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Abstract:	Background: Motor imagery (MI) was recently shown to be a promising tool in neurorehabilitation. The ability to perform motor imagery, however, may be impaired in part of the patients with neurological dysfunction. Objective: To assess the relation between cognitive and motor dysfunction and MI ability in patients with multiple sclerosis (MS). Methods: 30 patients with MS underwent a cognitive and motor screening, as well as performed a composite test battery to assess their MI ability. This test battery consisted of a questionnaire, a hand rotation task and a test based on mental chronometry. Patients' MI ability was compared with the MI ability of age-matched healthy controls. As well, their MI scores were compared between body sides and were correlated with their scores on tests on motor and cognitive functioning. Results: The average accuracy and temporal organisation of MI significantly differed between MS patients and controls. Patients' MI accuracy significantly correlated with impairments in cognitive functioning, but was independent of motor functioning. MI duration, on the other hand, was independent of cognitive performance, but differed between patients' most and least affected side.

	Conclusion: These findings are of use when considering the application of motor imagery practice in MS patients' rehabilitation.

Abstract

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Conclusion: These findings are of use when considering the application of motor imagery practice in MS patients' rehabilitation.

1. Introduction

Motor imagery (MI) can be defined as mental rehearsal of a motor act in the absence of overt motor output.[1] Recent studies showed that practice by means of MI can result in similar neural reorganization as actual physical practice.[2] Mainly in stroke patients[3] and patients with Parkinson's disease (PD)[4] the potential effect of combining MI and physical practice was shown. However, some studies question its applicability and effectiveness in part of the neurological patients, since cognitive and motor dysfunction could be related to impairments in imagery ability. Previous research showed that 40% of stroke patients were unable to perform MI.[3] The lack of imagery ability in these patients may be explained by the location of their lesion. Mainly lesions in the parietal cortex and left prefrontal area may result in a loss of imagery ability.[5,6] As well, studies have shown involvement of the basal ganglia in MI.[7] This was confirmed by behavioural studies showing impairments in MI in patients with PD.[8] Other studies, however, showed that, despite a severe slowness, PD patients are still able to accurately perform MI.[9] Since a relationship was shown between imagery ability and the effectiveness of MI practice[10], a thorough evaluation of patients' imagery ability is needed before considering using MI in rehabilitation.

In patients with multiple sclerosis (MS), MI ability has never been examined. MS is characterised by motor as well as cognitive symptoms.[11] Cognitive impairments, present in 40-70% of the patients, mainly relate to problems in attention, information processing speed, memory, mental flexibility and visuocontruction.[12] These deficits may be due to demyelination and axonal damage leading to loss of neuronal synchronization and functional disconnection amongst brain relays. Therefore, MS recently has been described as a multiple disconnection syndrome.[12,13] Recent studies showed that cognitive performance measured by processing speed and executive function is significantly associated with patients' motor function.[14] Motor symptoms include muscle weakness, spasticity and incoordination, leading to limitations in daily life functioning. In the present study, we particularly focused on upper limb movement capacity, since 76% of MS patients are confronted with upper limb dysfunction during the disease course.[15] The aim of this study was to investigate the relation between these motor and cognitive problems and MS patients' MI ability. To determine the relation between cognitive impairments and MI, the MI tests were correlated with patients' scores on a wide set of cognitive screening tests. To assess their relation with motor dysfunction, we correlated the MI scores with patients' outcome on motor tests, and compared patients' scores on MI tests performed with their most and least affected body side.

2. Materials and methods

2.1. Participants

30 MS patients (14 males; 50.5±10.9 years) and 30 healthy controls (14 males; 50.2±11.1 years) were recruited from consecutive admissions to the National MS Center Melsbroek by a neurologist using the Poser Criteria.[16] They were all right-handed as measured by the Edinburgh Handedness Inventory Questionnaire. Exclusion criteria were: Mini-Mental State Examination (MMSE) score <24, neurological or psychiatric comorbidity, severe visual deficit, severe orthopaedic problems of the upper limb and MS relapse or related corticosteroid therapy within eight weeks preceding study entry. The study was conducted in accordance with the sixth revision of the ethical standards laid down in the 1964 Declaration of Helsinki, and was approved by the Ethics Committees of the National MS Center Melsbroek and the Katholieke Universiteit Leuven. All participants gave written informed consent.

2.2. Experimental procedure

2.2.1. Screening of disease severity and cognitive and motor functions

First, patients were assessed by means of the Expanded Disability Status Scale (EDSS). Subsequently, patients' cognitive functioning was evaluated by means of the Symbol Digit Modalities Test (SDMT) and the Neuropsychological Screening Battery for Multiple Sclerosis (NSBMS). The NSBMS is composed of the i) Selective Reminding Test (SRT), ii) 7/24 Spatial Recall Test (7/24 SRT), iii) Paced Auditory Serial Addition Task (PASAT) and iv) Controlled Oral Word Association Test (COWAT). In addition, we evaluated patients' verbal and visuospatial working memory by means of the Digit Span and Corsi Block Tapping, respectively. Finally, patients' fine motor function was assessed by means of the Nine Hole Peg Test (9HPT) (Table 1).

2.2.2 Kinesthetic and Visual Imagery Questionnaire

The short version of the KVIQ (KVIQ-10) was used to evaluate participants' MI vividness. This questionnaire was specifically developed for assessing imagery ability in populations with restricted mobility.[17] The subjects first physically executed and then imagined doing the movements. Subjects who were unable to physically perform the movement were requested to use the other limb, or, in case both limbs were too severely impaired, to observe the experimenter performing the movement before imagining it. The KVIQ-10 comprises 5 visual and 5 kinesthetic items, scored on a 5-point visual analogue scale (1 = very clear image or intensity and 5 = no image or sensations at all). Lateralized items were performed at both body sides.

2.2.3. Hand rotation task

The hand rotation task was applied to measure imagery accuracy. 96 successive line drawings of hands (48 left and 48 right) were shown on a computer screen in four different views (back, palm, ulnar, radial) and 12 different rotations (30 degree steps).[18] Subjects were asked to judge as accurately as possible whether a left or right hand was shown without moving or seeing their own hands. This test requires mental rotation of their own hand and is as such an implicit MI test. Six practice pictures were given. Sharma et al.[18] described previously that a score below 75% indicates inability to perform accurate MI.

2.2.4. Mental chronometry

We applied mental chronometry on the Box and Block Test (BBT).[19,20] Mental chronometry is based on the comparison between the duration of physical execution and imagery of a task, with a close temporal relationship indicating correct MI. During the BBT, 2.5 cm^2 wooden blocks are transported from one to the other part of a box. We measured the time needed to transport 20 blocks.[9] After one practice trial, three trials of imagery and physical execution (in random order) were performed for each hand. During the imagery trials, participants were instructed to use visual imagery from a first person perspective. They were instructed to imagine the task in the same way as they had performed it physically.

2.3. Statistical analyses

We calculated the mean score on the KVIQ-10, mean hand rotation accuracy and mean duration of imagined and executed conditions of the BBT. After establishing normality assumptions for data distribution (Shapiro-Wilk test), patients' and controls' KVIQ scores were compared with an independent t-test. For the hand rotation task and BBT, a repeated measures ANOVA with group (MS, controls) as between-subject factor was used. As within-subject factor, dominant body side was included for the BBT and hand rotation task (left side, right side) and condition (physical execution, MI) for the BBT only. For significant effects at α=0.05, post hoc Tukey HSD tests were applied.

Pearson correlation coefficients were calculated to correlate the disease characteristics (EDSS, type of MS, years since diagnosis) and scores on cognitive (SDMT, NSBMS and its subcomponents, Digit Span, Corsi Block Tapping) and motor (9HPT) screening tests with scores on the imagery tasks. Finally, for the asymmetrically affected patients, subgroups were made for their most and least affected body side. The most affected side was defined as the body side at which physical execution of the BBT was at least 10% slower than at the other side. For all variables, dependent t-tests were performed to compare the most and least affected side. For the KVIQ-10, only the asymmetrical items were included in this analysis.

3. Results

3.1. KVIQ-10

Both groups rated their imagery vividness as good and no differences were found between groups (Table 2).

3.2. Hand rotation task

MS patients had a significantly lower accuracy score than controls ($F(1,58)=4.398$, $p=0.04$) (Table 2). For both groups, there were no significant differences in judging pictures from left or right hands. Nine MS patients failed to reach the 75% limit to define accurate MI, while for the control group this was the case for three persons.

3.3. Mental chronometry

For BBT duration, a significant interaction between condition and group was found ($F(1,58)=5.79$, $p=0.02$). During both imagery and execution, the task was performed faster by controls than by patients (execution: $F(1,58)=66.02$, $p<0.01$;

imagery: $F(1,58)=20.31$, $p<0.01$) (Table 2). In the control group, imagery was performed significantly slower than physical execution ($F(1,58)=23.82$, $p<0.01$) and both conditions were performed significantly faster with the right than with the left hand ($F(1,58)=5.99$, $p<0.01$). In the MS group, however, no significant differences for condition and dominant body side were found.

3.4. Correlations between screening and MI tests

There were no significant correlations between patients' EDSS score, type of MS and years since diagnosis with their performance on the MI tests. None of the cognitive tests correlated with the KVIQ-10 and with imagery of the BBT, but all of them showed a significant correlation with the hand rotation task (SDMT: r=0.54; NSBMS: r=0.58; SRT: r=0.52; 7/24 SRT: r=0.39; PASAT: r=0.40; COWAT: r=0.55; Digit Span: r=0.44; Corsi Block Tapping: r=0.48) (Figure 1). The 9HPT for fine motor function did not correlate significantly with the imagery tests.

3.5. Comparison between most and least affected side

21 out of 30 patients showed an asymmetry in upper limb function. Subgroups of the most and least affected side were significantly different, shown by differences in

physical execution of the BBT and the 9HPT (Table 3). Dependent t-tests showed, in line with physical execution, a significant difference between patients' most and least affected body side in imagery duration of the BBT. No differences were found between the most and least affected body side for the KVIQ-10 and the hand rotation task (Table 3).

4. Discussion

Recently, promising results were shown with regard to MI practice in the rehabilitation of stroke patients[3], but very limited research examined its potential for patients with MS. Before considering using MI based exercises as a therapy tool for these patients, however, it is important to consider to what extent patients' motor and cognitive impairments are related to their ability to generate correct motor images. Therefore, we evaluated the MI ability of 30 MS patients in comparison to 30 controls. Several aspects of MI ability were assessed, including vividness, accuracy and temporal organisation. We expected these aspects to be differentially affected in patients showing different degrees of cognitive and/or motor impairments.

As main results, it was found that imagery vividness did not differ between groups. Imagery accuracy, however, was significantly lower in patients than controls. Besides, significant correlations were found between imagery accuracy and patients' cognitive functioning. Furthermore, differences between groups were found in imagery duration. In general, patients were slower than controls during both execution and imagery. Whereas, in controls, imagery was performed slower than physical execution, no differences were found in MS patients. In the patients, imagery duration significantly differed between their most and least affected body side, indicating an association with motor functioning.

On the one hand, the results of the KVIQ may indicate that imagery vividness is well preserved in MS patients. However, caution is warranted when interpreting the results of questionnaires. First, it was previously shown that vividness measures predict performance on other imagery tasks rather weakly or not at all.[21] Besides, when using questionnaires participants perform an auto-evaluation of their MI ability, implying that they may overestimate their competence and that answers are subject to the individual's mood and to social desirability.[22] Furthermore, previous studies in MS have shown that patients' self-reports correlate with cognitive functioning and depression.[23] This is an important issue, since most studies on MI limit the assessment of imagery ability to self-evaluation questionnaires. More objective methods such as hand rotation and mental chronometry tasks should be considered in addition.

In contrast to imagery vividness, clear differences between groups were found in imagery accuracy. On average, patients were less accurate than controls and their imagery accuracy significantly correlated with their cognitive screening scores. Interestingly, the correlation of the hand rotation task with the total NSBMS score was higher than with each of its subcomponents. This indicates that MI involves several aspects of cognition. The hand rotation scores also significantly correlated with tests on working memory. This is in accordance with previous findings[24], showing an influence of working memory on MI in stroke patients. Imagery accuracy did not depend on patients' motor functioning, as shown by the lack of differences on the hand rotation task between patients' least and most affected side and the lack of correlation with the 9HPT.

A significant relation between imagery and motor functioning, however, was found with regard to patients' temporal organisation of MI, which significantly differed between patients' most and least affected body side. In the control group, imagery was performed slower than physical execution, which was not the case in the MS group. This can be interpreted in two ways. On the one hand, previous studies suggested that a close match between the duration of imagery and execution indicates correct MI.[20] As such, the BBT data show that patients were able to perform the task with good temporal organisation. On the other hand, other studies stated that if imagery is performed in accordance to the principles of motor control, it may not be performed faster than physical execution.[18] In healthy controls, on average, imagery was slightly slower than physical execution. In the patient group, however, there was on average no difference and some patients performed MI even faster than physical execution. This might indicate that these patients had an impaired temporal organisation of MI, called 'chaotic motor imagery'. Chaotic MI is defined as an inability to perform MI accurately or, if having preserved accuracy, the demonstration of temporal uncoupling.[18] Another explanation for the altered ratio between the duration of MI and execution in these patients, might be that instead of MI being abnormally speeded up, it may not include errors in patients' physical execution of the BBT. As such, we advise to be cautious when interpreting mental chronometry data in neurological patients, since these data might be affected by patients' disease symptoms.

In general, our results show that patients' cognitive and motor dysfunctions are related to their MI ability. When considering using MI based exercises in MS, a thorough screening of each patient's MI ability is needed, since it was shown that a relationship exists between imagery ability and the effectiveness of MI practice.[10] This does not necessarily mean that patients with diminished MI ability could not benefit from MI practice, but these patients might need additional training in using this technique first. For the patients who are able to successfully perform MI, imagery could be a valuable exercise method. Recent studies have shown that exercise training can induce positive effects in patients with MS. For example, Dalgas et al.[25,26] showed that progressive resistance training leads to improvements in lower limb muscle strength and functional capacity in moderately disabled patients with relapsing-remitting MS. Up to now, it is unclear if exercise training is also feasible and has similar effects in more severely disabled patients, and patients with other types of MS. Studies in gerontology suggest that exercise training might also have a beneficial effect on cognitive function. However, this requires further research in patients with MS.[27] A potential problem in severely affected MS patients, however, may be that physical exercise might be limited by the presence of motor fatigue, temporary decreasing physical performance and training intensity. Motor fatigue has been defined as a decline in motor performance during sustained or repetitive muscle activity.[28] We hypothesize that MI practice may serve as an alternative strategy to continue training at moments that motor fatigue hampers a patient from performing physical practice. On the other hand, MI requires mental resources, which may be not constantly be sufficiently present in case of cognitive fatigue, defined as a slowing in mental ability during the performance of repeated cognitive tasks.[29] The presence of primary fatigue, including cognitive fatigue, is high with approximately 65% of the MS patients reporting limitations in functioning due to fatigue.[30] The feasibility to efficiently perform physical and MI practice in patients with fatigue should be examined in the future.[31]

The present study is the first study investigating the applicability of MI in patients with MS with motor and/or cognitive impairment. Previously, Bovend'Eerdt et al.[32] investigated MI in 30 patients with various neurological pathologies, but only 1 of them suffered from MS. As well, no definitive conclusions could be drawn from this study since patients' compliance with the MI intervention was too low. These results point out that future studies are needed to explore the barriers and facilitators to uptake an MI intervention. Furthermore, future research should examine strategies to further optimise the quality of the MI process, especially in patients with diminished MI ability. In healthy persons[33], PD[34] and stroke patients[35], providing them with external cues during MI was shown to enhance MI quality. Although this approach seems promising, we should avoid generalizing results from studies investigating other types of neurological patients, since the etiology, affected anatomical areas, course of the disease and type of cognitive deficits can widely differ between patients. Even within patients with the same pathology, potentially a wide variation in MI quality can be found. The present study was limited to hospitalized patients who showed, on average, more severe motor symptoms than community-based MS patients. As well, we excluded patients with very severe cognitive dysfunctions. More research on a larger sample, consisting of patients with mild as well as severe motor and cognitive problems, should be performed in the future. As well, further research is needed to specifically validate the assessment battery that was used in the present study in patients with MS.

In summary, the current study showed that the MI vividness of patients with MS did not differ from healthy controls. However, MS patients did show significant differences in imagery accuracy and temporal organisation. Patients' MI accuracy significantly correlated with impairments in cognitive functioning, but was independent of motor functioning. MI duration, on the other hand, differed between body sides, implying an association with impaired motor functioning.

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Table 1. Patients' characteristics

Patient number	Age (years)/ gender	Years since diagnosis	Type of MS	EDSS score (/10)	MMSE (/30)	SDMT	NSBMS (/4)	SRT (/96)	7/24 SRT (/35)	PASAT (/60)	COWAT	Digit Span (/12)	Corsi Block Tapping (/12)	9HPT right side (s)	9HPT left side (s)
1	41/F	1	PP	7	30	55	4	51	26	54	47	8	8	31.2	26.8
2	77/M	41	SP	7	25	30	1	3	19	1	36	6	5	26.5	23.9
3	56/M	11	PP	6.5	29	27	4	45	33	29	29	6	5	49.6	105.0
4	41/F	2	RR	6.5	29	39	4	38	34	35	30	4	5	21.4	26.7
5	51/F	28	RR	6.5	30	31	1	15	18	1	20	7	5	29.3	25.2
6	62/F	15	RP	3	29	48	4	16	30	38	45	7	6	21.9	27.2
7	62/M	25	SP	6.5	27	26	4	24	19	35	32	1	3	34.5	42.8
8	52/F	4	SP	4	30	47	3	21	32	1	30	4	5	37.2	17.2
9	53/M	7	SP	7.5	28	29	2	22	26	1	28	3	5	27.0	29.7
10	50/F	17	RR	7	30	25	3	18	7	26	26	8	6	41.6	138.0
11	59/M	14	SP	7	28	31	3	8	25	40	43	5	6	193.0	63.0
12	45/F	16	PP	8	30	37	3	26	18	26	38	5	5	35.2	85.0
13	58/M	8	PP	7.5	30	47	4	21	30	42	46	9	6	24.3	47.4
14	46/M	13	SP	6.5	30	28	3	40	33	19	38	8	6	91.0	137.0
15	59/M	17	PP	6.5	30	42	4	29	35	23	50	8	5	26.7	34.6
16	42/M	2	RR	5.5	30	19	4	56	30	34	40	7	4	25.4	40.4
17	47/F	10	SP	7	28	34	2	4	32	34	18	8	7	27.5	44.9
18	51/F	5	PP	4	29	38	3	10	29	24	33	8	3	60.0	63.0
19	53/M	9	RR	6.5	30	31	4	23	32	24	32	4	6	39.6	77.3
20	65/F	16	RR	6.5	25	8	0	11	21	1	22	4	4	37.1	43.3
21	29/F	8	RR	7	30	42	4	18	31	49	39	8	7	55.7	28.9
22	56/M	14	SP	7	29	40	4	56	34	32	38	7	8	42.4	22.0
23	29/F	3	RR	4.5	29	54	4	65	35	54	39	7	6	20.9	23.5
24	34/M	9	RR	5.5	29	20	3	16	33	1	51	3	6	27.2	60.1
25	60/F	21	SP	6	29	53	4	58	27	47	43	8	7	24.9	26.8
26	40/F	18	RP	7.5	30	29	4	58	31	25	34	3	5	47.3	27.2
27	55/F	23	SP	5.5	27	30	2	13	26	1	48	6	5	32.8	31.3
28	52/F	7	RR	6	29	55	4	48	33	42	62	5	5	17.9	19.7
29	56/F	17	SP	6	30	54	4	63	28	26	26	9	4	24.2	34.0
30	35/M	12	SP	6.5	30	52	4	35	28	41	41	7	6	23.9	28.6

Abbreviations: PP, Primary Progressive; SP, Secundary Progressive; RR, Relapse Remitting; RP, Relapsing Progressive; EDSS, Expanded Disability Status Scale; MMSE, Mini Mental State Examination; SDMT, Symbol Digit Modalities Test; NSBMS, Neuropsychological Screening Battery for Multiple Sclerosis; SRT, Selective Reminding Test; 7/24 SRT, 7/24 Spatial Recall Test; PASAT, Paced Auditory Serial Addition Task; COWAT, Controlled Oral Word Association Test; 9HPT, Nine

Table 2. Test scores (group mean and standard deviation) per variable

Task	Variables	MS patients	Controls	Between-groups difference
KVIQ-10	Vividness score	40.0 ± 18.2	39.2 ± 15.1	p = 0.85
Hand rotation	Accuracy	82.1% ± 13.5%	88.4% ± 9.2%	p < 0.05
	Right side subscore	81.8% ± 13.8%	88.9% ± 9.7%	p < 0.05
	Left side subscore	82.4% ± 14.4%	87.8% ± 10.4%	p = 0.10
BBT	Duration execution	27.9s ± 7.8s	15.9s ± 1.9s	p < 0.01
	Duration imagery	26.4s ± 8.5s	18.6s ± 4.4s	p < 0.01
	Right side duration execution	26.6s ± 10.1s	15.3s ± 1.9s	p < 0.01
	Right side duration imagery	25.7s ± 9.7s	17.4s ± 4.2s	p < 0.01
	Left side duration execution	29.2s ± 8.3s	16.6s ± 2.0s	p < 0.01
	Left side duration imagery	27.2s ± 9.0s	19.7s ± 4.5s	p < 0.01

Abbreviations: KVIQ-10, Kinesthetic and Visual Imagery Questionnaire; BBT, Box and Block Test

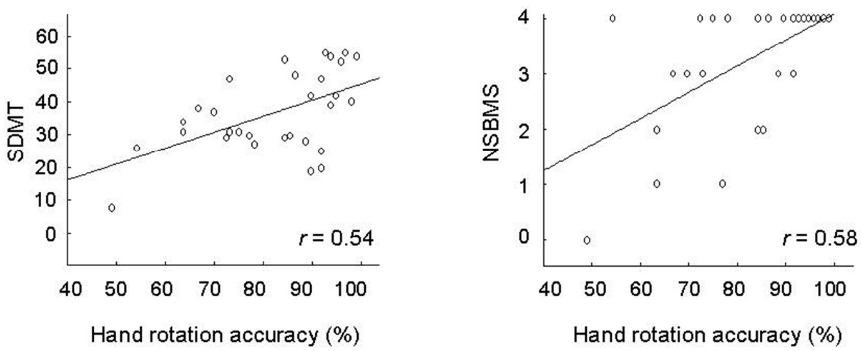
Table 3. MS patients' scores (group mean and standard deviation) per test for the most and least affected side

Test	Most affected side	Least affected side	Between-groups difference
9HPT	61.5s ± 46.3s	35.7s ± 18.6s	$p < 0.01$
BBT execution duration	32.5s ± 10.7s	23.3s ± 6.1s	$p < 0.01$
BBT imagery duration	28.0s ± 11.4s	23.6s ± 7.3s	$p = 0.03$
Asymmetric items KVIQ-10	20.0 ± 9.0	19.3 ± 8.9	$p = 0.20$
Hand rotation accuracy	83.2% ± 12.4%	83.5% ± 11.9%	$p = 0.88$

Abbreviations: 9HPT, Nine Hole Peg Test; BBT, Box and Block Test; KVIQ-10, Kinesthetic and Visual Imagery Questionnaire

Figure legends

Figure 1. Correlations between cognitive tests (Symbol Digit Modalities Test (SDMT) in the left panel and Neuropsychological Screening Battery for Multiple Sclerosis (NSBMS) in the right panel) and the accuracy score of the hand rotation task for the MS patients.



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