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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Overview of measurement methods of inter-limb coordination

Leen Boonen
Matthias Van Parijs

Eerste deel van het scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

PROMOTOR :
Prof. dr. Peter FEYS

COPROMOTOR :
Mevrouw Fanny VAN GEEL

2018
2019

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Overview of measurement methods of inter-limb coordination

“A lot of research has been done around coordination using expensive equipment in a neurologic setting”

“There is need for further research regarding coordination with clinical data.”

“*In neurologic patients, the efferent and afferent pathways may be damaged resulting in problems with muscle activation patterns.”*

“this review report different apparatuses and outcomes to obtain clinical data about coordination”

Leen Boonen & Matthias Van Parijs
1e master 2018-2019
Promotor: Prof. dr. Peter Feys
Co-promotor: Fanny Van Geel

Context of the master thesis

This master thesis belongs to the research domain of neurologic revalidation and is part of a doctorate study of Fanny Van Geel, co-promotor of this master thesis. The objective of this review is to define different ways to measure coordination using clinical data. Next year, in master thesis part 2, the findings of this study will be used to examine whether coordination is an influencing factor in walking fatigability in persons with Multiple Sclerosis (MS). This research will be done in REVAL Hasselt, at Hasselt University. In this review however, all neurologic patient groups will be included: there will be no distinction between MS and other neurologic conditions.

This literature study is written by two master students (LB and MVP) with counsel of promotor prof. dr. Peter Feys and daily mentoring by Fanny Van Geel. They chose for a central format for this thesis. Both students went through all steps of the literature study together.

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PART I: SYSTEMATIC REVIEW

PART I: SYSTEMATIC REVIEW

1 Abstract

Background:

A lot of research has been done around coordination. Most studies use expensive equipment in a neurologic setting. However, not a lot of research has been done using clinical data.

Methods:

A literature search was done in February 2019. Two electronic databases were consulted: Pubmed and Web of Science. The included studies were written in English and all look at the interlimb coordination in a neurologic population. 3D analysis and infrared cameras were excluded because data derived from these research methods can not be used in a clinical setting.

Results:

Eight articles were included. Two studies involved stroke patients, five studies focused on Parkinson's disease patients and one study was performed in pwMS. There were a total of four different research methods to examine coordination with clinical data. For every study, the task was different. Six studies had a walking task and in two studies patients were asked to perform a task while seated.

Discussion and conclusion:

In the articles we assessed, we found two types of data: sinusoidal waves and stepping phase value plots. The latter is analysed through the phase coordination index (PCI), whilst the former is analysed using frequency domain analysis or (continuous) relative phase.

Purpose of this research:

The objective of this study is to find the best method to evaluate interlimb coordination using clinical data in a neurologic population.

Operationalisation:

This review is part of the doctorate study of Fanny Van Geel under the direction of Peter Feys.

Important Keywords: Neurological condition, Interlimb coordination, Clinical data

2 Introduction

According to the Oxford English Dictionary, coordination is the ability to use different body parts smoothly and efficiently. According to this definition, efficiency is considered when a system achieves maximum productivity using minimal energy. Smoothness can be explained as the similarity of the parameters over a certain amount of time. Earlier research has identified the best parameters to examine coordination objectively, such as the cadence, stride length and speed[23]. However, more recent studies measure the variability of stepping phases to quantify coordination[1]. Others measure variability of the range of motion in joints[20].

Coordination is achieved by different kinds of muscle activation patterns learnt over time by practicing certain skills. Muscle activation patterns can be seen as the ability of the central nervous system to pass signals to different muscles in a specific order and with a certain force. Depending on the desired movement a different pattern with different muscles and forces will be activated[6]. To facilitate good coordination, three factors need to be present. Firstly, someone needs to be able to move in an alternating pattern, also known as the ability to work with agonist - antagonist muscle couples, where one relaxes if the other is contracting. The second aspect to good coordination is the ability to move in synergies. This is known as a spatiotemporal pattern of activity between muscles. A person has to be able to activate different muscles at the same time or in a certain sequence to reach the target goal[12]. Finally, accuracy is detrimental, which is acquired by the ability to estimate distances. This ensures a person can adjust the speed of a movement while it is still in process. (Physical rehabilitation, O'Sullivan, Ch 6, p217) In neurologic patients, the efferent and afferent pathways may be damaged resulting in problems with muscle activation patterns.

A recent study of Wallard L. et al. reports about the altered coordination in hemiplegic and osteoarthrosis patients compared to healthy controls. They found that an altered coordination leads to an increase in muscular mechanical work in both patient groups and an increase in energy expenditure for the hemiplegic group[22]. This increase in energy expenditure results in a person experiencing fatigue faster while performing the same task. The term fatigue is used here to refer to subjective sensations and fatigability to refer to objective changes in performance[8]. Research shows it is present in various neurologic conditions such as multiple

sclerosis, stroke, parkinson's disease and traumatic brain injury[4, 8, 11, 19]. In the same neurologic populations, walking can be problematic, this could be due to altered coordination. Therefore it is of the utmost importance to measure and objectify coordination as it would help identify people with increased fatigability while walking. A lot of research has been done regarding coordination with expensive equipment such as 3D video analyses and infrared cameras[3, 10, 14]. However, not a lot of research has been done on methods using clinical data such as accelerometers that can be used in a daily setting. In this review we will try to make an overview of different methods suited for the standard clinical setting to measure coordination in persons with a neurological disease, and how we can interpret this data.

3 Method

3.1 Research question

The research question led to a PICO (Population, Intervention, Control and Outcome) designed to extract relevant articles about our topic. The population in this review are people with a neurological condition. For this review there was no need for an intervention, nor a control group. The outcome was coordination defined as data specifically about interlimb coordination and not just walking asymmetry or walking variability.

Our research question was: “How can coordination between the limbs be measured and how is this data interpreted for persons with a neurological condition”.

3.2 Literature search

Using two electronic databases, “Pubmed” and “Web of Science”, we did a literature search for this review. We started the study in February 2019 and used the following five Medical Subject Headings(MeSH) and keywords: *interlimb coordination, lower extremity, upper extremity, gait and neurological conditions.* The following search strategy was: *((interlimb coordination) AND lower extremity[MeSH Terms]) AND upper extremity[MeSH Terms]) OR gait[MeSH Terms]) AND neurological conditions.*

3.3 Selection criteria

All included articles had to be written in English or Dutch, have a group of adults (18+) with a neurological condition and contain clinical data on interlimb coordination. Reviews, case reports and animal studies were instantly excluded by the evaluators. Studies without clinical data, like a 3D video analysis or camera system analysis for measuring interlimb coordination, were excluded. The reason for this exclusion was that the equipment is too expensive and not available to the researchers.

3.4 Quality assessment

The checklist used to assess the quality of each individual article was the Physiotherapy Evidence Database (PEDro) checklist. This checklist consists of eleven questions and is used to check the bias risk of the included articles. The maximum score is eleven points which was converted into a percentage in this review. The score was performed by one assessor and was verified by a different assessor in order to reduce the risk of bias.

3.5 Data-extraction

Taking our research question into consideration, relevant data was extracted from the included articles. The descriptive data includes the sample size and patient characteristics, being age and type of neurologic condition. Experimental data related to the apparatus that was used to measure coordination, and the particular outcome measures during the respective performed tasks were listed as well. Finally, the articles were examined to determine whether they had a control group or an intervention group. If the latter was the case, the differences between the groups were also reported. These differences are only used as extra info to have an indication if the method finds a difference between patients with coordination problems and those who do not.

4 Results

4.1 Results article selection

In February 2019, the search strategy resulted in 950 articles, 521 on Web of Science and 429 on Pubmed. After deduplication 880 remained, where 777 got excluded based on screening for title and abstract text. Reading the full text of the remaining 103 articles, resulted in only 3 articles including clinical measurements, and these were therefore automatically included in our research. Finally another 5 articles were included from cross referencing, which resulted in a total of 8 articles being included. Figure 1 portrays this process schematically.

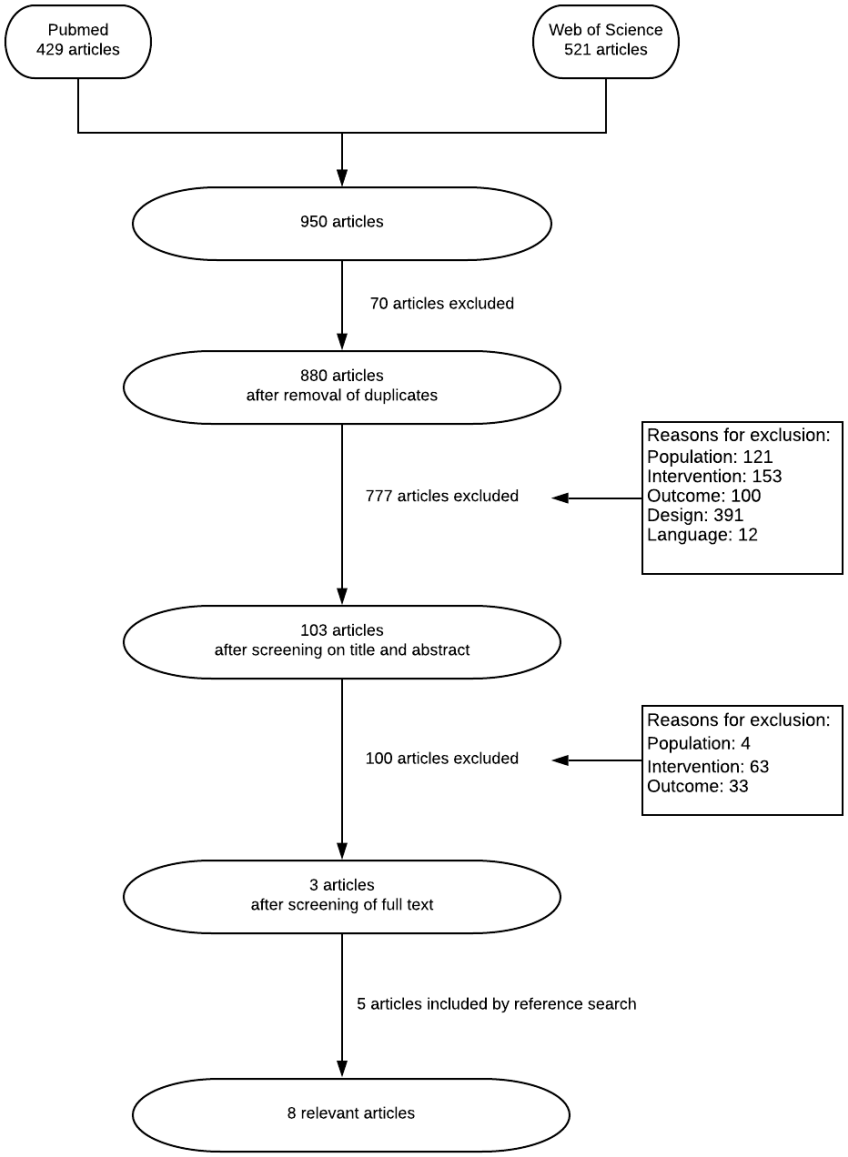

Fig. 1 *study selection process*

4.2 Results quality assessment

Results of the quality assessment are found in table 1. All articles except one had a minimum score of 55% (≥ 6/11). The remaining article had a score of 45% (5/11). For items C1 (eligibility criteria), C4 (groups were similar at baseline), C8 (variability of key outcome measures or more than 85% of the subjects), C9 (intention to treat analysis), C10 (between group statistical comparisons) and C11 (point measures and measures of variability) 95% of the articles were satisfied. No articles were excluded based on the quality assessment because we only had a small number of articles and the results of the quality assessment are still acceptable.

Table 1

Quality assessment of the included Studies Using the PEDro Checklist

Quality Assessment	type of study	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
Debaere et al. (2001)	clinical trial	Y	N	N	Y	N	Y	U	Y	Y	Y	Y
Kwakkel et al. (2002)	RCT	Y	Y	Y	Y	N	N	N	Y	N	Y	Y
Peterson et al. (2012)	clinical trial	Y	N	N	Y	N	U	U	Y	Y	Y	Y
Plotnik et al. (2009)	clinical trial	Y	N	N	Y	N	Y	U	Y	Y	Y	Y
Plotnik et al. (2008)	clinical trial	Y	N	N	Y	N	U	U	Y	Y	Y	Y
Plotnik et al. (2007)	clinical trial	Y	N	N	N	U	U	U	Y	Y	Y	Y
Swinnen et al. (1997)	clinical trial	Y	N	N	Y	U	Y	U	Y	Y	Y	Y
Wurdeman et al. (2011)	clinical trial	Y	N	N	Y	N	Y	U	Y	Y	Y	Y

RCT: Randomized controlled trial; C1: eligibility criteria; C2: randomly allocated to groups; C3: allocation was concealed; C4: groups were similar at baseline; C5: blinding of all subjects; C6: blinding of all therapists; C7: blinding of all assessors; C8: variability of key outcome measures of more than 85% of the subjects; C9: intention-to treat analysis; C10: between-group statistical comparisons; C11: point measures and measures of variability; Y: yes; N: No; U: unkown

4.3 Results data-extraction

4.3.1 Patient characteristics

In table 3, an overview of patient characteristics is listed. Sample size of each intervention group varies from 12 to 21 subjects. Average age varies from 26 to 76. There are different neurological groups in the articles, varying from multiple sclerosis (n=1)[24] and stroke (n=2)[2, 9] to Parkinson's disease (n=5)[15-18, 21]. Most studies (n=5)[2, 15, 18, 21, 24] contain a control group, 1 article included an intervention[17] and another 1 article included both[9].

4.3.2 Coordination task

The tasks that were performed by the subjects to measure coordination, vary for some studies, see table 2.

The majority (n=6)[9, 15-18, 24] used a walking task, the remaining articles (n=2)[2, 21] used a task while seated. The latter two used a coordination chair. This is a chair where subjects are seated and strapped on moveable 'manipulanda' so that movement is restricted to the sagittal plane. Movement registered was of flexion-extension in the examined joint[2, 10].

One study used four uniaxial accelerometers that were positioned at the distal tibia of both legs and at the lateral part of the wrist of both arms of the subjects[9]. Another four studies used force sensitive footswitches. These are placed in the soles of the shoes to measure vertical ground reaction forces. Using this data, a phase coordination index (PCI) can be calculated[15-18].

Lastly, one study used force plates over a distance of ten meters to measure ground reaction forces (GRF) in a single limb[24].

4.3.2.1 Walking task

Each study used a walking task with differing instructions and duration or distance. In one study, the subjects were asked to walk 10 meters at a comfortable walking pace and a maximal walking pace[9]. Another study used a series of six walking tasks, being forward- and backward walking, turning left and right in a small radius circle and lastly, turning to the left and right in a large radius circle[15]. For 3 studies, the subjects had to walk at a comfortable walking speed for two minutes[16], for ten meters[24] and for eighty meters[17]. The last study used a cognitive

dual task, where subjects had to walk for two minutes while making series of subtractions by seven[17].

4.3.2.2 Seated task

The seated coordination task was similar for both remaining studies, where the subjects had to perform a flexion-extension movement of the knee.[2, 21]

For the first study, subjects had to move cyclically with either one limb or two limbs simultaneously. There was a randomised order of trials that consisted of a trial with only forearm movement, a trial with only lower leg movement, a trial with both limbs in an isodirectional way and another trial with both limbs in an nonisodirectional way. The pace at which the subjects had to move was given by a metronome at 66 beats per minute[2].

The second study also used cyclical movements paced by a metronome at 60 beats per minute. There was a randomised order of trials that consisted of a trial in a homologue way, meaning the movement of two arms or two legs simultaneously. One trial in a homolateral way, this is either a combination of the left arm and left leg or the right arm and right leg. The third trial was one in a heterolateral way, being a combination of either the left arm and the right leg or the right arm and the left leg. Within each combination, half of the trials was performed in an isodirectional way, the other half was in a nonisodirectional way[21].

4.3.3 Outcome

The outcome measures are listed in table 2. Noteworthy outcomes are the phase coordination index (PCI), frequency domains and relative phase (RP) or continuous relative phase (CRP). The last two parameters are the same, but were given a different name by different authors. See figure 2 for a schematic overview of the following data analysis.

The PCI, obtained by the force sensitive footswitches, is a metric introduced by Plotnik and co-workers in 2007. To understand the PCI, the phase (φ) needs to be defined. It is the relative timing between two heel strikes (ideally 180 degrees). The PCI in return, is the sum of the variation of φ and the mean absolute difference between φ and 180 degrees. With this formula information is provided for both gait variability and accuracy. A higher value of PCI indicates that coordination is worse.

Relative phase/ continuous relative phase, obtained by the seated tasks and the uniaxial accelerometers, is calculated from a data set of two sinusoidal waves obtained from each examined limb. It is the difference between the angles of both waves at the same point (on the x-axis) of the wave. A larger difference, would mean more variability of the stepping pattern, indicating a worse interlimb coordination. This angle is derived from the tangent of each point. The formula used is the following:

$$\phi = \theta a - \theta l = tan^{-1}\left[\frac{\left(\frac{dX_a}{dt}\right)}{X_a}\right] - tan^{-1}\left[\frac{\left(\frac{dX_t}{dt}\right)}{X_l}\right]$$

Obtaining the standard deviation (SD) of all the angles of one curve allows us to determine the variability in this wave. A higher SD means more variability, which in turn means a worse coordination of the leg corresponding to that wave. A statistical difference between both legs, indicates bad interlimb coordination.

Frequency domain analysis, used by the walking task with force plates, is performed by calculating the integral of the sinusoidal curve. According to Wurdeman et al., using this type of analysis it is possible to analyse the entire gait cycle instead of discrete points or events in the cycle[24]. The data that is used in this case is derived from a force platform. To transfer this data into a sinusoidal wave, first a Fourier transformation needs to be applied. Then three different integrals are calculated. The first is that of the 99.5% frequency, meaning it is the integral of 99.5% of the wave. Then the integral of the median frequency is calculated. And lastly the bandwidth frequency, this is the integral of the maximum frequency subtracted by the minimum frequency. To determine whether there are any differences between the groups, an independent t-test was performed.

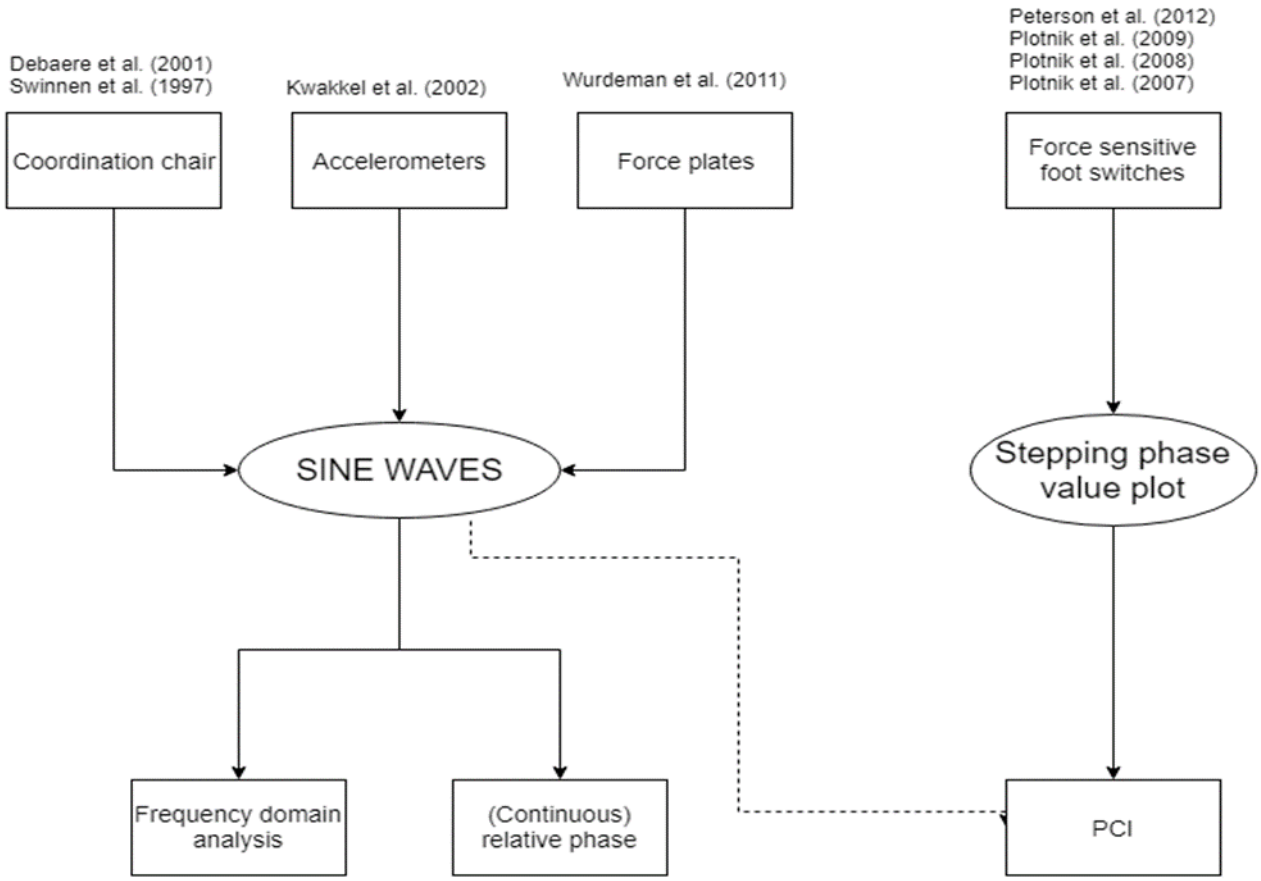

Fig. 2 *Representation of data analysis*

4.3.4 Difference or improvements

The difference between groups and controls or the improvements between intervention and controls are listed in table 3.

Debaere et al. (2001)[2], a study between healthy controls and stroke patients**,** found that the absolute deviation from target relative phase (RP) was larger in stroke patients (M=57.73°) compared to control subjects (M=28.52°). The isodirectional mode was significantly more accurate (M=25.13°) than the nonisodirectional mode (M=61.13°) (P<0.05).

Kwakkel et al. (2002)[9] had both a control group and two intervention groups. One of the intervention groups received 5x/week upper extremity training. The other group, received 5x/week lower extremity training. Comparing results at the end of the study with baseline, all three groups had improvements in mean comfortable walking speed going from 0.39m/s to 0.73m/s. Improvements were also found for the mean maximal walking speed, going from

0.53m/s to 0.96 m/s. For both these results, no significance level was mentioned suggesting no statistical analysis was performed on this data. However, statistical analysis was performed to investigate changes between the three groups. This showed there was a statistical difference for comfortable walking speed ($F=3.52$, $df=2$, $P=0.037$). After a post hoc analysis, it became clear that the lower extremity group had larger improvements for the comfortable walking speed compared to the control group ($t=-2.408$, $df=33$, $P=0.022$).

Peterson et al. (2012)[15] compared healthy controls and people with Parkinson's disease. The Parkinson group was divided into those with (PD +FOG) or without freezing of gait (PD-FOG). The control subjects had the lowest PCI values and the PD + FOG had the highest PCI in all walking conditions ($p<0.001$). Meaning the latter group had worse coordination.

Plotnik et al. (2009)[18] had a control group and a Parkinson's disease group. In the Parkinson's disease group (PD group), the PCI was significantly higher during dual tasks ($P<0.001$) compared to walking without dual tasks. This was not the case in healthy controls ($P= 0.29$). The change in PCI was associated with the changes in gait variability in the PD group.

Plotnik et al. (2008)[17] compared Parkinson's disease with freezing of gait (PD+FOG) and Parkinson's disease without freezing of gait (PD-FOG). They showed that mean values of ϕ_CV, ABS_ϕ and PCI were significantly higher in the 'off' state for the PD + FOG group in comparison with the PD - FOG group ($P \leq 0.034$). During the 'on' state, within group effects revealed that the PCI became less variable meaning a better coordination for both the PD + FOG group ($P = 0.059$) and the PD-FOG group ($P>0.9$). The proportion of gait adjustments were significantly different, where the converging shifts were higher than the diverging shifts ($P < 0.005$). This implied that both groups used more strides to make up for alterations in PCI.

Plotnik et al. (2007)[16] had 3 groups: one group of healthy elderly, one group of healthy adults and one with Parkinson's disease. They found different PCI values between all groups. The PCI values of the PD-group were higher compared to healthy elderly controls ($P<0.006$). Furthermore the PCI-values of the healthy elderly controls were higher than those of the young adults ($P<0.001$). Values for gait asymmetry were also significantly higher for the PD-

group compared with the healthy elderly subjects ($P<0.04$), and the same values were higher when comparing the healthy elderly to the young adults ($P<0.05$).

Swinnen et al. (1997)[21] report that PD patients had worse coordination compared to elderly subjects, with an absolute deviation from relative phase of 39.4° and 26.4° respectively ($P<0.05$).

According to the study of Wurdeman et al. (2011)[24], in which patients with Multiple Sclerose (MS) were compared to healthy controls, MS had a significantly lower 95% frequency ($P = 0.006$) and lower median frequency in the vertical direction ($P < 0.001$). Average walking speed was significantly lower in MS (1.02 m/s) than in healthy controls (1.23 m/s) ($P<0.001$).

Table 2

Main coordination

References	apparatus	Task	Outcome measure
Debaere et al. (2001) J.M. Exp Brain Res	Coordination chair	Sitting position: cyclical flexion-extension movements of either single limbs or two limbs at the same time (according to the isodirectional and nonisodirectional coordination modes) at the pace provided by the metronome (66 beats/min)	relative phase (accuracy and consistency); amplitude(mean and variability); cycle duration(mean and variability)
Kwakkel et al. (2002) J Phys Ther .	4 uniaxial accelerometers	Walk 10m at comfortable and maximal walking speeds.	walking speed; CRP: paretic arm and leg + nonparetic arm and leg
Peterson et al (2012) J.Parkreldis	Force sensitive footswitches	6 gait tasks: forward, backward, turning to the left and right in a small radius circle, and turning to the left and right in a large radius circle	PCI(vertical ground reaction forces): integration of accuracy and consistency of left-right stepping phases
Plotnik et al (2009) J Neurol Neurosurg Psychiatry.	Force sensitive footswitches	Usual walking with and without double task(repeatedly subtracting 7 from 500): the subjects walked, roughly in a straight line, for 2 min at a comfortable pace in a well-lit, obstacle free, 25m long, 2m wide corridor	PCI(vertical ground reaction forces): integration of accuracy and consistency of left-right stepping phases
Plotnik et al (2008) Eur J Neurosci.	Force sensitive footswitches	Walk for a total of 80m at their comfortable pace	PCI(vertical ground reaction forces): integration of accuracy and consistency of left-right stepping phases
Plotnik et al (2007) J.M. Exp Brain Res	Force sensitive footswitches	Walk at their normal pace for 2 min in a 25-m long, 2-m wide, well-lit corridor	PCI(vertical ground reaction forces): integration of accuracy and consistency of left-right stepping phases
Swinnen et al. (1997) Mov. Disord.	Coordination chair	Sitting position: cyclical flexion-extension movements using two of the four limbs at the pace provided by a metronome (60 beats/min). Three limb combinations were performed: homologous, homolateral and heterolateral(diagonal)	relative phase (accuracy and consistency); amplitude(mean and variability); cycle duration(mean and variability)
Wurdeman et al (2011) Clin Biomech (Bristol, Avon).	Force plates	Walking at a comfortable walking speed(10m), each limb was analysed separately	GRF frequency content values (Hz) for anterior-posterior and vertical directions (Sinus-waves); walking velocity

CRP: continuous relative phase; PCI: phase coordination index; GRF: ground reaction forces;

Table 3
Results of the included articles

Author		Age	Number of subjects	Apparatus	Neurological condition	Control group (Yes/No)	Difference (If control)	Intervention (Yes/No)	Improvement (If intervention)
Debaere et al. (2001) J.M. Exp Brain Res	Healthy controls	56,2	20	coordination chair	Stroke	Yes	Absolute deviation from target relative phase: Stroke: M=57.75° Control: M=28.52° The isodirectional mode: M=25.13° The nonisodirectional mode: M=61.13° (P<0.05)	No	
	Neurological group	58,5	20						
Kwakkel et al. (2002) J. Phys Ther .	Control group	62,1	18	4 uniaxial accelerometers	Stroke	Yes	Mean comfortable walking speed of the 3 groups improved from 0.39 m/s to 0.73 m/s. Mean maximal walking speed increased from 0.53 m/s to 0.96 m/s. Main effects were found for time (F=7.95; df=5,250; P<.001), walking speed (F=7.49; df=1,50; P=.009), and limb pair (F=26.06; df=1,50; P<.001)	Yes	comfortable walking speed: larger improvements in LE group vs control group (P=0.022) larger improvement in LE group vs UE group (P =0.039)
	UE Group	64,3	18						
	LE Group	60,8	17						
Peterson et al. (2012) j.parkreldis	Healthy controls	69	10	six round footswitches	parkinson	Yes	PCI index in all walking conditions(p<0.001): lowest in control highest in PD+FOG	No	
	Freezers	72	12						
	Non-freezers	71	19						
Plotnik et al. (2009) J Neurol Neurosurg Psychiatry.	Healthy controls	68,4	13	force sensitive footswitches	Parkinson	Yes	PCI: higher during dual task in PD (P<0.001) not significantly in healthy controls (P= 0.29) PD group: change PCI associated with changes gait variability	No	
	Neurological group	71,9	21						
Plotnik et al. (2008) Eur J Neurosci.	Freezers	60,6	21	force sensitive footswitches	Parkinson	No		Yes	During 'off' state: mean values of ϕ_CV, ABS_ϕ and PCI significantly higher for PD + FOG group vs PD - FOG group ($P \leq 0.034$). During 'on' state: PCI less variable for both groups (PD + FOG group (P = 0.059); PD-FOG group (P>0.9)) Diverging stride to stride adjustments: larger errors for PD + FOG group vs the PD - FOG group (P<0.006).
	Non-freezers	64,6	13						
Plotnik et al. (2007) J.M. Exp Brain Res	Healthy eldery	69,1	14	force sensitive footswitches	Parkinson	Yes	PCI values: higher in PD vs healthy elderly(P<0.006) higher in healthy elderly vs young adults (P<0.001) values gait assymetry: higher for PD group vs elderly subjects (P<0.04) higher for healthy elderly vs young adults (P<0.05)	No	
	Healthy young adults	26,3	15						
	Neurological group	71,9	21						

Author		Age	Number of subjects	Apparatus	Neurological condition	Control group (Yes/No)	Difference (If control)	Intervention (Yes/No)	Improvement (If intervention)
Swinnen et al. (1997) Mov. Disord.	Healthy controls	76,4	10	coordination chair	Parkinson	Yes	Absolute deviation from required phase(P<0,05): PD patients: 39,4° elderly subjects: 26,4°	No	
	Neurological group	67,8	10						
Wurdeman et al. (2011) Clin Biomech (Bristol, Avon).	Healthy controls	39,2	18	force plates	MS	Yes	MS: significantly lower 95% frequency in vertical direction (P=0.006), lower median frequency in vertical direction (P<0.001) Average walking speed(P<0.001): MS: 1,02m/s healthy controls: 1,23m/s	No	
	Neurological group	45,3	18						

UE group: Upper-Extremity Intervention; LE group: Lower-Extremity intervention; PCI: phase coordination inde; PD: Parkinson disease

5 Discussion

Two different types of datasets were obtained: sinusoidal waves and stepping phase value plots. Three different methods were found in the articles used for analysis. Most studies reported bigger changes in coordination in the neurologic groups when compared to healthy controls. The hypothesis of patients that were expected to have a worse coordination when compared to other patients got confirmed as well. This indicates that the aforementioned methods are a good tool to measure coordination in a neurologic population.

5.1 Reflection about quality studies

All included articles have a fair to high quality according to the PEDro checklist. This means the risk for bias is low. Most articles had a lack of blinding, for both the researchers and the subjects. Not a single article had blinding of the subjects or the assessors and only 2 articles had blinding of the therapists taking the tests. Due to the fact that all the articles had some issue with blinding, there could be an increased risk for performance bias and detection bias. Given the nature of the studies, this seems rather unimportant because blinding is not applicable to the research. Blinding the assessors is not possible because they need to understand the experiment. Blinding the subjects is not possible either, simply because they need to know what task to perform. Therefore, we think this performance or detection bias is only a minor bias, if there is any at all.

The sample size of all articles was at least 20. These subjects then got divided into their respective groups. Small sample sizes can lead to a larger variance or generalisation of the results, so these studies will be assessed critically.

5.2 Reflection on the findings in the review

There are several differences observed in the tasks and apparatuses used in the included articles making it hard to conclude which method is the most efficient or best to use. The coordination chair of Debaere et al. (2001)[2] and Swinnen et al. (1997)[21] are very different from the other six articles because the task performed is seated. This means some factors regarding coordination do change. When a person is seated, they do not have to adjust for postural

changes as much. However, this is the case in the walking tasks, making it particularly hard to generalise these findings to daily life activities. Datasets derived from this chair, is similar to the accelerometers used by Kwakkel et al.[9], more so, it is analysed in the same way. This leads to think that the coordination chair is a good way to observe interlimb coordination because it isolates coordination from potentially unrelated external factors. A more sophisticated approach to obtaining these sinusoidal waves are the force plates used in Wurdeman et al. (2011)[24]. Although in this study it is analysed differently, through frequency domain analysis. However, it is impossible to say which one is more valid without having more research done on the subject.

Lastly, the force sensitive footswitches used by Plotnik et al.[16-18] and Peterson et al.[15], yield different data compared to the above mentioned articles. The stepping phase value plots depicted in these articles are more simple in the way that they only give temporal information coming from heel strikes. In contrast to the coordination chair and the accelerometers, they also give information to limb swing speed and acceleration. The function 'position by time' can be used to calculate these parameters.

However, using these footswitches, it is possible to obtain a large pool of data points. Running this dataset through a program using the formula of the PCI, it is possible to see patterns in coordination changes throughout the day. This is achieved as a result of the offline gathering method attributed to the force sensitive footswitches.

Interestingly, sinusoidal data can also be analysed using the PCI method. Using the sine waves, a specific point on the graph can be used as the temporal input originally coming from the heel strikes. For example, using the coordination chair, a point of interest throughout the extension-flexion range, can be set as the position similar to the one seen in studies from Plotnik et al.[16-18] or Peterson et al.[15]. The accelerometers worn by subjects of Kwakkel et al.[9] were easier to use. There, it is possible to find the heel strikes as demonstrated in a study of Godfrey et al.[5]. The articles examined in this review did not use this method, however other authors have proven to use this metric with accelerometers[7, 14].

This makes the PCI a very compelling method to do more research with, because it could combine different forms of data into the same outcome results.
To the best of our knowledge, no research has been done to examine the validity of the PCI.

5.3 Limitations

We acknowledge several limitations in this review. Only two databases were used (Pubmed and Web of Science). This could mean relevant articles were not found and therefore not included in our pool of articles.

Five of the included articles are obtained from cross referencing. This was done because not a lot of research has been done with clinical data on a neurologic population. This could also be due to a flaw in our initial search string.

Only articles with the English or Dutch language were included, this could lead to a bias based on language. This selection had to be done because the assessors who analysed this review only had profound knowledge of these languages.

It is possible several studies never got published, leading to publication bias.

5.4 Recommendations for future research

There is need for further research regarding interlimb coordination with clinical data. This review only contains eight articles, of which three come from the same author. Therefore additional research is needed in the neurologic setting to determine whether neurologic patients have an altered coordination and what the impact would be in the daily lives of these patients. We suggest research around the validity of the PCI method, as well as the difference between frequency domain analysis compared to the relative phase methods.

Also, after this research, it is needed to find a way to integrate the formulas used in the PCI and relative phase into a software application useable by clinicians. Therapists could then identify altered coordination in their daily practice to adjust training modalities if possible.

6 Conclusion

Two different datasets, sine waves and stepping phase value plots, regarding coordination can be analysed in three different ways. Sine waves can be examined through frequency domain analysis and (continuous) relative phase. Where the stepping phase value plots can be analysed using the Phase Coordination Index. This PCI can also be used to analyse sine waves if the data set is altered a little bit by marking the heel strikes. This would generate a stepping phase value plot.

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8 Appendix part I – Overview tables

Table 4
Overview of number of hits and final search term in PubMed

Mesh-termen en key words		Hits februari 2019
#1	“Interlimb coordination” [All fields]	543
#2	Lower Extremity [Mesh]	18182
#3	Gait [Mesh]	25 390
#4	“Neurological condition” [All fields]	102 915
#5	#1 AND #2	56
#6	#1 AND #3	98
#7	#1 AND #4	11
#8	#2 AND #3	199
#9	#2 AND #4	77
#10	#3 AND #4	425
#11	#1 AND #2 AND #3	13
#12	#1 AND #2 AND #3 AND #4	1
#13	#1 AND (#2 OR #3) AND #4	6
#14	#1 AND #2 OR #1 AND #3	98
#15	#1 AND #2 AND upper extremity[Mesh] OR #3 AND #4	429

Table 5
Overview of number of hits and final search term in Web Of Science

Mesh-termen en keywords		Hits februari 2019
#1	“Interlimb coordination”	1242
#2	“Lower extremity”	55 659
#3	“Gait”	64 766
#4	“Neurological condition”	20 386
#5	#1 AND #2	44
#6	#1 AND #3	339
#7	#1 AND #4	5
#8	#2 AND #3	4367
#9	#2 AND #4	216
#10	#3 AND #4	483
#11	#1 AND #2 AND #3	24
#12	#1 AND #2 AND #3 AND #4	1
#13	#1 AND #2 AND 'upper extremity' OR #3 AND #4	521

Table 6

Overview of excluded articles on abstract and title

Reason of exclusion	Amount of articles	References
Population	125	Abu-Faraj et al. (2015); Acker et al. (2017); Akram et al. (2010); Alter et al. (2015); Ballesteros et al. (2019); Bona et al. (2017); Bondi et al. (2017); Bronas et al. (2018); Brott et al. (1994); Brunner et al. (2008); Cechetti et al. (2016); Clemson et al. (2012); Damiano et al. (2011); Darter et al. (2017); Delafontaine et al. (2018); Djukic et al. (2016); Donath et al. (2016); Duffy et al. (1997); Engstrom et al. (2018); Fecarotta et al. (2015); Fischer et al. (2015); Flensmark (2004); Foster et al. (2013); Franz et al. (2007); Getchell et al. (2003); Gomes et al. (2018); Gow et al. (2017); Gregory et al. (2016); Gregory et al. (2016); Guillebastre et al. (2009); Hamacher et al. (2016a); Hamacher et al. (2016b); Harada et al. (2009); Heffez et al. (2004); Heredia-Jimenez et al. (2016); Hocking et al. (2010); Holtzer et al. (2018); Holtzer et al. (2016); Howard et al. (2017); Hsieh et al. (2018); Insuga et al.(2018); Jordbru et al. (2014); Kalsi et al. (2016); Kaneko et al. (2018); Kannape et al. (2010); Kaski et al. (2012); Kim et al.(2018); Klarner et al. (2013); Kluzik et al. (2007); Knikou et al. (2013); Konig et al. (2018); Krasovsky et al. (2010); Kribus-Shmiel et al. (2018); Krishnan et al. (2017); Kwon et al. (2015); La Scaleia et al. (2018); Laufer (2003); Lee et al. (2017); Lee et al. (2008); Leung et al. (2014); Ma et al. (2016); Ma et al. (2018); Maidan et al. (2018); Marquez et al. (2014); Mazur et al. (2009); McIntosh et al. (2006); Menant et al. (2018); Menzer et al. (2010); Miguet et al. (2018); Mindler et al. (2014); Mirelman et al. (2017); Moevus et al. (2015); Montero-Odasso et al. (2016) ; Montero-Odasso et al. (2017); Moreira et al. (1992); Moreno et al. (2013); Morley et al. (2018); Moscufo et al. (2012); Nair et al. (2014); Nessler et al. (2009); Nessler et al. (2015); Nigro et al. (2015); O'Keefe et al. (2016); Oh et al. (2018); Ozinga et al. (2014); Pavcic et al. (2014); Pedoia et al. (2018); Pickett et al. (2012); Pizzamiglio et al. (2018); Preis et al. (1997); Ramos et al. (1997); Ready et al. (2019); Rebula et al. (2013); Reuben et al. (2013); Rhea et al. (2014); Rim et al. (2009); Romkes et al. (2017); Rosenblatt et al. (2014); Rosso et al. (2014); Rozumalski et al. (2008); Santos et al. (2014); Saussez et al. (2017); Schirinzi et al. (2018); Schneiders et al. (2010); Shah et al. (2018); Shu et al. (2016); Sivarajah et al. (2018); Solopova et al. (2017); Sorrentino et al. (2016); Steiger et al. (1993); Sukits et al. (2014); Swanson et al.(2018); Tavakoli et al. (2016); Teive et al. (2015); Thomas et al. (2007); Tian et al. (2018); Tian et al. (2016); Ungar et al. (2015); Vakili et al. (2013); Wang et al. (2019); Weiss et al. (2017); White et al. (2011); Wolfson et al. (1996); Yogev-Seligmann et al. (2012); Zwergal et al. (2012)
Intervention	216	Adams et al. (2016); Alcock et al. (2018); Allali et al.(2016); Allali et al. (2014); Anderson et al. (2019); Arcolin et al. (2015); Ardila (1993); Armand et al. (2006); Aurich-Schuler et al. (2017); Bach et al. (1990); Baker et al. (2018); Ballesteros et al. (2017); Bank et al. (2018); Barnes et al. (2007); Benninger et al. (2010); Bernad-Elazari et al. (2016); Bernhard et al. (2018); Bertoli et al (2018); Bilney et al. (2005); Buchman et al. (2014); Camerota et al. (2016); Canning et al. (1997); Cattaneo et al. (2012); Chaparro et al. (2017); Chiron et al. (2018); Cholewa et al. (2017); Chui et al. (2000); Crnalic et al. (2013); Cubo et al. (2000); Dagan et al. (2017); Dasgupta et al. (2018); del Olmo et al. (2005); Dennis et al. (2000); Di Russo et al. (2013); Do et al. (2011); Do et al. (2013); Dona et al. (2016); Doo et al. (2015); Ebersbach et al. (1999); Ellingsen et al. (2016); Esser et al. (2011); Fan et al. (2018): Fazio et al. (2013); Ferrari et al. (2016); Fok et al. (2010); Fok et al. (2012); Galiana et al. (2005); Ganesan et al. (2015); Gazzani et al. (1999); Geroin et al. (2015); Geroldi et al. (2003); Ghoseiri et al. (2009); Ghosh et al. (2014); Giladi et al. (1997); Gomez-Rodriguez et al. (2011); Grobbelaar et al. (2017); Gross et al. (1999); Haack et al. (2016); Hadjivassiliou et al. (1998); Haggard et al. (2000); Hannink et al. (2018); Hausdorff et al. (1997); Hedera et al. (2018); Hennerici et al. (1994); Hesse et al. (1994); Hickey et al. (2016); Hidler et al. (2008); Hopf et al. (2000); Hunt et al. (2018); Hunt et al. (2008); Hunter et al. (2018); Hwang et al. (2013); Iluz et al. (2014); Ishikawa et al. (1996); Jacobs et al. (2018); Jayaraman et al. (2018); Jenkins et al. (2009); Jensen et al. (2004); Kaczmarczyk et al. (2012); Kalron (2017); Kalron et al. (2016); Kang et al. (2012); Kastrup et al. (2010); Kim et al. (2010); Klawans (1986); Klein et al. (1987); Kohno et al. (1995); Kremen et al. (2011); Kroneberg et al. (2019); Kuruvilla et al. (2000); Laidet et al. (2015); LaPointe et al. (2010); Larsson et al. (1991); Lazaro et al. (2011); Leners

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Outcome	133	Abdalian et al. (2013); Abode-Iyamah et al. (2016); Aboud et al. (2019); Achiron et al. (1993); Agosti et al. (2016); Amboni et al. (2018); Araujo et al. (2015); Arya et al. (2016); Auvinet et al. (2012); Awai et al. (2017); Aziz et al. (2006); Banga et al. (2018); Bansal et al. (2016); Banz et al. (2008); Baratin et al. (2015); Bella et al. (2017); Benedetti et al. (2012); Bennett et al. (1999); Bertolucci et al. (2015); Bladh et al. (2012); Blumrosen et al. (2016); Borst et al. (2018); Braz et al. (2007); Bressel et al. (2002); Briley et al. (1997); Bruno et al. (2016); Brutsch et al. (2011); Brutsch et al. (2010); Buchowski et al. (2009); Burkhard et al. (2003); Burkhardt et al. (2017); Busse et al. (2004); Busse et al. (2006); Butler et al. (2017); Calancie et al.(1991); Chang et al. (2000); Chen et al. (2011); Cho et al. (2010); Chockalingaw et al. (2006); Combs et al. (2012); Connolly et al. (2000); Damiano et al. (2017); de Tommaso et al. (2015); Deligianni et al. (2018); DelMarco et al. (2017); Di Rienzo et al. (2013); Dietz et al. (1998); Do Carmo Vilas-Boas et al. (2017); Dziezyc et al. (2015); Elble et al. (1992); Esser et al. (2012); Fagert et al. (2017); Fasano et al. (2016); Forsell et al. (2017); Fox (2015); Gandolfi et al. (2017); Grasmucke et al. (2017); Halpern et al. (1991); Handojoseno et al. (2012); Heckman et al. (2017); Helweg-Larsen et al. (2000); Hidler et al. (2004); Ho et al. (2017); Hornby et al. (2012); Horst et al. (2009); Iosa et al.(2016); Jehu et al. (2018); Kautz et al. (2005); Kincses et al. (2017); King et al. (2008); Kizony et al. (2010); Kleiner et al. (2018); Lazennec et al. (2018); Lempert et al. (1991); Lencioni et al. (2017); Lencioni et al. (2018); Lexell et al. (2012); Liao et al. (2008); Lindenberg et al. (2014); Liouta et al. (2017); Lord et al. (1998); Macfarlane et al. (2015); Mackey et al. (2008); Manabe et al. (2010); Manosalva et al. (2018); Mari et al. (2014); Mashola et al. (2019); Michaud et al. (2004); Mikolajczyk et al. (2018); Mirek et al. (2018); Ni et al. (2003); Nishimura et al. (2018); Pagliano et al. (2011); Palmer et al. (2012); Pasluosta et al. (2018); Patane et al. (2017); Pehlivan et al. (2017); Pendharkar et al. (2008); Perumal et al. (2008); Pittaccio et al. (2013); Portnoy et al. (2018); Ricklin et al. (2018); Rodgers et al. (1999); Rodrigo et al. (2008); Roemmich et al. (2013); Roiz et al. (2011); Sant'Anna et al. (2011); Sawicki et al. (2006); Scafetta et al. (2009); Schlenstedt et al. (2017); Schmidt et al. (2001); Schmidt et al. (2002); Shan et al. (2001); Skinner et al. (2015); States et al. (2011); Stolze et al. (2000); Studer et al. (2015); Tunca et al. (2017); Tupa et al. (2015);Ustinova et al. (2017); van den Bogert et al. (2013); Vilas-Boas et al. (2017); Vitale et al. (2012); Wellner et al. (2007); Williams et al. (2011); Williamson et al. (2015); Wu et al. (2010); Yang et al. (2019); Yoneyama et al. (2016); Zehr et al. (2007); Zeng et al. (2016); Zesiewicz et al. (2017); Zivotofsky et al. (2018)

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Language	12	Anders et al. (2006); Bach et al. (1996); Fischer et al. (1994); Guillochon et al. (2010); Hesse et al. (1996); Hesse et al. (2004); Hiraoka et al. (1999); Mishina et al. (1995); Pernon et al. (2013); Pierre et al. (2003); Schiffter (1988); Useros-Olmo et al. (2015)

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PART II: RESEARCH PROTOCOL

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1 Introduction

It is known that people with a neurological condition can experience pathological fatigue. A lot of research has been done around the prevalence of fatigue in neurological conditions such as stroke (Seamon et al.2016; Kluger et al. 2013), Parkinson's disease (Kluger et al. 2013; Martino et al. 2016) and traumatic brain injury. For Multiple Sclerosis (PwMS), fatigue is one of the most common symptoms and is often one of the first symptoms (Severijns et al. 2017). Fatigue can be very impactful in the lives of people with MS this means that daily activities can be too strenuous. Some studies say that fatigue is the most disabling symptom in PwMS (Seamon et al. 2016; Kluger et al. 2013; Severijns et al. 2017; Loy et al. 2017).

A profound conceptualization of fatigue is needed to conduct thorough research on it. Therefore the following subdivisions can be made.

First, fatigue can be divided into two main domains: trait fatigue and state fatigue. Trait fatigue is something that is always present in a person. It is a general feeling that does not change harshly over time. On the other hand, there is something like state fatigue, also known as fatigability. Contrastingly, it changes quickly over time and depends on events that happen throughout the night or day.

Furthermore, fatigability can be divided on its own into two categories: cognitive fatigability and motor fatigability. Each of these have a perceived and a performance component. The latter can be measured objectively in both physical and cognitive parameters during and/or after an activity. Perceived fatigability however is subjective.

A lot of research has been done around the impact of fatigability in the upper limb (Severijns et al. 2016). The static fatigue index of the performance fatigability of the upper limb has a predictive value for functionality in the arm during daily life activities, together with physical experienced fatigue (Severijns et al. 2017). Even though the lower limb is more valuable than the upper limb according to patients, not a lot of research has been done in the lower limb with fatigability (Severijns et al. 2017; Leone et al. 2016; Phan-Ba et al. 2012). A lot of patients ask for more independence. Good ambulation can contribute to this factor, making it very important to examine. Some studies report changes in spatiotemporal and kinematic factors

after long walking tests. These are a decrease in walking speed or distance or changes in kinematic gait parameters (Leone et al. 2016; Phan-Ba et al. 2012; Sehle et al. 2014). There is no proof though that this actually exists.

The research group for neurologic rehabilitation in Hasselt university investigated a method to measure performance motor fatigability during walking. This is given by the decline in distance walked (DWI) of more than 15% during the 6MWT (Leone et al. 2016).

Different reasons for fatigability have been given for pathological performance motor fatigability in MS (Kluger et al. 2013; Severijns et al. 2017). In this research, we want to examine the effect of altered coordination on fatigability. If a correlation can be found, this could be very impactful in the future rehabilitation of patients with MS. More research could be performed around coordination training and what in turn, the effect on fatigability would be.

2 Study objective

2.1 Research question related to master thesis

The aim of this study is to investigate if coordination is an influencing factor of walking-related performance fatigability for people with MS.

3 Method

3.1 Research design

This study will be a cross-sectional observational research, there will be no experimental intervention.

3.2 Participants

A total of 60 people will participate in this study, of which 40 are with MS. Of these 40 people with MS there will be 20 with walking-related performance fatigability (fatigability group, FG) and 20 without (non-fatigability group, NFG). The other 20 subjects are ages- and gender matched healthy controls. Based on a 6MWT, patients will be assigned to one group after a distinction is made in the occurrence of walking related performance fatigability. A formula with a cut off value of -10% will be used this is based on Leone et all.

$$\frac{Distance\ walked\ in\ minute\ 6\ -\ Distance\ walked\ in\ minute\ 1}{Distance\ walked\ in\ minute\ 1}\ \text{x}\ 100$$

3.2.1 Inclusion criteria

In order to take part in this study, participants must meet the following criteria: (1) age between 18 and 70 years, (2) a confirmed MS-diagnosis according to the McDonald criteria and (3) able to walk independently or with unilateral support for 6 minutes without rest.

3.2.2 Exclusion criteria

Participants will be excluded when they (1) had a exacerbation or relapse within the last 3 months before the study and (2) when they have another medical condition that interferes with walking ability (e.g. cardiac or respiratory disease, arthritis and fibromyalgia, stroke, Parkinson).

3.2.3 Patient recruitment

The recruitment of in and out patients with Multiple Sclerose will be done via the rehabilitation and MS-centre Overpelt, the University of Hasselt and via flyers and posters that will be distributed.

3.3 Medical ethics

The Medical Ethics Committee of the University of Hasselt has already given its approval for this study.

3.4 Experimental procedure

3.4.1 Study procedure

The experiment for coordination consists of two test that will be taken in immediate succession, whilst seated. The order of which the tests will be taken is going to be randomised for each patient.

The subjects will be taking several cognitive and motor tests. The cognitive tests are the Stroop test, the PASAT, the SDMT and the DIGIT span. Motor tasks are the FTSS, NHPT, T25FW and the Jamar handgrip test. The order of these test will also be randomised.

Before any of the above tests occur, patients will be asked to do a 6MWT.

3.4.2 Apparatus

The apparatus that will be used to obtain the data is a metal chair in which a subject can sit. There is enough room for the subjects to move their legs in a pendulum. The legs are being contained in the sagittal plane to measure the flexion-extension range of motion in the knee. This is done by four, two by two, straps around the knee, one superior and another inferior to each knee joint. The apparatus obtains data from both legs simultaneously in an antiphase movement.

3.4.3 Tasks

Subjects have to complete two different tasks. The first being a 6 minute coordination test, similar to the 6MWT. For this test subjects will be instructed to move their legs in a pendular motion in an antiphase way for six minutes in total. The experiment leader will ask the patient to move their legs at a pace that is comfortable for them, although insist to move as fast as possible.

For the second task, subjects will be instructed to follow the pace of a metronome in three different test series. In between each serie, subjects have 1 minute to rest and will be asked to keep their legs motionless. The pace of the metronome will be 0.75 Hz, followed by 1 Hz and lastly 1.5 Hz.

3.4.4 Hypotheses

We hypothesise a distortion of phasing after a certain amount of time. In subjects with walking fatigability, this will happen faster than in controls and other patients without walking fatigability. If a distortion is present, this would indicate that the fatigability comes from an issue with the central drive.

We also hypothesise a distortion of phasing and synchronizing when a certain rhytm is given by a metronome. Therefore we expect people with walking fatigability to have more problems following the metronome at 0.75Hz, 1Hz and 1.5Hz.

3.5 Outcome measures

Fatigability will be measured using the DWI. This is the decline of distance walked of more than 15% during the 6MWT between the first minute and the last minute of the test.

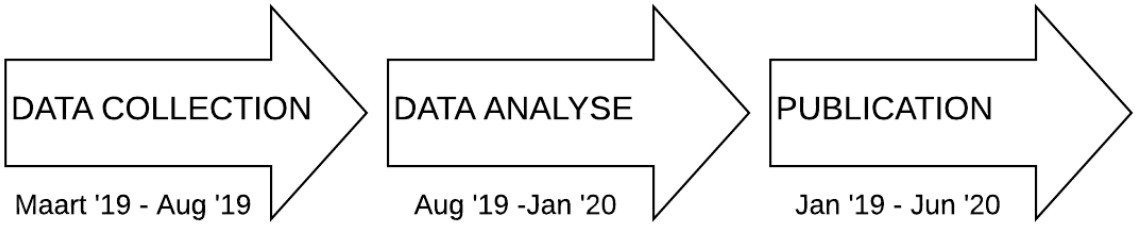
Relative phase/ continuous relative phase is calculated from a data set of two sinusoidal waves. The waves will come forth from the data obtained from the coordination chair. The relative phase is the difference between the angles of both waves at the same point (on the x-axis) of the wave. This angle is derived from the tangent of each point. The formula used is the following(Debaere et al. 2001; Swinnen et al 1997):

$$\phi = \theta a - \theta l = tan^{-1}\left[\frac{\left(\frac{dX_a}{dt}\right)}{X_a}\right] - tan^{-1}\left[\frac{\left(\frac{dX_t}{dt}\right)}{X_l}\right]$$

3.6 Data-analysis

To analyse data, we will be using SAS JMP. Tests for normality will be performed for each group. Data that has a variation of 3 SD, will be excluded. We will be using either an ANOVA or chi-square test to check for differences between the groups.

4 Time planning



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KNOWLEDGE IN ACTION

VOORTGANGSFORMULIER WETENSCHAPPELIJKE STAGE DEEL 1

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
5/11/'18	Afspraken masterproef + uitleg + contract	Promotor: Copromotor/begeleider: Student(e): B Student(e):
19/11/'18	zoekstrategie : Meshtermen	Promotor: Copromotor/begeleider: Student(e): B Student(e):
17/12/'18	zoekstrategie	Promotor: Copromotor/begeleider: Student(e): B Student(e):
18/2/'19	inclusie & exclusiecriteria	Promotor: Copromotor/begeleider: Student(e): B Student(e):
15/4/'19	bespreking gevonden artikels	Promotor: Copromotor/begeleider: Student(e): B Student(e):
2/5/'19	bespreking gevonden artikels + tabellen data-extractie	Promotor: Copromotor/begeleider: Student(e): B Student(e):
20/5/'19		Promotor: Copromotor/begeleider: Student(e): B Student(e):
6/6/'19		Promotor: Copromotor/begeleider: Student(e): Student(e):
		Promotor: Copromotor/begeleider: Student(e): Student(e):
6/6/'19	**Niet-bindend advies:** De promotor verleent hierbij het advies om de masterproef WEL/NIET te verdedigen.	Promotor: Copromotor/begeleider: Student(e): B Student(e):