University of Groningen

Perceived fatigue and muscle fatigability in persons with multiple sclerosis

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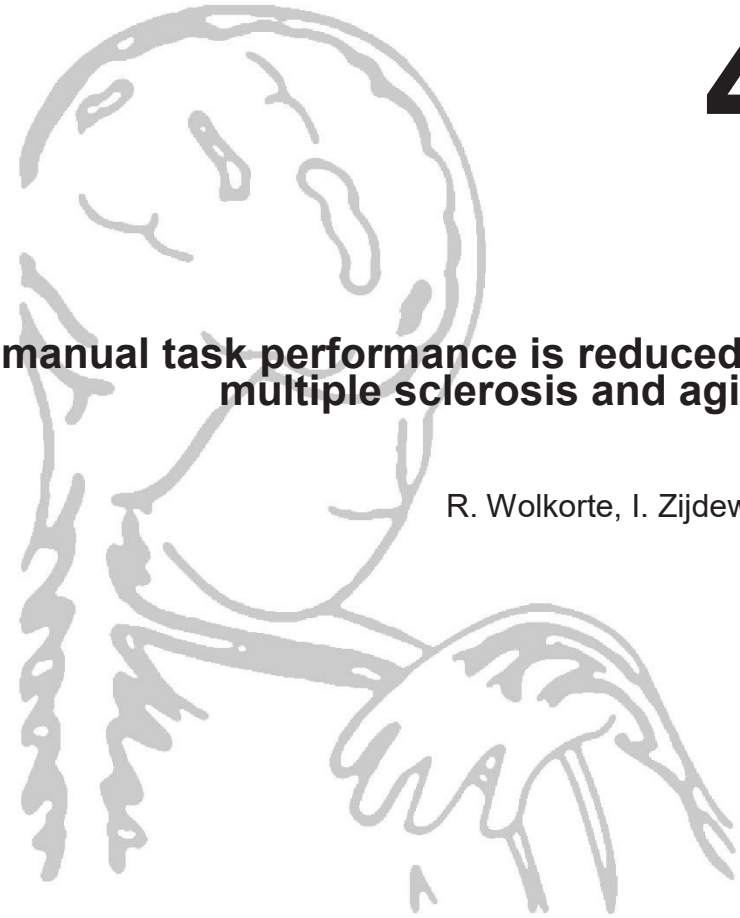

Bimanual task performance is reduced in multiple sclerosis and aging

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ABSTRACT

fIntroduction Dexterity becomes more important in today's society. MS patients and older individuals often report lower dexterity. Both MS patients and older individuals show increased cortical activation, especially of the ipsilateral motor cortex, during unimanual task performance. The increased cortical activation is possibly a compensatory mechanism. If older individuals already increase ipsilateral cortical activation, it is possible that MS patients are not able to increase cortical activation sufficiently to maintain function. However, it is not known whether age affects MS patients to a greater degree than controls.

Methods 115 patients with relapsing-remitting MS and 110 controls performed the Purdue Pegboard Test (PPT). The PPT measures both unimanual and bimanual task performance, and symmetrical and asymmetrical bimanual performance.

Results MS patients had overall lower dexterity than controls, and pegboard score was inversely associated with age ($r=-0.59$, $p<0.001$). A stronger decrease in task performance from a bimanual symmetric to a bimanual asymmetric task was found in both MS patients (Task by Group: $F1,220=154.7$, $p<0.001$) and older individuals (Task by Age: $F1,220=51.4$, $p<0.001$). No interaction effect of Task by Group by Age was found ($F1,220=0.05$, $p=0.829$).

Conclusion Patients with MS and older individuals have lower dexterity than controls and younger individuals, and this is more pronounced on an asymmetric versus symmetric bimanual task. The data suggest that MS patients are not differentially affected by age than controls.

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INTRODUCTION

Today's society is becoming increasingly dependent on the ability to manipulate small electronic devices. Precise bimanual control and dexterity is important in the work situation and for social interaction. Patients with multiple sclerosis (MS) often experience motor complaints, such as decreased dexterity.[37] Lower dexterity is also described in aging individuals.[42] Further parallels can be seen between patients with MS and an aging population. Both groups have reduced white matter integrity[132,190] and increased levels of inflammation[142,190] in the central nervous system. Furthermore, according to studies using fMRI and TMS, both MS patients[64,124,164,174,176,234] and older individuals[68,69,204] showed increased cortical activation during the performance of a motor task, especially in ipsilateral motor areas. Although there is still debate about the function of increased ipsilateral activation it is suggested for both MS patients[174,195] and elderly subjects[69] that it could point towards neuroplasticity to compensate for neuronal damage. This raised the question whether MS patients and elderly subjects show more interference with bimanual task performance. Bimanual performance demands even more attention when both hands perform different tasks compared to symmetrical bimanual tasks.[24,169] It is therefore expected, that if there is an interference between the compensatory (ipsilateral) activation and the bimanual activation, that MS patients and elderly subjects would show a larger performance decline during asymmetrical tasks. Furthermore, it is unclear what will happen to dexterity when MS patients age.

In the present pilot experiment we aimed to extend previous experiments regarding bimanual coordination in MS patients by including an asymmetrical bimanual task. Testing of both uni- and bimanual tasks, with both bimanual symmetrical and asymmetrical tasks makes the Purdue Pegboard test (#32020 Lafayette Instruments, Lafayette, USA; PPT) a good tool to monitor dexterity in MS patients. Most studies reported low dexterity values for MS patients[84,104,116,232] but did not study differences between unimanual and bimanual tasks and did not investigate aging effects in a patients population. In the present study we therefore focused on interaction effects across the Purdue Pegboard tasks and MS patients versus sex- and age matched controls. It was our hypothesis that MS patients and elderly subjects would have more difficulties with bimanual than unimanual task performance and that asymmetrical performance would be more difficult than symmetrical task performance. Furthermore, we expected that older MS patients would show a larger performance decline during symmetrical and even more during asymmetrical tasks.

Table 1 Subject characteristics and PPT performance scores.

	MS patients (N=115)	Controls (N=110)	p-value
Sex (m/f)	39/76 (34%/66%)	39/71 (35%/65%)	0.809
Age	41.0 (20-65)	40.5 (18-64)	0.761
Disease duration	8.4 (0-34)		
PPT right	12.6 (5.3-19.0)	15.8 (11.3-19.7)	<0.001
PPT left	11.9 (5.7-18.3)	15.0 (10.0-18.0)	<0.001
PPT unimanual	12.3 (5.5-18.0)	15.4 (11.7-18.8)	<0.001
PPT bimanual	9.7 (3.3-15.7)	12.5 (8.7-15.7)	<0.001
PPT assembly	26.9 (8.3-53.7)	39.5 (24.3-53.7)	<0.001
PPT z-score	-2.0 (-5.9-1.6)	0.0 (-2.5-2.0)	<0.001
RM ANOVA PPT	Effect	F-value	p-value
Unimanual-Bimanual	Task	$F_{1,220}$=124.4	<0.001
	Group	$F_{1,220}$=6.7	0.010
	Age	$F_{1,220}$=27.9	<0.001
	Task by Group	$F_{1,220}$=1.3	0.257
	Task by Age	$F_{1,220}$=0.3	0.566
	Task by Group by Age	$F_{1,220}$=0.4	0.521
Bimanual-Assembly	Task	$F_{1,220}$=464.1	<0.001
	Group	$F_{1,220}$=10.9	0.001
	Age	$F_{1,220}$=47.4	<0.001
	Task by Group	$F_{1,220}$=154.7	<0.001
	Task by Age	$F_{1,220}$=51.4	<0.001
	Task by Group by Age	$F_{1,220}$=0.05	0.829

PPT, Purdue pegboard test. MS, multiple sclerosis. Top: Subject characteristics and PPT. Data are represented as mean (range). Bottom: Main and interaction effects of RM ANOVA on the PPT.

METHODS

We included 115 MS patients with relapsing-remitting MS[159] and 110 controls. All but 3 were right-handed according to the Edinburgh Handedness questionnaire.[151]

All subjects performed the Purdue Pegboard Test. Subjects were seated at a table with the Purdue Pegboard in front of them. The test was explained to the participant according to the instructions manual. The test consists of 4 parts, which are all repeated three times: placing as many pins as possible in a board 1) using only the right hand, 2) using only the left hand, 3) using the right and left hand simultaneously, 4) placing pins and washers by using the right and left hand alternately. Subjects had 30 seconds for tasks 1-3, and 1 minute for task 4.

Statistical analyses

From one patient we only collected unimanual data. The data of three trials for each subtask were averaged. We calculated an overall score for PPT performance, by first calculating z-scores for each subtest with the following

equation: z-score=(score-$mean_{controls}$)/$sd_{controls}$, and then averaging the four z-scores per individual (zPPT-score).

To compare an unimanual with a bimanual task, we averaged the scores of the right and left hand as a measure of unimanual performance. To compare performance between the unimanual and (symmetrical) bimanual tasks, and between the symmetrical and asymmetrical bimanual task, we applied a repeated measures ANOVA with Task as a within-subjects factor, Group as a between-subjects factor and Age as a covariate. Although both main and interaction effects are presented, our interest concerns the interactions effects of Task by Group, Task by Age, and Task by Group by Age.

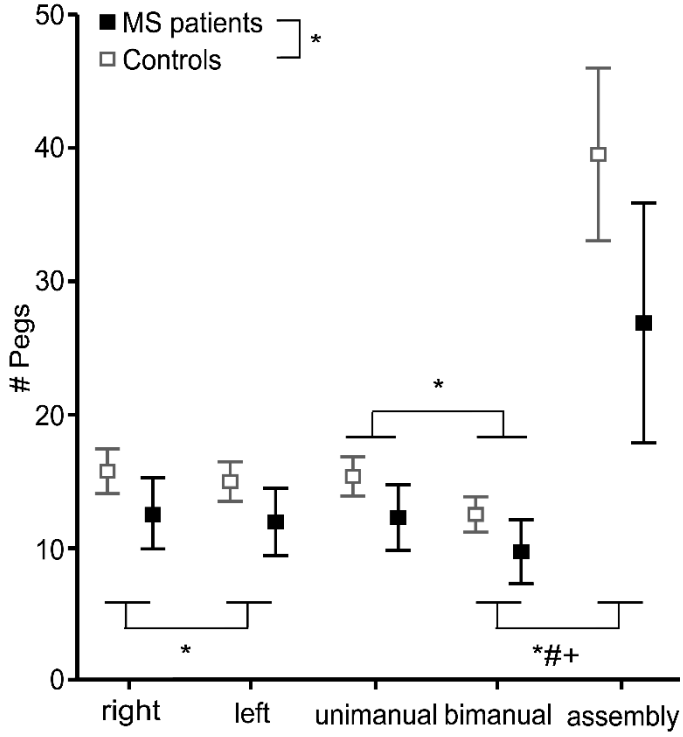

Figure 1 PPT scores in controls (n=110) and RRMS patients (n=115) *Data represent mean and SD. * main effects Task and Group; # Interaction effect Task by Group; + Interaction effect Task by Age.*

RESULTS

MS patients and controls did not differ in age nor sex (Table 1). Overall pegboard scores (Table 1, Figures 1 and 2) in controls were negatively associated with age ($r=-0.59$, $p<0.001$), with lower dexterity scores for older subjects.

Performance change

The analysis of unimanual versus symmetrical bimanual task revealed a main effect of Task, Age and Group (Table 1, Figure 2) but no interaction effects. Participants placed less pairs of pegs during the bimanual condition than the number of pegs in the unimanual condition, MS patients placed less pins on both tasks, and with increasing age less pegs were placed. The comparison between the symmetrical and asymmetrical bimanual task revealed - besides main effects of Task, Age and Group - an interaction effect of Task by Group ($F_{1,221}$=154.7, p<0.001) and Task by Age ($F_{1,221}$=51.4, p<0.001) (Table 1, Figure 2). These results indicate that the difference between the symmetrical and asymmetrical bimanual task was larger for the MS patients than the controls. Furthermore, the decline in performance in the asymmetrical task was also larger for older subjects compared with younger subjects.

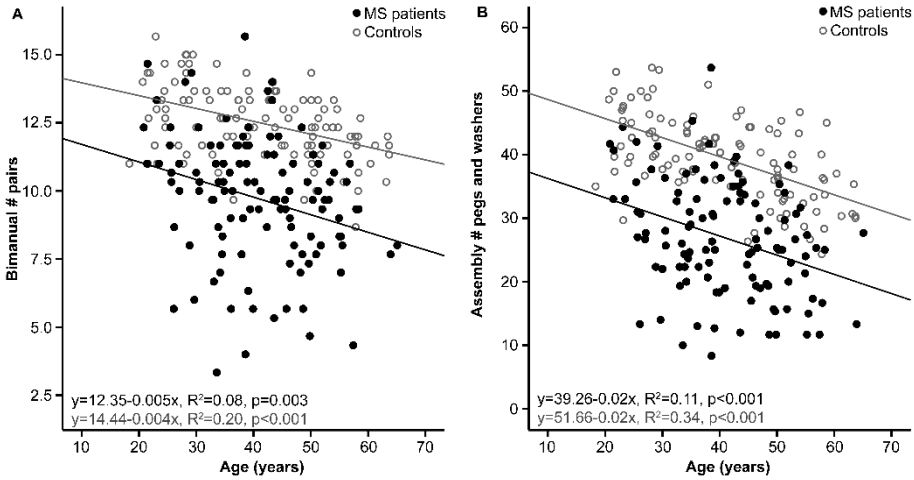

Figure 2 Bimanual task performance with age (A) *Symmetric bimanual task. (**B**) Asymmetric bimanual task.*

DISCUSSION

In comparison with an symmetrical bimanual task, during an asymmetrical bimanual task MS patients reduced their performance more than controls. Thus even after controlling for generalized slowness MS patients showed a reduced performance. For both older subjects and MS patients, performance was even more reduced when an asymmetrical bimanual task (compared to a symmetrical task) was performed.

The performance of a bimanual task can be considered a motor-motor dual task. Performance decline on a dual-task can be attributed to two reasons: if the

two tasks share input- or output modalities, competition can result in performance decline. If the two tasks do not share input- or output modalities, performance decline is most likely a result of insufficient attentional resources.[152,225]

Interference effects

During unimanual contractions, TMS and fMRI studies demonstrated more activity in ipsilateral cortical motor areas in both elderly subjects[68,69,204] and MS patients.[64,176] Whether the ipsilateral activation is functional in either MS patients[126,174] or older individuals[136,170] is still a subject of debate. It is expected that if ipsilateral motor areas are functionally involved in the unimanual contraction, interferences could take place during bimanual contractions which would result in the observed performance decline.

Attentional resources

Both MS patients[64,175] and elderly subjects[92,229] already require greater attention during unimanual task performance. Increased activation in MS patients[64,175] and older subjects[92,229] is found in areas involved in cognitive control of movements (frontal and parietal areas, including pre-motor cortex, posterior parietal cortex, anterior cingulate cortex). Under conditions with increased task demands both groups are less able to harness extra cognitive reserve resulting eventually to a decline in task performance, as shown on cognitive-motor dual-tasks.[Chapter 5,Chapter 6,72,218] The decreased cognitive reserve possibly accounts for the increased performance decline on the asymmetrical bimanual task of the PPT.

Bimanual task performance

Bimanual contractions are more complex than unimanual contractions.[203] Bimanual task performance requires action of both primary motor cortices and a complex bilateral neural network,[83,203] including the cerebellum, supplementary motor area (SMA), cingulate motor cortex, the (dorsal) premotor cortex, and the corpus callosum. It is therefore possible that both interference effects and decreased cognitive reserve are present in both MS patients and older individuals.

MS and aging

No interaction effect of Task by MS or Task by Age was found for an unimanual and bimanual task. Possibly, cortical activation can be increased to a level to maintain function, whereas the more difficult asymmetrical task did result in

additional performance decline. Both MS patients and older individuals had greater performance decline on an asymmetrical bimanual task. Since both groups have increased white matter disruption, increased levels of inflammation, and increased cortical activation during the performance of a task,[64,92,132,142,175,229] it is possible that similar mechanisms are responsible for functional decline in both groups, however further research is necessary to confirm this.

No interaction effect of Task by Group by Age was present, indicating no differential effects of aging for bimanual task performance in MS patients and controls. This is in agreement with the only other study that examined the interaction of aging and multiple sclerosis, by using a cognitive task.[26]

Implications and conclusions

Both MS patients and older subjects show similar performance decrease under asymmetrical bimanual task performance. This may have implications for the performance of MS patients in a work setting or during daily activities, especially on more complex tasks bimanual tasks. It is not known whether performance decline in both groups is the result of similar changes in cortical integrity and neuroplasticity. However similar compensatory activation strategies seem to be employed. Further research is therefore necessary to investigate the reasons for functional decline on bimanual tasks, for both MS patients and older subjects. Understanding the cause of increased performance decline can result in novel rehabilitation strategies for MS patients.

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