2013•2014

FACULTEIT GENEESKUNDE EN LEVENSWETENSCHAPPEN

master in de revalidatiewetenschappen en de kinesitherapie

Masterproef

The influence of hand dominance on the expression of arm-hand dysfunction and its relationship with the underlying neurophysiological disturbances in Mutliple Sclerosis

Promotor :
dr. Bart VAN WIJMEERSCH

Copromotor :
Prof. dr. Peter FEYS
Mevrouw Ilse LAMERS

Jessica Jacobs

Proefschrift ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

universiteit hasselt

KNOWLEDGE IN ACTION

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Dankwoord

Graag wil ik een woord van dank richten aan alle mensen die het mogelijk gemaakt hebben om deze masterproef tot een mooi resultaat te brengen.

Allereerst wil ik mijn promotor Prof. Dr. Bart Van Wijmeersch bedanken voor de begeleiding en voor de mogelijkheid tot samenwerking met het Revalidatie en MS centrum Overpelt.

Mijn copromotoren Dra. Ilse Lamers en Prof. Dr. Peter Feys wil ik extra bedanken voor hun inzet en nauwgezette begeleiding. Zij waren steeds bereikbaar en stonden altijd klaar met goede raad.

Daarnaast wil ik graag het Revalidatie en MS centrum in het algemeen bedanken voor het toestaan van thesis studenten, maar in het bijzonder wil ik de MS-verpleegkundigen Jan Kuppens en Cindy Vos bedanken voor de samenwerking tijdens de testmomenten.

De mensen die zeker niet vergeten mogen worden zijn de proefpersonen. Zonder hun deelname was het niet mogelijk geweest om de studie gegevens te bekomen. Hartelijk dank voor de medewerking!

Tenslotte een dankjewel voor de mensen rondom mij, familie, klasgenoten, vrienden, voor de steun en raad tijdens de totstandkoming van deze masterproef.

Halen, 28 mei 2014 J.J.

Situering

De wereldwijde incidentie van Multiple Sclerose (MS) kent een stijgend verloop en wordt geschat op 3.6/100.000 voor vrouwen en 2.0/100.000 voor mannen.(1) MS is een chronische en auto-immuun ziekte, gekarakteriseerd door inflammatie en degeneratie van het centraal zenuwstelsel.(2;3) Deze processen veroorzaken een variëteit aan symptomen zoals spierzwakte, spasticiteit, ataxie, etc.(4-6) Ongeveer ¾ van de MS populatie vertoont een verminderde arm- en handfunctie tengevolge van de bovenstaande symptomen.(5;7;8) Een verminderde arm- en handfunctie heeft een negatieve impact op de uitvoering van dagelijkse activiteiten en de levenskwaliteit.(5;7;8) Ondanks de klinische relevantie is onderzoek omtrent verminderde arm- en handfunctie beperkt. Zo is het bijvoorbeeld nog niet geweten of hand dominantie/hemisfeer dominantie een rol spelen in de manifestatie van arm- en hand disfunctie bij MS. Verder is het nog onduidelijk of deze klinische bevindingen van disfunctie consistent zijn met de resultaten van neurofysiologische metingen. Om arm- en hand disfunctie in MS beter te begrijpen is het belangrijk om hieromtrent meer inzicht in te winnen.

Deze masterproef past binnen het onderzoeksdomein neurologische revalidatie en wordt gefaciliteerd door het MS netwerk Limburg (http://www.uhasselt.be/msnetwerklimburg). Dit netwerk werd opgericht in 2007 om de samenwerking tussen REVAL, BIOMED en het Revalidatie en MS Centrum Overpelt te vergemakkelijken. Prof. Dr. Bart Van Wijmeersch (promotor van deze masterproef) is aangesteld als onderzoeker en neuroloog, gespecialiseerd in MS, binnen deze 3 partners van het netwerk.
Het onderzoek van deze masterproef kadert binnen het doctoraatsproject van Ilse Lamers (doctoraatsstudente aan de Universiteit Hasselt en copromotor van deze masterproef). Dit doctoraatsproject heeft als titel: Understanding upper limb function in multiple sclerosis; assessment and relationship between the levels of the International Classification of functioning.

In deze masterproef werden het onderzoeksprotocol en de methode opgesteld door Prof. Dr. Bart Van Wijmeersch, Prof. Dr. Peter Feys en Dra. Ilse Lamers, in samenspraak met mezelf als student. Mijn aandeel in dit onderzoek bestond erin de proefpersonen te rekruteren en de klinische testen, alsook de vragenlijst, af te nemen in samenwerking met de medewerkers van het Revalidatie en MS Centrum Overpelt . De neurofysiologische metingen werden uitgevoerd door één van de leden van het Revalidatie en MS centrum gespecialiseerd in het afnemen van neurofysiologische metingen. De dataverwerking en het academisch schrijfproces gebeurde door mezelf onder begeleiding van Dra. Ilse Lamers, copromotor.

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The influence of hand dominance on the expression of arm-hand dysfunction and its relationship with the underlying neurophysiological disturbances in Multiple Sclerosis

Opgesteld volgens de richtlijnen van Multiple Sclerosis Journal
Http://www.uk.sagepub.com/msg/msj.htm

Abstract

Background: The role of hand dominance on the expression of arm-hand dysfunction and the underlying neurophysiological processes are not well known in Multiple Sclerosis (MS).

Objective: This study aimed to acquire insights about the influence of hand dominance on the expression of arm-hand dysfunction in MS and the correlation between the clinical findings and neurophysiological output (Motor Evoked potentials (MEPs) and Somatosensory Evoked potentials (SSEPs)

Methods: 109 MS patients with a mean Expanded Disability Status Scale (EDSS) score of 3.0 were included. Arm-hand dysfunction was measured by using two clinical tests (Nine Hole Peg test (NHPT), JAMAR hand grip strength) and a questionnaire was used to assess hand dominance and perceived arm-hand dysfunction. MEPs and SSEPs were registered to evaluate the function of motor and sensory pathways.

Results: The NHPT revealed that the dominant arm became more impaired compared to the non-dominant arm. In contrast, perceived arm-hand function indicated a superior use of the dominant arm when performing activities of daily living, as well as a better perceived quality of performance.

Conclusions: According to the objective measures, the dominant hand was more impaired in PwMS, but this result was not confirmed by the subjective measures.

Keywords

Multiple Sclerosis, arm-hand dysfunction, hand dominance, NHPT, JAMAR, MEPs, SSEPs

Introduction

The majority of persons with Multiple Sclerosis (PwMS) experience arm-hand dysfunction. About 3/4 of the MS population reports an impaired arm-hand function as a result of several symptoms like muscle weakness, ataxia, spasticity, impaired sensation and fatigue.(1-3) This impaired arm-hand function impacts the ability to perform daily activities independently and decreases quality of life.(1-3)

Recently, there has been an emerging research interest towards understanding arm-hand dysfunction in MS and its impact on daily life. Lamers et al.(4) found that perceived and actual arm performance in daily life was decreased in PwMS. About 75% of the included subjects scored significant less on the Nine Hole Peg test (NHPT) with their non-dominant arm compared to their dominant arm. Furthermore, they also used their non-dominant arm less in daily life. However, it is not clear whether these results are representative for the entire MS population as only 30 highly disabled persons were included in the study.

The influence of hand dominance on the performance on clinical scales was also found in healthy subjects.(5;6) Oxford et al. found that healthy subjects had a better performance on the Nine Hole Peg test with their right arm, which was the dominant arm in most cases.(5) Similar results were found by Sartorio et al., who reported a lower time score for the dominant arm on de Functional Dexterity Test.(6) Both studies reported an impact of hand dominance on the performance on clinical scales.(5;6)

In the last decades, it is assumed in healthy subjects that hand dominance is linked to hemisphere dominance or asymmetry between the hemispheres.(7) Research regarding hand dominance, hemisphere dominance and asymmetry between the hemispheres has also been performed in MS. Filippi et al. found, in a small group of MS patients, a significant correlation between hand dominance and hemispheric lesion load.(8) The results of the study suggest that local events, which are probably related to the specialization of the hemisphere, may be responsible for the pathological processes in MS.(8) Furthermore, they found more lesions in the left hemisphere in the included sample.(8) However, it is unclear whether these findings can be generalized to the whole MS population as only 23 PwMS with a mean EDSS score of 3.0 were included. Charil et al. reported higher correlations between the EDSS score and hemispheric lesion distribution in the left hemisphere.(9)

When comparing the findings, we can state that hand dominance has an influence on the performance on clinical scales, both in healthy subjects and a small group of PwMS.(4-6) However, it is not clear if this statement also count for the entire MS population with different disability levels. Moreover, when comparing the findings of the clinical arm-hand manifestations of MS with the findings of lesion distribution in MS, it is clear that these findings are contradictory. Research verifying a possible link is missing. This link can be important with regard to a possible treatment for PwMS with arm-hand dysfunction. It is important to know which neurophysiological parameters correlate with the clinical manifestations and which of these neurophysiological parameters can make a difference in view of the rehabilitation. A cross-sectional study with a large population of PwMS with arm-hand dysfunction and the use of clinical and neurophysiological measures is required to find out if there is a correlation.

The aim of the present study was to acquire insights about the influence of hand dominance on the expression of arm-hand dysfunction in MS, more specifically differences between dominant arm non-dominant arm. This paper also focuses on the correlation between the clinical findings about arm-hand dysfunction and the function of motor and sensory pathways, measured with Motor Evoked potentials (MEPs) and Somatosensory Evoked potentials (SSEPs). These aims lead to four research questions that are the essence of this study;

1) Which arm is most affected in individuals with MS?
2) How many individuals with MS report a change in hand dominance as a result of the disease?
3) Which arm has the best performance on clinical tests?
4) Are the clinical findings correlated with the results of the neurophysiological measures?

Methods

Participants

PwMS were recruited from the Rehabilitation and MS center Overpelt. Participants of at least 18 year and with a diagnosis of MS according to the McDonald criteria(10) were included. They were excluded if they had additional mental and cognitive disorders, absence of arm-hand dysfunction (based on normative data related to age, gender and hand dominance)(1;5) or a relapse during the study period.

Design

This study was a cross-sectional study carried out in the Rehabilitation and MS center Overpelt, Belgium. All participants gave their informed consent for participation in the study, which was approved by the Human Ethics Committee of Hasselt University.

Outcome measures

Clinical tests to assess arm-hand function. The NHPT, in which the patient is asked to place nine pins in a pegboard and remove them as quickly as possible, was used to assess manual dexterity.(11) This procedure was performed for each hand separately and the mean time of two trials was noted in pegs/second. A measure of hand grip strength was obtained by using the JAMAR hand-held dynamometer(12), in which the subjects had to perform six times a maximal strength(kg) with both hands alternatively. A mean of three measures of each hand was calculated.

Questionnaire about hand dominance. This questionnaire consist of three parts.
The first part was the Edinburgh Handedness Inventory(13) to assess hand preference during several activities of daily life.
The second part consisted of four questions to assess if there is a change in handedness after the diagnosis of MS and to evaluate how their arm-hand were affected by the disease, if presence. Question one was ‘what was your hand dominance before MS diagnosis?’ Questions two and three were ‘to which extent is your left/right arm affected?’. The participants had to answer on these questions with not affected, little affected, affected, very affected or not usable. Final question four was ‘which arm is most affected if both arms are?’
The quantity and quality of the use of the arms in daily life were assessed in part three. The PwMS had to score both arms on two questions: ‘how often do you use your arm when performing activities of daily life (score A)’ and ‘how well can you use your arm in activities of daily life (score B)’. The score opportunities were similar to those of the Motor Activity Log(14). The arm was never, rarely, sometimes, often, usually or always used when performing activities of daily life were the possible answers of score A. Also score B implied six possible answers; the arm was not used, the arm moved but was not helpful, the arm moved very slowly or with difficulty, the arm movements were slow or made with some effort, the arm movements were almost normal, the arm functions as good as before diagnosis of MS.

Neurophysiological measures. These measures include the performance of MEPs (Transcranial magnetic stimulation-TMS) and SSEPs to assess the function of the motor and sensory pathways. MEPs are used to assess the corticospinal excitability via electromyographic (EMG) electrodes positioned at the musculus abductor pollicis brevis of the thumb.(15) The motor cortex will be stimulated by a magnetic impulse at the skull which causes contraction of the target muscle.(16) The function of the dorsal column-lemnical system is assessed by SSEPs via electrical stimulation of the median nerve in the arm, which sends impulses to the brain. These impulses are intercepted via electrodes attached to the head.(17;18) Both the MEPs and SSEPs are performed in a standardized way. The MEP and SSEP parameters measured for each hand were latency and amplitude.

Study procedure

Performance of the several clinical tests, as well as completing the questionnaire, were accomplished on the same day. This procedure was lasting about 15 minutes. The MEPs and SSEPs measures were registered in function of follow-up by the neurologist.

Statistical analysis

The data were processed and analysed using IBM SPSS Statistics. Non-parametric statistics were used because not all data were normally distributed (Shapiro Wilk tests). Frequency tables were used to represent perceived arm-hand dysfunction according to PwMS and to score how many individuals report a change in hand dominance because of MS. To investigate differences between the dominant and non-dominant hand, a Wilcoxon Signed Rank test was used. To investigate the relationship between clinical tests and MEPs and SSEPs, Spearman Rank correlation coefficients were calculated (very high (>0.90), high (0.70-0.89), moderate (0.50-0.69), low (0.30-0.49) or small (≤0.29))(19). The significance level was set to $p<0.05$.

All analysis were performed in the total MS group and in the disability subgroups based on their EDSS score: mild (0-3.5), moderate (4-5.5) and severe (6-9.5). A Kruskal Wallis Test was used to investigate differences between the mild, moderate and severe EDSS subgroups, with a Mann-Whitney U test for the specific significance level between the subgroups.

Results

Participants

111 PwMS met the inclusion and exclusion criteria and gave informed consent. Two participants were excluded because of missing data concerning the questionnaire. In total, 109 PwMS (table 1) were assigned to the study (mean age=46.94, SD=11,5years, 84female). PwMS without arm-hand dysfunction, based on norm values +1SD(1;5), were excluded from analysis of the clinical tests. These norm values were based on gender, age and hand dominance. A flowchart projecting the process of inclusion of the PwMS in the clinical, neurophysiological and subjective measures are presented in figure 1. In total, 78 PwMS were included in the clinical and subjective measures and 60 PwMS in the neurophysiological measures. For all analysis, the total MS group was also divided into disability subgroups based on their EDSS score: mild (0-3.5), moderate (4-5.5) and severe (6-9.5).

In the total MS group, 96 patients were right-handed before diagnosis of MS of whom six patients changed their hand dominance (Table1). When looking at the EDSS subgroups, two patients of the mild group changed their hand dominance, while four patients in the severe group.

Table 1. Descriptive characteristics of the PwMS (n=109)

Gender (m/f)	25 / 84		
Mean age ± SD (years)	46.94	± 11.50	[23-75]
Mean disease duration from MS onset ± SD (years)	11.3	± 9.26	[0-41]
Mean disease duration from MS diagnosis ± SD (years)	8.4	± 8.31	[0-37]
Median EDSS	3.0	± 1.92	[0-7.5]
Type MS (n)			
Relapsing Remitting	74		
Secondary progressive	24		
Primary progressive	7		
Progressive relapsing	4		
Hand dominance (n) previous / current			
Right	96 / 94		
Left	9 / 9		
Ambidextrous	4 / 6		
Change in hand dominance (n)			
No change	103		
Change from right to left	3		
Change from left to right	1		
Change from left to ambidextrous	2		
Arm-hand dysfunction based on norm values NHPT			
No impairment	31		
Impairment one arm / hand	19		
Impairment both arms / hands	59		

SD: standard deviation; EDSS: Expanded Disability Status Scale

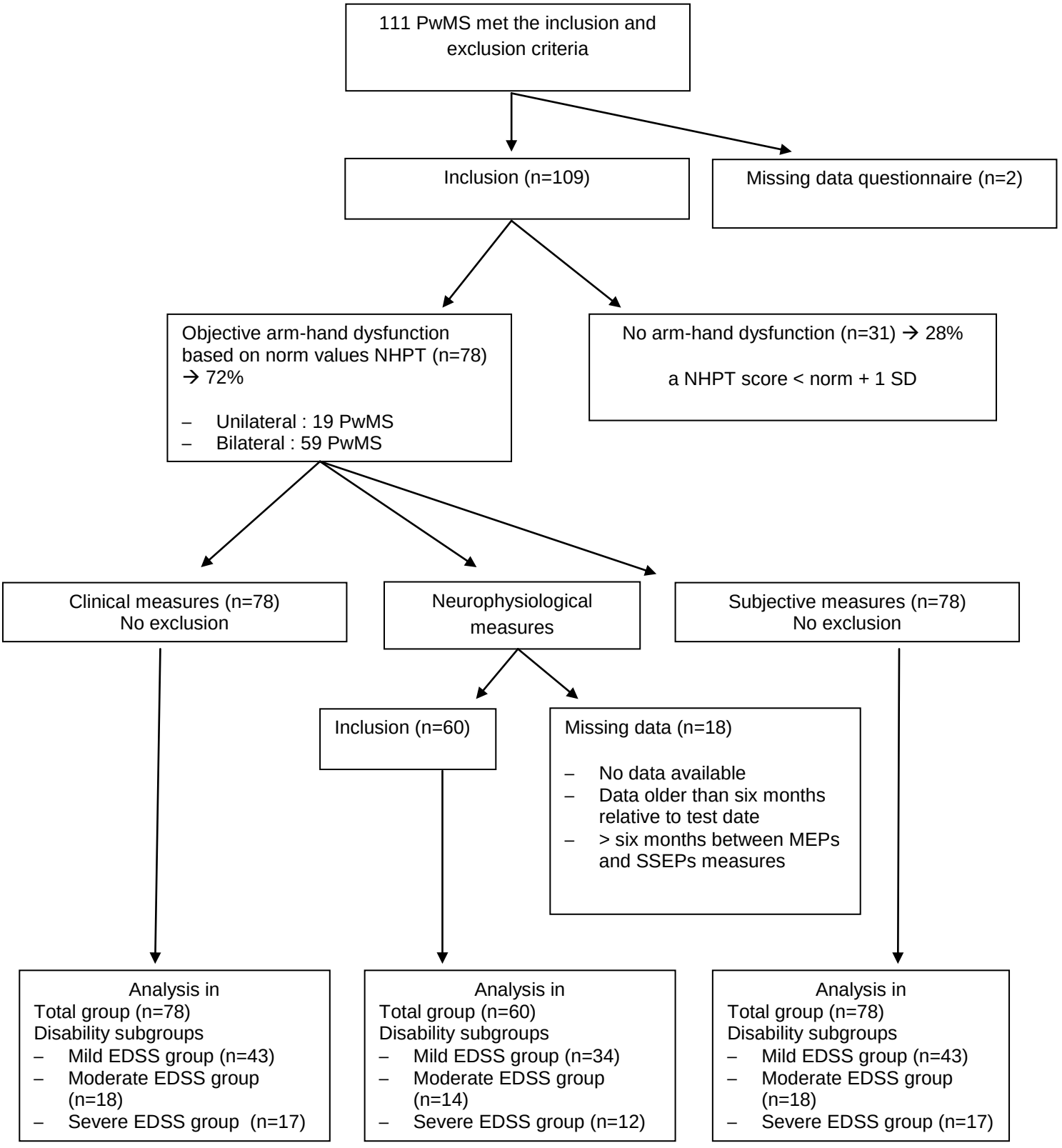

Figure 1. Inclusion of PwMS

Differences between dominant and non-dominant arm for perceived arm-hand performance

51% and 60% of the PwMS reported that their dominant arm, respectively non-dominant arm was impaired, but this difference was not significant (Figure 2).

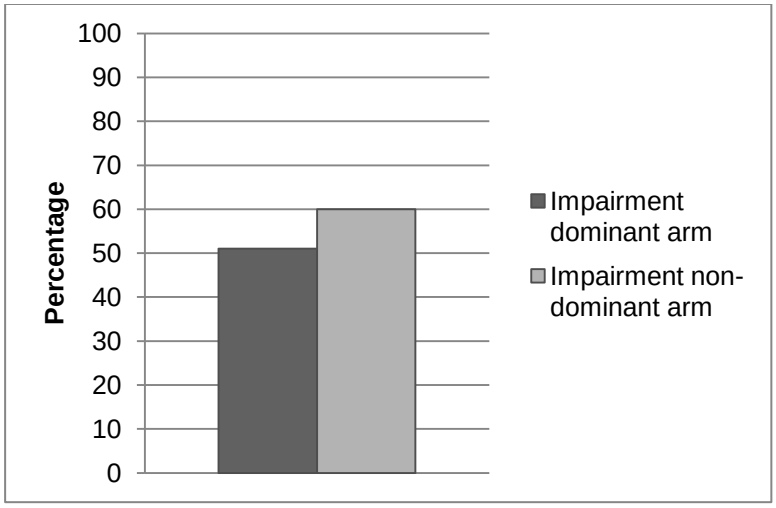

Figure 2. Perceived impairment of dominant and non-dominant arm

Similar results were found when comparing the different EDSS subgroups. There is a trend towards more impairment of the non-dominant arm in each group but without significant difference between the dominant and non-dominant arm (Figure 3).

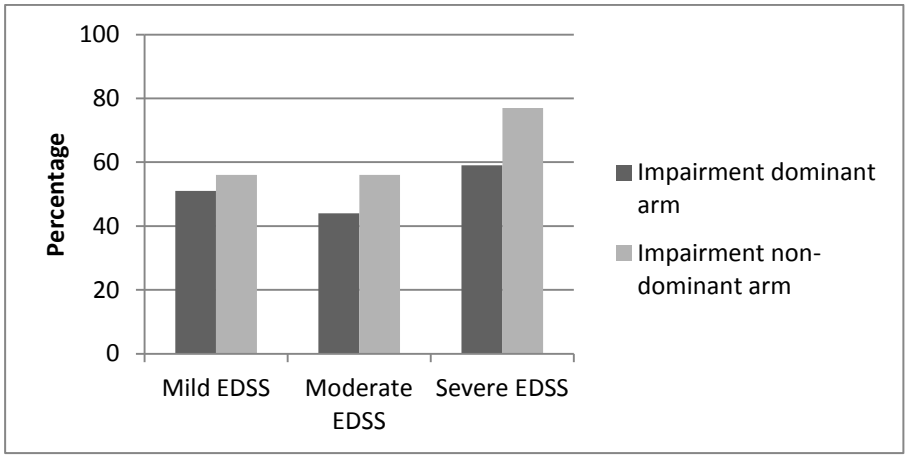

Figure 3. Perceived impairment of dominant and non-dominant arm in the different EDSS subgroups

The subjective questionnaire about the quantity and quality of the use of the arms in daily life revealed significant differences between the dominant and non-dominant arm in the total MS group (Table2a). They reported using their dominant arm more compared to their non-dominant arm. The dominant arm showed also a better quality in the performance of activities of daily life.

Also in all EDSS subgroups (Table 2b), PwMS reported to use their dominant arm significantly more compared to their non-dominant arm. For the quality of use, only a significant better performance of the dominant arm was found in the severe EDSS subgroup.

Differences between dominant and non-dominant arm for clinical and neurophysiological measures

Table 2a. Differences between the dominant and non-dominant arm in the total MS population

	Dominant arm		Non-dominant arm		
Objective outcome measures (n=78)	Median	[1st-3rd IQR]	Median	[1st-3rd IQR]	P value°
JAMAR	26.00	[19.70-31.33]	23.25	[16.88-29.60]	<0.001
NHPT (pegs per sec)	0.36	[0.32-0.43]	0.35	[0.28-0.43]	0.152
Subjective outcome measures (n=78)	Median	[1st-3rd IQR]	Median	[1st-3rd IQR]	P value°
Amount of use (0-5)	5	[5-5]	2	[2-4]	<0.001
Quality of use (0-5)	4	[4-5]	4	[3-5]	0.010
Neurophysiological measures (n=60)	Median	[1st-3rd IQR]	Median	[1st-3rd IQR]	P value°
MEP amplitude	2.60	[1.00-4.50]	1.90	[1.10-4.30]	0.318
MEP latency	20.80	[19.47-23.13]	20.61	[19.27-24.33]	0.670
SSEP amplitude	3.10	[1.70-5.00]	3.15	[1.90-5.05]	0.063
SSEP latency	20.28	[19.18-21.70]	20.17	[19.35-22.57]	0.329

SD: standard deviation; IQR:interquartile range; °Wilcoxon Signed Rank test

Clinical measures

PwMS showed a significant better hand grip strength with their dominant arm compared to their non-dominant arm, measured with the JAMAR test. No significant difference was found between the dominant and non-dominant arm for manual dexterity, based on the NHPT (Table2a).

In the different EDSS subgroups (Table 2b), the dominant arm was significant stronger than the non-dominant arm in the mild and severe EDSS group, measured with the JAMAR test. For manual dexterity (NHPT), no significant results were found between the dominant and non-dominant arm in each EDSS group.
Significant differences were found between the different EDSS subgroups for manual dexterity. The performance on the NHPT became worsen with increasing disability (Table 2b en 2c) .

Neurophysiological measures

No significant differences were found between the dominant and non-dominant arm for MEP and SSEP amplitude and latency in the total MS group (Table2a).

When comparing the different EDSS subgroups, the same findings returned with no significant difference between dominant and non-dominant arm for MEP and SSEP amplitude and latency (Table 2b).

Table 2b. Differences between dominant and non-dominant arm in the different EDSS subgroups

	Mild EDSS (0-3.5) Clinical/subjective measures : n=43 Neurophysiological measures : n =34					**Moderate EDSS (4-5.5)** Clinical/subjective measures : n=18 Neurophysiological measures : n =14					**Severe EDSS (6-9.5)** Clinical/subjective measures : n=17 Neurophysiological measures : n =12					**Pvalue between EDSS subgroups[a]**	
	Dom		Non-dom		P value*	Dom		Non-dom		P value*	Dom		Non-dom		P value*	Dom	Non-dom
Objective outcome measures (n=78)	Median	[1st-3rd Q]	Median	[1st-3rd Q]		Median	[1st-3rd Q]	Median	[1st-3rd Q]		Median	[1st-3rd Q]	Median	[1st-3rd Q]			
JAMAR	26.17	[18.20-30.70]	23.20	[17.60-28.40]	0.030*	28.05	[22.08-39.70]	25.85	[19.15-36.10]	0.193	22.30	[18.95-30.85]	20.40	[13.20-27.75]	0.022*	0.233	0.211
NHPT (pegs per sec)	0.40	[0.34-0.44]	0.40	[0.32-0.46]	0.391	0.34	[0.32-0.39]	0.36	[0.31-0.40]	0.931	0.29	[0.18-0.36]	0.26	[0.10-0.33]	0.163	<0.001[a]	<0.001[a]
Subjective outcome measures (n=78)	Median	[1st-3rd Q]	Median	[1st-3rd Q]		Median	[1st-3rd Q]	Median	[1st-3rd Q]		Median	[1st-3rd Q]	Median	[1st-3rd Q]			
Amount of use (0-5)	5	[5-5]	2	[2-3]	<0.001*	5	[4-5]	2	[1-4]	0.001*	5	[5-5]	3	[1-5]	0.002*	0.226	0.889
Quality of use (0-5)	5	[4-5]	5	[3-5]	0.152	4	[3-5]	4	[3-5]	0.359	4	[3-5]	3	[1-4]	0.038*	0.051	0.005[a]
Neurophysiological measures (n=60)	Median	[1st-3rd Q]	Median	[1st-3rd Q]		Median	[1st-3rd Q]	Median	[1st-3rd Q]		Median	[1st-3rd Q]	Median	[1st-3rd Q]			
MEP amplitude	3.30	[1.70-5.48]	3.45	[1.78-4.88]	0.561	2.20	[1.00-3.40]	1.70	[1.30-2.43]	0.505	1.35	[0.58-2.95]	1.20	[0.40-3.10]	0.484	0.028[a]	0.020[a]
MEP latency	19.65	[18.96-21.21]	20.05	[18.96-21.48]	0.538	22.25	[20.35-24.72]	20.98	[19.85-26.51]	0.972	23.40	[21.18-27.46]	25.30	[22.67-28.12]	1.000	<0.001[a]	<0.001[a]
SSEP amplitude	3.10	[2.08-3.93]	3.15	[2.00-5.13]	0.080	3.10	[1.45-5.33]	3.20	[1.68-5.10]	0.490	2.90	[0.90-5.00]	3.05	[1.28-4.40]	0.859	0.932	0.753
SSEP latency	19.37	[18.84-20.29]	19.61	[19.09-20.28]	0.260	21.55	[20.31-21.77]	21.30	[20.02-22.98]	0.777	21.75	[20.73-24.50]	24.06	[20.59-25.47]	0.965	<0.001[a]	<0.001[a]

*Wilcoxon Signed Rank test (between dominant and non-dominant arm); [a]Kruskal Wallis Test; *[a]Significance is set at p<0.05; Dom: dominant arm; Non-dom: non-dominant arm

Table 2c. Differences between the mild, moderate and severe EDSS subgroups

	Post-hoc[b]					
	Dominant arm			Non-dominant arm		
	Mild vs. moderate	Mild vs. severe	Moderate vs. severe	Mild vs. moderate	Mild vs. severe	Moderate vs. severe
Objective outcome measures (n=78)						
JAMAR	0.150	0.694	0.109	0.214	0.394	0.086
NHPT (pegs per sec)	0.010*	<0.001*	0.011*	0.097	<0.001*	0.001*
Subjective outcome measures (n=78)						
Amount of use (0-5)	0.223	0.418	0.113	0.566	0.953	0.865
Quality of use (0-5)	0.430	0.015*	0.177	0.504	0.001*	0.022
Neurophysiological measures (n=60)						
MEP amplitude	0.069	0.021	0.384	0.028	0.031	0.294
MEP latency	0.005*	<0.001*	0.237	0.052	<0.001*	0.090
SSEP amplitude	0.874	0.702	0.891	0.683	0.483	0.719
SSEP latency	0.001*	<0.001*	0.262	0.002*	<0.001*	0.123

[b]Mann-Whitney U test; *significant Pvalue <0.016 (bonferroni correction)

Relationship between clinical and neurophysiological measures

Correlation coefficients between the objective, subjective and neurophysiological measures are provided in table 3a.

For the clinical tests, the NHPT showed low correlations (0.30-0.49) with MEP and SSEP latency for both arms and a small correlation (<0.29) with MEP amplitude for the dominant arm. In contrast, the JAMAR test had only a small (<0.29) to low (0.30-0.49) correlation with SSEP latency and amplitude for the dominant arm.

Furthermore, the subjective use of the non-dominant arm showed a low correlation (0.30-0.49) with SSEP amplitude. Also the quality of use of the non-dominant arm had small (<0.29) to low (0.30-0.49) correlations with MEP and SSEP latency.

Tabel 3a. Correlation between objective/subjective outcome measures and neurophysiological measures in the total MS population with arm-hand dysfunction (n=60)

	MEP amplitude		MEP latency		SSEP amplitude		SSEP latency	
	dom	non-dom	dom	non-dom	dom	non-dom	dom	non-dom
JAMAR	0.00	-0.04	0.13	0.13	-0.49**	-0.20	0.26*	0.13
NHPT pegs/sec	0.29*	0.18	-0.46**	-0.39**	0.06	0.22	-0.45**	-0.38**
Amount of use	0.18	-0.04	0.02	0.01	-0.03	0.30*	0.09	-0.01
Quality of use	0.13	0.20	-0.12	-0.34**	0.00	0.23	-0.03	-0.28*

Spearman correlation coefficients; p<0.05* ; p<0.01**; dom:dominant arm; non-dom:non-dominant arm

The correlation coefficients between the objective/subjective outcome measures and neurophysiological measures for the mild, moderate and severe EDSS subgroups are provided in table 3b, 3c and 3d.

In the mild EDSS group, there was a low correlation (0.30-0.49) between hand grip strength and SSEP amplitude and latency for the dominant arm. Also the use of the arms in daily life had a low correlation (0.30-0.49) with MEP amplitude of the dominant arm.

In the moderate EDSS group, only one moderate correlation (0.50-0.69) was found between the NHPT and SSEP amplitude of the non-dominant arm.

The JAMAR test had a moderate correlation (0.50-0.69) with SSEP amplitude for the dominant arm in the severe EDSS group. Additional, a moderate correlation (0.50-0.69) was found between the NHPT and SSEP latency for the dominant arm. The NHPT had also a high correlation (0.70-0.89) with SSEP amplitude for the non-dominant arm. Furthermore, the quality of the use of the non-dominant arm had a high correlation (0.70-0.89) with SSEP amplitude.

The correlation coefficients in the different EDSS subgroups will not be discussed further because no clear interpretations can be made from the results.

Table 3b. Correlation between objective/subjective outcome measures and neurophysiological measures in the mild EDSS group with arm-hand dysfunction (n=60)

	MEP amplitude		MEP latency		SSEP amplitude		SSEP latency	
	dom	non-dom	dom	non-dom	dom	non-dom	dom	non-dom
JAMAR	-0.24	-0.05	0.15	0.22	-0.40*	-0.25	0.38*	0.33
NHPT pegs/sec	0.10	-0.10	-0.13	-0.25	-0.24	-0.02	0.09	-0.14
Amount of use	0.35*	-0.13	0.16	0.00	-0.07	0.27	0.14	-0.02
Quality of use	-0.14	0.15	0.29	-0.29	-0.32	0.13	0.34	-0.16

Spearman correlation coefficients; p<0.05* ; dom:dominant arm; non-dom:non-dominant arm

Table 3c. Correlation between objective/subjective outcome measures and neurophysiological measures in the moderate EDSS group with arm-hand dysfunction (n=60)

	MEP amplitude		MEP latency		SSEP amplitude		SSEP latency	
	dom	non-dom	dom	non-dom	dom	non-dom	dom	non-dom
JAMAR	0.23	-0.37	0.02	0.43	-0.52	-0.50	0.15	-0.08
NHPT pegs/sec	0.47	0.53	-0.38	0.01	0.44	0.59*	-0.36	-0.37
Amount of use	0.10	0.19	-0.31	-0.06	0.01	0.16	0.01	-0.13
Quality of use	0.20	0.17	-0.45	-0.07	0.18	0.04	-0.27	-0.15

Spearman correlation coefficients; p<0.05* ; dom:dominant arm; non-dom:non-dominant arm

Table 3d. Correlation between objective/subjective outcome measures and neurophysiological measures in the severe EDSS group with arm-hand dysfunction (n=60)

	MEP amplitude		MEP latency		SSEP amplitude		SSEP latency	
	dom	non-dom	dom	non-dom	dom	non-dom	dom	non-dom
JAMAR	0.44	0.20	0.42	-0.10	-0.63*	0.46	0.12	-0.07
NHPT pegs/sec	0.08	0.24	-0.27	-0.50	0.30	0.84**	-0.69*	-0,53
Amount of use	0.10	-0.06	-0.07	0.12	0,12	0.50	0.05	-0.01
Quality of use	0.20	0.14	-0.27	-0.55	0.36	0.73**	-0.30	-0.53

Spearman correlation coefficients; p<0.05* ; p<0.01**; dom:dominant arm; non-dom:non-dominant arm

Discussion

Differences between dominant and non-dominant arm for perceived arm-hand performance

We can state that there is a trend towards more impairment of the non-dominant arm compared to the dominant arm in how PwMS reported about their arm-hand dysfunction, but without significant results. This trend was found in the total MS group and in the mild, moderate and severe EDSS subgroups.

PwMS used their dominant arm more in daily life, with no influence of disability level which indicated that both the PwMS with a low and high EDSS score used their dominant arm more in daily living. This may relate to the findings of Lamers et al., who found that the dominant arm is more used in more disabled PwMS.(4) Also healthy subjects reported to use their dominant arm significantly more in daily life compared to their non-dominant arm.(4) One can state that these results about the superior use of the dominant arm in daily life in PwMS is normal, as it correspond to the results in healthy subjects. We can conclude that hand dominance has an influence on the use of the arms in daily life in both PwMS and healthy subjects.

For the quality of performance, the dominant arm had a significant better performance in daily life in PwMS. Also an increase of disability level led to a greater decrease in quality of the non-dominant arm compared to the dominant arm. These findings are in contrast to what would be expected in healthy subjects. Lamers at al., found that healthy subjects reported no significant differences between both arms for perceived quality of performance.(4) One can assume that PwMS consider their non-dominant arm as more impaired because they use their non-dominant arm less in daily life. They will link the minor use of the non-dominant arm to impairment of the non-dominant arm in which, in some cases, no or very little objective impairment of the non-dominant arm will be present. They perceive impairment because they have the diagnosis of MS, even though there is no impairment present.

Differences between dominant and non-dominant arm for clinical and neurophysiological measures

PwMS had significant more hand grip strength in their dominant arm compared to their non-dominant arm, measured with the JAMAR test. This was also the case for PwMS in the mild and severe EDSS group. The same findings were found in healthy subjects. The study of Puh. U. revealed norm values, based on gender and age, which indicated that the dominant arm had 7% more strength than the non-dominant arm.(20) One can state that there is an influence of hand dominance on the measure of hand grip strength in PwMS.

Furthermore, performance on the NHPT revealed that there were no significant differences found for manual dexterity between the dominant and non-dominant arm. These results are in contrast with Oxford et al., who revealed that the right arm had a slightly better score on the NHPT in healthy subjects. This indicates that there is an influence of hand dominance in healthy subjects, because 90% of the male participants and 93% of the female participants were right hand dominant.(5) One can assume that the dominant arm became more impaired than the non-dominant arm with regard to manual dexterity in PwMS because normally the dominant arm is quicker than the non-dominant arm

in healthy subjects. The significant difference between the dominant and non-dominant arm in healthy subjects, with a better performance of the dominant arm, disappears in PwMS indicating more impairment of the dominant arm compared to the non-dominant arm.
Additional, differences were found between the mild, moderate and severe EDSS subgroups, indicating that manual dexterity decreases with increasing disability in MS. In fact, the NHPT is associated with the severity of MS.

The dominant arm showed impairment for manual dexterity, measured with the NHPT, but without loss of strength. The objective impairment of the dominant arm can be demonstrated with the NHPT, but not with the JAMAR test. We can assume that the JAMAR test is not sufficient enough for demonstration of 'functional' deterioration.

Neurophysiological measures, based on MEP and SSEP amplitude/latency, revealed no significant differences between the dominant and non-dominant arm in the total MS group, nor in the different EDSS subgroups. The same findings returned in healthy subjects. Livingston et al., found that MEP amplitude and latency were not influenced by hand dominance(21) and Chen et al., found no significant sensory differences between the hemispheres for the nervus medianus and ulnaris.(22) Furthermore, significant differences were found between the mild, moderate and severe EDSS subgroups with higher values of MEPs and SSEPs with increasing disability. One can state that MEP and SSEP measures are associated with the severity of MS because of the deterioration of the motor and sensory pathways with increasing disability.

Relationship between clinical and neurophysiological measures

MEP and SSEP amplitude and latency were negatively correlated with the NHPT (pegs/sec), which means that greater values of amplitude and latency led to fewer pegs/minute on the NHPT for both arms. The influence of abnormal SSEPs on the performance of the NHPT was also shown in the study of Notici et al., who observed that PwMS with abnormal SSEPs needed more time to complete the NHPT.(23) Based on these findings, we can say that impairment of motor and sensory pathways has a great influence on manual dexterity in PwMS, more than on hand grip strength. Abnormal values of MEP and SSEP amplitude/latency are more likely to lead to a functional decline than to strength loss.

The severe EDSS subgroup showed generally higher correlations than the mild and moderate EDSS subgroups. This can be explained by more impairment in the severe EDSS subgroup in which 88% of the PwMS had impairment of both arms, compared to 79% and 70% in the moderate and mild EDSS subgroups. We can notice that there is more impairment in the severe EDSS subgroup, but also higher values of impairment based on the MEP and SSEP amplitude/latency in which more delayed signals in the motor and sensory pathways are associated with a higher degree of impairment (higher EDSS score).

In summary, one can state that the EDSS score, and thus the severity of MS, is associated with the NHPT and the measures of MEPs and SSEPs. Hand dominance will have a minor influence on the NHPT and the measures of MEPs and SSEPs in PwMS because these tests are able to show some

impairment if present, also of the dominant arm. Hand dominance will have an influence on the JAMAR test because the present impairment of the dominant arm is not shown is this test. Also the subjective thoughts of the PwMS, for both the use and the quality of the arms in daily life, are related to the hand dominance of the PwMS. Summarizing, we cannot exclude the influence of hand dominance in PwMS.

Furthermore, our results suggest that despite the objective impairment of the dominant arm, measured with the NHPT, the dominant arm is more used in daily life and with a better quality according to the PwMS. There is no consistency between the objective measures, which reveal impairment of the dominant arm, and what the PwMS experience about their arm-hand dysfunction (subjective). One can state that there is a subclinical impairment present in PwMS which can be measured objectively, but not subjectively. This can be related to four possible assumptions. First the experience of the PwMS in which they do not report impairment of the dominant arm because of the fact that the dominant arm can still do the major activities in daily life. Secondly, PwMS underestimate the use of the non-dominant arm in daily life because this arm only serves as support of the activities mainly performed by the dominant arm. Thirdly, PwMS report faster impairment, in which the impairment is mainly linked to the use of the arms in daily life, because they have the label of 'MS patient'. Finally, neural plasticity can play a role in which the dominant arm has to be more impaired before it will no longer compensate for lesions in PwMS.

On the other hand, it is also possible that there is clinical deterioration present in the non-dominant arm which cannot be demonstrated with the NHPT and JAMAR test. Several other tests are required in order to answer this finding.

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