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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

The influence of a 4-week walking intervention with auditory-motor coupling compared to walking in silence on gait parameters in pwMS: a randomized feasibility study

Anne Ceulemans
Febe Schuurmans

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

PROMOTOR :
Prof. dr. Peter FEYS

COPROMOTOR :
dr. Lousin MOUMDJIAN

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Acknowledgements

We would like to acknowledge Dr. Lousin Moumdjian and Prof. Peter Feys for their invaluable mentorship and advice on this master thesis.

Also, we want to thank the institution Noorderhart Rehabilitation & MS centre for letting us use their property to do the intervention and the therapists to do the recruitment of our participants.

Hamont-Achel, 06/06/2022 A.C.

Peer, 06/06/2022 F.S.

1. Context of master thesis

The research topic of this master's thesis situates in the domain of neurological rehabilitation, especially in the area of music-based interventions. Walking constitutes a significant problem in neurological populations. There is limited proof of a positive effect on the walking ability of music cued gait training in Multiple Sclerosis (MS). Also, a limited amount of studies examine the ability to perceive beats of this population and the effect of music cued gait training on that synchronisation ability. Therefore, an investigation into the influence of auditory-motor coupling on gait parameters (primary) and synchronisation ability (secondary) is appropriate.

This master thesis will be part of an intervention study: "The Effect of a 4 Week Auditory-motor Coupling Intervention on Walking, Information Processing Speed and Fatigue in Persons with Multiple Sclerosis: Three-Armed Pilot Intervention" (NCT04856345). This study includes 30 persons with MS. The intervention study investigates the effect of a four-week auditory-motor coupling intervention on walking, information processing speed and fatigue. Due to a postponement of four months at the initial phase, followed by strict recruiting rules, and temporary hold on testing, of the hospital due to the covid-19 pandemic combined with less support of their clinical staff for obvious prioritization of work, the study was delayed. Therefore, this master thesis includes fewer participants than in the original protocol of the intervention study.

Prof. Dr Peter Feys promotes this duo-master thesis by Anne Ceulemans and Febe Schuurmans as the promoter, and Dr Lousin Moumdjian co-promotes. The first part of this master thesis was already established last year. It consisted of a systematic review 'A review on beat perception ability and its influence on gait parameters with RAS on patients with neurological disorders and a protocol. The second part of this master thesis contains an intervention study conducted at the Noorderhart Rehabilitation & MS centre. This second part will be represented in the subsequent article.

The research team of Dr Lousin Moumdjian had already written the protocol and methodology. Nevertheless, both thesis students helped with the ethical commission application. The study subjects were recruited with the help of therapists at Noorderhart

Revalidation & MS centre, who distributed self-made flyers for our study. The equipment of the intervention, the Biodex Gait trainer containing music training ingredients, was provided in-kind from the company BIODEX. Both students were actively involved in the collection of the data and had an equal contribution to this article's data processing and writing process.

2. Article

2.1. Abstract

Background: The decrease in walking ability in persons with Multiple Sclerosis (pwMS) is a prevalent impairment which affects the quality of life. One innovative way to improve gait ability may be with auditory-motor-coupling. However, is it the presence of coupling or the instruction to synchronise that effects the spatiotemporal gait parameters?

Objectives: To investigate the superior effect of synchronisation during coupling on gait parameters compared to walking in silence and in addition, the effect on synchronisation ability, fatigue and motivation after coupling to music compared to walking in silence.

Participants: Five pwMS, with an average duration of diagnoses over eight years.

Methods: All participants received walking training on a self-paced treadmill twice per week for four weeks with a week prior the pre-testing and a week after the post-testing. Participants in arm A received instructions to synchronise their steps to personalised music based on their cadence. Arm B walked on personalised music at a cadence of +20% of their baseline without these instructions. Arm C walked in silence. The primary outcome measures included cadence, step interval, stride interval and 12MWT. The secondary outcome measures were the relative phase angle (rPA) and the result vector length (RVL), perceived fatigue (physical and cognitive) and motivation during the training session. The statistical analyses of fatigue and motivation were done with paired t-tests and MANOVA.

Results: The baseline demographic information (age, education, EDSS…) were the same for all five participants. A four-week treadmill-intervention with or without music showed inconclusive results on the influence on gait parameters. For the secondary outcomes, the synchronisation outcomes also showed inconclusive results. Furthermore, there were no significant differences found within the three groups between the first and last session in physical and cognitive fatigue and motivation. Between the arms, there was a significant difference in fatigue and motivation between pre-and post-intervention session.

Conclusion: Making a general conclusion based on the results is not possible. However, the insights could be interesting for future studies regarding music-based treadmill interventions in pwMS.

Keywords: Multiple Sclerosis, auditory-motor-coupling, gait, synchronisation, motivation and fatigue

2.2. Introduction

Multiple sclerosis (MS) is a chronic, predominantly autoimmune disease of the central nervous system, mainly characterised by demyelination, inflammation and axonal loss (Dobson & Giovannoni, 2019; Garg & Smith, 2015; McGinley et al., 2021; Oh et al., 2018; Vidal-Jordana & Montalban, 2017). The disease prevalence is worldwide very heterogeneous but highest in North America and Europe, respectively 140 and 108 per 100000 people (Belbasis et al., 2015; Leray et al., 2016). The objective evidence about the aetiology of the disease is still lacking. However, a multifactorial cause is acknowledged, where environmental and genetic factors play a significant role (Dobson & Giovannoni, 2019; Garg & Smith, 2015; Oh et al., 2018). The disease can appear in four different phenotypes: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS (PPMS) and progressive remitting MS (PRMS) or recently called the clinically isolated syndrome (CIS) (Vidal-Jordana & Montalban, 2017). The prognosis of the disease depends on many variables: the time between two relapses, the total number of relapses, the recovery extent from a relapse, the localization of the first relapse and the cognitive impairment (Rotstein & Montalban, 2019). A relapse in MS is a patient's reported or observed episode of an acute inflammatory demyelinating event. Throughout a relapse, an exacerbation of the common symptoms of MS can be observed, including sensory alterations, visual acuity loss (optic neuritis), muscle weakness, imbalance (ataxia), fatigue and cognitive difficulty (Galea et al., 2015). Thus, it is not surprising that balance problems and gait disorders are pervasive in persons with MS (pwMS) (Cameron & Nilsagard, 2018). Even in an early stage of the disease (EDSS < 1.5), changes in gait ability are visible compared to healthy controls (Novotna et al., 2016). Together with pain and depression, walking difficulties are among the strongest predictors of life quality diminution in pwMS, irrespective of the MS type. Improving walking ability is thus an essential component of the rehabilitation of pwMS (Zhang et al., 2021). Much research is available about gait improvements after an intervention with rhythmic auditory stimulation (RAS), especially in PD patients (Burrai et al., 2021; Wang et al., 2022). RAS is a gait rehabilitation approach aiming for footsteps synchronizing to musical beats or a metronome (Leow et al., 2015). Nevertheless, there is proof that RAS can also be an auspicious way to improve gait in pwMS (Ghai & Ghai, 2018; Moumdjian, Moens, Maes, Van Geel, et al., 2019; Shahraki et al., 2017). An essential factor to consider when using RAS is the groove of the music (Leow et al., 2014;

Leow et al., 2021). The groove is defined as the experience of music that makes people tap their feet and want to dance (Madison et al., 2011). Music rated as high on groove elicited faster gait than music rated as low on groove (Leow et al., 2014; Leow et al., 2021). Other factors to look at are the type and tempo of the music. Less physical and cognitive fatigue are registered when pwMS walk on music than on a metronome (Moumdjian, Moens, Maes, Van Geel, et al., 2019). Further, the highest synchronisation for music is found between +2% and +6% of the preferred walking cadence in pwMS (Moumdjian, Moens, Maes, Van Nieuwenhoven, et al., 2019). All three factors are thus also considered in this study.

Another promising tool to improve walking in pwMS is via rhythmic-cued motor imagery, where significant improvements in walking speed, distance and walking perception were found (Seebacher et al., 2017).

Both different rehabilitation methods rely on the terms of the mechanism of auditory-motor coupling, whereby entrainment and synchronisation play a significant role. *Entrainment* defines itself as the process that manages the dynamic alignments of the auditory and motor domains. In contrast, *synchronisation* is the stable maintenance of timing during auditory-motor alignment (Moumdjian et al., 2018). Another factor that can be discussed in both methods is motivation. Higher perceived motivation is found when walking to music than to metronome or silence. This could be explained by the cognitive-motivational theory involving the experience of musical agency. The theory states that in combination with physical effort and expression, successful sensorimotor prediction engages emotional arousal of satisfaction and experience of pleasantness (Moumdjian, Moens, Maes, Van Nieuwenhoven, et al., 2019).

Because of the limited evidence about the effect of auditory-motor coupling in pwMS, this pilot study is designed. The following main research question is formulated:
Is walking in synchrony to music superior to walking without synchronising to music and to walking in silence after a four-week training to observe improvements in gait parameters?

We hypothesise that gait parameters improve more when walking in synchrony to music after an auditory-motor coupling intervention.

2.3. Methods

2.3.1. Participants

2.3.1.1. Inclusion criteria

The following criteria should be met by the participants entering this study. MS should be diagnosed longer than a year ago with no relapse in the last two months. Also, the participant must have the ability to walk for twelve minutes and walk independently on a treadmill with a minimum speed of 0,8 m/s and a maximum speed of 1,2 m/s.

2.3.1.2. Exclusion criteria

If the participant experienced the following criteria, they were excluded from the intervention study. Severe cognitive impairment that ensures that the participant would not be able to understand or perform the intervention. Also, participants who experienced deafness and amusia were excluded. Finally, pregnant participants were not included in this study.

2.3.1.3. Descriptive criteria

The participant's personal information such as gender, date of birth, weight, height, physical activity and work was included as general information. Furthermore, the nature and duration of education were included. Specific information related to MS-like date of diagnosis or first MS symptom, type of MS, date of last relapse and medication were also described. Also, information about EDSS like assessment date, who did the assessment and the scores were asked and described. Finally, music-related information was included. Furthermore, some motor function tests (the Nine Hole Peg Test (NHPT), Timed Up and Go (TUG), Six Minute Walking Test (6MWT), Timed 25-Foot Walk Test (T25FWT), Dynamic Gait Index (DGI), Motricity Index (MI) and Modified Ashworth Scale (MAS)), a few cognitive evaluations (Paced Auditory Serial Addition Test (PASAT), Symbols Digit Modalities Test (SDMT)) and a rhythm discrimination task (Montreal Battery of Evaluation of Amusia (MBEA)) were included as a descriptive test. Also, a few self-reported questionnaires were included to look at the impact of MS on the participant’s daily life. The following questionnaires were included: the Multiple Sclerosis Walking Scale (MSWS-12), Activities-Specific Balance Confidence Scale (ABC-NL), Modified Fatigue Impact Scale (MFIS) and the Hospital Anxiety and Depression Scale (HADS).

2.3.2. Procedure

2.3.2.1. Recruitment

The participants were recruited through the therapist of their rehabilitation centre (i.e., Noorderhart Rehabilitation & MS centre). The therapists were provided with flyers that contained all the information.

2.3.2.2. Randomisation

A block randomisation procedure was used, wherein numbered tickets were placed inside sealed brown envelopes. Every brown envelope was matched with a white envelope by a sign in the upper corner. In each brown envelope, there were three numbered tickets. The participant chose a brown envelope. Thereafter, the participant took a numbered ticket out of the brown envelope. This numbered ticket was placed into the white envelope by the assessor. Randomisation was performed right before the first intervention session.

2.3.2.3. Study arms

The participants were allocated into three arms/groups based on the randomisation. The intervention of the first arm/group (A) consisted of walking on music while synchronising to the beats. The intervention of the second arm/group (B) consisted of walking on music without the instruction to synchronise, and lastly, the third group/arm (C) walked in silence.

2.3.2.4. Intervention

The participants engaged in a four-week training intervention. A week before and a week after the intervention, the participants underwent pre-and post-testing. These consisted of a two-hour session, with multiple periods of rest implemented, to collect different data. The intervention sessions lasted 20 minutes and were conducted two times a week at Noorderhart Rehabilitation & MS centre. The intervention sessions took place before or after their regular rehabilitation session that day. Each training intervention consisted of walking twice for ten minutes with rest on a Biodex treadmill (Gait trainer 3, Biodex Medical Systems, Inc. 2022). The resting period in between lasted as long as needed for the participant. Depending on which group they were divided in, the participants walked on music, with or without the instruction to synchronise, or in silence. A three-minute walk on the treadmill was performed

in the first session to find their average walking speed. Also, the participants underwent a familiarisation task; a metronome was used to instruct the participant to synchronise by stepping to the beat. After these baseline testings, the participants were equipped with two sensors attached at the ankles and were asked to complete the walking intervention on the Biodex treadmill. If the participants were allocated in the first two arms of the study, the intervention included walking to music at different tempi. The music used was fitted to the participant's baseline by the participants in the first arm. If the participant was allocated in the second arm, the music used was 20% above their baseline beats per minute (bpm). For the music, a personalised database was used. The database contained songs with a range from 70 to 140 bpm. Furthermore, each week the music genre alternated between pop-rock and pop. The songs were randomly selected based on the participants' baseline cadence. During the intervention, progression occurred by increasing walking speed while obtaining the balance with synchronisation ability. A more detailed prescription regarding the organisation of testing-and intervention sessions can be found in Figure 1.

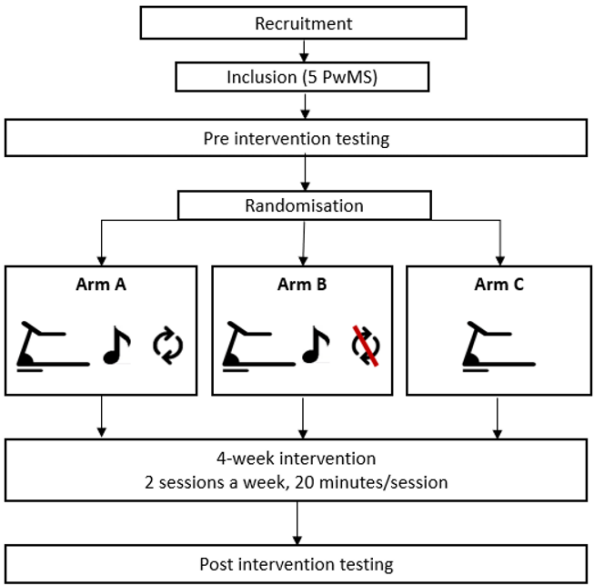


Figure 1: Organisation of testings and intervention

2.3.2.5. COVID-19 precautionary measures

The study took place during the COVID-19 pandemic. Therefore, extra precaution was taken to create the safest possible environment. As required by the government, face masks were always worn. Furthermore, hygienic measurements such as disinfecting hands and materials were respected. The researcher would always remain 1,5 meters from the participants except to strap on the sensors.

In case the researcher or the participant experienced one of the following symptoms: fever, sore throat, cough, respiratory problems, loss of sense of smell or taste, aches and pains or diarrhoea, the intervention session was cancelled. When the participant or the researcher has had a high-risk contact, the session was also cancelled.

2.3.3. Outcome Measures

2.3.3.1. Descriptive outcome measures

In the pre-testing, the following descriptive tests: Montreal Battery of Evaluation of Amusia (MBEA), Nine Hole Peg Test (NHPT), Timed Up and Go (TUG), Six Minute Walking Test (6MWT), 12 Minute Walking Test (12MWT), Timed 25-Foot Walk Test (T25FWT), Dynamic Gait Index (DGI), Motricity Index (MI), Modified Ashworth Scale (MAS), Paced Auditory Serial Addition Test (PASAT), Symbols Digit Modalities Test (SDMT), Multiple Sclerosis Walking Scale (MSWS-12), Activities-Specific Balance Confidence Scale (ABC-NL), Modified Fatigue Impact Scale (MFIS), Hospital Anxiety and Depression Scale (HADS), and outcome measures were conducted: walking paradigm with measurement of the relative phase angle (rPA), result vector length (RVL) and spatiotemporal gait parameters. A last descriptive test was conducted during the post-testing: credibility and expectations questionnaire. Below each test is explained (Meetinstrumenten in de zorg, z.d.). A more detailed prescription regarding the organisation of the pre-testing session can be found in the Figure 1.

Rhythm discrimination task

Montreal Battery of Evaluation of Amusia (MBEA)

In this study, only the rhythm subscale of the MBEA was used to examine the amusia of the participants. Furthermore, a short version of fifteen pairs of rhythms was used where the participants must decide whether they had the same rhythm. The MBEA is sensitive and has a good test-retest reliability (Pfeifer & Hamann, 2015).

Motor function

Nine Hole Peg Test (NHPT)

The NHPT measures fine motor skills and the speed of movement of the upper limb. The participant should take nine pegs, one for one, and put them into the holes in the board.

Afterwards, the participant should remove the nine pegs from the holes and place them back into the starting position. This should be done as fast as possible. Furthermore, the participant can only use one hand at a time. The time that the participant needs to do this task is measured. 33,3 seconds is considered the cut-off score to differentiate between mild versus marked to severe upper limb dysfunction. The NHPT has a high inter-rater (ICC: 0.84-0.96), a high intra-rater (ICC: 0.91-0.99) and test-retest reliability (r = 0.86-0.98/ICC: 0.88). Furthermore, the test has a very high internal consistency (Cronbach's alpha: 0.93) (Feys et al., 2017; Rasova et al., 2012).

Timed Up and Go (TUG)

The TUG gives information about balance and gait, indicating a possible fall risk. The test measures the participant's time to get up out from the chair, walk three metres comfortably, turn around, walk back, and sit back down. If necessary, the participant can use a walking aid, but otherwise, no encouragement or help is allowed. There are no specific cut-off values for persons with MS. However, the cut-off value for community-dwelling adults is 13,5 seconds (Shumway-Cook et al., 2000). The TUG has an excellent test-retest reliability (ICC= 0.973) (Bennett et al., 2017).

Six Minute Walking Test (6MWT)

The 6MWT measures the functional capacity of the participant by measuring the maximal distance that the participant can walk within six minutes. The participant walks at a comfortable pace and is allowed to use a walking aid or orthoses.

The 6MWT records an excellent inter-rater reliability (ICC = 0.91) and excellent intra-rater reliability (ICC = 0.95) (Goldman et al., 2008). Furthermore, the test-retest variability is excellent (ICC = 0.965) (Bennett et al., 2017).

12 Minute Walk Test (12MWT)

The 12MWT also measures the functional capacity of the participant by measuring the maximal walking distance within twelve minutes. During the 12MWT, the participant needs to walk at a comfortable pace for twelve minutes. Meanwhile, sensors are placed on the participants' feet and ankles (D-Jogger and APDM) to measure spatiotemporal parameters.

Timed 25-Foot Walk Test (T25FWT)

The T25FWT measures mobility and leg function performance. The participant starts at one end of the 25-foot course and is instructed to walk as quickly as possible but safely. While the participant walks, the time to complete the course is measured. The participant is allowed to use a walking aid. The T25FWT has adequate reliability with an ICC of 0.94 and can be interpreted as a valid measure of walking (Motl et al., 2017). Furthermore, the T25FWT has a very high test-retest reliability (ICC: 0.95) and a very high internal consistency (Cronbach's alpha: 0.96) (Rasova et al., 2012).

Dynamic Gait Index (DGI)

The DGI measures gait, balance and fall risk. The test consists of eight different domains: walking on an even surface, changing walking speed, walking with head turned left and right, walking with head turned up and down, walking and turning 360°, stepping over an obstacle, avoiding obstacles and climbing stairs. The test scores range from zero (severe impairment) to three (normal function). The maximum score of the DGI is 24.

The DGI records an excellent test-retest reliability (ICC= 0.955) (Bennett et al., 2017).

Motricity Index (MI)

The MI measures the degree of hemiplegia for the arms and legs by looking at the ability to move randomly and the maximal isometric force. The total score of the MI is 100 (99+1). A high score correlates with higher force production. In this study, only the legs are evaluated. Therefore, the hip flexors, knee extensors and ankle dorsiflexors are evaluated. Looking at the psychometric properties, the MI has a moderate test-retest reliability (ICC: 0.56) and an excellent internal consistency (Cronbach's alpha: 0.87) (Rasova et al., 2012).

Modified Ashworth Scale (MAS)

The MAS measures the degree of spasticity for muscle groups. The researcher scores the muscle tone from zero to four. In this study following muscle groups were evaluated: Mm. Hamstrings, Mm. Triceps Surae, Mm. Quadriceps. The scores range from zero to four (zero means no spasticity, and four means rigid in both flexion and extension). The MAS has a good

internal consistency (Cronbach's alpha: 0.78) but a poor test-retest reliability (ICC; 0.49). However, it is susceptible to post-treatment changes (Rasova et al., 2012).

Cognitive function

Paced Auditory Serial Addition Test (PASAT)

The PASAT measures the cognitive ability of auditory information processing speed and flexibility as well as the calculation of ability. During the test, single digits are presented every three seconds. The participant needs to remember the last digit and add the next digit. The score of the PASAT is the total number of correct answers out of 60 possible answers. The PASAT has a high inter-rater (ICC: 0.90-0.97) and a high intra-rater reliability (ICC: 0.94-0.98). Also, the internal consistency is excellent (split-half reliability: 0.96) (Rasova et al., 2012). Furthermore, the PASAT has good reliability (ICC 0.86) (Strober et al., 2019).

Symbols Digit Modalities Test (SDMT)

The SDMT measures also measure information processing speed. The participant gets 90 seconds to link geometric figures to the correct number. The answer can be written or given orally. The score of the SDMT is the total number of correct answers given in 90 seconds. The SDMT has good reliability (ICC: 0.85). Furthermore, the test is susceptible to changes. It captures MS-related changes that are not detected by the EDSS (kappa coefficients: -0.02 - +0.03) (Strober et al., 2019).

Questionnaires

Multiple Sclerosis Walking Scale (MSWS-12)

The MSWS-12 is a self-report questionnaire about the impact of MS on walking ability. The test consists of twelve questions where the participants give a score from one (no limitation) to five (extreme limitation). The maximum score of the MSWS-12 is 60.

This test has a good test-retest reliability (ICC = 0.863) (Bennett et al., 2017).

Activities-Specific Balance Confidence Scale (ABC-NL)

The ABC-NL is a self-report questionnaire that measures the confidence level of participants in holding their balance while doing certain activities. The test consists of sixteen items, and the participants need to score their confidence level from 0% to 100% for each item. The

higher the score, the more confident the participant feels. The internal consistency of the ABC was 0.96, while the minimal detectable change was 11.28. Furthermore, an excellent test-retest reliability was found (ICC = 0.98) (Alghwiri et al., 2020).

Modified Fatigue Impact Scale (MFIS)

The MFIS is a self-report questionnaire about the impact of fatigue on physical, cognitive and psychosocial functioning. The MFIS is divided into psychosocial, physical, and cognitive subscales. The higher the scores, the more significant the influence of fatigue in daily life.
The internal consistency of the overall score of MFIS is excellent ($\alpha = 0.81$). For the different parts, the internal consistency for physical is 0.91, cognitive 0.95 and psychosocial 0.81. Also, the test-retest of this test is excellent (ICC = 0.91) (Larson, 2013).

Hospital Anxiety and Depression Scale (HADS)

The HADS is a self-report questionnaire about participants' fear and depression during the past week, independent of their physical condition. The HADS is divided into two subscales consisting of seven items: fear and depression. The higher the scores, the more fear or depression. The cut-off value of the depression subscale is eight, and a cut-off value of eleven for the fear subscale. The HADS-D has a high specificity with a cut-point of eleven but a low sensitivity with a cut-point of eleven. However, the HADS-A has a high sensitivity with a cut-point of eight but a lower specificity with a cut-point of eight. The HADS has a good internal consistency (HADS-D: ICC = 0.82, HADS-A: ICC = 0.86) and a good test-retest reliability (HADS-D: ICC= 0.83, HADS-A: ICC = 0.83) (Marrie et al., 2018).

Credibility and expectations questionnaire

The credibility and expectations questionnaire needs to be filled in at the post-testing.
This questionnaire is a self-report questionnaire about the participant's feelings or beliefs about the influence of the intervention/therapy on the improvement of their lifestyle and functioning. The questionnaire consists of two parts. The first part is about the intervention/therapy in general. The second part is about how the participants feel or think about intervention/therapy and the possible success of the participant himself. This questionnaire has good validity and reliability (Devilly & Borkovec, 2000).

A more detailed prescription regarding the organisation of the post-testing session can be found in Figure 1.

2.3.3.2. Experimental primary outcome measures

Spatiotemporal gait parameters

At the beginning of pre-testing, the participants will be asked to walk a baseline in silence to determine their comfortable speed. After that, the walking paradigm will be measured. As described above (see walking paradigm), the participants will walk under six conditions for three minutes. During these conditions following spatiotemporal gait parameters will be recorded: cadence, step interval and stride interval. The walking paradigm will be performed during both pre-and post-testing sessions.

2.3.3.3. Experimental secondary outcome measures

Synchronisation ability

Walking paradigm

During the walking paradigm, the participants walk using a headphone and the D-Jogger equipment on a flat surface. The participants need to synchronise to the beat of the music. There are six conditions the participants need to perform: 'high' 0%, 'high' 6%, 'high' 10%, 'low' 0%, 'low' 6% and 'low' 10%. High or low indicates the clarity of the beat of the played music. The percentages indicate the pace based on their comfortable walking cadence. Therefore, 'high' 5% means that the participant will walk five percent faster than their comfortable tempo to music with a clear beat. Each condition has a duration of three minutes with rest in between. By randomisation by a digital randomisation program, the order of the conditions is determined. During these paradigms, the following measurements are recorded for data collection:

Relative phase angle (rPA)

The rPA measures the timing of the participant's footfall in relation to the beat. The unit of the rPA is degrees and can either be a positive or negative angle. If the outcome is positive, the footfall is before the beat. If the outcome is negative, the footfall is after the beat. The closer to zero, the better the synchronisation to the beat of the music.

Result vector length (RVL)

The RVL expresses the ability of the stability of the rPA over time. It is a value between zero and one. The value one means that the rPA has a precipitous distribution over time which indicates that all footfalls have an equal timing relationship with the rhythmic beats of the music. However, when the RVL has a value of zero, it indicates that the rPA has a more diverse distribution, meaning no stable synchronisation.

The following two secondary outcome measures were collected before and after an intervention session:

Fatigue

A Visual Analogue Scale was used to measure the perceived cognitive and physical fatigue before and after each intervention session. The VAS is a numeric scale ranging from zero to ten. If the participant indicates a score of zero, he or she perceives no fatigue. If the participant indicates a ten score, he or she perceives the worst fatigue possible.

Motivation

The Likert scale measures the participant's motivation before and after each intervention session. Furthermore, this scale was also used to indicate the music's familiarity and amusement after each intervention session. The scores of this scale range from zero to five. If the participant is not motivated, does not know or likes the music to participate, a score of zero will be given. However, when the participant is fully motivated, very familiar with the music or likes the music very much, a score of five will be given.

2.3.4. Equipment

2.3.4.1. Synchronisation and gait measures

D-Jogger

The D-Jogger consists of headphones, sensors and a laptop with custom made software (Figure 2) (Moens & Leman, 2015). The APDM and NGIMU sensors were strapped to the participant's feet and ankles for the walking paradigm. The NGIMU sensors were used to conduct data on the gait parameters. The participants heard the music through wireless

headphones. The music used for the pre-and post-testing sessions was standardised and different from those used in the intervention sessions. (NGIMU, UK, https://x-io.co.uk/NGIMU/)

Figure 2: A few items making up the D-Jogger

APDM sensors for spatiotemporal gait parameters

The APDM sensors were used for all the walking tests during the pre-and post-testing sessions (Figure 3). The sensors were strapped around the feet and measured the spatiotemporal gait parameters as described in the secondary outcome measures. (OPAL, USA, https://www.apdm.com/wearable-sensors/)

Figure 3: APDM sensors

2.3.4.2. Training devices

BIODEX gait trainer 3

The BIODEX gait trainer 3 is a treadmill where a tablet and a speaker are attached to the frame (Figure 4). The tablet is used to play and adapt the music and gait parameters to the participant's needs. (Biodex Medical Systems, New York, https://www.biodex.com/physical-medicine/products/treadmills/gait-trainer-3)

Figure 4: BIODEX gait trainer 3

Intervention laptop

For this study, a laptop with a custom-made software program to log the data was used (Figure 5). Furthermore, this laptop ran on a specific internal network. In the software program, the participants' ID, number of the session and the intervention arm had to be filled in before it was possible to start logging the data. Also, the connection with the left and right NGIMU sensors needed to be checked, and the songs used in the session (this is not the case if the participant needs to walk in silence) needed to be uploaded to the program. However, when the song changed on the treadmill, the researcher needed to change the song in the program manually. The intervention laptop was linked to the BIODEX gait trainer 3 and the NGIMU sensors (Biodex Medical Systems, New York, https://www.biodex.com/physical-medicine/products/treadmills/gait-trainer-3) (NGIMU, UK, https://x-io.co.uk/NGIMU/). The participant's ID and study arm were selected when opening the program. Also, the connection to the NGIMU sensors was checked. Then the songs were selected for every participant individual, and the session was established and administered on the program. Lastly, the participant's ID and songs were selected on the treadmill. The intervention session was started and recorded when the assessors clicked the start button on the laptop and the treadmill.

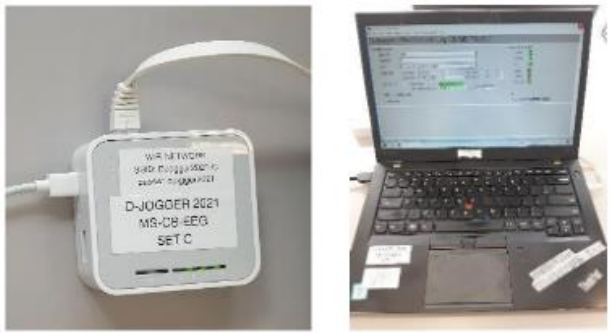


Figure 5: Laptop

2.3.5. Study design & Data-analysis

The originally planned study was not achievable due to the COVID-19 pandemic. Therefore, the researchers present the results as a feasibility study. The data analyses of the originally planned study will be described but not fully executed in the results of this article. Instead, a power analysis will be performed for future studies.

2.3.5.1. Original study: study design

In the original study 30 pwMS would be participating in this study. These 30 participants would be randomly divided into three intervention groups: the instructed synchronised group, the non-instructed synchronised group or the silence group (control group). The instructed synchronised group will walk on music during their treadmill training sessions and will be instructed to synchronise their steps to the music. The non-instructed synchronised group will also walk on music but will not be instructed to synchronise their steps. The silence group will walk without any music during the treadmill training sessions. Each group would contain ten participants. Every walking intervention would be done at the preferred cadence of the participant. The pre-and post testings, intervention, and study equipment will be the same as described in this feasibility study. Primary outcomes would consist of the walking and tapping paradigm, 6MWT and MSWS-12. Secondary outcomes would include the spatiotemporal gait parameters, TUG, MFIS and perceived fatigue. All other performed tests would have been descriptive measures.

2.3.5.2. Statistical analyses

Here will the statistical analysis be described that would have been conducted in the case of recruitment of 30 PwMS in the three randomised arms to answer the research question: is training four-weeks walking in synchrony to music superior to walking without synchronising to music and to walking in silence to observe improvements on synchronisation, motor walking and walking variability?

Sample size and power were not calculated at the beginning of the study. First, the normality of the descriptive data would have been checked by the Shapiro-Wilk test. Next, the data will be analysed with a t-test when normality is proven. If not, it would be analysed by the

Wilcoxon signed-rank test. Analyses of the differences per group of each session in spatiotemporal gait parameters and perceived physical and cognitive fatigue would be done by a mixed model analysis of variance (ANOVA). Another two mixed models ANOVA, with two factors (groups and time) in common, will be performed. One will be used to interpret the motor and cognitive outcomes. One will add another two factors (tempi and sessions) to interpret the outcome measures from the tapping and walking paradigm between the three intervention groups. A multiple comparison Bonferroni test would be used as a post-hoc test to analyse the outcome measures pre and post within one group or in case of interactions. All the analyses would be based on intention to treat. The statistical analyses of all the data would be performed with SAS JMP Pro 16.2.0 (JMP®, Version 16.2.0. SAS Institute Inc., Cary, NC, 1989–2022). The confidence intervals (CI) would be set at 95%, and a probability of $p<0.05$ will be used.

The following is the statistical analysis that was conducted within this thesis due to the limited number of participants:

First, the demographic data of the different participants (gender, age, type of MS, EDSS score, duration of MS diagnosis, handiness, hand function by 9HPT, height, weight, BMI, education, musical experience, activity level and frequency of therapy) was analysed. For every variable for the three groups, the descriptive statistics were calculated and presented as the mean (standard deviation, SD) for continuous variables and the number of participants per group (%) for categorical variables. The primary outcome measures included spatiotemporal gait outcomes (cadence, step interval and stride interval). The secondary outcome measures were the synchronisation outcomes (relative phase angle (rPA) and the result vector length (RVL)), perceived fatigue (physical and cognitive) and motivation. All the analyses were based on the intention-to-treat principle. Statistical analysis of the overall effect between the three intervention groups for the spatiotemporal gait parameters and synchronisation outcomes was not possible due to the low sample size. To provide some clinical evidence, the outcomes of the pre-post session of the participants were compared to their baseline. In addition, a power analysis is performed to calculate the power of the overall study. For fatigue and motivation, the statistical analysis to examine the difference between the first and last intervention session was done by a paired t-test, signed-rank test for groups B and C, and a mixed model ANOVA for group A. Normality of the data was checked by Shapiro-Wilk test. To

compare fatigue and motivation between the three arms, multivariate analysis of variance (MANOVA) was used. The statistical analysis of the data was performed with the software program SAS JMP Pro 16.2.0 (JMP®, Version 16.2.0. SAS Institute Inc., Cary, NC, 1989–2022). Data are presented in tables and graphs made in SAS JMP Pro or Excel. The confidence intervals (CI) were set at 95%, and a probability of $p<0.05$ will be used. A priori and post-hoc power analysis of ANOVA repeated measures, conducted within-between interaction. The a priori analysis is done for sample size estimation for future studies, based on data from this pilot study. The post-hoc analyses calculated the power of this pilot study. The effect size used in both power analysis was based on Cohen's criteria (Cohen, 1992). The significance criterion was set at $\alpha = 0.025$ to test two-sided and power at 80%. The correlation among repeated measures was fixed at 0.5 and the nonsphericity correction at one, assuming that sphericity is met. The power analysis was conducted using G*Power version 3.1.9.7 (Faul et al., 2007).

The decision trees of the statistical analysis can be found in Appendix.

2.4. Results

2.4.1. Participants

In total five pwMS participated in the study. All the recruited participants were randomised in one of the three intervention groups. The results of the randomisation can be seen in Figure 6. One participant dropped out after the first intervention session in group A due to excessive fatigue problems after the intervention. Finally, four participants completed the post-intervention assessment.

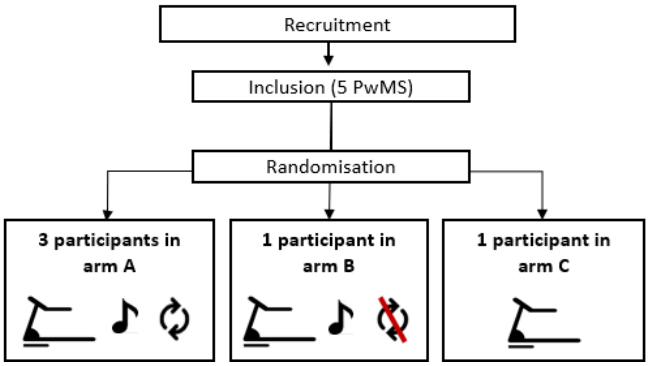


Figure 6: Results of the randomisation

2.4.2. Descriptive measures

One participant of group A and the participants in arms B and C have the secondary progressive type of MS. The information about the type of MS of the other two participants of arm A was not available. The EDSS scores of the participants in arms B and C were between 4,5 and 5,5. Unfortunately, the score was missing for the subjects in arm A. The average duration of the diagnosis was in arm A: 8,6 (7,37) years, in arm B: 9 years and arm C: 13 years. The other baseline characteristics of the participants of the three arms can be seen in Table 1. The descriptive measures of the disease and global characteristics were similar between the three arms. Furthermore, the test results of the motor function tests, the cognitive abilities test and the self-reported questionnaires are summarised in Table 2, Table 3 and Table 4. Due to an error made by the assessors, the results of the SDMT were not reliable and could not be included in this study. Also, the results of the MBEA could not be included in this study due to missing of the correct answers.

Characteristic	Arm A (n=3)	Arm B (n=1)	Arm C (n=1)
Gender (#female)	1 (33.33%)	1	1
Age	65,59 (5,98)	55	53
Handiness (#right)	1 (33,33%)	1	1
Hand function by 9HPT (s)	R: 22,48 (2,13) L: 31,04 (8,81)	L: 29,26 R: 40,88	L: 21,18 R: 32,53
Height (cm)	176,33 (5,77)	178	168
Weight (kg)	72,67 (5,77)	81	68
BMI	23,38 (1,77)	25,56	24,09
Education (#high school)	1 (33,33%)	1	1
Musical experience (#yes)	0 (0%)	0	0
Sports (#yes)	2 (66,67%)	1	0
Rehab (#times/week)	2,5 (0,58)	3	3

Values are presented as mean (SD) for continuous variables or number of participants per group (%) for categorical variables for n = 5 participants at baseline. #: number of; RM: relapsing-remitting; SP: secondar progressive; PP: primary progressive; NK: not known

Table 1: Descriptive information

Motor function test		**Arm A (n=3)**		**Arm B (n=1)**	**Arm C (n=1)**
	Participant 1	Participant 2	Participant 3	Participant 4	Participant 5
TUG (s)	13,32 s	11,88s	10,64s	9,53s	16,78s
6MWT (m)	176,44m	164,37m	153,47m	192,32	154,43m
T25FWT (s)	7,76s	10,41s	10,05s	7,91s	10,43s
DGI (range)	9/24	19/24	11/24	15/24	18/24
MI Lower limb (0-100)	R: 23/99 L: 99/99	R: 91/99 L: 69/99	R: 37/99 L: 85/99	R: 99/99 L: 99/99	R: 75/99 L: 99/99
MAS (0-4)*	Triceps surae: 3	0	0	0	0

*Values are presented as mean; *only spastic muscles presented, no spasticity present resulted in an overall score of 0*

Table 2: Motor function tests

Cognitive abilities test		**Arm A (n=3)**		**Arm B (n=1)**	**Arm C (n=1)**
	Participant 1	Participant 2	Participant 3	Participant 4	Participant 5
PASAT (0-60)	23	50	45	45	/

Raw scores were used for this test

Table 3: Cognitive abilities test

Questionnaires		**Arm A (n=3)**		**Arm B (n=1)**	**Arm C (n=1)**
	Participant 1	Participant 2	Participant 3	Participant 4	Participant 5
MSWS-12 (0-60)	46	/	54	55	56
MFIS (0-84)	56	/	59	52	47
HADS (0-42)	20	/	22	12	10
ABC-NL (0-100%)	45%	/	56%	44%	82%

Total scores are used. For the ABC-NL, the values are presented as mean.

Table 4: Questionnaires

2.4.3. Primary outcome measures

2.4.3.1. Arm A (walking in sync to music)

A.1) Participant 1

To describe the spatiotemporal gait parameters, the average values of the left and right leg were used as measurements. Unfortunately, due to an error of the APDM sensors, the data of the NGIMU sensors could only be used as outcome measures.

Gait Cadence

At the pre-testing session, the participant's cadence was higher than the baseline for all tempi except when walking at their comfortable walking cadence with a 'high level' of beat clarity. The increase was also the case when comparing the baseline cadence of the post-testing with the baseline cadence of the pre-testing. However, when comparing the cadence of the participant at the post-testing with their baseline, a slower cadence was measured for all the tempi.

An overview of the results can be found in Table 5.

For the 12MWT, the participant reached an average baseline cadence of 91,310 steps/min at the pre-testing session. The participant's cadence was 99,048 steps/min at the post-testing session. (+8,47%).

Stride interval

Left foot

At the pre-testing session, the participant's stride interval was larger than the baseline when walking with a 'high level' of beat clarity. When walking with a ‘low level’ of beat clarity or when walking with an increase of 10% of their comfortable walking cadence, the stride interval was smaller compared to the baseline. When comparing the baseline stride interval of the post-testing with the baseline stride interval of the pre-testing, the stride interval showed a decrease. However, when comparing the stride interval of the participant at the post-testing with their baseline, a larger stride interval was measured for all the tempi.

An overview of the results can be found in Table 6.

For the 12MWT, the participant reached an average baseline stride interval of 1334,714 mm at the pre-testing session. At the post-testing session, the participant's stride interval was 1292,888 mm (-3,13%).

Right foot

At the pre-testing session, the participant's stride interval was larger compared to the baseline when walking with a 'high level' of beat clarity. When walking with a 'low level' of beat clarity or when walking with an increase of 10% of their comfortable walking cadence, the stride interval was smaller compared to the baseline. When comparing the baseline stride interval of the post-testing with the baseline stride interval of the pre-testing, the stride interval showed a decrease. However, when comparing the stride interval of the participant at the post-testing with their baseline, a larger stride interval was measured for all the tempi.
An overview of the results can be found in Table 7.

For the 12MWT, the participant reached an average baseline stride interval of 1334,766 mm at the pre-testing session. At the post-testing session, the participant's stride interval was 1283,896 mm. (+3,81%).

Step interval

Left foot

At the pre-testing session, the participant's step interval was larger compared to the baseline for all tempi. When comparing the baseline step interval of the post-testing with the baseline step interval of the pre-testing, the step interval showed a decrease. However, when comparing the step interval of the participant at the post-testing with their baseline, a larger step interval was measured for all the tempi.
An overview of the results can be found in Table 8.

For the 12MWT, the participant reached an average baseline step interval of 738,402 mm at the pre-testing session. The participant's step interval was 733,207 mm at the post-testing session (-0,70%).

Right foot

At the pre-testing session, the participant's step interval was smaller compared to the baseline for all tempi except when walking at their comfortable walking cadence with a 'high level' of beat clarity. When comparing the baseline step interval of the post-testing with the baseline step interval of the pre-testing, the step interval showed a decrease. However, when comparing the step interval of the participant at the post-testing with their baseline, a larger step interval was measured for all the tempi.

An overview of the results can be found in Table 9.

For the 12MWT, the participant reached an average baseline step interval of 596,048 mm at the pre-testing session. At the post-testing session, the participant's step interval was 589,875 mm (-6,17%).

A.2) Participant 2

Gait Cadence

At the pre-testing session, the participant's cadence was higher compared to the baseline for all tempi except when walking at a 'high level' of beat clarity at their comfortable walking cadence or at an increase of 6% of their comfortable walking cadence. Due to the drop-out of this patient, there were no post-testing values available.

An overview of the results can be found in Table 5.

Stride interval

Left foot

At the pre-testing session, the stride interval of the participant was larger compared to the baseline when walking with a 'high level' of beat clarity at their comfortable walking cadence, an increase of 6% of their comfortable walking cadence and when walking with a 'low level' of beat clarity at an increase of 10% of their comfortable walking cadence. For the other tempi, a decrease in stride interval was shown. Due to the drop-out of this patient, there were no post-testing values available.

An overview of the results can be found in Table 6.

Right foot

At the pre-testing session, the participant's stride interval was larger compared to the baseline for all tempi. Due to the drop-out of this patient, there were no post-testing values available. An overview of the results can be found in Table 7.

Step interval

Left foot

At the pre-testing session, the participant's step interval was larger compared to the baseline for all tempi. Due to the drop-out of this patient, there were no post-testing values available. An overview of the results can be found in Table 8.

Right foot

At the pre-testing session, the participant's step interval was larger compared to the baseline for all tempi. Due to the drop-out of this patient, there were no post-testing values available. An overview of the results can be found in Table 9.

There was no data of the 12MWT for this participant.

A.3) Participant 3

Gait Cadence

At the pre-testing session, the participant's cadence was lower compared to the baseline for all tempi. Unfortunately, there was no data of the tempi 'walking at an increase of 10% of the comfortable walking cadence'. However, a decrease in cadence was shown when comparing the baseline cadence at the pre-testing with the baseline cadence at the post-testing. When comparing the cadence of the participant at the post-testing with their baseline, a faster cadence was measured for walking at an increase of 6% of their comfortable walking cadence and when walking at an increase of 10% of their comfortable walking speed in combination with a 'high level' of beat clarity. For the other three tempi, a decrease in cadence was measured.

An overview of the results can be found in Table 5.

For the 12MWT, the participant reached an average baseline cadence of 77,180 steps/min at the pre-testing session. The participant's cadence was 78,583 steps/min at the post-testing session. (+1,82%).

Stride interval

Left foot

At the pre-testing session, the participant's stride interval was larger compared to the baseline for all tempi. When comparing the baseline stride interval of the post-testing with the baseline stride interval of the pre-testing, the stride interval showed an increase. However, when comparing the stride interval of the participant at the post-testing with their baseline, a larger stride interval was measured for all the tempi except when walking at their comfortable walking cadence with a 'high level' of beat clarity.

Due to an error in the system, there was no data available for walking at an increase of 10% of their comfortable walking cadence at the pre-testing and no data available for walking at their comfortable walking speed with a 'low level' of beat clarity at the post-testing.

An overview of the results can be found in Table 6.

For the 12MWT, the participant reached an average baseline stride interval of 1600.395 mm at the pre-testing session. At the post-testing session, the participant's stride interval was 1561.589 mm (-2,42%).

Right foot

At the pre-testing session, the participant's stride interval was larger compared to the baseline for all tempi. When comparing the baseline stride interval of the post-testing with the baseline stride interval of the pre-testing, the stride interval showed an increase. However, when comparing the stride interval of the participant at the post-testing with their baseline, a smaller stride interval was measured for all the tempi except when walking at their comfortable walking cadence.

Due to an error in the system, there was no data available for walking at an increase of 10% of their comfortable walking cadence at the pre-testing.

An overview of the results can be found in Table 7.

For the 12MWT, the participant reached an average baseline stride interval of 1649,227 mm at the pre-testing session. The participant's cadence was 1564,111 mm at the post-testing session (+5,16%).

Step interval

Left foot

At the pre-testing session, the participant's step interval was larger compared to the baseline for all tempi. When comparing the baseline step interval of the post-testing with the baseline step interval of the pre-testing, the step interval showed an increase. However, when comparing the step interval of the participant at the post-testing with their baseline, a smaller step interval was measured when walking at a 'high level' of beat clarity with an increasing of 6% or 10% of their comfortable walking cadence. For the other tempi, a larger step interval was measured.

Due to an error in the system, there was no data available for walking at an increase of 10% of their comfortable walking cadence at the pre-testing and no data available for walking at their comfortable walking speed with a 'low level' of beat clarity at the post-testing.

An overview of the results can be found in Table 8.

For the 12MWT, the participant reached an average baseline step interval of 962,978 mm at the pre-testing session. The participant's step interval was 855,521 mm at the post-testing session (+11,16%).

Right foot

At the pre-testing session, the step interval of the participant was larger compared to the baseline for all tempi. When comparing the baseline step interval of the post-testing with the baseline step interval of the pre-testing, the step interval showed an increase. However, when comparing the step interval of the participant at the post-testing with their baseline, a smaller step interval was for all tempi.

Due to an error in the system, there was no data available for walking at an increase of 10% of their comfortable walking cadence at the pre-testing and no data available for walking at their comfortable walking speed with a 'low level' of beat clarity at the post-testing.

An overview of the results can be found in Table 9.

For the 12MWT, the participant reached an average baseline step interval of 721,017 mm at the pre-testing session. At the post-testing session, the participant's step interval was 706,945 mm (-1,95%).

2.4.3.2. Arm B (walking non-sync to music)

B) Participant 4

Gait Cadence

At the pre-testing session, the participant's cadence was higher compared to the baseline for all tempi except when walking at their comfortable walking cadence. However, when comparing the baseline cadence at the pre-testing with the baseline cadence at the post-testing, a decrease in cadence was shown. When comparing the cadence of the participant at the post-testing with their baseline, a faster cadence was measured for all tempi except when walking at their comfortable walking cadence.

An overview of the results can be found in Table 5.

For the 12MWT, the participant reached an average baseline cadence of 90,443 steps/min at the pre-testing session.

Stride interval

Left foot

At the pre-testing session, the participant's stride interval was smaller compared to the baseline for all tempi except when walking at their comfortable walking cadence. When comparing the baseline stride interval of the post-testing with the baseline stride interval of the pre-testing, the stride interval showed an increase. However, when comparing the stride interval of the participant at the post-testing with their baseline, a smaller stride interval was measured for all the tempi except when walking at their comfortable walking cadence with a 'high level' of beat clarity.

Due to an error in the system, there was no data available for walking at their comfortable walking cadence with a 'low level' of beat clarity at the post-testing.

An overview of the results can be found in Table 6.

For the 12MWT, the participant reached an average baseline cadence of 1331,265 mm at the pre-testing session.

Right foot

At the pre-testing session, the participant's stride interval was smaller compared to the baseline for all tempi except when walking at their comfortable walking cadence. When comparing the baseline stride interval of the post-testing with the baseline stride interval of the pre-testing, the stride interval showed an increase. When comparing the stride interval of the participant at the post-testing with their baseline, a larger stride interval was measured for all the tempi except when walking at an increase of 6% of their comfortable walking cadence with a 'low level' of beat clarity.

Due to an error in the system, there was no data available for walking at an increase of 6% or 10% of their comfortable walking cadence with a 'low level' of beat clarity at the pre-testing and also no data available for walking at an increase of 10% of their comfortable walking cadence with a 'high level' of beat clarity at the post-testing.

An overview of the results can be found in Table 7.

For the 12MWT, the participant reached an average baseline cadence of 1354,646 mm at the pre-testing session.

Step interval

Left foot

At the pre-testing session, the participant's step interval was smaller compared to the baseline for all tempi. When comparing the baseline step interval of the post-testing with the baseline step interval of the pre-testing, the step interval showed an increase. However, when comparing the step interval of the participant at the post-testing with their baseline, a smaller step interval was measured for all tempi.

Due to an error in the system, there was no data available for walking at an increase of 6% of their comfortable walking speed with a 'low level' of beat clarity at the pre-testing and no data available for walking at their comfortable walking cadence with a 'low level' of beat clarity or when walking at an increase of 10% of their comfortable walking cadence with a 'high level' of beat clarity at the post-testing.

An overview of the results can be found in Table 8.

For the 12MWT, the participant reached an average baseline step interval of 1334,766 mm at the pre-testing session.

Right foot

At the pre-testing session, the step interval of the participant was larger compared to the baseline when walking at their comfortable walking cadence. However, the step interval showed a decrease compared to the baseline for the other tempi. When comparing the baseline step interval of the post-testing with the baseline step interval of the pre-testing, the step interval showed an increase. However, when comparing the step interval of the participant at the post-testing with their baseline, a smaller step interval was measured for all tempi except when walking at their comfortable walking cadence with a 'high level' of beat clarity.

Due to an error in the system, there was no data available for walking at an increase of 6% of their comfortable walking speed with a 'low level' of beat clarity at the pre-testing and no data available for walking at their comfortable walking cadence with a 'low level' of beat clarity or when walking at an increase of 10% of their comfortable walking cadence with a 'high level' of beat clarity at the post-testing.

An overview of the results can be found in Table 9.

For the 12MWT, the participant reached an average baseline step interval of 651,024 mm at the pre-testing session.

For this participant, there was no data available for the 12MWT at the post-testing session.

2.4.3.3. Arm C (walking in silence)

C) Participant 5

Gait Cadence

At the pre-testing session, the participant's cadence was higher compared to the baseline for all tempi. However, when comparing the baseline cadence at the pre-testing with the baseline cadence at the post-testing, a decrease in cadence was shown. When comparing the cadence

of the participant at the post-testing with their baseline, a slower cadence was measured for all tempi except when walking at their comfortable walking cadence with a ‘low level’ of beat clarity and when walking at an increase of 6% of their comfortable walking cadence with a ‘high level’ of beat clarity.
An overview of the results can be found in Table 5.

Stride interval

Left foot

At the pre-testing session, the participant's stride interval was smaller compared to the baseline for all tempi except when walking at their comfortable walking cadence with a ‘high level’ of beat clarity. When comparing the baseline stride interval of the post-testing with the baseline stride interval of the pre-testing, the stride interval showed an increase. When comparing the stride interval of the participant at the post-testing with their baseline, a larger stride interval was measured for all the tempi except when walking at an increase of 6% of their comfortable walking cadence with a ‘high level’ of beat clarity.
Due to an error in the system, there was no data available for walking at their comfortable walking cadence with a ‘low level’ of beat clarity at the pre-testing.
An overview of the results can be found in Table 6.

Right foot

At the pre-testing session, the participant's stride interval was smaller compared to the baseline for all tempi except when walking at an increase of 6% of their comfortable walking cadence with a ‘low level’ of beat clarity. When comparing the baseline stride interval of the post-testing with the baseline stride interval of the pre-testing, the stride interval showed an increase. When comparing the stride interval of the participant at the post-testing with their baseline, a larger stride interval was measured for all the tempi except when walking at an increase of 6% of their comfortable walking cadence with a ‘high level’ of beat clarity.
An overview of the results can be found in Table 7.

Step interval

Left foot

At the pre-testing session, the participant's step interval was smaller compared to the baseline for all tempi. When comparing the baseline step interval of the post-testing with the baseline step interval of the pre-testing, the step interval showed an increase. However, when comparing the step interval of the participant at the post-testing with their baseline, a smaller step interval was measured for all tempi.

Due to an error in the system, there was no data available for walking at their comfortable walking speed with a 'low level' of beat clarity at the pre-testing.

An overview of the results can be found in Table 8.

Right foot

At the pre-testing session, the step interval of the participant was smaller compared to the baseline for all tempi except when walking at their comfortable walking cadence with a 'high level' of beat clarity and when walking at an increase of 6% of their comfortable walking cadence with a 'low level' of beat clarity. When comparing the baseline step interval of the post-testing with the baseline step interval of the pre-testing, the step interval showed an increase. Furthermore, when comparing the step interval of the participant at the post-testing with their baseline, a larger step interval was measured for all tempi.

Due to an error in the system, there was no data available for walking at their comfortable walking speed with a 'low level' of beat clarity at the pre-testing.

An overview of the results can be found in Table 9.

For this participant, there was no data of the 12MWT.

	Baseline	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
Participant 1 (Arm A)							
PRE	92,998	91,136	93,942	91,262	93,951	95,146	93,545
		-2,00%	+2,09%	-1,876%	+1,02%	+0,16%	+0,59%
POST	96,990	93,597	95,296	93,791	92,638	93,152	93,517
	+4,19%	-3,40%	-1,65%	-3,20%	-4,39%	-3,48%	-3,86%
Participant 2 (Arm A)							
PRE	80,970	67,375	75,287	73,696	78,563	75,395	73,994
		-16,70%	-7,34%	-8,65%	-2,86%	-6,89%	-8,26%
POST	/	/	/	/	/	/	/
Participant 3 (Arm A)							
PRE	86,393	77,343	77,175	74,001	73,792	/	/
		-10,48%	-10,67%	-11,96%	-14,34%		
POST	70,716	70,237	69,082	76,0654	73,199	75,329	70,196
	-18,15%	-0,68%	-2,31%	+3,51%	+4,35%	+6,52%	-0,74%
Participant 4 (Arm B)							
PRE	95,193	94,725	94,288	100,013	99,701	103,550	97,688
		-0,49%	-0,95%	+5.06%	+4,74%	+8,78%	+2,62%
POST	89,667	89,345	88,877	94,494	94,383	97,236	97,745
	-6,16%	-0,36%	-0,88%	+5,35%	+5,26%	+8,44%	+9,00%
Participant 5 (Arm C)							
PRE	95,110	95,902	95,415	98,776	95,250	101,028	95,578
		+0,83%	+0,32%	+3,85%	+0,15%	+6,22%	+0,49%
POST	92,084	92,048	91,689	92,231	91,592	91,224	91,591
	-3,18%	-0,04%	+3,44%	+0,16%	-0,53%	-0,93%	-0,53%

Table 5: Gait cadence (spm); values are compared to baseline (%)

	Baseline	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
Participant 1 (Arm A)							
PRE	1297,650	1317,079	1287,055	1335,290	1289,084	1276,559	1300,461
		+1,14%	-0,74%	+2,65	-0,47%	-1,36%	+0,08
POST	1255,339	1294,725	1276,851	1290,784	1310,876	1301,371	1298,254
	-3,26%	+3,10%	+1,69%	+3,33%	+4,29%	+3,59%	+3,32
Participant 2 (Arm A)							
PRE	1502,500	1788,463	1611,538	1650,949	1548,214	1613,856	1631,467
		+19,03	+7,26%	+9,88%	+3,04%	+7,41%	+,58%
POST	/	/	/	/	/	/	/
Participant 3 (Arm A)							
PRE	1394,285	1565,092	1561,156	1589,199	1634,974	/	/
		+12,25%	+11,97%	+13,98%	+17,26%		
POST	1716,384	1734,922	/	1641,570	1645,336	1600,262	/
	+23,10%	+1,02%		-4,42%	-4,14%	-6,77%	
Participant 4 (Arm B)							
PRE	1265,395	1275,460	1274,826	1204,907	1203,434	1162,714	1238,188
		+0,80%	+0.75%	-4,78%	-4,90%	-8,11%	-2,15%
POST	1343,101	1350,667	/	1274,929	1276,367	1233,787	1233,135
	+6,14%	+0,56%		-5,08%	-4,97%	-8,14%	-8,19%
Participant 5 (Arm C)							
PRE	1271,825	1256,724	/	1221,185	1267,185	1192,989	1264,068
		+1,19%		-3,94%	-0,32%	-6,16%	-0,57%
POST	1310,895	1311,214	1315,456	1307,937	1312,502	1319,573	1314,159
	+3,12%	+0,02%	+0,35%	-0,23%	+0,12%	+0,66%	+0,25%

Table 6: Stride interval left foot (mm); values are compared to baseline (%)

	Baseline	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
Participant 1 (Arm A)							
PRE	1298,140	1312,461	1288,063	1332,055	1291,588	1280,009	1298,664
		+1,10%	-0,78%	+2,61%	-0,50%	-1,40%	+0,04%
POST	1252,110	1294,213	1276,518	1294,204	1309,232	1300,364	1297,028
	-3,55%	+3,36%	+1,95%	+3,36%	+4,65%	+3,85%	+3,59%
Participant 2 (Arm A)							
PRE	1502,415	1792,020	1607,117	1654,401	1550,901	1612,983	1633,204
		+19;28%	+6;97%	+10,12%	+3,23%	+7,36%	+8,71%
POST	/	/	/	/	/	/	/
Participant 3 (Arm A)							
PRE	1394,105	1565,221	1563,990	1594,363	1638,414	/	/
		+2,27%	+2,18%	+14,36%	+17,52%		
POST	1714,801	1735,075	1736,026	1642,383	1646,105	1708,869	1598,440
	+22,99%	+1,18%	+1,24%	-4,22%	-4,01%	-0,58%	-6,79%
Participant 4 (Arm B)							
PRE	1262,965	1273,598	1275,206	1204,097	/	1162,703	1234,957
		+0,84%	+0,97%	-4,66%		-7,94%	-2.22%
POST	1342,931	1350,957	1349,903	1274,158	1274,065	/	1232,698
	+6,33%	+0,60%	+0,52%	+5,12%	-5,13%		-8,21%
Participant 5 (Arm C)							
PRE	1270,369	1256,888	1257,303	1221,888	1270,427	1193,014	1263,113
		-1,06%	-1,03%	-3,82%	+0.01%	-6,09%	-0,57%
POST	1308,001	1308,152	1314,851	1306,423	1311,063	1320,712	1311,871
	+2,96%	+0,01%	+0,52%	-0,12%	+0,23%	+0,97%	+0,30%

Table 7: Stride interval right foot (mm); values are compared to baseline (%)

	Baseline	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
Participant 1 (Arm A)							
PRE	694,614	702,778	696,563	733,828	710,218	711,562	723,457
		+0,18%	+0,28%	+5,65%	+2,25%	+2,44%	+4,15%
POST	671,937	696,657	691,973	698,005	695,684	711,976	712,661
	-3,26%	+3,68%	+2,98%	+3,88%	+3,53%	+5,96%	+6,06%
Participant 2 (Arm A)							
PRE	831,211	939,884	877,447	911,009	856,837	893,883	875,985
		+13,07%	+5,56%	+9,60%	+3,08%	+7,54%	+5,38%
POST	/	/	/	/	/	/	/
Participant 3 (Arm A)							
PRE	695,100	831,250	813,630	774,732	885,188	/	/
		+19,59%	+17,05%	+11,46%	+27,35%		
POST	838,569	952,730	/	811,222	901,591	767,006	/
	+20,64%	+13,61%		-3,26%	+7,52%	-8,53%	
Participant 4 (Arm B)							
PRE	661.317	659,583	656,243	617,722	/	609,439	644,718
		-0,22%	-0,77%	-6,59%		-7,84%	-2,51%
POST	689,832	675,879	/	645,931	646,338	/	622,444
	+4,13%	-2,02%		-6,36%	-6,30%		-9,77%
Participant 5 (Arm C)							
PRE	686,794	671,274	/	659,960	681,795	636,808	679,962
		-2,26%		-3,91%	-0,73%	-7,28%	-0,99%
POST	700,690	688,525	698,245	685,0.37	688,853	692,247	689,934
	+2,02%	-1,74%	-0,35%	-2,33%	-1,69%	-1,20%	-1,54%

Table 8: Step interval left foot (mm); values are compared to baseline (%)

	Baseline	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
Participant 1 (Arm A)							
PRE	603,251	613,601	588,442	599,404	578,248	564,577	574,416
		+1,72%	-2,45%	-0,64%	-4,14%	-6,41%	-4,78%
POST	579,285	599,454	581,856	594,281	610,967	586,049	587,244
	-3,55%	+3,48%	+0,44%	+2,59%	+5,47%	+1,37%	+1,17%
Participant 2 (Arm A)							
PRE	670,902	848,626	732,012	738,289	690,451	720,748	756,221
		+26,49%	+9,11%	+6,94%	+2,01%	+7,43%	+12,72%
POST	/	/	/	/	/	/	/
Participant 3 (Arm A)							
PRE	698,388	731,420	750,080	812,159	753,056	/	/
		+4,73%	+7,40%	+16,29%	+7,83%		
POST	874,508	778,918	/	831,105	742,934	830,556	/
	+25,26%	-10,93%		-4,96%	-15,05%	-5,03%	
Participant 4 (Arm B)							
PRE	602,950	613,314	616,850	585,215	/	554,412	589,981
		+1,71%	+2,31%	-2,94%		-8,05%	-1,82%
POST	652,138	671,788	/	627,253	627,151	/	609,177
	+8,16%	+3,01%		-3,82%	-3,83%		-6,59%
Participant 5 (Arm C)							
PRE	584,613	584,699	/	562,005	586,698	556,856	583,077
		+0,01%		-3,87%	+0,36%	-4,75%	-0,26%
POST	608.787	618,460	615,880	619,630	622,117	626,173	620,751
	+4,14%	+1,59%	+1,17%	+1,78%	+2,19%	+2,86	+1,97

Table 9: Step interval right foot (mm); values are compared to baseline (%)

2.4.4. Secondary outcome measures

2.4.4.1. Synchronisation consistency and accuracy

Arm A (walking in sync to music)

A.1) Participant 1

Result vector length

At the pre-testing session, when the participant walked at their comfortable walking cadence (CWC) with a 'high level' of beat clarity, the RVL was 0,602. At CWC with a 'low level' of beat clarity, the measured RVL was 0,537. Increasing the CWC by 6% in combination with a 'high level' of beat clarity resulted in a RVL of 0,066. While walking at 6% faster than their CWC in combination with a 'low level' of beat clarity, a value of 0,077 was measured. When increasing the CWC with 10% in combination with a 'high level' of beat clarity, the RVL showed a value of 0,021. When increasing the CWC with 10% in combination with a 'low level' of beat clarity, the RVL had a value of 0,040.

At the post-testing session, when walking at the CWC with a 'higher level' of beat clarity, a difference of 0,533 (-88,54%) was shown compared to the pre-testing data meaning a less stable synchronisation. When the participant walked at their CWC with a 'low level' of beat clarity, the synchronisation was 0,398 (-74,12%) less stable compared to the pre-testing data. Increasing the CWC by 6% in combination with a 'high level' of beat clarity, resulted in a less stable synchronisation of 0,041 (-62,12%) compared to the pre-testing data. While walking at 6% faster than their CWC in combination with a 'low level' of beat clarity, the synchronisation was less stable resulting in a RVL of 0,043 in comparison to the pre-testing data. When increasing the CWC with 10% in combination with a 'high level' of beat clarity, the RVL showed a difference of 0,014 (-66,67%) compared to the pre-testing data meaning a less stable synchronisation. When increasing the CWC with 10% in combination with a 'low level' of beat clarity, the RVL showed a difference of 0,012 (-30,00%) compared to the pre-testing data meaning a less stable synchronisation.

Relative phase angle

The data of the relative phase angle are shown in Table 10. A negative value means the step came before the beat and a positive value means the step came after the beat. The closer to zero, the better the synchronisation.

	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
PRE	-37,527	-59,463	-159.934	45,293	-143,731	98,020
POST	65.667	-52,530	162,631	-135,771	53,260	16,539

Table 10: Relative phase angle (°) participant 1

A.2) Participant 2

Result vector length

At the pre-testing session, when the participant walked at their comfortable walking cadence (CWC) with a 'high level' of beat clarity, the RVL was 0,137. At CWC with a 'low level' of beat clarity, the measured RVL was 0,037. Increasing the CWC by 6% in combination with a 'high level' of beat clarity resulted in a RVL of 0,039. While walking at 6% faster than their CWC in combination with a 'low level' of beat clarity, a value of 0,054 was measured. When increasing the CWC with 10% in combination with a 'high level' of beat clarity, the RVL showed a value of 0,026. When increasing the CWC with 10% in combination with a 'low level' of beat clarity, the RVL had a value of 0,038.

Relative phase angle

The data of the relative phase angles are shown in **Fout! Verwijzingsbron niet gevonden.**. A negative value means the step came before the beat and a positive value means the step came after the beat. The closer to zero, the better the synchronisation. For this participant, there was no data of the post-testing session. The participant dropped out after the first intervention session.

	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
PRE	73,117	-71,776	-86,518	-164,966	6,435	133,528
POST	/	/	/	/	/	/

Table 11: Relative phase angle (°) participant 2

A.3) Participant 3

Result vector length

At the pre-testing session, when the participant walked at their comfortable walking cadence (CWC) with a 'high level' of beat clarity, the RVL was 0,304. At CWC with a 'low level' of beat clarity, the measured RVL was 0,245. Increasing the CWC by 6% in combination with a 'high level' of beat clarity resulted in a RVL of 0,168. While walking at 6% faster than their CWC in combination with a 'low level' of beat clarity, a value of 0,158 was measured. When increasing the CWC with 10%, an error occurred so no valid data was available.

At the post-testing session, when walking at the CWC with a 'higher level' of beat clarity, a difference of 0,509 (+67,43%) was shown compared to the pre-testing data meaning a more stable synchronisation. When the participant walked at their CWC with a 'low level' of beat clarity, the synchronisation was 0,670 (+276,47%) more stable compared to the pre-testing data. Increasing the CWC by 6% in combination with a 'high level' of beat clarity, resulted in a more stable synchronisation of 0,634 (+377,38%) compared to the pre-testing data. While walking at 6% faster than their CWC in combination with a 'low level' of beat clarity, the synchronisation was more stable resulting in a RVL of 0,830 in comparison to the pre-testing data. When increasing the CWC with 10% in combination with a 'high level' of beat clarity, the RVL was 0.676. When increasing the CWC with 10% in combination with a 'low level' of beat clarity, the RVL resulted in a value of 0,205.

Relative phase angle

The data of the relative phase angles are shown in Table 12. A negative value means the step came before the beat and a positive value means the step came after the beat. The closer to zero, the better the synchronisation.

	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
PRE	124,150	94,348	143,234	151,201	/	/
POST	-52,421	-64,905	-19,627	-19,320	39,628	69,654

Table 12: Relative phase angle (°) participant 3

Arm B (walking non-sync to music)

B) Participant 4

Result vector length

At the pre-testing session, when the participant walked at their comfortable walking cadence (CWC) with a 'high level' of beat clarity, the RVL was 0,887. At CWC with a 'low level' of beat clarity, the measured RVL was 0,938. Increasing the CWC by 6% in combination with a 'high level' of beat clarity resulted in a RVL of 0,905. While walking at 6% faster than their CWC in combination with a 'low level' of beat clarity, a value of 0,903 was measured. When increasing the CWC with 10% in combination with a 'high level' of beat clarity, the RVL showed a value of 0,841. When increasing the CWC with 10% in combination with a 'low level' of beat clarity, the RVL had a value of 0,541.

At the post-testing session, when walking at the CWC with a 'higher level' of beat clarity, a difference of 0,023 (-2,59%) was shown compared to the pre-testing data meaning a less stable synchronisation. When the participant walked at their CWC with a 'low level' of beat clarity, the synchronisation was 0,160 (-17,06%) less stable compared to the pre-testing data. Increasing the CWC by 6% in combination with a 'high level' of beat clarity, resulted in a less stable synchronisation of 0,012 (-1,33%) compared to the pre-testing data. While walking at 6% faster than their CWC in combination with a 'low level' of beat clarity, the synchronisation was less stable resulting in a RVL of 0,892 in comparison to the pre-testing data. When increasing the CWC with 10% in combination with a 'high level' of beat clarity, the RVL showed a difference of 0,089 (-10,58%) compared to the pre-testing data meaning a less stable synchronisation. When increasing the CWC with 10% in combination with a 'low level' of beat clarity, the RVL showed a difference of 0,253 (+46,77%) compared to the pre-testing data meaning a more stable synchronisation.

Relative phase angle

The data of the relative phase angles are shown in Table 13. A negative value means the step came before the beat and a positive value means the step came after the beat. The closer to zero, the better the synchronisation.

	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
PRE	-26,570	-51,485	-34,909	-41,318	-20,835	-36,599
POST	-60,415	-71,100	-25,096	-64,784	-15,710	-48,029

Table 13: Relative phase angle (°) participant 4

Arm C (walking in silence)

C) Participant 5

Result vector length

At the pre-testing session, when the participant walked at their comfortable walking cadence (CWC) with a 'high level' of beat clarity, the RVL was 0,853. At CWC with a 'low level' of beat clarity, the measured RVL was 0,873. Increasing the CWC by 6% in combination with a 'high level' of beat clarity resulted in a RVL of 0,458. While walking at 6% faster than their CWC in combination with a 'low level' of beat clarity, a value of 0,316 was measured. When increasing the CWC with 10% in combination with a 'high level' of beat clarity, the RVL showed a value of 0,523. When increasing the CWC with 10% in combination with a 'low level' of beat clarity, the RVL had a value of 0,147.

At the post-testing session, when walking at the CWC with a 'higher level' of beat clarity, a difference of 0,167 (-19,58%) was shown compared to the pre-testing data meaning a less stable synchronisation. When the participant walked at their CWC with a 'low level' of beat clarity, the synchronisation was 0,099 (-11,34%) less stable compared to the pre-testing data. Increasing the CWC by 6% in combination with a 'high level' of beat clarity, resulted in a more stable synchronisation of 0,268 (+58,52%) compared to the pre-testing data. While walking at 6% faster than their CWC in combination with a 'low level' of beat clarity, the synchronisation was less stable resulting in a RVL of 0,737 in comparison to the pre-testing data. When increasing the CWC with 10% in combination with a 'high level' of beat clarity, the RVL showed a difference of 0,331 (-63,29%) compared to the pre-testing data meaning a less stable synchronisation. When increasing the CWC with 10% in combination with a 'low level' of beat clarity, the RVL showed a difference of 0,446 (+303,40%) compared to the pre-testing data meaning a more stable synchronisation.

Relative phase angle

The data of the relative phase angles are shown in Table 14. A negative value means the step came before the beat and a positive value means the step came after the beat. The closer to zero, the better the synchronisation.

	High 0%	Low 0%	High 6%	Low 6%	High 10%	Low 10%
PRE	-9,180	-22,335	7,289	-157,524	29,331	27,582
POST	-10,989	-22,335	-45,812	-59,517	121,813	-39,362

Table 14: Relative phase angle (°) participant 5

2.4.4.1. Perceived fatigue

Physical fatigue

Between first and last session

The calculated differences of pre and post-tests of the first session and last session of all the participants (n=3) in arm A can be seen in Table 15. Due to a drop-out, only two post measurements were available. The differences in the first session (p= 0,2983) and last session (p= 1,0000) were normal distributed. There were no statistical differences among the participants in the first session (p= 0,3356 and p= 0,5000) and last session (p= 0,5000 and 1,0000) found in physical fatigue within arm A. Also, the difference between the first and last session within the three participants were not significant (p>0,05).

	First session			Last session			First-last session
Group A	Pre	Post	Difference post-pre	Pre	Post	Difference post-pre	
Participant 1	3	9	6	2	7	5	
Participant 2	5	5	0	/	/	/	
Participant 3	5	6	1	6	6	0	
p-value			0,3356* 0,5000**			0,5000* 1,0000**	0,9597***

**t-test; **signed-ranked test; ***ANOVA*

Table 15: Results difference between first and last session in physical fatigue within arm A

The calculated differences of pre and post-tests of the first and last session in arms B and C were normal distributed (p=1,00). There were in both arms no statistical differences (p>0,05) found in physical fatigue in the first and last session (Table 16).

	First session			Last session			p-value
	Pre	Post	Difference post-pre	Pre	Post	Difference post-pre	
Group B							
Participant 4	7	9	2	6	9	3	P=0,1257* p=0,5000**
Group C							
Participant 5	3	8	5	3	6	3	P=0,1560* p=0,5000**

*t-test; **signed-ranked test

Table 16: Results difference between first and last session in physical fatigue within arm B and C

Between arms

There was a significant difference (p< 0,001) between the three groups in physical fatigue. In Figure 7, there was a tendency for less physical fatigue after the intervention in walking in sync to the music group compared to the other two groups, but no statistical analyses could be done.

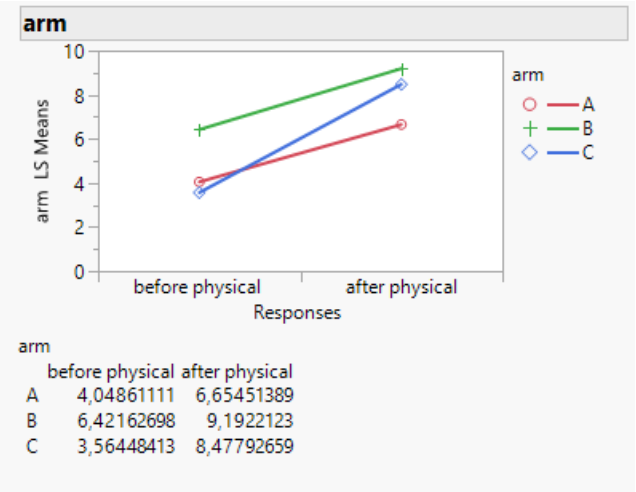


Figure 7: Differences in physical fatigue between the three groups

Cognitive fatigue

Between first and last session

The calculated differences of pre and post-tests of the first session of all the participants (n=3) were not normally distributed (p<0,0001). The differences of the last session were normally distributed (p= 1,0000). Due to a drop-out, only two post measurements were available. For both sessions, there were no statistical differences (p>0,05) found in cognitive fatigue within the participants in arm A (Table 17). Furthermore, the difference between the first and last session among the three participants was insignificant (p>0,05).

	First session			**Last session**			**First-last session**
Group A	Pre	Post	Difference post-pre	Pre	Post	Difference post-pre	
Participant 1	3	7	4	2	7	5	
Participant 2	5	5	0	/	/	/	
Participant 3	2	2	0	4	5	1	
p-value			1,0000**			0,3743* 0,5000**	0,5172***

**t-test; **signed-ranked test; ***ANOVA*

Table 17: Results difference between first and last session in cognitive fatigue within arm A

The calculated differences of pre-and post-tests of the first and last session were normally distributed (p= 1,00) in arm B. There were no statistical differences (p>0,05) found in physical fatigue in the first and last session in arm B (Table 18). In arm C, no statistical analyses were possible due to a similar result in the calculated difference between pre and post-tests. There was no difference found in cognitive between the first and last session in arm C (Table 18).

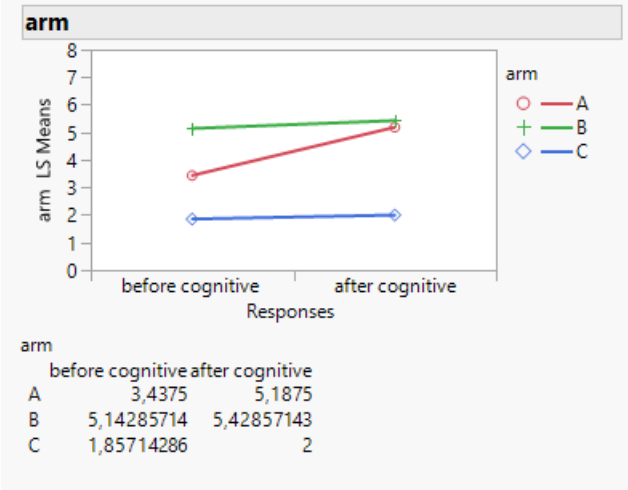
	First session			Last session			p-value
	Pre	Post	Difference post-pre	Pre	Post	Difference post-pre	
Group B							
Participant 4	5	6	1	5	5	0	p=0,5000* p= 1,0000**
Group C							
Participant 5	1	1	0	0	0	0	/

**t-test; **signed-ranked test*

Table 18: Results difference between first and last session in cognitive fatigue within arm B and C

Between arms

There was a significant difference (p<0,0008) in cognitive fatigue between the three arms. In Figure 8, there was a tendency for less cognitive fatigue after the intervention in walking in silence group compared to the other two groups, but no statistical analyses could be done.



arm

	before cognitive	after cognitive
A	3,4375	5,1875
B	5,14285714	5,42857143
C	1,85714286	2

Figure 8: Differences in cognitive fatigue between the three groups

2.4.4.2. Motivation

Between first and last session

The calculated differences of pre and post-tests of the first session of all the participants (n=3) were not normally distributed (p<0,0001). The differences of the last session were normally distributed (p= 1,0000). Due to a drop-out, only two post measurements were available. There were no statistical differences (p>0,05) found in motivation within the participants in arm A for both sessions. Furthermore, the difference between the first and last session among the three participants in arm A was not significant (p>0,05) (Table 19Table 19).

	First session			**Last session**			**First-last session**
Group A	Pre	Post	Difference post-pre	Pre	Post	Difference post-pre	
Participant 1	4	4	0	4	4	0	
Participant 2	4	4	0	/	/	/	
Participant 3	2	3	1	2	3	1	
p-value			1,0000**			0,5000* 1,0000**	0,7888***

**t-test; **signed-ranked test; ***ANOVA*

Table 19: Results difference between first and last session in motivation within arm A

No statistical analyses were possible within arms B and C due to a similar result in the calculated difference between pre and post-tests of the first and the last session. There was no difference in motivation between the first and last session in arms B and C (Table 20).

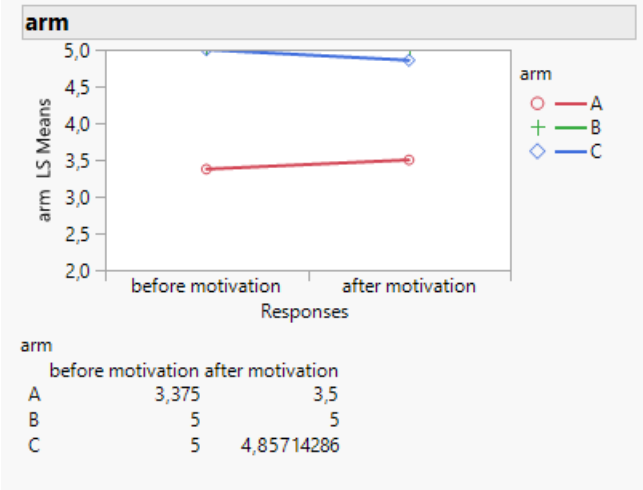
	First session			**Last session**			**p-value**
	Pre	Post	Difference post-pre	Pre	Post	Difference post-pre	
Group B							
Participant 4	5	5	0	5	5	0	/
Group C							
Participant 5	5	5	0	5	5	0	/

**t-test; **signed-ranked test*

Table 20: Results difference between first and last session in motivation within arm B and C

Between arms

There was a significant difference (p<0,0001) in motivation between the three arms. In Figure 9, there was a tendency for less motivation after the intervention in walking in sync to the music group compared to the other two groups, but no statistical analyses could be done.



arm	before motivation	after motivation
A	3,375	3,5
B	5	5
C	5	4,85714286

Figure 9: Differences in motivation between the three groups

2.4.5. Power analysis

2.4.5.1. A priori analyses future studies

The used data and results of the different effect sizes of the a priori power analysis can be seen in Figure 10. Depending on the magnitude of effect size f (Cohen, 1992), different sample sizes are required to get a chance greater than 80 percent to reject the null hypothesis correctly with a significance level of 5%. When a small effect size f (red line in Figure 10) wants to be detected, a minimum sample size of n=244 is obtained. For a medium effect size f (yellow line in Figure 10), a minimal sample size of n=42 and a large effect size f (burgundy line in Figure 10), a minimal sample size of n=18 is necessary.

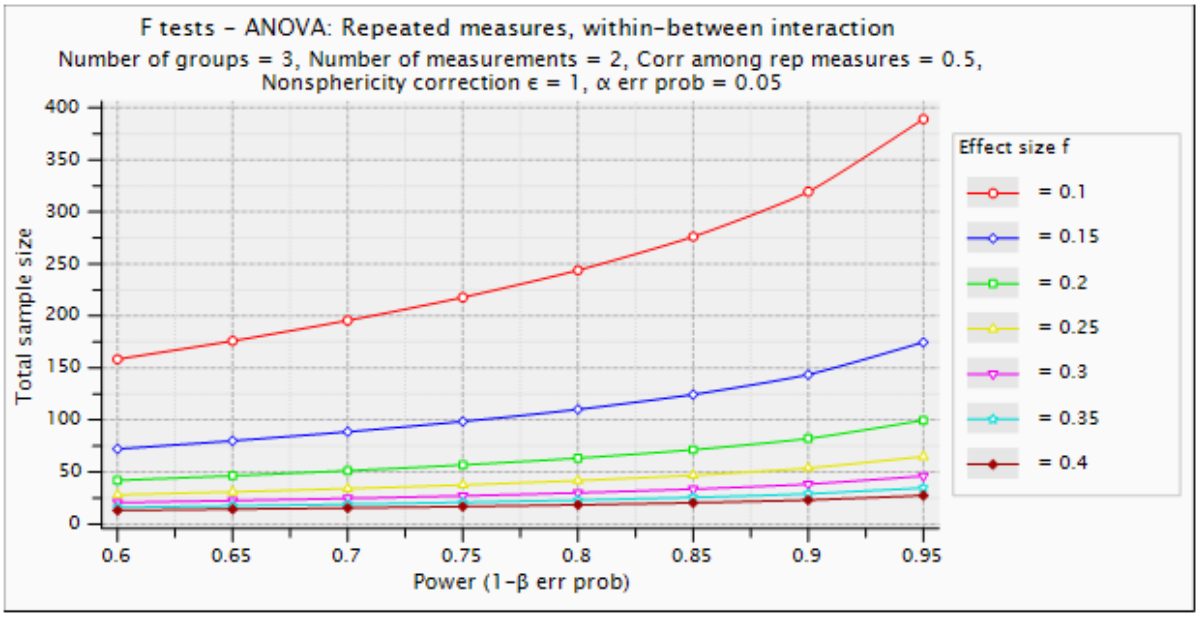


Figure 10: Results a priori analyses

2.5. Discussion

When comparing the pre and post measurements of all the participants, inconclusive results make it difficult to say if a four-week treadmill intervention with or without music influences gait parameters (gait cadence, stride and step interval and 12mwt). Also, the influence on the synchronisation ability (result vector length and relative angle phase) gave inconclusive results. There were no significant differences between the three groups between the first and last session in perceived physical and cognitive fatigue and motivation. However, there was a significant difference between the three groups found in fatigue and motivation. Thus, using RAS in therapy, awareness of the influence on perceived fatigue and motivation of the patient is crucial.

This trial provides limited evidence of the effect of RAS on gait performance of pwMS. Looking at the effect of RAS on gait performance, many studies already looked into this area. Most of the studies are about Parkinson's Disease. (Burrai et al., 2021; Wang et al., 2022), but also about other neurological pathologies there is evidence available about the benefits of RAS. Two systematic reviews and meta-analyses about stroke and acquired brain injury patients revealed improvements in walking velocity, cadence and stride length (Magee et al., 2017; Yoo & Kim, 2016).

Looking at the secondary outcome measure synchronisation, there is a lack of studies looking into this area. Furthermore, most of these studies include stroke patients, persons with Parkinson's Disease (pwPD) or healthy controls. (Crosby et al., 2020) investigated the influence of the rhythm abilities in stroke patients on the benefits of RAS on gait but found no significant influence of the strength of rhythm abilities of patients on the improvements of gait. In pwPD concluded (Benoit et al., 2014) that the benefits of auditory cueing go further than only improvements in gait. As a result, the pwPD improved their ability to synchronise and time perception after a four-week music program. Another two studies with pwPD (Dalla Bella et al., 2017; Leow et al., 2014) also stated that sensorimotor timing skills could predict the success of RAS. Lastly, a study with healthy controls (Ready et al., 2019) found that beat perception ability and giving instructions to synchronise influence spatiotemporal gait parameters when walking to music-and metronome-based rhythmic auditory stimuli.

Auditory-motor coupling plays thus a crucial role in the practice of neurological gait rehabilitation (Moumdjian et al., 2018).

The statistically significant differences between the three groups are not new for fatigue and motivation, but the found tendencies in this study were not consistent with previous findings in this area. In a study in 2019, a lower fatigue perception and higher motivation was observed in the music group (Moumdjian, Moens, Maes, Van Geel, et al., 2019).

Although this feasibility study indicates the possible benefits of RAS on gait performance in pwMS, there are limitations. Given the design/format of this study, adequate statistical data cannot be provided. Furthermore, the sample size was too small to provide statistically relevant or meaningful effects. At the beginning of the study, five participants were included. Unfortunately, one participant decided to drop out. This drop-out could lead to an attrition bias. Also, the assessors were not blinded, leading to detection bias.

The pre-and post-testing sessions were divided over two days. The number of tests could lead to more physical or cognitive fatigue. Fatigue is one of the most common MS-related symptoms (Oliva Ramirez et al., 2021), so it could have affected on our outcomes. As a pre- and post-test, the MBEA provided information about beat perception. Due to the lack of the correct answers, the test results could not be included in this study. Sadly, the APDM sensors gave errors during the pre-and post-testing sessions. So, the data about the stride length, stride width and other specific gait parameters could not be included in this study. Also, cognitive ability was not included in this study due to an error of the assessors. Cognitive dysfunction is highly prevalent in pwMS, so the question arises if this could influence the results of this intervention (Sandroff et al., 2016).

Different assessors conducted the intervention study. Despite that the assessors were educated the same way; this could have led to differences in the data based on the way assessors explained the intervention session or saved the data on the laptop. Also, not every participant succeeded in performing all eight intervention sessions, which makes it difficult to compare the participants. Furthermore, the testing of the participants was spread over a long time (> one year). This could have led to a decrease in accuracy in the testing sessions of the

assessors. All the participants were recruited from only one clinic. This can lead to a selection bias. Moreover, a study in 2019 already found that higher motivation was seen in walking to music than in metronomes and silence (Moumdjian, Moens, Maes, Van Nieuwenhoven, et al., 2019). So, a performance bias could be present given that the participants who walked on music could be more motivated than the participants walking in silence.

Looking at the results of this study, many errors have occurred. This should be avoided in upcoming literature to provide a more decisive conclusion about the influence of auditory-motor coupling on gait and synchronisation performances. Because of a limitation of the software program SAS JMP Pro 16.2.0, no post hoc tests, for example, Bonferroni, of the secondary outcome measures (perceived fatigue and motivation) were executed. The statistical analysis was done by MANOVA, whereby the software does not support post-hoc tests for repeated measures models. So, in future studies a more detailed analysis of fatigue and motivation could be interesting. Given the lack of statistical support, a power analysis was performed for future studies. This power analysis used standard values for Cohens' F, sphericity and correlation between measures. The power analysis was done with the G*Power software. Although the considerable effort has been put into evaluating the program, there is no warranty that all the data is correctly calculated (Faul et al., 2009).

Although there are limitations, this study also has strengths. The participants were blinded to the intervention. This randomisation avoided an allocation bias. Furthermore, many descriptive measures were included in this study, and the participants showed no large differences based on these measures. Also, the assessors were coupled to participants, so the participants always had the same assessor. The risk of differences in measuring per participant was, in this way, lowered. Although there was one drop-out, this study used an intention to treat analysis. Lastly, a power analysis was performed for future studies.

No general conclusion can be made because of the small sample size and the study design. Also, general implications for the work field cannot be formed. However, this study showed a fascinating insight into influence of RAS on spatiotemporal gait parameters and secondary on the synchronisation ability. So, it could be a starting point for further studies. To form a general conclusion a larger sample size is needed. The power analysis mentioned in this study shows

the number of needed participants to succeed. Furthermore, the inclusion of beat perception tests such as MBEA and the inclusion of cognitive abilities is recommended to give a complete picture of the participants and the influence of it on their capabilities. To reduce the number of biases, blinding the assessors and less switching between them would be recommended. Also, the right way of using the sensors and looking to improve their functioning, would lead to more detailed data and a more sophisticated way of presenting them.

2.6. Conclusion

Looking at the results, it is not possible to make a general conclusion about the influence of auditory-motor coupling on gait and secondary on synchronisation ability for pwMS. However, statistically significant differences in motivation and perceived fatigue were found between the three study arms.

Despite the insufficient evidence of the reported results in this thesis, the insights could be interesting for future studies regarding music-based treadmill interventions in pwMS. Therefore, a larger sample size and more statistical analysis are needed to address the effectiveness of a music-based treadmill intervention in patients with MS.

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3. Appendices

3.1. Declaration of honour

3.2. Inventarisation form

3.3. Advice promotor

3.4. Decision trees statistics

3.5. List of abbreviations

3.1. Declaration of honour

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit RWS 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 RWS aan de UHasselt. Dit onderzoek wordt beleid door Prof. Peter Feys 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 Neurorehabilitation (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. Peter Feys/Dr. Lousin Moumdjian.

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: Ceulemans Anne

Adres: Mortel 22 3930 Achel

Geboortedatum en –plaats : 08/04/1999 te Lommel

Datum: 13/12/2022

Handtekening:

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit RWS 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 RWS aan de UHasselt. Dit onderzoek wordt beleid door Prof. Peter Feys 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 Neurorehabilitation (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. Peter Feys/Dr. Lousin Moumdjian.

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: Schuurmans Febe

Adres: Apotheker Hendrixstraat 13 3990 Peer

Geboortedatum en –plaats : 05/04/1999 te Hasselt

Datum: 13/12/2022

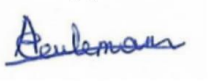
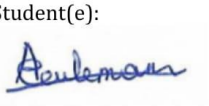
Handtekening:

3.2. Inventarisation form

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
13/12/2022	Meeting about start writing thesis 2	Promotor: Copromotor/Begeleider:  Student(e):  Student(e): 
29/03/2022	Information about statistics + forming & filling in templates of the data sets	Promotor: Copromotor/Begeleider:  Student(e):  Student(e): 
12/04/2022	Answering questions about the thesis (methodology, statistics…)	Promotor: Copromotor/Begeleider:  Student(e):  Student(e): 

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): Febe Schaumans Anne Ceulemans **Datum:** 27/5/2022

Titel Masterproef: 'The influence of a 4-week walking intervention with auditory-motor coupling compared to walking in silence on gait parameters in pwMS: a randomized feasibility study. '

1) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:
   - NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
   - 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
   - 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
   - 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering
   - 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.
   - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag	O	O	O	O	O	O
Methodologische uitwerking	O	O	O	O	O	O
Data acquisitie	O	O	O	O	O	O
Data management	O	O	O	O	O	O
Dataverwerking/Statistiek	O	O	O	O	O	O
Rapportage	O	O	O	O	O	O

2) Niet-bindend advies: Student(e) krijgt toelating/geen toelating (schrappen wat niet past) om bovenvermelde Wetenschappelijke stage/masterproef deel 2 te verdedigen in bovenvermelde periode. Deze eventuele toelating houdt geen garantie in dat de student geslaagd is voor dit opleidingsonderdeel.

3) Deze wetenschappelijke stage/masterproef deel 2 mag wel/niet (schrappen wat niet past) openbaar verdedigd worden.

4) Deze wetenschappelijke stage/masterproef deel 2 mag wel/niet (schrappen wat niet past) opgenomen worden in de bibliotheek en docserver van de UHasselt.

Datum en handtekening Student(e)	Datum en handtekening promotor(en)	Datum en handtekening Co-promotor(en)
27/05/2022	27/5/2022	

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): Febe Schuurmans **Datum:** 27/5/2022

Titel Masterproef: 'The influence of a 4-week walking intervention with auditory-motor coupling compared to walking in silence on gait parameters in pwMS: a randomized feasibility study. '

1) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:
   - NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
   - 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
   - 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
   - 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering
   - 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.
   - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	**NVT**	**1**	**2**	**3**	**4**	**5**
Opstelling onderzoeksvraag	O	O	O	O	O	O
Methodologische uitwerking	O	O	O	O	O	O
Data acquisitie	O	O	O	O	O	O
Data management	O	O	O	O	O	O
Dataverwerking/Statistiek	O	O	O	O	O	O
Rapportage	O	O	O	O	O	O

2) Niet-bindend advies: Student(e) krijgt toelating/geen toelating (schrappen wat niet past) om bovenvermelde Wetenschappelijke stage/masterproef deel 2 te verdedigen in bovenvermelde periode. Deze eventuele toelating houdt geen garantie in dat de student geslaagd is voor dit opleidingsonderdeel.

3) Deze wetenschappelijke stage/masterproef deel 2 mag wel/niet (schrappen wat niet past) openbaar verdedigd worden.

4) Deze wetenschappelijke stage/masterproef deel 2 mag wel/niet (schrappen wat niet past) opgenomen worden in de bibliotheek en docserver van de UHasselt.

Datum en handtekening Student(e)	Datum en handtekening promotor(en)	Datum en handtekening Co-promotor(en)
	27/5/2022 Peter Feys PF	

3.3. Advice promotor

Inschrijvingsformulier verdediging masterproef academiejaar 2021-2022, semester 2
Registration form jury Master's thesis academic year 2021-2022, semester 2

GEGEVENS STUDENT - *INFORMATION STUDENT*

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

Stamnummer + naam: **1746586 Ceulemans Anne**
Student number + name

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

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:* **The influence of a 4-week walking intervention with auditory-motor coupling compared to walking in silence on gait parameters in pwMS: a randomized feasibility study**

O behouden - *keep*

O wijzigen - *change to*:

UHvoorlev5 1/06/2022

Interne Promotor/*Internal Supervisor*: **Prof. dr. Peter FEYS**

O behouden - *keep*

O wijzigen - *change to*:

Interne Promotor/*Internal Supervisor*: **dr. Lousin MOUMDJIAN**

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)*: **Schuurmans Febe**

O 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)


31/05/2022

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


31/05/2022

Inschrijvingsformulier verdediging masterproef academiejaar 2021-2022, semester 2
Registration form jury Master's thesis academic year 2021-2022, semester 2

GEGEVENS STUDENT - *INFORMATION STUDENT*

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

Stamnummer + naam: **1747358 Schuurmans Febe**
Student number + name

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

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:* **The influence of a 4-week walking intervention with auditory-motor coupling compared to walking in silence on gait parameters in pwMS: a randomized feasibility study**

O behouden - *keep*

O wijzigen - *change to*:

UHvoorlev5 1/06/2022

Interne Promotor/*Internal Supervisor*: **Prof. dr. Peter FEYS**

O behouden - *keep*

O wijzigen - *change to*:

Interne Promotor/*Internal Supervisor*: **dr. Lousin MOUMDJIAN**

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)*: **Ceulemans Anne**

O 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)

31/05/2022

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

Peter Feys 31/05/2022

3.4. Decision trees statistics

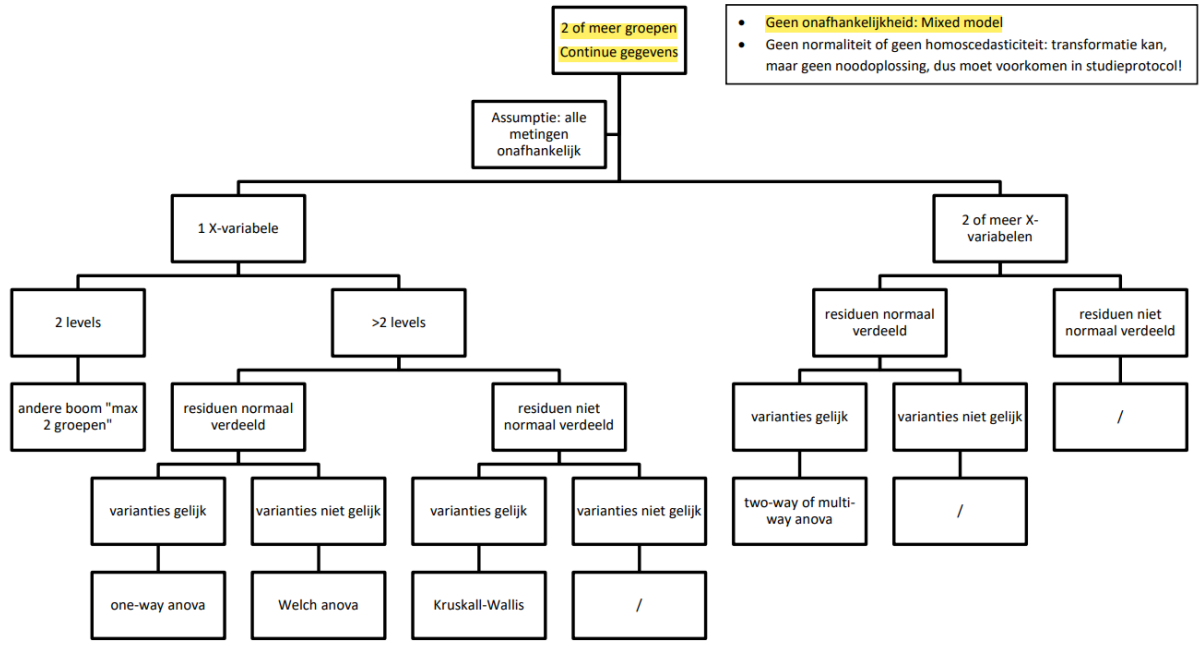


Figure 11: Decision tree original study

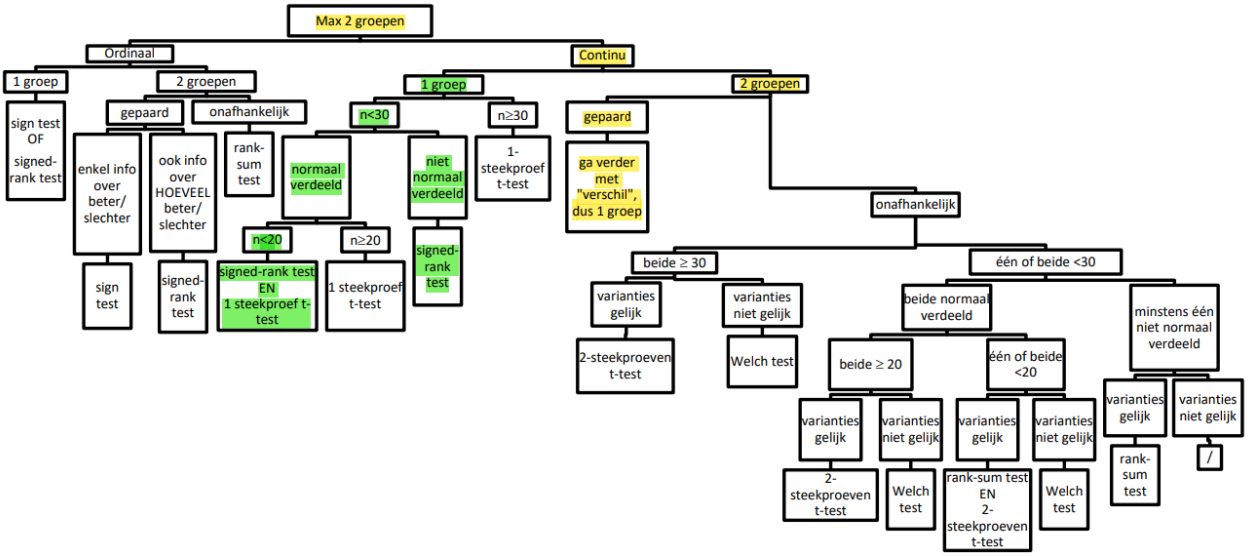


Figure 12: Decision tree feasibility study

3.5. List of abbreviations

LIST OF ABREVIATIONS

MS	Multiple Sclerosis
pwMS	persons with Multiple Sclerosis
RRMS	Relapsing-Remitting Multiple Sclerosis
SPMS	Secondary Progressive Multiple Sclerosis
PPMS	Primary Progressive Multiple Sclerosis
PRMS	Progressive Remitting Multiple Sclerosis
EDSS	Expended Disability Status Scale
RAS	Rhythmic Auditory Stimulation
rPA	relative Phase Angle
RVL	Result Vector Length
BMI	Body Mass Index
12MWT	12-minute walk test
6MWT	6-minute walk test
NHPT	Nine Hole Pec Test
TUG	Timed Up and Go
T25FWT	Timed 25-Foot Walk Test
DGI	Dynamic Gait Index
MI	Motricity Index
MAS	Modified Ashworth Scale
PASAT	Paced Auditory Serial Addition Test
SDMT	Symbols Digit Modalities Test
MBEA	Montreal Battery of Evaluation of Amusia
MSWS-12	Multiple Sclerosis Walking Scale
ABC-NL	Activities-Specific Balance Confidence Scale
MFIS	Modified Fatigue Impact Scale
HADS	Hospital Anxiety and Depression Scale
bpm	beats per minute
ICC	Intraclass Correlation Coefficient
r	Pearson’s Correlation Coefficients

VAS	Visual Analogue Scale
SD	Standard Deviation
CI	Confidence Interval
ANOVA	Analysis Of Variance
MANOVA	Multivariate Analysis Of Variance
CWC	Comfortable Walking Cadence
pwPD	persons with Parkinson's Disease