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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Test-retest reliability of cognitive fatigability and relation between cognitive and walking fatigability in moderately disabled persons with Multiple Sclerosis

Charlotte Deschryvere
Maite Noels

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij kinderen

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Research context

This article is created in the context of the second part of the master's thesis in the second master year of Rehabilitation Sciences and Physiotherapy at University of Hasselt (UHasselt) by two second master students, Charlotte Deschryvere (C.D.) and Maite Noels (M.N.), under supervision of Prof. Dr. Peter Feys (promotor), Dr. Cintia Ramari Ferreira (copromotor) and Drs. Felipe Balistieri Santinelli (supervisor). It is written according to the sixth edition of the American Psychological Association (APA) style guidelines and predetermined guidelines of the master's thesis.

This master's thesis is situated in the neurological rehabilitation research domain of physiotherapy. Multiple Sclerosis (MS)-related fatigue is the most reported and chronic disabling symptom (Lenaert, Jansen, & van Heugten, 2018). It has a multidimensional impact on daily living activities and quality of life (QoL) (Romani et al., 2004).

Fatigability is an aspect of MS-related fatigue and can be defined as a decline of a prolonged performance (Kluger, Krupp, & Enoka, 2013). Fatigability can occur to everyone, but in persons with MS (pwMS) in an abnormal way. This multidimensional construct will investigate two domains of fatigability, namely cognitive and walking fatigability.

Cognitive performance over time is a method to measure cognitive fatigability. This could determine a significant decline in short-term memory and information processing speed of the cognitive function in pwMS. According to Kluger et al. (2013), this can be measured by the Symbol Digit Modalities Test (SDMT) and Paced Auditory Serial Addition Test (PASAT). It has been proven that cognition has an influence on walking (Motl et al., 2021). So, cognitive fatigability can possibly be an important factor in walking and walking fatigability (Kluger et al., 2013).

A decrease in walking performance can be affected by fatigue (Van Geel et al., 2021), and the Distance Walked Index (DWI_{6-1}) is a discriminative reliable measurement for walking fatigability (Van Geel, Veldkamp, Severijns, Dalgas, & Feys, 2020a). In that way, increased walking-related performance fatigability can result in potential symptoms, such as muscle weakness, gait impairment, balance disorders, pain, spasticity and dizziness (Van Geel et al., 2021). The relationship between cognitive and walking fatigability in pwMS is still un-

assessed. The possibility of this relationship is important to implement in the multidisciplinary rehabilitation of MS.

The focus of this article is also to investigate the test-retest reliability of an objective measure for cognitive fatigability. Further research is needed to assess psychometric properties of standard cognitive tests such as SDMT and PASAT to measure errors and normality cut-off scores to interpret intervention changes. Past research only investigated the reliability of cognitive tests for cognitive function in general, not for cognitive fatigability. A standard clinical test to assess cognitive fatigability would be important to implement in future research.

This article is written in the context of a current experimental research project at UHasselt. Of that project, part A will assess the psychometric properties of cognitive and coordination fatigability measurements in MS, to which this master's thesis relates. The aim of this master's thesis is to investigate the test-retest reliability of cognitive fatigability and the relationship between cognitive and walking fatigability in moderately disabled pwMS.

Data collection was performed in REVAL research centre of the faculty of rehabilitation sciences at UHasselt, building B and at two MS rehabilitation centres, the National Multiple Sclerosis Centre (NMSC) in Melsbroek and the MS centre 'Noorderhart' in Pelt. The research design and method of this broad research project is initiated and designed by the research team of Prof. Dr. Peter Feys.

The recruitment of participants and data collection were done by C.D. and M.N. with the help of our supervisors and 1st master students assigned to this team. The scheduling of participants, data analysis and academic writing of this article is done by the two second master students, C.D. and M.N. None of the authors have potential competing interests.

Abstract

Background: One way to quantify fatigability is by the decline of prolonged performance. There are two domains of fatigability, namely cognitive and motor fatigability. Previous research already showed significant results for cognitive and walking fatigability in persons with Multiple Sclerosis (pwMS). But the relationship has not yet been investigated.

Objectives: This study aims to investigate the test-retest reliability of cognitive fatigability and the relationship between cognitive and walking fatigability in moderately disabled pwMS.

Methods: Twenty-four pwMS (Expanded Disability Status Scale (EDSS) 4.75; 56.1±8.6 years; 14F/10M) and 17 healthy controls (HCs) (51±6.9 years; 16F/1M). To measure cognitive fatigability, Symbol Digit Modalities Test (SDMT) and Paced Auditory Serial Addition Test (PASAT) were used with the Cognitive Fatigability Index (CFI). Walking fatigability was measured with a 6-minute walk test and using the Distance Walked Index (DWI_{6-1}). All tests were performed in two separate days (5-7 days apart).

Results: SDMT-CFI and PASAT-CFI showed low test-retest reliability, examined with Intraclass Correlation Coefficient (ICC), for both subgroups separately and combined, with no statistical significance. Group averages for SDMT-CFI day 2 ($p=0.017$) and 6MWT-DWI_{6-1} day 1 and 2 ($p<0.001$) were significantly different between both groups. So, there is a difference between pwMS and HCs in terms of DWI_{6-1} and SDMT-CFI, where the HC group showed less fatigability. In the MS group a significant moderate relationship between PASAT-CFI and 6MWT-DWI% on day 1 ($p=0.017$;$r=0.483$) was found, while no significant relationship was found in the HC group.

Conclusion: Both assessments for cognitive fatigability showed low test-retest reliability, indicating a difference in performance between day 1 and 2. In addition, a significant relation was observed between PASAT-CFI and 6MWT-DWI_{6-1} in day 1, in pwMS. This indicates to a relationship between cognitive and walking fatigability, whereby cognitive fatigability can influence walking fatigability.

Keywords: Multiple Sclerosis, cognitive fatigability, walking fatigability, test-retest reliability

Introduction

Multiple sclerosis (MS) is a chronic, inflammatory, and demyelinating disease of the central nervous system (Thompson, Baranzini, Geurts, Hemmer, & Ciccarelli, 2018). The heterogeneous presentation and progressive course of MS consist of a variety of unpredictable neurological symptoms starting from onset (Filippi et al., 2018). The disability progression develops in symptoms such as fatigue, cognitive dysfunction, and walking difficulties (Gustavsen et al., 2021).

MS-related fatigue is a frequently reported chronic symptom with a prevalence between 36.5% and 78.0% (Ramirez et al., 2021). The general definition of fatigue is "the subjective perception of tiredness, lack of physical and/ or mental energy and reduced capacity", which affects functioning, daily activities, participation, and quality of life (QoL) in persons with MS (pwMS) (Ramirez et al., 2021; Romani et al., 2004). Fatigue can be divided into two domains, namely perception of fatigue and performance fatigability. Loy, Taylor, Fling, and Horak (2017) showed a significant relation between perceived fatigue, assessed with e.g. BORG scale, and fatigability in pwMS, while they do not assess the same underlying construct.

This study will focus on fatigability defined as "the magnitude of change in a performance relative to a reference value over a given time" (Kluger et al., 2013). The assessment of fatigability can be measured in different ways. There is self-reported fatigability, and performance fatigability quantified by the decrease of a prolonged performance (Kim et al., 2018). Self-reported fatigability measures perceived fatigability subjectively, while performance fatigability can be objectively measured. A distinction can be made between two domains of fatigability, namely a cognitive and motor factor (Kluger et al., 2013).

On one hand, for the cognitive factor, there is cognitive fatigability. Cognitive performance over time is a method to measure cognitive fatigability and could determine a significant decline in short-term memory and information processing speed of cognitive function in pwMS. Currently, evidence is lacking to select the best objective measurement tool for cognitive fatigability. However according to Harrison, das Nair, and Moss-Morris (2017), the Paced Auditory Serial Addition Test (PASAT) is one of the most promising and advanced tools in minimizing possible confounders, and according to Kluger et al. (2013), cognitive fatigability can be measured by the Symbol Digit Modalities Test (SDMT) and PASAT. Research for

objective measurements of cognitive fatigability whose psychometric properties are investigated, are inconsistent at present (Harrison et al., 2017). So, the focus of this study is to operationalize these objective measures for cognitive fatigability measured by decreased accuracy by comparing the first one-third and last one-third of the SDMT, an information processing speed test, or the PASAT, a working memory test (Harrison et al., 2017). The dimension of test-retest reliability in this study is important for the evaluation of the consistency and applicability of the cognitive fatigability measurement to identify changes in clinical settings. For cognitive fatigability, using an objective measure, the test-retest reliability is not yet determined in pwMS. In addition, another interesting but uncertain indication is a possible link with walking. Motl et al. (2021) has found a significant and strong correlation between the SDMT and six-minute walk test (6MWT). Since walking is strongly correlated with cognition in MS (Bollaert, Sandroff, Stine-Morrow, Sutton, & Motl, 2019), cognitive fatigability can potentially influence walking fatigability (Kluger et al., 2013).

On the other hand, there is the motor factor, especially walking fatigability. This is characterized by a deterioration or change in speed and distance during a task-related performance, and usually, this can be measured during prolonged walking by the 6MWT (Van Geel et al., 2021). A 10% decline in distance during the 6MWT is considered a discriminating value to define abnormal walking fatigability, and is called the Distance Walked Index (DWI_{6-1}) (Van Geel et al., 2020a). Fatigability could measure the reduced productivity of a walking performance resulting increased potential symptoms, such as muscle weakness, gait impairment, balance disorders, pain, spasticity and dizziness (Van Geel et al., 2021).

The aim of the study is to assess the test-retest reliability of cognitive fatigability in moderately disabled pwMS. It will also assess the relationship between cognitive and walking fatigability in moderately disabled pwMS. For both the PASAT-Cognitive Fatigability Index (CFI) and SDMT-CFI, a good test-retest reliability is expected. Findings of the SDMT total score and PASAT total score in other studies appear to support this hypothesis (Benedict et al., 2017; Koh et al., 2011; Sonder, Burggraaff, Knol, Polman, & Uitdehaag, 2014). For the PASAT-CFI, there is a study that does not seem to support this hypothesis, because it has found that the PASAT total score had a low test-retest reliability due to high sensitivity to learning effects (Tombaugh, 2006). It is also expected that pwMS with higher levels of cognitive fatigability will likely present higher levels of walking fatigability.

Methods

Participants

Twenty-four pwMS in the MS group and 17 matched healthy controls (HCs) in the HC group were recruited in this study.

HCs were contacted by a Facebook repost of University of Hasselt (UHasselt), faculty rehabilitation sciences. Ambulatory individuals affected by all types of MS were contacted by Facebook posts of UHasselt and via information posters and banners in two MS rehabilitation centres, namely 'Noorderhart' in Pelt and the National Multiple Sclerosis Centre (NMSC) in Melsbroek.

The selection criteria for HCs and pwMS were similar. Participants were aged between 35 and 70 years. The included participants needed to have the ability to walk for six minutes, whereby walking assistive devices were allowed for pwMS if necessary.

PwMS with a diagnosis by a neurologist according to McDonald's criteria (Thompson et al., 2018) were included if they also met the following inclusion criteria: (1) disability level, defined by the Expanded Disability Status Scale (EDSS) (Kurtzke, 1983), ranging from 4 to 6.5, (2) relapse free in the past month preceding the start of this study.

The exclusion criteria for both groups were defined as: (1) a cognitive impairment that would interfere with understanding the study instructions, (2) pregnancy, (3) musculoskeletal disorders in the lower limbs not related to MS.

For HCs, demographics of age, gender, weight, and height were collected. For pwMS, the same demographics were collected, with in addition the EDSS, years since diagnosis and type of MS.

Experimental procedure

The measurements of this experimental procedure were collected in two different sessions separated by five to seven days, around the same time of the day. All participants completed the test battery in the same order. Between all tests, they were allowed to rest if needed. The participants were informed about the experimental procedures and signed the informed consent allowing their participation in the present study. In Figure 1, the study flow can be found.

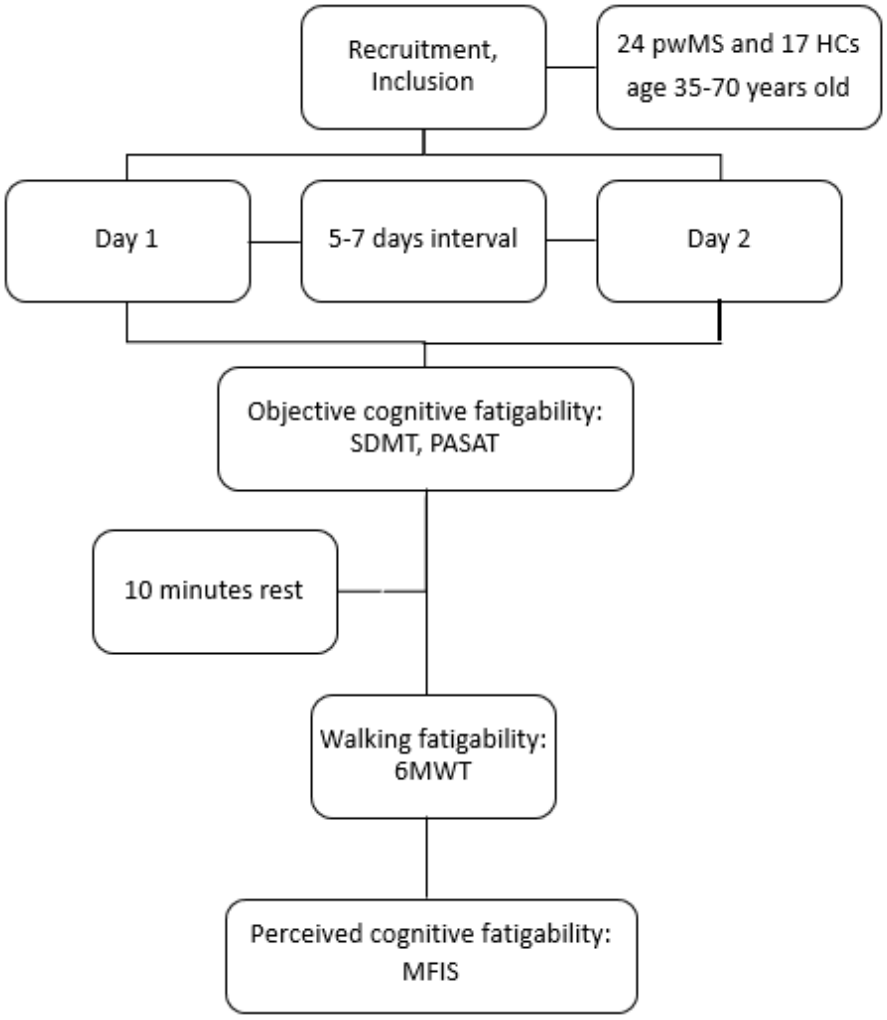

Figure 1. Study Flow.

Cognitive fatigability.

The participants started with a cognitive test battery. The SDMT and PASAT were verbally solved by the participant and the researcher wrote down the answers.

The SDMT was performed first. It is a valid test to measure information processing speed by matching as many one to nine digits as possible to nine different symbols in 90 seconds (Harrison et al., 2017). Every 30 seconds, the current location of the participant was indicated. To calculate the cognitive fatigability, the following formula was used for the SDMT Cognitive Fatigability Index (SDMT-CFI). A negative score indicates cognitive fatigability.

$$SDMT\ CFI = \left(\frac{last\ 30\ sec - first\ 30\ sec}{first\ 30\ sec}\right) X100$$

The PASAT was performed in sequence of the SDMT. It is a valid measure of the working memory and processing speed in pwMS (Morrow, Rosehart, & Johnson, 2015). Each time, the participant pronounced the sum of the last two numbers of the recording at a rate of one new number every five seconds for three minutes in total. Cognitive impaired pwMS showed a decrease in correct responses (Bryant, Chiaravalloti, & Deluca, 2004). The score of cognitive fatigability was calculated according to the following formula PASAT-CFI. A negative score indicates cognitive fatigability.

$$PASAT\ CFI = \left(\frac{last\ \frac{1}{3th}\ of\ the\ test - first\ \frac{1}{3th}\ of\ the\ test}{first\ \frac{1}{3th}\ of\ the\ test}\right) X100$$

After performing the 6MWT, discussed under the following subsection walking fatigability, all participants completed the Modified Fatigue Impact Scale (MFIS) to report perceived cognitive fatigability. It is a self-report instrument to measure the effects of fatigue on physical, mental and psychosocial status. This assessment tool contains several questions, indicated by a score of 0 (‘no problem’) to 4 (‘extreme problem’). The maximum score is 84 and a higher score indicates a greater effect on QoL. The reliability of this measurement is acceptable, but limitations in interpreting the scores must be considered (Larson, 2013).

Walking fatigability.

The second part of a session included the measurement of walking fatigability. Each participant performed the 6MWT once, covering a maximum distance in six minutes. The travelled distance was tracked minute by minute, and taken by a researcher. PwMS were allowed to use their walking assistance devices if necessary. The total 6MWT distance was a valid indicator of walking endurance in pwMS (Goldman, Marrie, & Cohen, 2008). It was a moderate-intensity exercise because they were instructed to walk as fast as they could, back and forth, in a 25-30 meters corridor depending on their test location.

The 6MWT-$DWI_{6\text{-}1}$ reflected walking-related fatigability during a prolonged walking performance, previously investigated by Van Geel et al. (2020a). A distance decline of 10% or more between the first and last minute of the 6MWT reflected objective assessment of walking fatigability. The score of walking fatigability was calculated with the following formula.

$$DWI = \left(\frac{Distance\ walked\ at\ minute\ 6 - Distance\ walked\ at\ minute\ 1}{Distance\ walked\ at\ minute\ 1}\right) X100$$

Statistical analysis

The data analytical software, named the Statistical Package for the Social Sciences (SPSS) Statistics version 22 (Hoyt, Snider, Thompson, & Mantravadi, 2016) was used for all statistical tests, with a level of significance set at 0.05. The normal distribution of continuous parameters was checked using the Shapiro-Wilk test. For non-normally distributed data, the median was reported rather than mean ± standard deviation (SD) for interpretability.

To assess the test-retest reliability of cognitive function and cognitive fatigability, the Intraclass Correlation Coefficient (ICC) was calculated. A two-way random-effects model was chosen. An ICC above 0.70 was considered acceptable, an ICC above 0.80 was perceived as good, and an ICC above 0.90 was considered excellent (Koo & Li, 2016). The lower the ICC, the more variation the method of assessment had caused and therefore the worse the agreement between assessments. Group comparisons, in terms of cognitive fatigability and walking fatigability, clinical evaluation, and anthropometric measures, were performed by an independent t-test. In case of non-normally distribution, the Mann–Whitney U test was used. Group comparison was made to characterise the cohort and examined the equality of population means. To research the discriminative validity, the cognitive fatigability scores were compared between both groups. For this purpose, the data of group comparison is used (Naghdi et al., 2020).

For the second research question, the hypothesized bivariate relationship between cognitive and walking-related fatigability was tested by the Pearson's Correlation Coefficient (r). In case of non-normally distribution, the Spearman test was used. The correlation coefficient can be categorized as follows. Correlation coefficients below 0.10 were interpreted as negligible, between 0.10-0.39 as weak, between 0.40-0.69 as moderate, between 0.70-0.89 as strong and above 0.90 as very strong (Schober, Boer, & Schwarte, 2018).

Results

The participant characteristics are described for both groups using group means and standard deviations, except for EDSS where the median was used due to not normal distribution (see Table 1). The EDSS, assistive device and onset were observed in the MS group only. One third of the MS group used a walking assistive device. The range of onset was from 35 years ago until 4 years ago. The sample was 66.66% female in the MS group and 82.35% in the HC group. To avoid drop-outs as much as possible, two MS participants had more than seven days between two test sessions due to availability or health reasons and the test session of one MS participant was continued at two different test locations.

In Table 2, the clinical data can be found. The MS group showed a relevant decline for the SDMT-CFI day 2 and for the 6MWT-$DWI_{6\text{-}1}$ day 1 and 2, the HC group showed a relevant decline for PASAT-CFI on day 1. The mean and SD from all parameters, including the results of the tests, are reported in Table 2.

In both Table 1 and 2, the p-values of the group comparison are reported. Cognitive fatigability (MFIS, SDMT-CFI and PASAT-CFI) and walking fatigability (6MWT-$DWI_{6\text{-}1}$) of both groups were compared. The group averages for all subcomponents of the MFIS were significantly different, whereby the MS group reported higher levels of fatigue. For SDMT-CFI day 2 and both 6MWT-$DWI_{6\text{-}1}$, the group averages were significantly different in the subgroups, where the HC group had higher averages. This means that the HC group showed less cognitive and walking fatigability for those parameters. The group averages of other parameters were not significantly different. Figures 2 to 5 illustrate the group comparison.

Table 1

Participant characteristics

Group	MS	HC	Group comparison p-values
Age in years	56.1 ± 8.6	51.0 ± 6.9	0.051
Height in cm	169.8 ± 8.9	169.7 ± 6.6	0.948
Body mass in kg	76.2 ± 18.2	73.7 ± 13.0	0.638
Female sex [n(%)]	16 (66.66%)	14 (82.35%)	
Assistive device [n(%)]	8 (33.33%)		
EDSS [median (range)]	4.75 (4-6.5)		
Duration of disease in years (range)	17.5 (4 – 35)		

Abbreviations: cm=centimetre; EDSS=Expanded Disability Status Scale; HC=healthy control; kg=kilograms; MS=multiple sclerosis; n=number; SD=standard deviation.

Table 2

Parameter characteristics

Group	MS	HC	Group comparison p-values
MFIS physical	22.8 ± 4.3	9.2 ± 6.5	**<0.001**
MFIS cognitive	18.4 ± 6.1	11.3 ± 6.6	**0.002**
MFIS psychosocial	5.0	1.5 ± 1.2	**<0.001***
MFIS total	45.7 ± 10.3	21.8 ± 13.4	**<0.001**
SDMT day 1	50.0	60.7 ± 9.0	**<0.001***
SDMT day 2	55.0	66.0 ± 8.2	**0.003***
SDMT CFI day 1	-6.7 ± 15.8	-9.2 ± 12.3	0.596
SDMT CFI day 2	-11.2 ± 13.0	-1.8 ± 9.3	**0.017**
PASAT day 1	47.0	47.3 ± 8.4	0.095*
PASAT day 2	44.9 ± 10.7	54.0	0.078*
PASAT CFI day 1	-5.0 ± 23.7	-16.7 ± 19.6	0.103
PASAT CFI day 2	-8.6	-6.3	0.841*
6MWT day 1	298.3 ± 129.4	574.7 ± 63.1	**<0.001**
6MWT day 2	303.6 ± 130.9	595.9 ± 73.8	**<0.001**
6MWT DWI_{6-1} day 1	-11.6 ± 7.7	0.3 ± 7.1	**<0.001**
6MWT DWI_{6-1} day 2	-16.0 ± 11.7	-1.6 ± 6.5	**<0.001**

Bold ones represent significant values

*Mann-Whitney U Test due to not-normally distributed data

Abbreviations: 6MWT=6-minute walk test; CFI=cognitive fatigability index; DWI=distance walked index; HC=healthy control; MFIS=Modified Fatigue Impact Scale; MS=multiple sclerosis; PASAT=Paced Auditory Serial Addition Test; SDMT=Symbol Digit Modalities Test; Sig: significance.

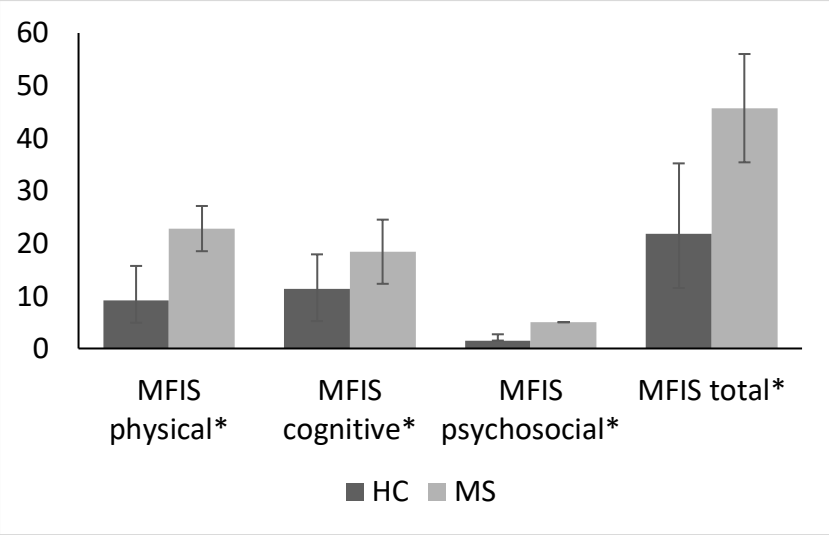

Figure 2. Group comparison MFIS.
*Correlation is significant at the 0.05 level

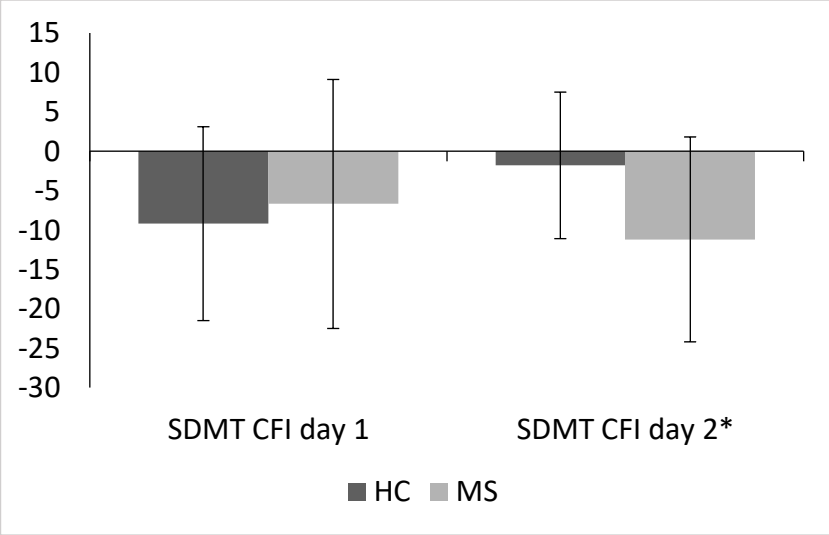

Figure 3. Group comparison SDMT-CFI.
*Correlation is significant at the 0.05 level

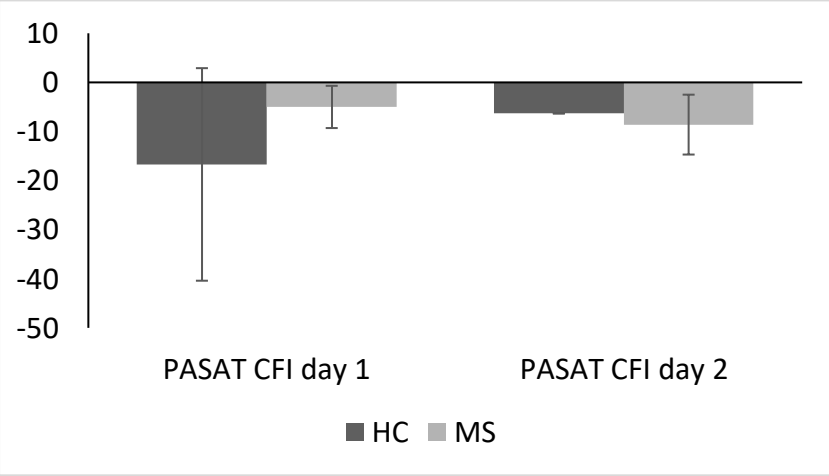

Figure 4. Group comparison PASAT-CFI.
*Correlation is significant at the 0.05 level

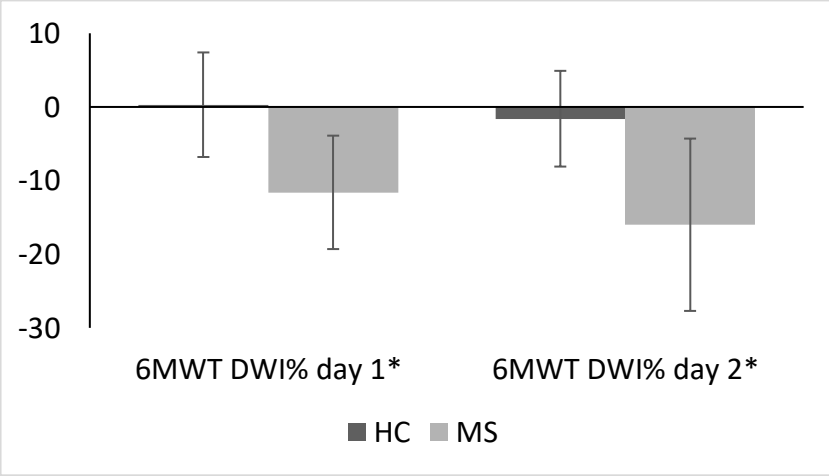

Figure 5. Group comparison 6MWT-DWI%.
*Correlation is significant at the 0.05 level

Discriminative validity was examined for objective cognitive fatigability. The independent t-test showed a significant difference for the SDMT-CFI day 1 (Table 2). For the PASAT-CFI, there was no difference in group averages present.

The test-retest reliability for cognitive function (SDMT and PASAT) and cognitive fatigability (SDMT-CFI and PASAT-CFI) was calculated using the ICC and categorized according to Koo and Li (2016) (see Table 3). For interpretation, the single measures were used since this indicates the reliability for tests of participants between two test days. For cognitive function, both the SDMT and PASAT showed significant results for the groups together and separately. The SDMT had ICC values below 0.70 which shows to a low agreement. The PASAT demonstrated a good agreement for the HC group and both groups together and an acceptable agreement for the MS group. In addition, for cognitive fatigability following results were found.

In terms of calculation for both groups separately, the MS group had a low test-retest reliability for cognitive fatigability (SDMT-CFI and PASAT-CFI). The HC group also showed a low test-retest reliability for cognitive fatigability (SDMT-CFI and PASAT-CFI). In terms of calculation for both groups combined, there was generally low test-retest reliability for cognitive fatigability (SDMT-CFI and PASAT-CFI). There was no significant p-value found for all comparisons of cognitive fatigability.

Table 3
ICC

		ICC	95% Confidence Interval		p-value
	Group		Lower bound	Upper bound	
SDMT total	HC	0.687	0.051	0.899	**<0.001**
	MS	0.390	-0.016	0.690	**0.009**
	HC and MS	0.579	0.146	0.794	**<0.001**
PASAT total	HC	0.846	0.258	0.956	**<0.001**
	MS	0.791	0.530	0.977	**<0.001**
	HC and MS	0.819	0.559	0.917	**<0.001**
SDMT CFI	HC	0.083	-0.309	0.506	0.355
	MS	-0.253	-0.626	0.193	0.871
	HC and MS	-0.156	-0.462	0.176	0.822
PASAT CFI	HC	0.302	-0.190	0.674	0.113
	MS	-0.062	-0.468	0.352	0.613
	HC and MS	0.068	-0.250	0.369	0.338

Bold ones represent significant values
Abbreviations: CFI=cognitive fatigability index; HC=healthy control; MS=multiple sclerosis; PASAT=Paced Auditory Serial Addition Test; SDMT=Symbol Digit Modalities Test.

The correlation analysis was performed to explore the hypothesized relationship between cognitive and walking fatigability separately in both groups and categorized according to Schober et al. (2018) (see Figure 6 and Appendix 4). In the HC group, there were no statistically significant relationships found between cognitive and walking fatigability. In the MS group one statistically significant relationship between the PASAT-CFI day 1 and the 6MWT-$DWI_{6\text{-}1}$ day 1 was found, more specifically a positive, moderate correlation. The other relations were not statistically significant. There, a weak correlation can be seen between cognitive and walking fatigability in the HC and MS group for cognitive and walking fatigability. In Figure 7 and 8, a correlation matrix can be found for both groups.

MS group

	SDMT CFI day 1	SDMT CFI day 2	PASAT CFI day 1	PASAT CFI day 1	6MWTDWI day 1	6MWTDWI day 2
SDMT CFI day 1	1					
SDMT CFI day 2	-0.247	1				
PASAT CFI day 1	0.059	-0.097	1			
PASAT CFI day 2	-0.117*	-0.006*	0.09*	1*		
6MWTDWI day 1	0.226	-0.013	**0.483**	0.247*	1	
6MWTDWI day 2	0.361	-0.064	0.276	0.298*	**0.605**	1

HC group

	SDMT CFI day 1	SDMT CFI day 2	PASAT CFI day 1	PASAT CFI day 1	6MWTDWI day 1	6MWTDWI day 2
SDMT CFI day 1	1					
SDMT CFI day 2	0.101	1				
PASAT CFI day 1	-0.095	-0.006	1			
PASAT CFI day 2	-0.307*	0.078*	0.407*	1*		
6MWTDWI day 1	0.179	0.138	-0.12	0.158*	1	
6MWTDWI day 2	-0.24	-0.26	0.207	0.361*	0.197	1

1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
-0.8
-0.9
-1

Bold ones represent significant values

*Spearman test due to not normally distributed data

Abbreviations: 6MWT=6-minute walk test; CFI=cognitive fatigability index; DWI=distance walked index; HC=healthy control; MS=multiple sclerosis; PASAT=Paced Auditory Serial Addition Test; SDMT=Symbol Digit Modalities Test.

Figure 6. Correlation heat map.

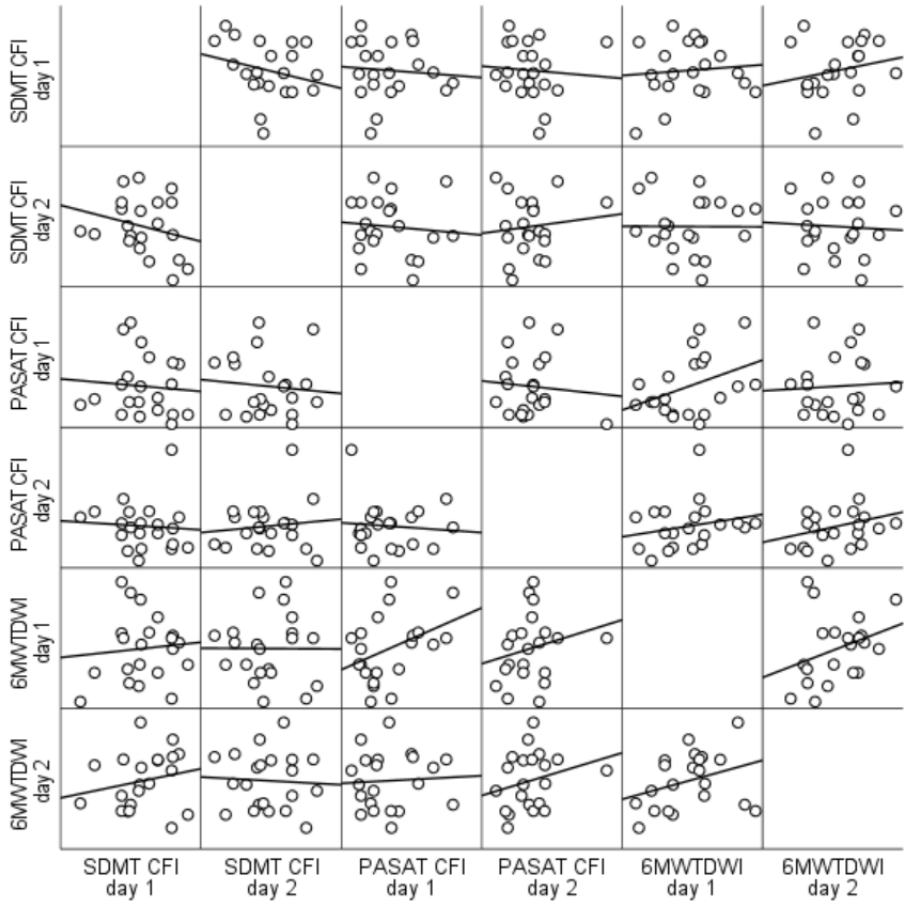

Figure 7. Correlation matrix HC group.

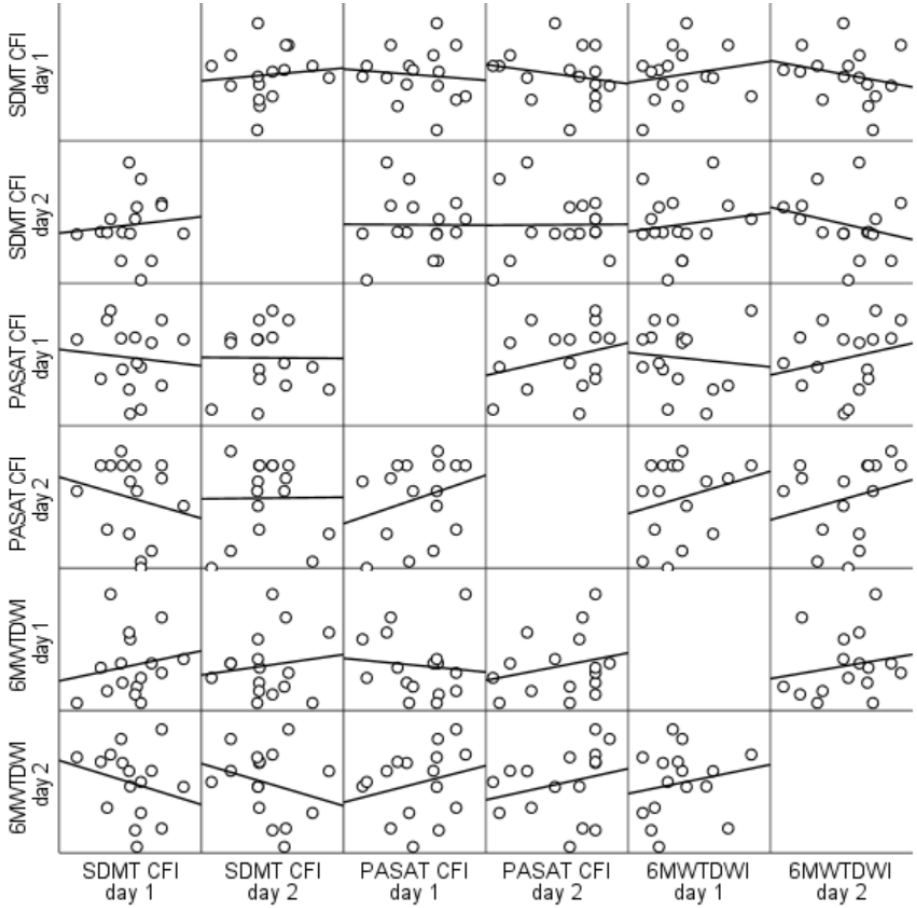

Figure 8. Correlation matrix HC group.

Discussion

Key findings

This study aimed to investigate the test-retest reliability of cognitive fatigability using the SDMT and PASAT to detect if they provide reliable objective measurements in moderately disabled pwMS. The results showed that there was a low test-retest reliability with not statistically significance for both cognitive tests. For the PASAT-CFI, this did not confirm the hypothesis, but instead the related findings on the PASAT total score of a study (Schwid et al., 2003; Tombaugh, 2006). For the SDMT-CFI, an unexpected result was found according to the hypothesis and related findings on the SDMT total score of other studies (Benedict et al., 2017; Koh et al., 2011; Sonder et al., 2014). In addition, the relationship between cognitive and walking fatigability was researched. No statistically significant relationships were found in the HC group between cognitive and walking fatigability, which was to be expected. In the MS group, one statistically significant relationship was found between the PASAT-CFI and the 6MWT-DWI_{6-1}, both on day 1. This finding supports the hypothesis that higher levels of cognitive fatigability will likely present higher levels of walking fatigability in moderately disabled pwMS. The interpretation of these findings is presented in the following sections.

Test-retest reliability for cognitive fatigability.

Sonder et al. (2014) showed significant test-retest reliability for both cognitive tests, SDMT and PASAT. That study found that the coefficients of the SDMT were the highest, which suggests that this cognitive test may be more valid and reliable over time compared to PASAT. The SDMT also showed to be less susceptible for possible learning effects, however, Koh et al. (2011) and Roar, Illes, and Sejbaek (2016) reported a small learning effect if the SDMT is performed twice in a week. Also Benedict et al. (2017) reported a good test-retest reliability higher than 0.70. There, it is also proven that a one month and two-year interval showed sufficient reliability for the SDMT. An excellent test-retest reliability for the SDMT total score was found in Koh et al. (2011). For the PASAT, also a good to excellent test-retest reliability has been found, although there is a presence of learning effects (Tombaugh, 2006).

This study showed significant test-retest reliability for the SDMT and PASAT total scores for the groups together and separately, this was to be expected according to studies (Benedict et al., 2017; Koh et al., 2011; Sonder et al., 2014; Tombaugh, 2006). Simultaneously a low test-

retest reliability for the SDMT-CFI and PASAT-CFI for both groups together and separately was found, with no statistical significance. Contrary to these results, the expectation was that there is significant test-retest reliability for the cognitive tests. It could point out that the assessment of cognitive fatigability can be influenced by various factors (Harrison et al., 2017; Kluger et al., 2013).

Kluger et al. (2013) reported multiple factors that could influence fatigue. Homeostatic factors such as energy consumption and protection, psychological factors like, expectations, motivation and mood, peripheral factors, for example physical changes in nerves and muscles, and central factors like the functioning of the central nervous system, can influence fatigue and fatigability. Also, administration of the cognitive tests already suggested to see a possible learning effect, for example performing two test moments in short succession, which was also found in other studies (Koh et al., 2011; Roar et al., 2016; Tombaugh, 2006). Test-retest reliability and its possible learning effects could be a pioneering addition in the scientific literature for the assessment of objective cognitive fatigability in pwMS. It is an added value to make the research more reliable by eliminating as many confounders as possible, e.g. no therapy, medication, mood (Harrison et al., 2017), and using a larger sample size to be able to draw conclusions with greater certainty. The identification of measurement errors will result in better interpretation of changes in future clinical settings and research.

Relationship between cognitive and walking fatigability.

Mackay, Johnson, Moodie, Rosehart, and Morrow (2021) showed that subjective cognitive fatigability, measured by MFIS, and objective cognitive fatigability were not significantly related. Therefore, this study will only focus comparing the findings of this study with objective cognitive fatigability.

For the SDMT-CFI, calculated with a formula of the correct answers in the first one-third and last one-third of the test, a significant decrease in accuracy and reaction time was found in pwMS (Harrison et al., 2017; Van Geel, Geurts, Abasıyanık, Coninx, & Feys, 2020b). As well for the PASAT-CFI, multiple studies report significant findings for a decrease in accuracy comparing the first and last part of the test (Berard, Smith, & Walker, 2018; Morrow et al., 2015; Schwid et al., 2003; Van Geel et al., 2020b). Also, Van Geel et al. (2021) proved that pwMS, who showed walking-related performance fatigability, have more problems with e.g.

balance and pain after the 6MWT. In addition, Motl et al. (2021) has found a significant and strong correlation between the SDMT and 6MWT. Since cognition showed significant effects on walking, cognitive fatigability can potentially influence walking fatigability (Kluger et al., 2013).

When previous research is compared to the findings of this study, the following can be seen. In the MS group a statistically significant, moderate relationship between the PASAT-CFI and the 6MWT-$DWI_{6\text{-}1}$ on day 1 was found. This confirms the assumption made, based on the results of other studies (Kluger et al., 2013; Motl et al., 2021; Van Geel et al., 2021). The other relationships were not statistically significant and weakly correlated, which can explain the finding of previous research that the PASAT is one of the most advanced tools for cognitive fatigability and that HCs show less decline in fatigability (Harrison et al., 2017; Van Geel et al., 2021).

The reason for low correlations could be that no distinction was made in the MS group for pwMS with and pwMS without fatigability. As a result, pwMS without fatigability will probably influence the researched relationships. The found significant relationship between the two types of fatigabilities may reflect the relevance of cognitive fatigability for walking dysfunctions and potentially related fatigability in daily activities in pwMS with moderate disability. Since the relationship has proven to influence each other, an impact on decreased motor functions (e.g. increased symptoms of muscle weakness, gait impairment, balance disorders, pain, spasticity and dizziness) should be considered when walking-related performance fatigability is present in the MS population (Van Geel et al., 2021). This is important information to implement in the multidisciplinary rehabilitation of MS. By these findings, there is, for the first time as far as we know, significant evidence for the relationship between cognitive and walking fatigability in pwMS with moderate disability. These results should be interpreted with caution as there might be a large influence of unexamined confounders such as mood, medication, type of MS etc. (Kluger et al., 2013; Shah, 2009).

Group comparison and discriminative validity.

In addition to our research questions, group comparison was also investigated. The group averages for all subcomponents of MFIS (assessing perceived cognitive fatigability) were significantly different, whereby the MS group reported the expected higher levels of fatigue (Kos et al., 2003). For the SDMT-CFI day 2 (assessing objective cognitive fatigability) and 6MWT-DWI_{6-1} day 1 and 2 (walking fatigability) significant differences were found between both groups. So, there is a difference between pwMS and HCs in terms of DWI_{6-1} and SDMT-CFI, where the HC group had higher averages. This indicates less decline of a prolonged performance. Thus, the HC group showed less cognitive and walking fatigability for those parameters, which is to be expected in participants without fatigability (Kluger et al., 2013). The fact that not all cognitive fatigability parameters were significantly different may be attributed to a possible learning effect on cognitive tests (Roar et al., 2016; Tombaugh, 2006), and because the PASAT is less discriminating and sensitive than the SDMT according to Sonder et al. (2014). Based on the group comparison, discriminative validity was examined. The SDMT-CFI day 1 showed a significant difference between the subgroups. In this study, only the group comparison was examined. Further studies may investigate a cut-off to determine in which subgroup a specific participant would be placed according to results.

Strengths and weaknesses

This study has several strengths. Firstly, the test-retest reliability and the relationship between cognitive (CFI) and walking (DWI_{6-1}) fatigability were still not investigated and document in evidence-based literature. This opens up the possibility for other studies to investigate this further. Secondly, the method including the recruitment strategy and mainly the experimental procedure is extensively described in detail which reduced the risk of sampling bias and increased the reproducibility of this study. Thirdly, the MS group is compared to active HCs. This will investigate the pathological influence of the chronic neurological disease to fatigability and will present a broad overview of the differences and results of pwMS. Fourthly, the participants were recruited via various communication channels or related to one of the two involved Flemish rehabilitation MS centres. In this way, the risk of selection bias is reduced. Fifthly, this study examined cognitive fatigability by using two different tests for cognitive function (SDMT and PASAT). Lastly, the ratio of genders was

not balanced in both subgroups, but the MS group was structured according to prevalence of the disease, specifically the female majority (ratio 3:1) (McGinley, Goldschmidt, & Rae-Grant, 2021). Thereby, this fact may contribute to the correct estimation of differences due to higher prevalence of fatigue in female pwMS. Kister, Bacon, and Cutter (2021) proved that women suffered more from MS-related fatigue burden than the male MS population.

One inherent weakness of this study is the small sample size of both intervention groups, which reduced the consistency, generalizability to the MS population and the applicability of our findings. Also, we tried to control a distinction between researchers collecting data and the statistical researchers, by giving the same instructions and following the protocol strictly, but if it is not fully satisfied, it may increase the risk of detection bias. Lastly, the EDSS is a scale to examine the level of disability in MS and the range is divided in two parts (Kurtzke, 1983). The subdivision below four and a half is done by measuring functional impairments in eight categories such as pyramidal, cerebellar, brain stem, sensory, bowel and bladder, visual, cerebral and other not defined functions. The subdivision starting at five is done by evaluating the walking invalidity with focus on distance and the use of assistive devices. Cognition or fatigue are barely or not at all scored in the EDSS. Thereby, the rescaling of the EDSS by the neurologist is done only annually. Our included EDSS range was from four to six and a half. Due to above-described limitations of the EDSS, it is a must to interpret the results of the MS group with caution.

Recommendations

To the best of our knowledge, the test-retest reliability for measurements of objective cognitive fatigability has not been evidence-based explored to date. When looking for research on the relationship between cognitive and walking fatigability, no studies were found either. Jones et al. (2020) discovered that walking fatigability and cognitive fatigability do not differ based on age, but suggested that it is more likely to be affected by the disability level in pwMS. Harrison et al. (2017) showed that there are measurements for objective cognitive fatigability, but that these are not reliable and sensitive enough at this moment. There were no predictable factors investigated for objective cognitive fatigability proven by Bailey, Channon, and Beaumont (2007) and Mackay et al. (2021). Van Geel et al. (2021) examined if pwMS with more severe symptoms showed more gait impairment and decline of

speed, which proved to be effectively significant. So, there is growing evidence for cognitive and walking fatigability separately, but more research is needed to link both domains and understand more of the impact of cognitive fatigability on walking fatigability. Further research is needed to investigate these hypotheses of this study. Due to the lack of research on cognitive fatigability, the interpretation of these study results is difficult. Not only in the MS population would research on the applicability of cognitive and walking fatigability be interesting but also in other pathologies.

It is useful to investigate the differences in several objective walking parameters (e.g. arm swing and balance) between four MS groups, pwMS with and without both types of fatigability, pwMS with cognitive fatigability and pwMS with walking fatigability. In this way, the influence of cognitive fatigability on walking fatigability can be investigated more specifically with parameters of the gait pattern. Afterwards, attention can be paid to these findings to make the rehabilitation of walking-related performance fatigability more specific to improve the gait pattern and considering increased potential symptoms such as muscle weakness, gait impairment, balance disorders, pain, spasticity and dizziness (Van Geel et al., 2021).

In future studies of fatigability in MS, it is also recommended to consider confounders and medication effects. It can also be made more specific by taking the type of MS into account.

Conclusion

This master's thesis showed a low test-retest reliability, with no statistical significance, for the psychometric properties of cognitive fatigability with the SDMT and PASAT, indicating a difference in performance between day 1 and 2. In addition, it was able to prove one significant correlation between PASAT-CFI and 6MWT-$DWI_{6\text{-}1}$ on day 1 in moderately disabled pwMS, which refers to a relationship between cognitive and walking fatigability, whereby cognitive fatigability influences walking fatigability. Future research in the MS population is recommended to confirm or disprove these findings with a greater sample size to find out more about the impact of fatigability and implement it in multidisciplinary neurological rehabilitation.

List of abbreviations

American Psychological Association (APA)

Charlotte Deschryvere (C.D.)

Cognitive Fatigability Index (CFI)

Distance Walked Index (DWI_{6-1})

Expanded Disability Status Scale (EDSS)

Fatigue Impact Scale (FIS)

Healthy controls (HCs)

Intraclass correlation coefficient (ICC)

Maite Noels (M.N.)

Modified Fatigue Impact Scale (MFIS)

Multiple Sclerosis (MS)

National Multiple Sclerosis Centre (NMSC)

Paced Auditory Serial Addition Test (PASAT)

Persons with MS (pwMS)

Quality of Life (QoL)

Six-minute walking test (6MWT)

Standard deviations (SD)

Statistical Package for the Social Sciences (SPSS)

Symbol Digit Modalities Test (SDMT)

University of Hasselt (UHasselt)

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Appendices

Appendix 1: Statistical decision tree ICC

Appendix 2: Statistical decision tree group comparison

Appendix 3: Statistical decision tree correlation

Appendix 4: Addition to statistical analysis

Appendix 5: Declaration on honour of Charlotte Deschryvere

Appendix 6: Declaration on honour of Maite Noels

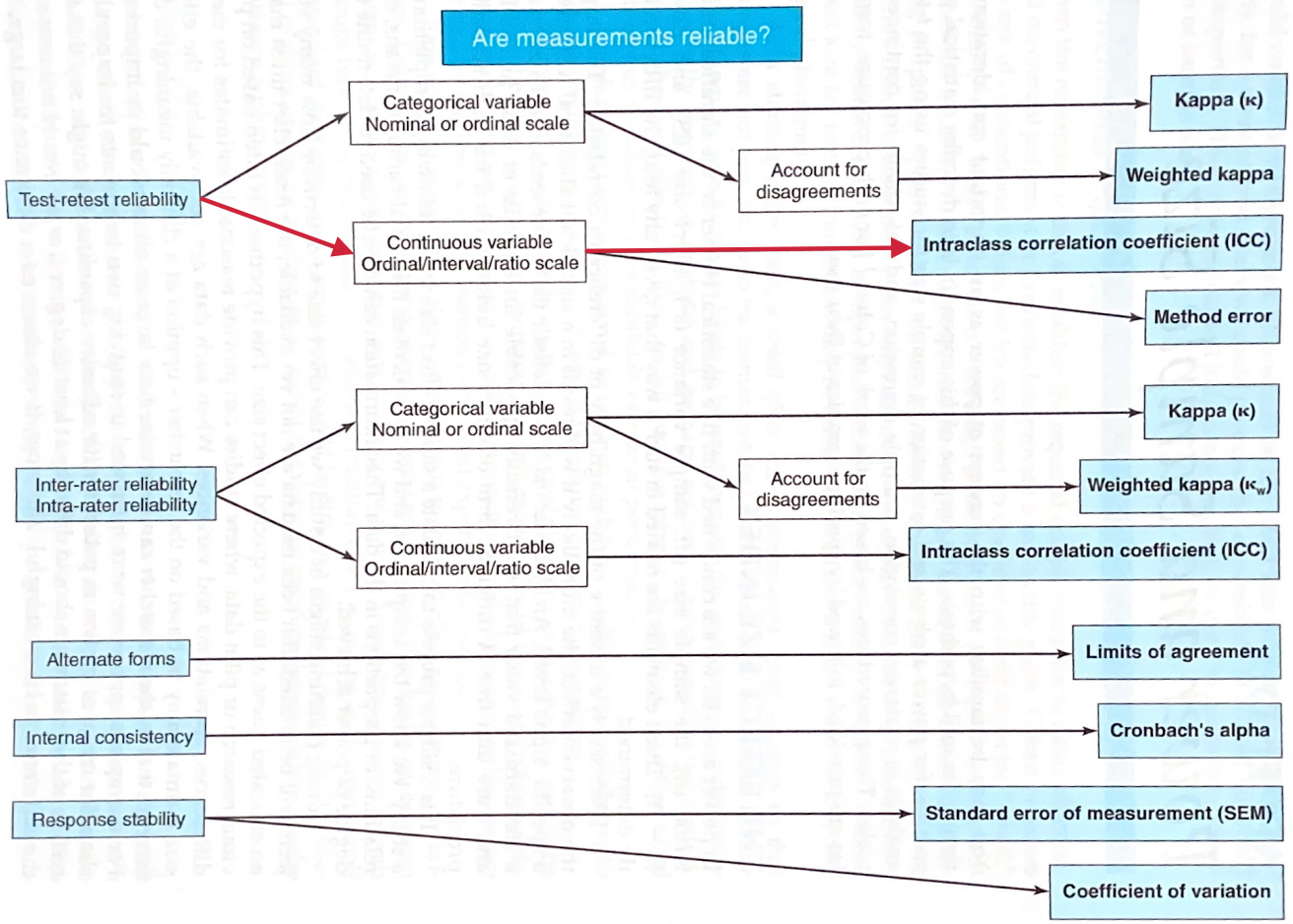
Appendix 7: Registration form jury Master's thesis of Charlotte Deschryvere

Appendix 8: Registration form jury Master's thesis of Maite Noels

Appendix 9: Advice promotor

Appendix 10: Inventory form

Appendix 1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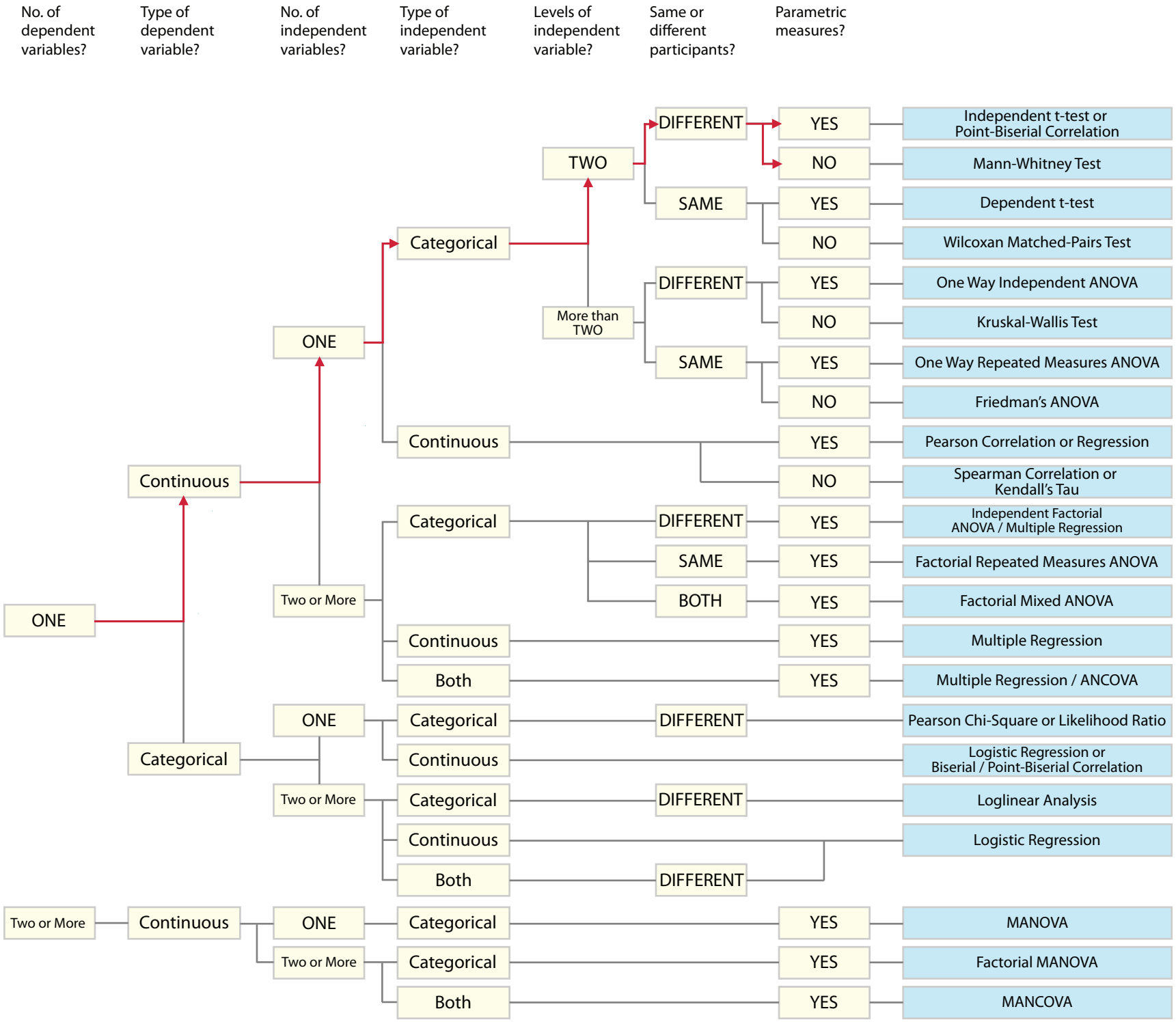
Test-retest reliability
Categorical variable
Nominal or ordinal scale
Kappa (κ)
Account for
disagreements
Weighted kappa
Continuous variable
Ordinal/interval/ratio scale
Intraclass correlation coefficient (ICC)
Method error
Inter-rater reliability
Intra-rater reliability
Categorical variable
Nominal or ordinal scale
Kappa (κ)
Account for
disagreements
Weighted kappa (κw)
Continuous variable
Ordinal/interval/ratio scale
Intraclass correlation coefficient (ICC)
Alternate forms
Limits of agreement
Internal consistency
Cronbach's alpha
Response stability
Standard error of measurement (SEM)
Coefficient of variation

Appendix 2

STATISTICS DECISION TREE

FACULTY OF HEALTH SCIENCES

THE UNIVERSITY OF SYDNEY

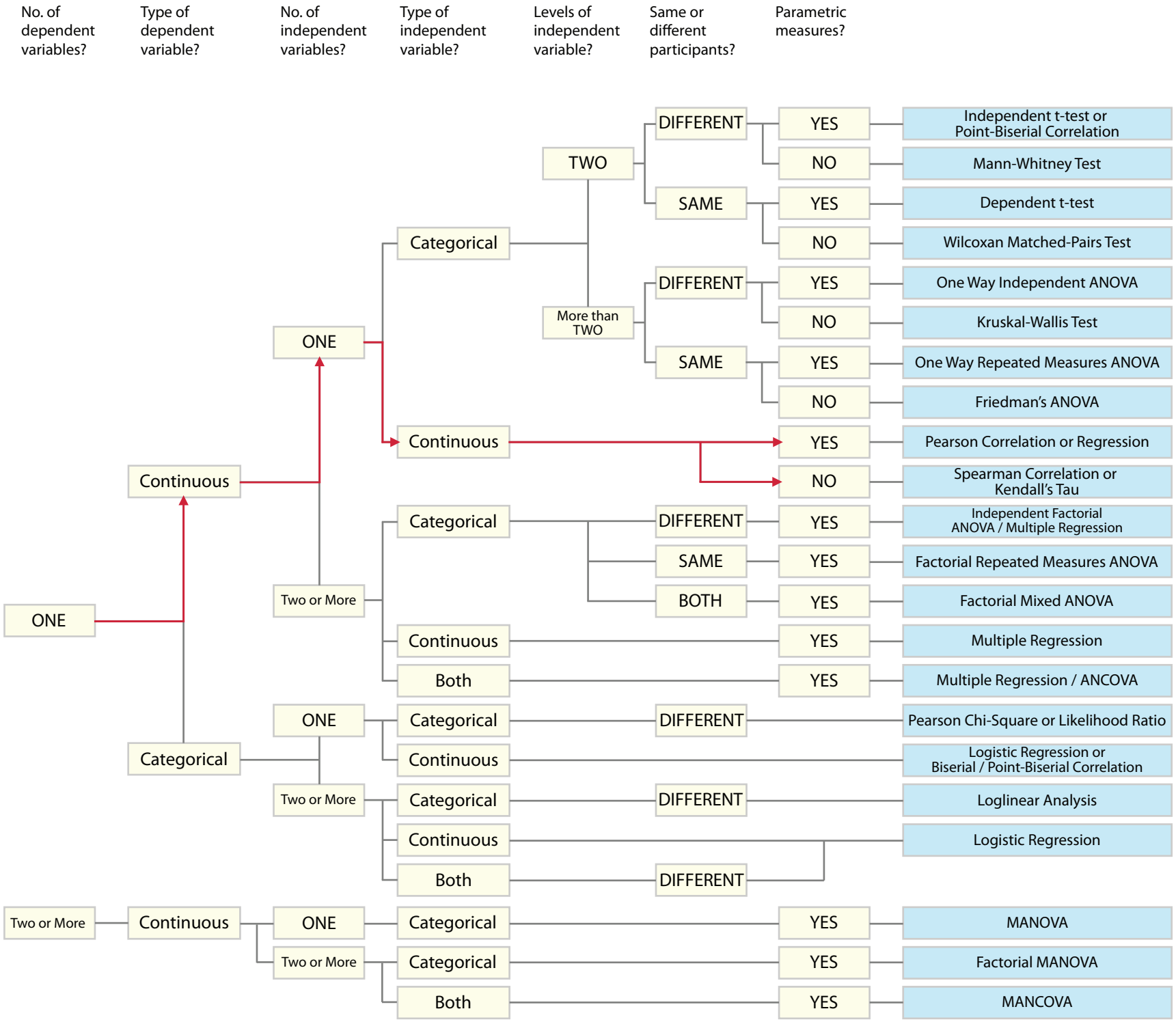


Appendix 3

STATISTICS DECISION TREE

FACULTY OF HEALTH SCIENCES

THE UNIVERSITY OF SYDNEY



Appendix 4

Complementary to statistical analysis.

Normality testing was performed separately for both groups to be more conservative and avoid a type II error. Results can be found in Table 1. For EDSS, a not normal distribution was found. Because of this, the median was calculated instead of the mean. There can also be seen that some of the parameters were not normally distributed. For these parameters, non-parametric tests were used.

Table 1
Tests of Normality

Group		Shapiro-Wilk		
		Statistic	df	Sig.
HC	Age	0.945	17	0.382
	Height	0.920	17	0.150
	Body mass	0.919	17	0.140
	MFIS physical	0.908	14	0.148
	MFIS cognitive	0.966	14	0.826
	MFIS psychosocial	0.849	14	**0.022**
	MFIS total	0.922	14	0.236
	SDMT total day 1	0.951	16	0.507
	SDMT total day 2	0.964	16	0.737
	SDMT CFI day 1	0.989	16	0.998
	SDMT CFI day 2	0.956	16	0.592
	PASAT total day 1	0.935	17	0.263
	PASAT total day 2	0.846	17	**0.009**
	PASAT CFI day 1	0.941	17	0.330
	PASAT CFI day 2	0.856	17	**0.013**
	6MWT distance day 1	0.962	17	0.673
	6MWT distance day 2	0.938	17	0.291
	6MWTDWI day 1	0.917	17	0.131
	6MWTDWI day 2	0.973	17	0.869
MS	Age	0.955	22	0.401
	Height	0.950	22	0.316
	Body mass	0.976	22	0.846
	EDSS	0.826	24	**0.001**
	MFIS physical	0.963	23	0.530
	MFIS cognitive	0.973	23	0.765
	MFIS psychosocial	0.864	23	**0.005**
	MFIS total	0.937	23	0.156
	SDMT total day 1	0.877	23	**0.009**
	SDMT total day 2	0.881	23	0.011
	SDMT CFI day 1	0.967	23	0.621
	SDMT CFI day 2	0.978	23	0.879
	PASAT total day 1	0.865	24	**0.004**

PASAT total day 2	0.948	24	0.249
PASAT CFI day 1	0.928	24	0.086
PASAT CFI day 2	0.873	24	**0.006**
6MWT distance day 1	0.964	24	0.519
6MWT distance day 2	0.973	23	0.757
6MWTDWI day 1	0.962	24	0.477
6MWTDWI day 2	0.936	23	0.150

Bold ones represent significant values

Abbreviations: 6MWT=6-minute walk test; CFI=cognitive fatigability index; df=degrees of freedom; DWI=distance walked index; HC=healthy control; MFIS=Modified Fatigue Impact Scale; MS=multiple sclerosis; PASAT=Paced Auditory Serial Addition Test; SDMT=Symbol Digit Modalities Test; Sig: significance.

For group comparison, the T-values can be found in Table 2.

Table 2

Group comparison

Parameter	t-test	df
MFIS physical	-7.107	19.851
MFIS cognitive	-3.320	35
MFIS psychosocial	28.500*	
MFIS total	-6.071	35
SDMT CFI day 1	-0.534	37
SDMT CFI day 2	2.509	37
PASAT CFI day 1	-1.671	39
PASAT CFI day 2	196.500*	
6MWT DWI% day 1	5.053	39
6MWT DWI% day 2	4.965	35.552

*Mann Withney-U Test due to not normal distribution

Abbreviations: 6MWT=6-minute walk test; CFI=cognitive fatigability index; df=degrees of freedom; DWI=distance walked index; MFIS=Modified Fatigue Impact Scale; PASAT=Paced Auditory Serial Addition Test; SDMT=Symbol Digit Modalities Test.

In addition to the correlation coefficients, the p-values can be found in Table 3.

Table 3

Correlation p-values

		SDMT CFI day 1	SDMT CFI day 2	PASAT CFI day 1	PASAT CFI day 1
HC	6MWTDWI day 1	0.508	0.611	0.646	0.545*
	6MWTDWI day 2	0.371	0.331	0.426	0.155*
MS	6MWTDWI day 1	0.301	0.952	**0.017**	0.244*
	6MWTDWI day 2	0.099	0.779	0.202	0.168*

Bold ones represent significant values

*Spearman due to not normal distribution

Abbreviations: 6MWT=6-minute walk test; CFI=cognitive fatigability index; DWI=distance walked index; HC=healthy control; MS=multiple sclerosis; PASAT=Paced Auditory Serial Addition Test; SDMT=Symbol Digit Modalities Test.

Appendix 5

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit Revalidatiewetenschappen aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

1. Ik ben ingeschreven als student aan de UHasselt in de opleiding Revalidatiewetenschappen en kinesitherapie, waarbij ik de kans krijg om in het kader van mijn opleiding mee te werken aan onderzoek van de faculteit Revalidatiewetenschappen aan de UHasselt. Dit onderzoek wordt beleid door Prof. Peter Feys en PhD Cintia Ramari Ferreira en kadert binnen het opleidingsonderdeel Wetenschappelijke stage/masterproef deel 2. Ik zal in het kader van dit onderzoek creaties, schetsen, ontwerpen, prototypes en/of onderzoeksresultaten tot stand brengen in het domein van neurologische revalidatie (hierna: "De Onderzoeksresultaten").

2. Bij de creatie van De Onderzoeksresultaten doe ik beroep op de achtergrondkennis, vertrouwelijke informatie[1], universitaire middelen en faciliteiten van UHasselt (hierna: de "Expertise").

3. Ik zal de Expertise, met inbegrip van vertrouwelijke informatie, uitsluitend aanwenden voor het uitvoeren van hogergenoemd onderzoek binnen UHasselt. Ik zal hierbij steeds de toepasselijke regelgeving, in het bijzonder de Algemene Verordening Gegevensbescherming (EU 2016-679), in acht nemen.

4. Ik zal de Expertise (i) voor geen enkele andere doelstelling gebruiken, en (ii) niet zonder voorafgaande schriftelijke toestemming van UHasselt op directe of indirecte wijze publiek maken.

5. Aangezien ik in het kader van mijn onderzoek beroep doe op de Expertise van de UHasselt, draag ik hierbij alle bestaande en toekomstige intellectuele eigendomsrechten op De Onderzoeksresultaten over aan de UHasselt. Deze overdracht omvat alle vormen van intellectuele eigendomsrechten, zoals onder meer – zonder daartoe beperkt te zijn – het auteursrecht, octrooirecht, merkenrecht, modellenrecht en knowhow. De overdracht geschiedt in de meest volledige omvang, voor de gehele wereld en voor de gehele beschermingsduur van de betrokken rechten.

6. In zoverre De Onderzoeksresultaten auteursrechtelijk beschermd zijn, omvat bovenstaande overdracht onder meer de volgende exploitatiewijzen, en dit steeds voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding:

   - het recht om De Onderzoeksresultaten vast te (laten) leggen door alle technieken en op alle dragers;
   - het recht om De Onderzoeksresultaten geheel of gedeeltelijk te (laten) reproduceren, openbaar te (laten) maken, uit te (laten) geven, te (laten) exploiteren en te (laten) verspreiden in eender welke vorm, in een onbeperkt aantal exemplaren;

[1] Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo snel mogelijk op de hoogte brengt.

- het recht om De Onderzoeksresultaten te (laten) verspreiden en mee te (laten) delen aan het publiek door alle technieken met inbegrip van de kabel, de satelliet, het internet en alle vormen van computernetwerken;
- het recht De Onderzoeksresultaten geheel of gedeeltelijk te (laten) bewerken of te (laten) vertalen en het (laten) reproduceren van die bewerkingen of vertalingen;
- het recht De Onderzoeksresultaten te (laten) bewerken of (laten) wijzigen, onder meer door het reproduceren van bepaalde elementen door alle technieken en/of door het wijzigen van bepaalde parameters (zoals de kleuren en de afmetingen).

De overdracht van rechten voor deze exploitatiewijzen heeft ook betrekking op toekomstige onderzoeksresultaten tot stand gekomen tijdens het onderzoek aan UHasselt, eveneens voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding.

Ik behoud daarbij steeds het recht op naamvermelding als (mede)auteur van de betreffende Onderzoeksresultaten.

7. Ik zal alle onderzoeksdata, ideeën en uitvoeringen neerschrijven in een "laboratory notebook" en deze gegevens niet vrijgeven, tenzij met uitdrukkelijke toestemming van mijn Uhasseltbegeleider Prof. Dr. Peter Feys en PhD Cintia Ramari Ferreira.

8. Na de eindevaluatie van mijn onderzoek aan de UHasselt zal ik alle verkregen vertrouwelijke informatie, materialen, en kopieën daarvan, die nog in mijn bezit zouden zijn, aan UHasselt terugbezorgen.

Gelezen voor akkoord en goedgekeurd,

Naam: Deschryvere Charlotte

Adres: Lindeveldweg 1, 1750 Lennik

Geboortedatum en –plaats : 09/04/1998, Asse

Datum: 04/10/2021

Handtekening:

Appendix 6

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit Revalidatiewetenschappen aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

1. Ik ben ingeschreven als student aan de UHasselt in de opleiding Revalidatiewetenschappen en kinesitherapie, waarbij ik de kans krijg om in het kader van mijn opleiding mee te werken aan onderzoek van de faculteit Revalidatiewetenschappen aan de UHasselt. Dit onderzoek wordt beleid door Prof. Dr. Peter Feys en PhD. Cintia Ramari Ferreira en kadert binnen het opleidingsonderdeel Wetenschappelijke Stage/masterproef deel 2. Ik zal in het kader van dit onderzoek creaties, schetsen, ontwerpen, prototypes en/of onderzoeksresultaten tot stand brengen in het domein van neurologische revalidatie (hierna: "De Onderzoeksresultaten").

2. Bij de creatie van De Onderzoeksresultaten doe ik beroep op de achtergrondkennis, vertrouwelijke informatie[1], universitaire middelen en faciliteiten van UHasselt (hierna: de "Expertise").

3. Ik zal de Expertise, met inbegrip van vertrouwelijke informatie, uitsluitend aanwenden voor het uitvoeren van hogergenoemd onderzoek binnen UHasselt. Ik zal hierbij steeds de toepasselijke regelgeving, in het bijzonder de Algemene Verordening Gegevensbescherming (EU 2016-679), in acht nemen.

4. Ik zal de Expertise (i) voor geen enkele andere doelstelling gebruiken, en (ii) niet zonder voorafgaande schriftelijke toestemming van UHasselt op directe of indirecte wijze publiek maken.

5. Aangezien ik in het kader van mijn onderzoek beroep doe op de Expertise van de UHasselt, draag ik hierbij alle bestaande en toekomstige intellectuele eigendomsrechten op De Onderzoeksresultaten over aan de UHasselt. Deze overdracht omvat alle vormen van intellectuele eigendomsrechten, zoals onder meer – zonder daartoe beperkt te zijn – het auteursrecht, octrooirecht, merkenrecht, modellenrecht en knowhow. De overdracht geschiedt in de meest volledige omvang, voor de gehele wereld en voor de gehele beschermingsduur van de betrokken rechten.

6. In zoverre De Onderzoeksresultaten auteursrechtelijk beschermd zijn, omvat bovenstaande overdracht onder meer de volgende exploitatiewijzen, en dit steeds voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding:

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   - het recht om De Onderzoeksresultaten geheel of gedeeltelijk te (laten) reproduceren, openbaar te (laten) maken, uit te (laten) geven, te (laten) exploiteren en te (laten) verspreiden in eender welke vorm, in een onbeperkt aantal exemplaren;

[1] Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo snel mogelijk op de hoogte brengt.

- het recht om De Onderzoeksresultaten te (laten) verspreiden en mee te (laten) delen aan het publiek door alle technieken met inbegrip van de kabel, de satelliet, het internet en alle vormen van computernetwerken;
- het recht De Onderzoeksresultaten geheel of gedeeltelijk te (laten) bewerken of te (laten) vertalen en het (laten) reproduceren van die bewerkingen of vertalingen;
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Ik behoud daarbij steeds het recht op naamvermelding als (mede)auteur van de betreffende Onderzoeksresultaten.

7. Ik zal alle onderzoeksdata, ideeën en uitvoeringen neerschrijven in een "laboratory notebook" en deze gegevens niet vrijgeven, tenzij met uitdrukkelijke toestemming van mijn UHasseltbegeleider Prof. Dr. Peter Feys en PhD. Cintia Ramari Ferreira.

8. Na de eindevaluatie van mijn onderzoek aan de UHasselt zal ik alle verkregen vertrouwelijke informatie, materialen, en kopieën daarvan, die nog in mijn bezit zouden zijn, aan UHasselt terugbezorgen.

Gelezen voor akkoord en goedgekeurd,

Naam: Maite Noels

Adres: Stotert 43, 2491 Olmen

Geboortedatum en –plaats : 21/04/1998, Mol

Datum: 04/10/2021

Handtekening:

Appendix 7

Inschrijvingsformulier verdediging masterproef academiejaar 2021-2022,
Registration form jury Master's thesis academic year 2021-2022,

GEGEVENS STUDENT - *INFORMATION STUDENT*

Faculteit/School: **Faculteit Revalidatiewetenschappen**
Faculty/School: ***Rehabilitation Sciences***

Stamnummer + naam: **1745659 Deschryvere Charlotte**
Student number + name

Opleiding/*Programme*: **2 ma revalid. & kine inwendige**

INSTRUCTIES - *INSTRUCTIONS*

Neem onderstaande informatie grondig door.

Print dit document en vul het aan met DRUKLETTERS.

In tijden van van online onderwijs door COVID-19 verstuur je het document (scan of leesbare foto) ingevuld via mail naar je promotor. Je promotor bezorgt het aan de juiste dienst voor verdere afhandeling.

Vul luik A aan. Bezorg het formulier aan je promotoren voor de aanvullingen in luik B. Zorg dat het formulier ondertekend en gedateerd wordt door jezelf en je promotoren in luik D en dien het in bij de juiste dienst volgens de afspraken in jouw opleiding.
Zonder dit inschrijvingsformulier krijg je geen toegang tot upload/verdediging van je masterproef.

Please read the information below carefully.

Print this document and complete it by hand writing, using CAPITAL LETTERS.

In times of COVID-19 and during the online courses you send the document (scan or readable photo) by email to your supervisor. Your supervisor delivers the document to the appropriate department.

Fill out part A. Send the form to your supervisors for the additions in part B. Make sure that the form is signed and dated by yourself and your supervisors in part D and submit it to the appropriate department in accordance with the agreements in your study programme.
Without this registration form, you will not have access to the upload/defense of your master's thesis.

LUIK A - VERPLICHT - IN TE VULLEN DOOR DE STUDENT
PART A - MANDATORY - TO BE FILLED* OUT *BY THE STUDENT

Titel van Masterproef/*Title of Master's thesis:*

O behouden - *keep*

● wijzigen - *change to*:
TEST-RETEST RELIABILITY OF COGNITIVE FATIGABILITY AND RELATION BETWEEN COGNITIVE AND WALKING FATIGABILITY IN MODERATELY DISABLED PERSONS WITH MULTIPLE SCLEROSIS

/:

O behouden - *keep*

O wijzigen - *change to*:

In geval van samenwerking tussen studenten, naam van de medestudent(en)/*In case of group work, name of fellow student(s)*:

● behouden - *keep*

O wijzigen - *change to:*

LUIK B - VERPLICHT - IN TE VULLEN DOOR DE PROMOTOR(EN)
PART B - MANDATORY - TO BE FILLED OUT BY THE SUPERVISOR(S)

Wijziging gegevens masterproef in luik A/*Change information Master's thesis in part A:*

O goedgekeurd - *approved*

O goedgekeurd mits wijziging van - *approved if modification of:*

Scriptie/*Thesis:*

O openbaar (beschikbaar in de document server van de universiteit)- *public (available in document server of university)*

O vertrouwelijk (niet beschikbaar in de document server van de universiteit) - *confidential (not available in document server of university)*

Juryverdediging/*Jury Defense:*

De promotor(en) geeft (geven) de student(en) het niet-bindend advies om de bovenvermelde masterproef in de bovenvermelde periode/*The supervisor(s) give(s) the student(s) the non-binding advice:*

O te verdedigen/*to defend the aforementioned Master's thesis within the aforementioned period of time*

O de verdediging is openbaar/*in public*

O de verdediging is niet openbaar/*not in public*

O niet te verdedigen/*not to defend the aforementioned Master's thesis within the aforementioned period of time*

LUIK C - OPTIONEEL - IN TE VULLEN DOOR STUDENT, alleen als hij luik B wil overrulen
PART C - OPTIONAL - TO BE FILLED OUT BY THE STUDENT, only if he wants to overrule part B

In tegenstelling tot het niet-bindend advies van de promotor(en) wenst de student de bovenvermelde masterproef in de bovenvermelde periode/*In contrast to the non-binding advice put forward by the supervisor(s), the student wishes:*

O niet te verdedigen/*not to defend the aforementioned Master's thesis within the aforementioned period of time*

O te verdedigen/*to defend the aforementioned Master's thesis within the aforementioned period of time*

LUIK D - VERPLICHT - IN TE VULLEN DOOR DE STUDENT EN DE PROMOTOR(EN)
PART D - MANDATORY - TO BE FILLED OUT BY THE STUDENT AND THE SUPERVISOR(S)

Datum en handtekening student(en)
Date and signature student(s)

Charlotte Deschryvere
22/05/2022

Datum en handtekening promotor(en)
Date and signature supervisor(s)

Peter Feys 30/5/2022

We raden je aan om de komende week nog zorgvuldig verder te wreken aan de masterpoef, en verdere te reflecteren over de inhoud van de discussie.

Appendix 8

Inschrijvingsformulier verdediging masterproef academiejaar 2021-2022,
Registration form jury Master's thesis academic year 2021-2022,

GEGEVENS STUDENT - *INFORMATION STUDENT*

Faculteit/School: **Faculteit Revalidatiewetenschappen**
Faculty/School: ***Rehabilitation Sciences***

Stamnummer + naam: **1747598 Noels Maite**
Student number + name

Opleiding/*Programme*: **2 ma revalid. & kine kinderen**

INSTRUCTIES - *INSTRUCTIONS*

Neem onderstaande informatie grondig door.

Print dit document en vul het aan met DRUKLETTERS.

In tijden van van online onderwijs door COVID-19 verstuur je het document (scan of leesbare foto) ingevuld via mail naar je promotor. Je promotor bezorgt het aan de juiste dienst voor verdere afhandeling.

Vul luik A aan. Bezorg het formulier aan je promotoren voor de aanvullingen in luik B. Zorg dat het formulier ondertekend en gedateerd wordt door jezelf en je promotoren in luik D en dien het in bij de juiste dienst volgens de afspraken in jouw opleiding.
Zonder dit inschrijvingsformulier krijg je geen toegang tot upload/verdediging van je masterproef.

Please read the information below carefully.

Print this document and complete it by hand writing, using CAPITAL LETTERS.

In times of COVID-19 and during the online courses you send the document (scan or readable photo) by email to your supervisor. Your supervisor delivers the document to the appropriate department.

Fill out part A. Send the form to your supervisors for the additions in part B. Make sure that the form is signed and dated by yourself and your supervisors in part D and submit it to the appropriate department in accordance with the agreements in your study programme.
Without this registration form, you will not have access to the upload/defense of your master's thesis.

LUIK A - VERPLICHT - IN TE VULLEN DOOR DE STUDENT
PART A - MANDATORY - TO BE FILLED* OUT *BY THE STUDENT

Titel van Masterproef/*Title of Master's thesis:*

O behouden - *keep*

● wijzigen - *change to*:

TEST-RETEST RELIABILITY OF COGNITIVE FATIGABILITY AND RELATION BETWEEN COGNITIVE AND WALKING FATIGABILITY IN MODERATELY DISABLED PERSONS WITH MULTIPLE SCLEROSIS

/:

O behouden - *keep*

O wijzigen - *change to*:

In geval van samenwerking tussen studenten, naam van de medestudent(en)/*In case of group work, name of fellow student(s)*:

● behouden - *keep*

O wijzigen - *change to:*

LUIK B - VERPLICHT - IN TE VULLEN DOOR DE PROMOTOR(EN)
PART B - MANDATORY - TO BE FILLED OUT BY THE SUPERVISOR(S)

Wijziging gegevens masterproef in luik A/*Change information Master's thesis in part A:*

☑ goedgekeurd - *approved*

O goedgekeurd mits wijziging van - *approved if modification of:*

Scriptie/*Thesis:*

☑ openbaar (beschikbaar in de document server van de universiteit)- *public (available in document server of university)*

O vertrouwelijk (niet beschikbaar in de document server van de universiteit) - *confidential (not available in document server of university)*

Juryverdediging/*Jury Defense:*

De promotor(en) geeft (geven) de student(en) het niet-bindend advies om de bovenvermelde masterproef in de bovenvermelde periode/*The supervisor(s) give(s) the student(s) the non-binding advice:*

☑ te verdedigen/*to defend the aforementioned Master's thesis within the aforementioned period of time*

☑ de verdediging is openbaar/*in public*

O de verdediging is niet openbaar/*not in public*

O niet te verdedigen/*not to defend the aforementioned Master's thesis within the aforementioned period of time*

LUIK C - OPTIONEEL - IN TE VULLEN DOOR STUDENT, alleen als hij luik B wil overrulen
PART C - OPTIONAL - TO BE FILLED OUT BY THE STUDENT, only if he wants to overrule part B

In tegenstelling tot het niet-bindend advies van de promotor(en) wenst de student de bovenvermelde masterproef in de bovenvermelde periode/*In contrast to the non-binding advice put forward by the supervisor(s), the student wishes:*

O niet te verdedigen/*not to defend the aforementioned Master's thesis within the aforementioned period of time*

O te verdedigen/*to defend the aforementioned Master's thesis within the aforementioned period of time*

LUIK D - VERPLICHT - IN TE VULLEN DOOR DE STUDENT EN DE PROMOTOR(EN)
PART D - MANDATORY - TO BE FILLED OUT BY THE STUDENT AND THE SUPERVISOR(S)

Datum en handtekening student(en)
Date and signature student(s)

22/05/2022

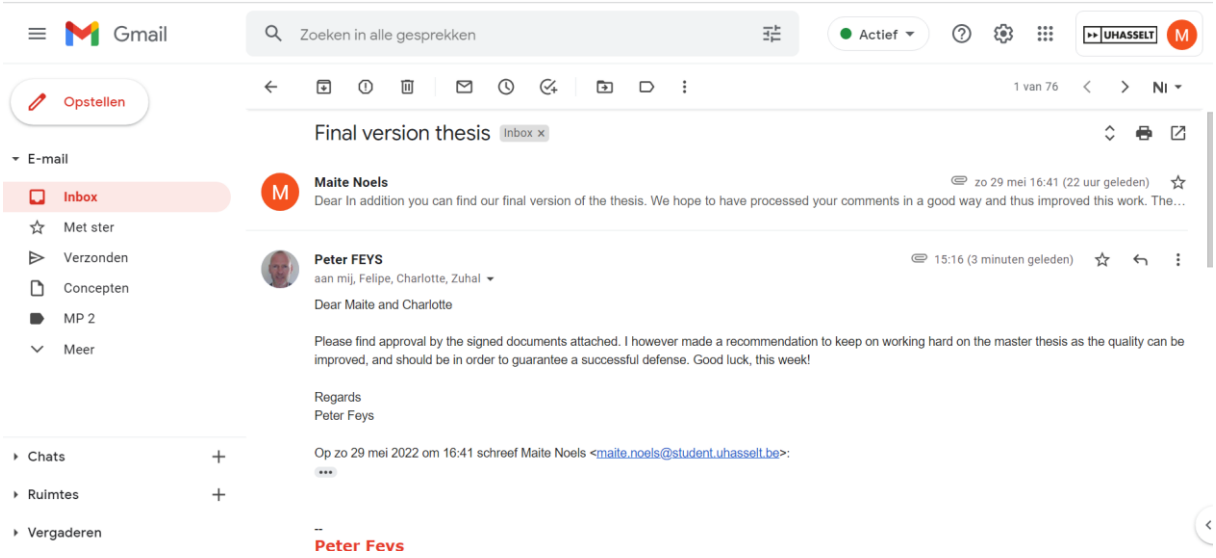
Datum en handtekening promotor(en)
Date and signature supervisor(s)

Peter Feys

30/5/2022

We raden je aan om deze week nog zorgvuldig verder te werken aan de hele masterproef, en te reflecteren hoe je de discussie nog verder inhoudelijk kan verdiepen.

Appendix 9


Gmail
Zoeken in alle gesprekken
Actief
UHASSELT
Opstellen
E-mail
Inbox
Met ster
Verzonden
Concepten
MP 2
Meer
Chats
Ruimtes
Vergaderen
1 van 76
Final version thesis
Inbox
Maite Noels
zo 29 mei 16:41 (22 uur geleden)
Dear In addition you can find our final version of the thesis. We hope to have processed your comments in a good way and thus improved this work. The…
Peter FEYS
15:16 (3 minuten geleden)
aan mij, Felipe, Charlotte, Zuhal
Dear Maite and Charlotte
Please find approval by the signed documents attached. I however made a recommendation to keep on working hard on the master thesis as the quality can be improved, and should be in order to guarantee a successful defense. Good luck, this week!
Regards
Peter Feys
Op zo 29 mei 2022 om 16:41 schreef Maite Noels <maite.noels@student.uhasselt.be>:
--
Peter Feys

Appendix 10

www.uhasselt.be
Campus Hasselt | Martelarenlaan 42 | BE-3500 Hasselt
Campus Diepenbeek | Agoralaan gebouw D | BE-3590 Diepenbeek
T + 32(0)11 26 81 11 | E-mail: info@uhasselt.be

UHASSELT
KNOWLEDGE IN ACTION

INVENTARISATIEFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
22/12/2021	- Bespreken onderzoek en planning	Promotor: Prof. Dr. Peter Feys Copromotor/Begeleider: Cintia Ramari Ferreira Student(e): Maite Noels Student(e): Charlotte Deschryvere
14/03/2022	- Feedback bespreken op introductie en methode - Brainstorm over aanpassing onderzoeksvraag	Promotor:Prof. Dr. Peter Feys (niet aanwezig) Copromotor/Begeleider: Cintia Ramari Ferreira, Felipe Balistieri Santinelli Student(e): Maite Noels Student(e): Charlotte Deschryvere
10/05/2022	- Feedback inleiding en methode - Bespreken uitvoering statistiek	Promotor:Prof. Dr. Peter Feys (niet aanwezig) Copromotor/Begeleider: Felipe Balistieri Santinelli, Zuhal Abasiyanik Student(e): Maite Noels Student(e): Charlotte Deschryvere
23/05/2022	- Feedback bespreken volledige MP - Bespreken uitvoering discriminatieve validiteit	Promotor:Prof. Dr. Peter Feys (niet aanwezig) Copromotor/Begeleider: Felipe Balistieri Santinelli Student(e): Maite Noels Student(e): Charlotte Deschryvere
01/06/2022	- Bespreken feedback volledige MP	Promotor:Prof. Dr. Peter Feys (niet aanwezig) Copromotor/Begeleider: Felipe Balistieri Santinelli, Zuhal Abasiyanik Student(e): Maite Noels Student(e): Charlotte Deschryvere