreased accuracy in mental rotation tasks.

A more detailed examination of the BICAMS subtests revealed differential contributions to mental rotation performance. Among the three subtests, SDMT -which evaluates processing speed- demonstrated the strongest and most consistent associations with both reaction times and accuracy percentages. This finding aligns with prior evidence suggesting that cognitive processing speed is particularly critical in spatial transformation tasks [7–9]. In contrast, CVLT II and BVMT-R showed significant but more modest relationships with accuracy outcomes, especially in lower extremity responses, suggesting that verbal and visuospatial memory may support the precision of perspective taking but contribute less to processing speed. The pattern of results also suggests that lower limb responses may be prioritized over upper limb function in MS, potentially reflecting the impact of ambulation-related cognitive processing demands.

In addition to statistical significance, effect size analyses further supported the clinical relevance of the observed cognitive differences. The large effect size found for SDMT ( $d = -1.27$ ) highlights the substantial impairment in information processing speed among individuals with MS. Moderate and small-to-moderate effects in BVMT-R ( $d = -0.87$ ) and CVLT-II ( $d = -0.61$ ), respectively, suggest that although visuospatial and verbal memory are also affected, processing speed may be the primary cognitive domain influencing egocentric mental rotation performance. Taken together, these findings support the notion that egocentric mental rotation in MS is mediated by multiple cognitive domains, with a predominant reliance on information processing speed. This highlights the relevance of incorporating cognitive processing speed training into rehabilitation strategies for individuals with MS.

Our study's strengths include rigorous participant inclusion criteria. Studies on MS suggests that the relationship between fatigue, anxiety, and depression and cognitive functions should be prioritized in research [37]. Previous research [9, 10, 38] indicates depression and fatigue influence mental rotation in MS, and we ensured both groups were comparable in these aspects. An innovative aspect is the use of the RLD for accurate direction identification. Functional system scores have been suggested to be a more sensitive assessment tool compared to the total EDSS score in detecting the progressive phase of the disease [39]. Our

study's the first to explore the FSS and mental rotation relationship.

The study had several limitations. Although the predominance of females in MS provides generalizable data, gender-based differences in mental rotation were not assessed. Due to the high prevalence of RRMS [40], our results reflect the general MS population; however, further research is needed on mental rotation in PPMS, which is less common. Additionally, our study focused primarily on egocentric mental rotation tasks. Including both egocentric and object-based tasks in future assessments may offer more comprehensive insights. Another limitation is the exclusion of left-handed individuals, which, while ensuring consistency in motor laterality and neural processing, may restrict the generalizability of the findings. Future research should consider including both right- and left-handed participants to evaluate the potential influence of handedness on egocentric mental rotation performance in MS.

## Conclusion

This study examined mental rotation tasks in individuals with MS and HS, revealing significant impairments in right-hand and right-foot performance in right-dominant individuals with MS. Increased disease duration, EDSS, and FSS were linked to mental rotation performance, with cognitive status also playing a role. Given the clinical variability in MS, grouping all individuals with MS as a single population may be inappropriate. Stratifying individuals with MS by FSS could clarify changes in mental rotation and inform treatment targets. Further research, including longitudinal studies and imaging, is needed to explore the relationship between mental rotation and clinical parameters in MS. Moreover, approaches that activate cognitive pathways, such as mental rotation tasks, could be incorporated into the rehabilitation of individuals with MS.

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## Declarations

**Conflict of interest** The authors declare no competing interests.

**Ethical approval** The study was carried out in accordance with the ethical principles and the Helsinki Declaration. Informed consent of the patients was obtained. The study was approved by the Non-Interventional Clinical Research Ethics Committee of Hacettepe University (GO22/832).

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