

Abnormalities of Motor Imagery and Relationship With Depressive Symptoms in Mildly Disabling Relapsing-Remitting Multiple Sclerosis

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Background and Purpose: The effectiveness of motor imagery (MI) as an adjunct to physical rehabilitation has previously been shown. Motor imagery ability can be affected by neurologic disorders that affect motor and cognitive function. This study was designed to assess MI ability in persons with mildly disabling relapsing-remitting multiple sclerosis (RRMS) based on the functional and cognitive dysfunctions.

Methods: Twenty-two participants with RRMS and 23 age-, gender-, and education-matched comparison subjects were evaluated by a battery of MI tasks, including a kinesthetic and visual imagery questionnaire, a mental hand rotation task, and a visual guided pointing task.

Results: There was no significant difference in MI vividness between the participants with MS and the comparison group, but the accuracy and temporal correspondence of MI in the participants with MS differed significantly from those in the comparison group. Depression scores were significantly higher in participants with MS ($P < 0.001$), and depression was significantly correlated with disability ($r = 0.4$; $P < 0.05$). The correlation between accuracy of MI in the participants with MS and their cognitive ability was significant ($r = 0.57$; $P < 0.05$). The MI duration of participants with MS was significantly correlated with their disability ($r = 0.59$; $P < 0.05$) and their cognitive ability ($r = -0.38$; $P = 0.009$).

Discussion: The preservation of MI ability was observed in participants with RRMS; however, abnormalities in accuracy and temporal aspects of MI were observed even in the participants with mild disease. Abnormalities in temporal aspects and accuracy of MI were related to disability and cognitive ability, respectively. In participants with MS, depression should be considered as a confounding factor for the MI task results.

Conclusions: Our finding could be considered in the application of MI during the rehabilitation of persons with MS.

Video abstract available (see Video, Supplemental Digital Content 1, <http://links.lww.com/JNPT/A67>, for more insights from the authors).

Key words: *imagery, mental hand rotation, motor imagery, multiple sclerosis, questionnaire, rehabilitation*

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INTRODUCTION

Multiple sclerosis (MS) is one of the most common disorders of the central nervous system. It is characterized by chronic demyelination, which causes various symptoms leading to motor and cognitive disability. Multiple sclerosis is a disorder with typical onset in early adulthood, having a progressive course and a long duration, and has a high prevalence of accompanying disabilities.^{1,2} Multiple sclerosis is categorized into relapsing-remitting MS (RRMS, the most common subtype), secondary progressive MS, and primary progressive MS. The quality of life for many persons with MS deteriorates over time; therefore, treatment of symptoms is essential and requires a multidisciplinary approach including drug therapy, psychological counseling, and physical therapy.

Studies have shown that physical therapy leads to a significant improvement in disability and quality of life in persons with MS.^{3,4} There is some evidence to suggest that the effectiveness of physical therapy can be improved with the use of motor imagery (MI) as an adjunct therapy.⁵ Motor imagery is the ability to mentally perform movement without overt movement execution.⁶ Motor imagery has been used by athletes to learn motor skills for years,⁷ and recently it has been given more attention as a therapeutic tool for persons with neurological disorders.⁸ The effectiveness of MI in the treatment of some neurological disorders (ie, stroke,⁹ spinal cord injury,¹⁰ and Parkinson disease¹¹) has been shown in previous studies. When MI is considered for use as part of a rehabilitation program, it is important that the MI ability of patients be evaluated in advance.⁸

Recently, Heremans et al¹² studied MI ability in hospitalized patients with MS who had severe motor and cognitive dysfunction. Their results showed that these patients differed from unaffected people in the accuracy and temporal

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organization of MI. Because a variety of cognitive and motor dysfunctions are associated with different subtypes of MS, variation in MI ability is expected to be found among persons with MS of different stages and subtypes. The primary goal of this study was to assess MI ability in a group of participants with mild disability due to RRMS.

Different aspects of MI ability, including vividness, accuracy, and temporal correspondence between actual and imagined movement, are usually measured using questionnaires, mental chronometry, and computer tasks. Heremans et al¹² evaluated MI ability in their participants, using the short version of the Kinesthetic and Visual Imagery Questionnaire (KVIQ-10), hand rotation (HR) task, and Box and Block test (as a mental chronometric task). In this study, a battery of MI tests comprising KVIQ-20 (the long version of KVIQ), visual-guided pointing task (VGPT), and HR were used. Compared with the Box and Block test, VGPT measures either the timing of physical and imagined movements or the relationship between the duration of movement (physical and imagined) and difficulty of the task (as reflected in the speed-accuracy trade-off of Fitts' law).

Cognitive impairment is found in approximately 65% of persons with MS.¹³ The most affected domains are attention, speed of information processing, and working memory.^{14,15} Impaired working memory is observed in the early stages of MS, when other cognitive impairments are subtle and asymptomatic.¹⁶ Importantly, working memory is among the cognitive processes involved in MI.¹⁷ Therefore, investigating the extent of the effect of working memory impairment on MI abilities in persons with MS is of particular interest, and this was another aim of this study.

Depressive symptoms are common in persons with MS¹⁸⁻²⁰ and studies have found that the prevalence of clinical depression is higher among persons with MS than in the general population. Depressive symptoms, particularly psychomotor retardation, tend to be associated with adverse effects on the performance in neuropsychological tests, particularly in capacity-demanding tasks such as working memory.²¹ It is expected that the performance of MI tasks is affected by depressive symptoms in persons with MS. Therefore, the final aim of the present study was to assess the effects of patient clinical characteristics, such as depressive symptoms, disease duration, and level of disability on their MI abilities. To avoid bias of age, sex, and educational level, which are known to influence the results of cognitive testing results, participants with MS were individually matched to healthy comparison subjects.

METHODS

Participants

The study sample included 22 participants with RRMS who were recruited by a neurologist working in an MS clinic (the 23rd participant who did not complete procedure was excluded from the study) and 23 age-, gender-, and education-matched healthy participants. All participants with MS met the McDonald criteria for the diagnosis of MS²² and were assessed with the Kurtzke Expanded Disability Status Scale (EDSS).²³ Persons with EDSS > 3.5 were excluded. All par-

ticipants had normal or corrected normal vision and all were right-handed on the basis of the Edinburgh Handedness Inventory Questionnaire. The exclusion criteria included having had a new neurologic episode during the month before the study, neurological comorbidity (stroke, seizure), head trauma, chronic psychiatric disorders, alcohol or drug abuse, and treatment with deep stimulants. The Beck Depression Inventory (BDI-II) was used to assess depression symptoms.^{24,25} The study was approved by the Ethics Committee of Kerman University of Medical Science, Kerman, Iran. All participants gave written informed consent to participate in the study.

Procedure

All participants completed an assessment battery designed to measure MI ability comprising the KVIQ, mental HR test, and VGPT. The battery was used to evaluate vividness, accuracy, and temporal aspects of MI ability in MS and lasted approximately 2 hours. All participants were instructed to use a first-person perspective MI, wherein they were encouraged to use the vantage point they would have if they were actually performing the activity. In addition, all participants were assessed by the standard Paced Auditory Serial Addition Task (PASAT), a cognitive test.

Testing Battery Administration

Paced Auditory Serial Addition Task. PASAT test is commonly used and combines elements of both a working memory task and information-processing speed²⁶ and its results were correlated with memory tasks in participants with MS.²⁷ The standard PASAT test consists of 61 single digits with a 3-second inter-stimulus interval. Participants were asked to add consecutive single digit numbers as they were heard and to respond orally with the accurate sum. PASAT score was calculated on the basis of the total number of correct responses, ranging from 0 to 60.

Kinesthetic and Visual Imagery Questionnaire. The long version of KVIQ (KVIQ-20) was used to assess the imagery vividness. KVIQ-20 is an MI questionnaire adapted for persons with disabilities who are unable to stand or perform physically complex movements.²⁸ After demonstration of the movements by the experimenter, the participants were instructed to first physically execute the movement only once and then imagine performing the same movements. The KVIQ-20 consists of 20 items (10 movements in each of the visual and kinesthetic subscales) representing gestures from different body parts. Participants performed the movements while seated. KVIQ-20 uses a 5-point scale (5 = clear and intense image; 1 = no image, no sensation) to rate the clarity of the image (visual subscale) and the intensity of the sensation (kinesthetic subscale).

Mental HR task. To examine imagery accuracy, the Parson classical HR paradigm is often used. In this task, participants judge the laterality of pictures, representing left or right hand in different rotation angles.²⁹ The participants were comfortably seated on a chair in front of a table. The stimuli consisted of line drawings of left and right hands in back and palm views (Figure 1), presented in a random order. The hand pictures were rotated in 6 different orientations (0°, 60°, 120°, 180°, 240°, and 300°). Each picture was repeated 15 times, resulting in 360 trials (6 × 2 × 2 × 15). The participants were

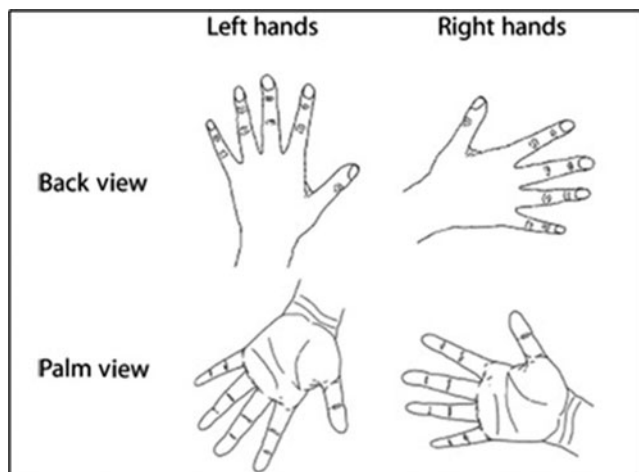


Figure 1. The stimuli in the hand rotation task consisted of line drawings of left and right hands in back and palm views with different rotation angles (0° , 60° , 120° , 180° , 240° , and 300°).

asked to judge whether it was a picture of a left or right hand by pressing left or right button as quickly and accurately as possible. Response time and accuracy rate (percentage of correct responses) were registered via a key press. A score lower than 75% indicated an inability to accurately perform MI.³⁰

Visual-guided pointing task. This test was used to measure the speed-accuracy trade-off of real and imagined movements.³¹ Each trial consisted of a plain sheet of paper upon which an 80-mm vertical line and a black target box were drawn (Figure 2). The closest edge of the target box was 30 mm away from the line. Five sheets were used with different target widths (3.0, 5.3, 10.6, 18.9, or 28 mm). Each hand movement was defined from the far side of the vertical line to touch the target and then back to the far side of the vertical line. The participants made 5 of these movements for each target-width trial. A stopwatch was used to record the duration of the hand movements of the subject. The participants were tested under 2 conditions including “physical execution (VGPT) and imagined movements (VGPTI).” In the imagined condition, participants were instructed to hold the pen at the starting position (with their eyes open) and imagine that they were moving the pen back and forth between the far side of the vertical line and target, as quickly and accurately as possible. The participants were requested to use imagery from a first-person perspective. They completed 2 sets of the 5 target widths for each condition. Timing of each trial began when the experimenter said “go.” The timing for real movements stopped when the subjects completed the fifth imagined movement and the timing for imagined movement stopped when the subject said “stop” after the fifth imagined movement was completed. The order of administration was randomized between the target-widths and real and imagined movements. According to Fitts’ law, the index of difficulty (ID) for each target width was calculated using the equation: $ID = \log_2(2A/W)$, where A is amplitude of the movement and W is the width of the targets. Fitts’ law, which states that movement (both actual and imagined) dura-

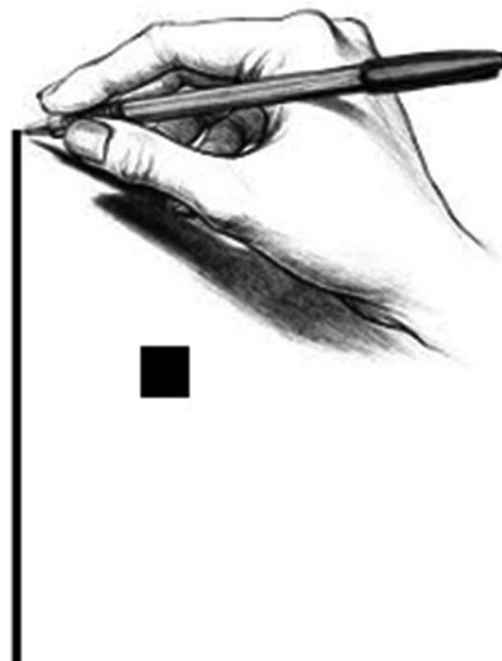


Figure 2. Visual guided pointing task (VGPT). Participants were required to move a pencil from the starting point at the top of the line to anywhere within the target square as quickly and as accurately as possible.

tion is inversely related to the ID, expresses speed-accuracy trade-off during real- and imagined-movement trials.

Analysis

The mean score of the KVIQ-20, the mean movement time of 5 different target-widths in VGPT and VGPTI, the overall mean response time and the accuracy rate of 6 different rotation angles (after combining similar angles from right and left in back or palm views) in the HR task were calculated. Data distributions were assessed for normality using the Shapiro-Wilk test. To evaluate potential confounding or interrelations between the results of imagery tests and BDI-II scores, a Pearson correlation was conducted. For comparison of the 2 groups, independent t tests, or analysis of covariance (ANCOVA; to control confounding effect of depression) with results of the imagery tests as dependent variables and groups (MS and comparison) as factors were run. The accuracy and response time of the HR task were analyzed using repeated-measures ANOVA, with groups (MS, CMP) as between subject, HR angles (0° , 60° , 120° , 180° , 240° , and 300°), and hand side (left, right) as within subject. Repeated-measures ANOVA was also carried out with groups as between subjects and condition (executed and imagined) and ID as within subjects for the VGPT task. The relationship between the participant characteristics and imagery task results was studied using the Pearson correlation test. Multivariate regression was used to determine the predictive factors (between independent variables) of the VGPT result. Data analysis was conducted using SPSS. V.17 (Version 17.0. Chicago: SPSS Inc). For all significant effects, the α level was 0.05.

RESULTS

The demographic and clinical characteristics of the participants are shown in Table 1. The mean time since diagnosis in participants with MS was 6.16 years. While the MS and comparison groups were well-matched for gender, age, and education, there was a significant difference between groups on BDI-II scores, and participants with MS had significantly higher scores than the comparison group. On the basis of a BDI-II cutoff score of 15, 74% of the participants with MS had depressive symptoms. BDI-II was significantly correlated with EDSS ($r = 0.4$; $P < 0.05$) and PASAT ($r = -0.36$; $P < 0.05$) in the MS group; however, there were no significant correlations between BDI-II and other patient characteristics (disease duration, age, and education level). Moreover, significant correlations ($r \geq 0.3$) between BDI-II and some imagery measures (KVIQ, VGPT, and VGPTI) were found; therefore, BDI-II was used as a covariate in analyses of these variables. The 2 groups were not significantly different on the PASAT score.

Between-Groups Comparisons

Imagery Questionnaire

After adjusting for BDI-II, there was no significant difference in the mean scores of KVIQ between the 2 groups (Table 2).

HR Task

Response time. Repeated-measure ANOVA analysis for group \times stimulus angle \times stimulus side showed a significant main effect of group ($F_{1,43} = 7.29$, $P = 0.01$), stimulus angle ($F_{1,43} = 148.44$, $P < 0.001$), and stimulus side ($F_{1,43} = 38.31$, $P < 0.001$), while no interaction effect of group \times rotation angle was found. These results indicate significantly slower response times in the participants with MS relative to the comparison group. Also, these findings show an increase in response times of HR with an increase in rotation angles (Figure 3A), and response times to the left-hand stimuli were significantly slower than those to the right-hand stimuli in both groups. The interacting effects of group \times stimulus angle, group \times stimulus side, and stimulus angle \times stimulus side

Table 1. Participant Characteristics

Measure	MS	CMP	P Value
Age, years	32.31 \pm 5.38	31.82 \pm 4.91	ns
Gender (females/males), proportion	17/5	17/6	ns
Education, mean (range), years	12 (5-18)	12 (5-16)	ns
Duration of disease (years)	6.16 (1-23)		
EDSS	1.8 (1-3.5)		
BDI-II	22.65 \pm 10.33	11.73 \pm 6.92	<0.001
PASAT	34.90 \pm 14.12	40.78 \pm 11	ns

Abbreviations: BDI, Beck Depression Inventory score; CMP, comparison group; EDSS, Kurtzke Expanded Disability Status Scale; MS, multiple sclerosis group; ns, nonsignificant; PASAT, paced auditory serial addition test.

All data are presented in mean and SD unless otherwise indicated.

Table 2. Test Scores (Group Mean and Standard Deviation) and Comparison Results

Imagery Tasks	MS	CMP	P Value
KVIQ	3.67 \pm 0.73	4.11 \pm 0.47	0.27 ^a
VGPT	6.2 \pm 1.57	4.84 \pm 1.11	0.01 ^a
VGPTI	5.73 \pm 1.58	4.16 \pm 0.90	0.003 ^a
HRT	1629.9 \pm 255.9	1444.3 \pm 203.1	0.01 ^b
HRA	83.82 \pm 9.15	89.46 \pm 6.89	0.02 ^b

Abbreviations: CMP, comparison group; HRA, hand rotation accuracy rate (percent of accuracy); HRT, hand rotation reaction time; KVIQ, Kinesthetic and Visual Imagery Questionnaire (was assessed on a 5-point VAS, with a score of 1 indicating minimum vividness and a score of 5 maximum); MS, multiple sclerosis group; VGPT, visual pointing guided test (physical executive form); VGPTI, visual pointing guided test (imagery form).

^aANCOVA after adjusting for Beck Depression Inventory II.

^bIndependent *t* test.

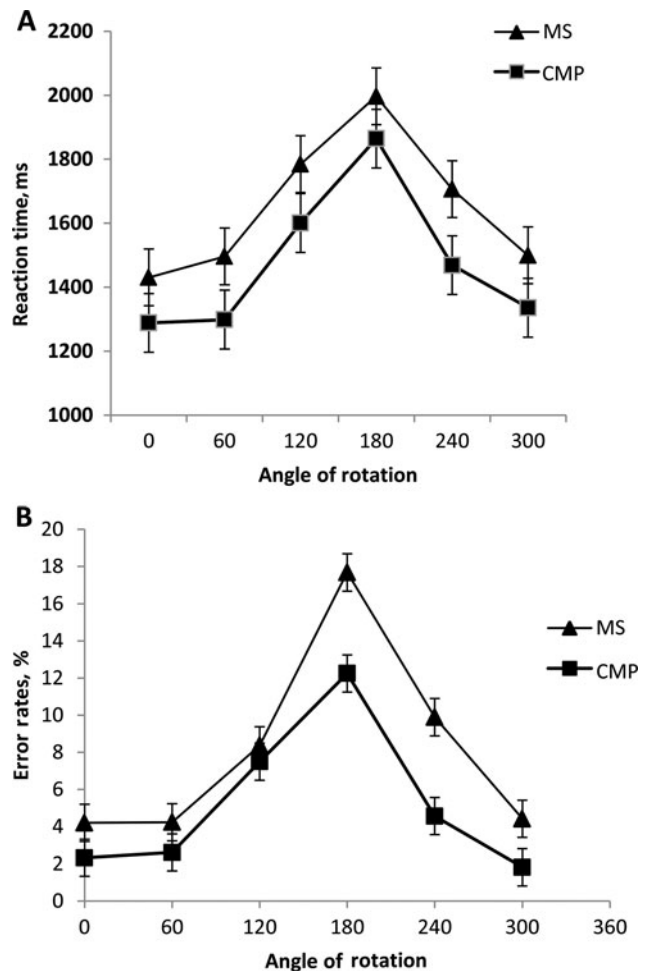


Figure 3. (A) Reaction time and (B) error rate in mental hand rotation task for the multiple sclerosis (MS) group and control (CMP) group.

were not significant, showing similar behavior of the 2 groups across different orientations and stimulus sides.

Accuracy. ANOVA analysis for group \times stimulus angle \times stimulus side showed main effect of group ($F_{1,43} = 5.8$,

$P = 0.02$) and angle ($F_{1,43} = 74.13, P < 0.001$), while the main effect of stimulus side was not significant. These findings indicate that accuracy rates were significantly lower in participants with MS compared with the comparison group, and that accuracy rates decreased with increasing rotation angles in both groups (Figure 3B). The interaction effect of group \times stimulus angle was significant, indicating different behaviors of the 2 groups across different angles. Post hoc analysis demonstrated that the 2 groups were significantly different at 240° and 300° rotation angle.

Visual-Guided Pointing Task

The results of repeated-measure ANOVA showed a significant main effect of group ($F_{1,43} = 20.57, P < 0.001$), indicating that the participants with MS ($M = 6.01$) took significantly longer to perform both the executed and imagined movements than the comparison group ($M = 4.24$). In addition, the main effect of condition (executed or imagined) was significant ($F_{1,43} = 14.07, P = 0.001$), while the interaction effect between groups and movement condition was not significant, showing that both groups performed imagery movements faster ($M = 4.91$) than physical movements ($M = 5.36$). There was also a significant main effect of ID ($F_{1,43} = 12.39, P < 0.001$). This indicates that the participants performed the easiest target (ID = 1.09), the fastest ($M = 4.90$) and the most difficult condition (ID = 4.32), the slowest ($M = 5.28$). The interaction of ID with group was not significant, indicating similar lengthening of performance time with an increase in ID in both groups (Figure 4). Finally, the correlation between VGPT and VGPTI was high in MS group ($r = 0.82, P < 0.001$).

Correlations Among the Participant Characteristics and Imagery Tasks

Correlations among the characteristics of participant with MS (ie, disease duration, BDI-II, EDSS, and PASAT) and imagery test (KVIQ, VGPT, VGPTI, HR response time, and accuracy) were investigated (Table 3).

Imagery Questionnaire

None of the correlations between the KVIQ scores and the characteristics of participants with MS were significant.

Visual Pointing Guided Test (Physical Executive Form)

Simple bivariate analysis showed that VGPT scores were significantly related to EDSS, BDI-II score, and PASAT, while no significant correlations were found with other variables. To find the variables contributing to the prediction of VGPT, a multiple regression analysis was performed. The results showed adequate goodness of fit for the applied model (adjusted $r^2 = 0.31, df = 3, F = 4.21, P = 0.02$). Expanded Disability Status Scale was a significant predictor ($\beta = 1, t = 3.01, P < 0.001$) but BDI-II ($\beta = 0.006, t = 0.20, P = 0.84$) and PASAT ($\beta = -0.02, t = -1.26, P = 0.22$) were not significant predictors of VGPT.

Visual Pointing Guided Test (Imagery Form)

Correlation analysis showed that VGPTI scores were significantly correlated with BDI-II, EDSS, and PASAT scores, but no significant correlations were found with other characteristics of participants with MS. The multiple regression analyses showed that EDSS was a significant predictor for VGPTI ($\beta = 1.18, t = 3.03, P = 0.007$), while BDI-II, PASAT, and EDSS were not significant.

Hand Rotation

The correlation analysis between HR response time and patient characteristics was not significant, but accuracy rate of HR in the participants with MS had a significant correlation with PASAT.

DISCUSSION

The potential role of MI in rehabilitation of some neurological diseases such as stroke, Parkinson disease, and spinal cord injury has been shown.⁸⁻¹¹ However, there is scarce evidence for the effectiveness of using MI in the different stages of MS disease. The present study aimed to assess different aspects of MI (vividness, accuracy, and temporal aspects) using a

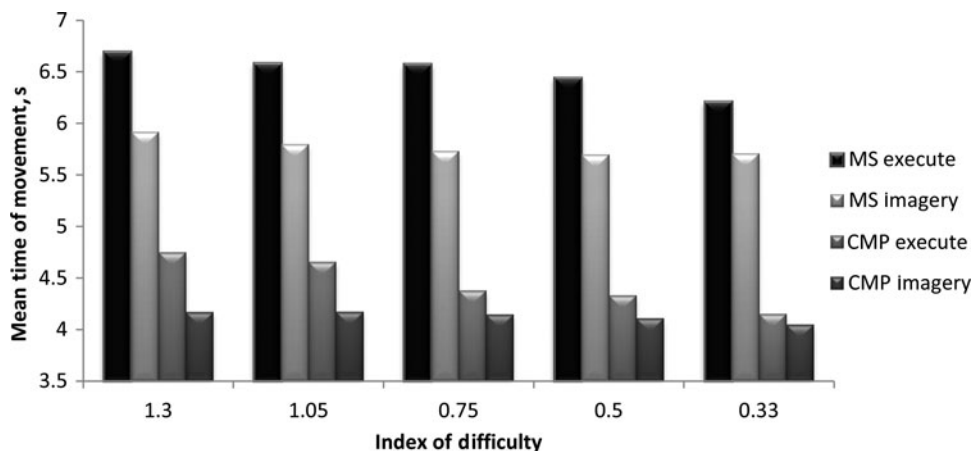


Figure 4. Mean time of movement in visual guided pointing task (VGPT) for participants with multiple sclerosis (MS) and comparison subjects (CMP) in execution and imagined movement.

Table 3. Correlation Between Patients' Characteristics and Imagery Tasks^a

	KVIQ	VGPT	VGPTI	HRT	HRA
Disease duration	ns	ns	ns	ns	ns
BDI-II	0.4 (<0.05)	0.55 (<0.001)	0.38 (0.009)	ns	ns
EDSS	ns	0.59 (<0.05)	0.59 (<0.05)	ns	ns
PASAT	ns	-0.49 (<0.001)	-0.38 (0.009)	ns	0.57 (<0.05)

Abbreviations: BDI, Beck depression inventory score; EDSS, Kurtzke Expanded Disability Status Scale; HRA, hand rotation accuracy rate (percent of accuracy); HRT, hand rotation reaction time; KVIQ, Kinesthetic and Visual Imagery Questionnaire; VGPT, visual pointing guided test (physical executive form); VGPTI, visual pointing guided test (imagery form); PASAT, Paced auditory serial addition test; ns, nonsignificant.

^aValues are Pearson's *r* (*P* value).

battery of MI tasks in participants with mild disability (EDSS ≤ 3.5) due to RRMS compared with a healthy comparison group.

For the imagery questionnaire (KVIQ-20), consistent with a recent study on persons with severe motor dysfunction (EDSS ≥ 4),¹² our results showed no significant difference in imagery vividness between MS and control groups, indicating that imagery vividness is preserved in persons with MS. Moreover, there were no significant correlations between vividness scores and patient disabilities (EDSS) and cognitive abilities (PASAT). In support of this, previous studies have also reported that persons with brain lesions affecting the motor system are likely to be able to imagine movements but that their performances, either physical or imagined, are similarly affected.^{8,32} Our finding about preservation of MI vividness in participants with MS reveals their capability of performing MI as a complement to physical rehabilitation.

The results of this study indicated that while the participants with MS were similar to the health comparison group in imagery vividness, the 2 groups were significantly different in duration and accuracy of imagery when assessed by the VGPT and HR tasks. The participants with MS were significantly slower in imagery tasks than the comparison group. This finding is consistent with the results of the study by Heremans et al,¹² which reported slow MI performance using the Box and Block test in participants with MS, reflecting a temporal problem of imagery. The prolonged response during the mental chronometric task in the patient group could be a result of both cognitive and motor slowing.³³ In the present study, the participants were without relevant impaired speech, but the verbal feedback slowing in VGPT result should be considered as a confounding effect in participants with MS. In addition, our results showed that the response slowing of the MS group in both forms of VGPT (physical and imagined) was significantly correlated with EDSS of the participants with MS. Our results indicated that among the 3 variables (EDSS, BDI-II, and PASAT), only EDSS was a significant predictor of both forms of VGPT (physical and imagined), showing the effect of physical disability on performance slowing in participants with MS. Previous studies have reported slower reaction times in participants with MS even in the early stage of the disease compared with the comparison group,^{33,34} which correlated with their disabilities.^{15,33-35}

In the HR task, accuracy rates of the participants with MS were significantly lower than those of the comparison group, consistent with the study of Heremans et al,¹² indicating that the participants with MS imagine less accurately than control

subjects. Moreover, the positive correlation between HR accuracy and PASAT score in participants with MS indicates an association between a decrease in cognitive abilities (working memory, attention, or processing speed) and less accurately performing MI. This is in accordance with a previous study showing an effect of working memory on MI.³⁶

Regarding the VGPT task, the 2 groups showed a more rapid performance in imagined movements than executed ones, and both conditions of movements complied with Fitts' law. In addition, the relationship between imagined movement duration and ID (increasing movement time with decreasing target size) was in accordance with the central movements limits reflected in Fitts' law,³¹ indicating the relative preservation of MI in the participants with MS despite disruption of both accuracy and temporal aspects. Our finding of shorter duration of movement time in the imagined condition compared with the executed condition was in agreement with some studies.³⁷ However, other studies have found a slower performance in imagined conditions compared with real conditions.^{31,38} It is possible that both groups imagined performing VGPT in a less constrained way than when physically performing. There is no way of confirming whether participants were imagining correctly and accurately, although both groups demonstrated imagined movement in accordance with Fitts' law.

In agreement with other studies, our results indicated a high prevalence of depressive symptoms (74%) in the MS group. It should be mentioned that the prevalence of depressive symptoms in MS has been reported differently (approximately 70%),^{18,19} because of differences in screening measures, gender ratio, and age.²⁰ Moreover, consistent with previous findings,³⁹ the present study showed that depressive symptoms were related to EDSS score in participants with MS. It is suggested that the risk for depression begins with the onset of MS before commencing sequel of MS including fatigue, physical disability, cognitive dysfunction, and pain.⁴⁰

In addition, a significant relationship between depressive symptoms (BDI-II) and the results of some imagery tasks (KVIQ and VGPT) was observed in participants with MS. It has been shown initiation of voluntary responses and psychomotor retardation.⁴¹ Depression seems to reduce the activation of the behavioral system that regulates motor behavior associated with initiation of locomotion and movement toward desired objects.⁴² Importantly, slowed performance on mental rotation tasks has been found in persons diagnosed with depression,⁴³ indicating an impairment of MI and planning in depression. Our results suggest the importance of considering

the role of depression in interpreting motor and imagery tasks in MS.

In this study, PASAT was used to evaluate the working memory in participants. PASAT, as a highly sensitive and commonly used cognitive test in participants with MS,²⁶ evaluates working memory, attention, and information-processing speed. Despite some limitations (effect of practice, intelligence, and mathematical ability), PASAT (particularly the 3s version) can be considered as an appropriate tool to differentiate working memory capacity in participants with MS from that of the comparison group.²⁷ Our results showed similar performances of participants with MS and the comparison group on PASAT. While most studies have shown impaired performance on PASAT, even in the early stages of MS,^{34,44} some studies have also reported comparable results with the comparison subjects.^{27,45} These discrepancies in the literature may be related to the effect of confounding factors, stages of disease, intelligence, and mathematical ability.⁴⁶ It must be taken into account that in the present study, depression was assumed to be a confounding factor and the participants with MS had mild disability (EDSS < 3.5) and some were in the early stages of disease. In addition, the correlation between PASAT scores and the patient demographic characteristics (disease duration and EDSS) were not significant. This finding is in agreement with previous studies that have shown that cognitive dysfunction in MS is weakly correlated with other neurological disabilities (EDSS) or disease duration.⁴⁷

Finally, our results showed slowing response rates in the participants with MS on VGPTE negatively correlated with their PASAT scores. This finding, consistent with other studies, indicates an association between response slowing and a decrease in the speed of information processing in participants with MS.³³ The relationship between response slowing with both motor slowing and a decline in sustained attention (not perceptual or decisional process) has been reported.³³ As described before, the impairment of processing speed is common in participants with MS, leading to general slowing (motor execution and mental processing) even in the early stage of RRMS with minimal physical disability.

The results of KVIQ showed preserved vividness of MI in participants with MS, although we should be careful in interpreting this result. In fact, the KVIQ is an autoevaluation measurement tool, which may lead to overestimation of the patient's abilities. Therefore, other objective methods such as HR and mental chronometry tasks should be applied in studies of MI. Motor imagery has a concealed nature and screening for MI ability is important before considering it in the rehabilitation of participants with MS.⁴⁸ Regarding the relationship between sensory-motor structures and mental HR,²⁹ this test could be introduced as an objective tool to evaluate MI ability (the accuracy and duration) in persons with MS. Moreover, given the effects of depressive symptoms and cognitive dysfunction on MI ability of participants with MS, evaluation of these factors gives a better insight to their abilities. It should be noted that observed impairment in temporal and accuracy aspects of MI can improve by using external cues, as studies have shown that visual and auditory cues can increase the spatial accuracy and MI duration in participants with MS.⁴⁹

There are 2 limitations to our study. First, this study was limited to examining upper-limb function, while examination of the lower limbs may have given different results. Second, there were small numbers of evaluating tools for motor and cognitive functions. Future MI studies of persons with MS should use a wide set of motor and cognitive neuropsychological tests.

Our finding of preserved MI ability in participants with MS has several clinical implications. First, MI practice may be considered as a supportive therapy in these participants to increase the level of their activity and independence. In fact, MI as a home-based exercise can be used by patients without the need for the presence of a therapist and a special equipment. Second, because the presence of attention deficits has been well established in MS, MI practice may reduce attention load during actual performance.⁵⁰ Third, MI practice could increase self-efficacy, motivation, and independency⁵¹ and improve the quality of life in persons with MS and other neurological disorders.

In summary, this study indicated the preservation of MI ability in participants with RRMS, with impairment of the temporal and accuracy aspects of MI, which were correlated with participants' EDSS and PASAT scores, respectively.

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REFERENCES

- Weinshenker B, Bass B, Rice G, et al. The natural history of multiple sclerosis: a geographically based study. *Brain*. 1989;112:133-146.
- Kantarci OH, Weinshenker BG. Natural history of multiple sclerosis. *Neurol Clin*. 2005;23:17-38.
- Solari A, Filippini G, Gasco P, et al. Physical rehabilitation has a positive effect on disability in multiple sclerosis patients. *Neurology*. 1999;52:57-57.
- Wiles C, Newcombe R, Fuller K, et al. Controlled randomised crossover trial of the effects of physiotherapy on mobility in chronic multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2001;70:174-179.
- Warner L, McNeill ME. Mental imagery and its potential for physical therapy. *Phys Ther*. 1988;68:516-521.
- Mulder T. Motor imagery and action observation: cognitive tools for rehabilitation. *J Neural Transm*. 2007;114:1265-1278.
- Murphy SM. Imagery interventions in sport. *Med Sci Sports Exerc*. 1994;26:486-494.
- Jackson PL, Lafleur MF, Malouin F, Richards C, Doyon J. Potential role of mental practice using motor imagery in neurologic rehabilitation. *Arch Phys Med Rehabil*. 2001;82:1133-1141.
- Sharma N, Pomeroy VM, Baron JC. Motor imagery: a backdoor to the motor system after stroke? *Stroke*. 2006;37:1941-1952.
- Cramer SC, Orr ELR, Cohen MJ, Lacourse MG. Effects of motor imagery training after chronic, complete spinal cord injury. *Exp Brain Res*. 2007;177:233-242.
- Tamir R, Dickstein R, Huberman M. Integration of motor imagery and physical practice in group treatment applied to subjects with Parkinson's disease. *Neurorehabil Neural Repair*. 2007;21:68-75.
- Heremans E, D'Hooghe M, Bondt S, Helsen W, Feys P. The relation between cognitive and motor dysfunction and motor imagery ability in patients with multiple sclerosis. *Mult Scler*. 2012;18:1303-1309.
- Gmeindl L, Courtney SM. Deconstructing spatial working memory and attention deficits in multiple sclerosis. *Neuropsychology*. 2012;26:57-70.

14. Denney DR, Gallagher KS, Lynch SG. Deficits in processing speed in patients with multiple sclerosis: evidence from explicit and covert measures. *Arch Clin Neuropsychol*. 2011;26:110-119.
15. De Sonneville L, Boringa J, Reuling I, Lazeron R, Ader H, Polman C. Information processing characteristics in subtypes of multiple sclerosis. *Neuropsychologia*. 2002;40:1751-1765.
16. Pelosi L, Geesken J, Holly M, Hayward M, Blumhardt L. Working memory impairment in early multiple sclerosis. Evidence from an event-related potential study of patients with clinically isolated myelopathy. *Brain*. 1997;120:2039-2058.
17. Decety J, Grèzes J. Neural mechanisms subserving the perception of human actions. *Trends Cogn Sci*. 1999;3:172-178.
18. Figved N, Klevan G, Myhr K, et al. Neuropsychiatric symptoms in patients with multiple sclerosis. *Acta Psychiatr Scand*. 2005;112:463-468.
19. Ayatollahi P, Nafissi S, Eshraghian M, Kaviani H, Tarazi A. Impact of depression and disability on quality of life in Iranian patients with multiple sclerosis. *Mult Scler*. 2007;13:275-277.
20. Patten SB, Metz LM, Reimer MA. Biopsychosocial correlates of lifetime major depression in a multiple sclerosis population. *Mult Scler*. 2000;6:115-120.
21. Benedict RHB, Fischer JS, Archibald CJ, et al. Minimal neuropsychological assessment of MS patients: a consensus approach. *Clin Neuropsychol*. 2002;16:381-397.
22. McDonald WI, Compston A, Edan G, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. *Ann Neurol*. 2001;50:121-127.
23. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33:1444-1452.
24. Richter P, Werner J, Heerlein A, Kraus A, Sauer H. On the validity of the Beck Depression Inventory. *Psychopathology*. 1998;31:160-168.
25. Benedict RHB, Fishman I, McClellan M, Bakshi R, Weinstock-Guttman B. Validity of the beck depression inventory—fast screen in multiple sclerosis. *Mult Scler*. 2003;9:393-396.
26. Tombaugh TN. A comprehensive review of the paced auditory serial addition test (PASAT). *Arch Clin Neuropsychol*. 2006;21:53-76.
27. Litvan I, Grafman J, Vendrell P, et al. Multiple memory deficits in patients with multiple sclerosis: exploring the working memory system. *Arch Neurol*. 1988;45:607-610.
28. Malouin F, Richards CL, Jackson PL, Lafleur MF, Durand A, Doyon J. The Kinesthetic and Visual Imagery Questionnaire (KVIQ) for assessing motor imagery in persons with physical disabilities: a reliability and construct validity study. *J Neurol Phys Ther*. 2007;31:20-29.
29. Parsons LM. Temporal and kinematic properties of motor behavior reflected in mentally simulated action. *J Exp Psychol Hum Percept Perform*. 1994;20:709-730.
30. Sharma N, Jones P, Carpenter T, Baron JC. Mapping the involvement of BA 4a and 4p during motor imagery. *Neuroimage*. 2008;41:92-99.
31. Sirigu A, Cohen L, Duhamel J, Pillon B. Congruent unilateral impairments for real and imagined hand movements. *Neuroreport*. 1995;6:997-1001.
32. Decety J, Boisson D. Effect of brain and spinal cord injuries on motor imagery. *Eur Arch Psychiatry Clin Neurosci*. 1990;240:39-43.
33. Stoquart-El-Sankari S, Bottin C, Roussel-Pieronne M, Godefroy O. Motor and cognitive slowing in multiple sclerosis: an attentional deficit? *Clin Neurol Neurosurg*. 2010;112:226-232.
34. Achiron A, Barak Y. Cognitive impairment in probable multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2003;74:443-446.
35. Amato MP, Ponziani G, Siracusa G, Sorbi S. Cognitive dysfunction in early-onset multiple sclerosis: a reappraisal after 10 years. *Arch Neurol*. 2001;58:1602-1606.
36. Malouin F, Belleville S, Richards CL, Desrosiers J, Doyon J. Working memory and mental practice outcomes after stroke. *Arch Phys Med Rehabil*. 2004;85:177-183.
37. McLennan N, Georgiou N, Mattingley J, Bradshaw JL, Chiu E. Motor imagery in Huntington's disease. *J Clin Exp Neuropsychol*. 2000;22:379-390.
38. Maruff P, Wilson P, Fazio JD, Cerritelli B, Hedt A, Currie J. Asymmetries between dominant and non-dominant hands in real and imagined motor task performance. *Neuropsychologia*. 1999;37:379-384.
39. Amato M, Ponziani G, Rossi F, Liedl C, Stefanile C, Rossi L. Quality of life in multiple sclerosis: the impact of depression, fatigue and disability. *Mult Scler*. 2001;7:340-344.
40. Arnett PA, Barwick FH, Beene JE. Depression in multiple sclerosis: review and theoretical proposal. *J Int Neuropsychol Soc*. 2010;14:691-724.
41. Buyukdura JS, McClintock SM, Croarkin PE. Psychomotor retardation in depression: biological underpinnings, measurement, and treatment. *Prog Neuropsychopharmacol Biol Psychiatry*. 2011;35:395-409.
42. Mayberg H. Limbic-cortical dysregulation: a proposal model of depression. *J Neuropsych Clin N*. 1997;9:471-481.
43. Rogers M, Bradshaw J, Phillips J, Chiu E, Mileskin C, Vaddadi K. Mental rotation in unipolar major depression. *J Clin Exp Neuropsychol*. 2002;24:101-106.
44. Deloire M, Salort E, Bonnet M, et al. Cognitive impairment as marker of diffuse brain abnormalities in early relapsing remitting multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2005;76:519-526.
45. Staffen W, Mair A, Zauner H, et al. Cognitive function and fMRI in patients with multiple sclerosis: evidence for compensatory cortical activation during an attention task. *Brain*. 2002;125:1275-1282.
46. Brooks JBB, Giraud VO, Saleh YJ, Rodrigues SJ, Daia LA, Fragoso YD. Paced auditory serial addition test (PASAT): a very difficult test even for individuals with high intellectual capability. *Arq Neuropsiquiatr*. 2011;69:482-484.
47. Filippi M, Alboroni M, Martinelli V, et al. Influence of clinical variables on neuropsychological performance in multiple sclerosis. *Eur Neurol*. 1994;34:324-328.
48. Goss S, Hall C, Buckolz E, Fishburne G. Imagery ability and the acquisition and retention of motor skills. *Mem Cognit*. 1986;14:469-477.
49. Heremans E, Nieuwboer A, Spildooren J, et al. Cued motor imagery in patients with multiple sclerosis. *Neuroscience*. 2012;206:115-121.
50. Murphy SM, Woolfolk RL. The effects of cognitive interventions on competitive anxiety and performance on a fine motor skill accuracy task. *Int J Sport Psychol*. 1987;18:152-166.
51. Van Leeuwen R, Inglis TJ. Mental practice and imagery: a potential role in stroke rehabilitation. *Phys Ther Rev*. 1998;3:47-52.