



**UHASSELT**

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## Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

### Masterthesis

***Walking to beats in music and metronomes in persons with progressive MS: preliminary pilot study results***

#### Jirte Mertens

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

#### PROMOTOR :

Prof. dr. Peter FEYS

#### COPROMOTOR :

dr. Lousin MOUMDJIAN

#### BEGELEIDER :

Mevrouw Nele VANBILSEN



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**2023**



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## **Acknowledgment**

This master's thesis is situated within the research area of gait and balance. The effects of auditory stimuli and the adaptive strategy on different gait parameters in patients with multiple sclerosis are discussed.

The results of this research can be incorporated into the treatments of patients with multiple sclerosis to achieve preservation or improvement in their gait.

This master's thesis is situated within an ongoing doctoral study by Nele Vanbilsen: 'Understanding the effect of variances on precision in predictive coding when walking to music and metronomes in persons with multiple sclerosis with progressive subtypes'. This is an FWO-funded project under the supervision of Prof. Peter Feys and Dr. Lousin Moundjian. This research was conducted at REVAL, the technology center in the Science Park in Diepenbeek, and the Rehabilitation and MS center in Pelt and Melsbroek. Participants were asked to walk on different auditory stimuli during two-hour sessions.

My research question resulted from the doctoral study of Nele Vanbilsen and was drafted with her. I would now also like to take the opportunity to thank her, as she has guided me throughout my master's thesis and has also proofread it several times. Likewise, I want to thank Prof. Peter Feys, Hasselt University, and the Rehabilitation and MS centers in Pelt and Melsbroek for giving me the opportunity to write this master's thesis.



## **Abstract**

**Background:** Synchronizing steps to beats in auditory stimuli seems feasible in persons with Multiple Sclerosis (PwMS) with progressive subtypes, showing positive effects on gait parameters. However, it remains to be investigated whether patients can maintain this synchronization during prolonged walking tasks and possibly benefit from adaptive strategies.

**Objectives:** This study investigates whether synchronization can be maintained when walking to auditory stimuli in which assistive adaptations are presented, compared to silence, in PwMS versus healthy controls (HC). Furthermore, the effects on gait parameters during eight minutes of walking are reviewed.

**Methods:** Participants were assessed when walking on their preferred baseline cadence for eight minutes in three conditions: walking to music or metronomes without adaptations (standard condition), walking to music or metronomes with adaptations (adaptive condition), and silence. While walking, cadence, stride length, speed, and synchronization were measured.

**Results:** Data were obtained from ten HC and ten PwMS. PwMS (age 49 (SD 9.9), EDSS 4.4 (2.5-6.0)) started walking above their baseline in all conditions but decreased their cadence, speed, and stride length towards the end of the walking period. HC seemed to achieve the best results when walking in silence. Both groups were able to synchronize, best with the adaptive condition, meaning the adaptive strategy is proven effective.

**Conclusion:** Walking to adaptive metronomes led to a higher cadence for PwMS, while walking in silence benefited their stride length and speed. The highest synchronization was captured when walking to adaptive music.

**Keywords:** Auditory-motor coupling; Metronome; Multiple sclerosis; Music; Prolonged walking; Spatiotemporal parameters; Synchronization.



## 1. Introduction

There are two forms of progressive Multiple Sclerosis (MS); Primary Progressive MS (PPMS) and Secondary Progressive MS (SPMS). PPMS is the least common form of MS and occurs in merely five percent of people with MS. No more relapses appear in this form, but the spinal cord is affected, and deterioration develops immediately; both legs stiffen and weaken, and strength decreases (Test, 2022). The most common form of MS is Relapsing and Remitting MS (RRMS), where active inflammation arises in the central nervous system. About 30 percent of patients with RRMS progress to a new stage after ten years: SPMS. Hardly any relapses occur in this phase, but the body's functions are impaired. In general, people with MS (PwMS) with progressive subtypes encounter problems with activities of daily living, speech, gait, contractures, and cognition, among other things (Test, 2022). To a large extent, these can be diminished or prevented by rehabilitation. Many rehabilitation strategies already exist, including physical therapy, occupational therapy, speech-language pathology, neuropsychology, driver rehabilitation, occupational rehabilitation, vision rehabilitation, and rehabilitation using technology or medical devices (Rehabilitation, 2021). In some patients, cognitive problems are one of the first symptoms of MS (MS Symptoms, 2023). This manifests in depleted information processing, memory, attention, concentration, executive functions such as planning and prioritizing, verbal fluency, and visuospatial functions, which is the capability to associate visual information with the space around (MS Symptoms, 2023). Hence, for PwMS, it may be challenging to engage in training as it requires conscious and sustained attention as well as visuospatial functions. Considering this difficulty, a task-oriented rehabilitation strategy for walking is proposed. It has been proven that several aspects of gait are affected in PwMS during sustained walking. Among other things, fatigability and a decrease in walking speed have been observed during prolonged walking tasks (Leone et al., 2016; Goldman et al., 2008; Shema-Shiratzky et al., 2019). Therefore, it appears that PwMS have trouble maintaining walking for extended periods of time. This is also seen in patients with Parkinson's disease. In a study by Ginis and colleagues (2017) on prolonged walking in Parkinson's patients, rhythmic auditory cueing was shown to improve the ability to walk for longer periods of time. When they walked on cues, patients with Parkinson's were better able to maintain their cadence as well as their attention, and it also helped them fight weariness (Ginis et al., 2017). Given these facts, auditory-motor coupling is proposed as a task-oriented rehabilitation strategy. Auditory-motor coupling occurs as the



individual aligns his or her footsteps with the beats of the music or metronomes during a process called entrainment (Moumdjian et al., 2019a). Moumdjian and colleagues (2019) mentioned that synchronization occurs once the footsteps and beats couple in terms of phase or period. This synchronization can then be considered a quantifiable result of the coupled system (Moumdjian et al., 2020).

To address the previously declared gait problems in PwMS, this study examines whether auditory-motor coupling can be used for rehabilitation. The previous research on music-based therapies in neurological populations served as the foundation for this study. It has been proven that auditory-motor coupling positively affects gait parameters in Parkinson's (Schaefer, 2014) and stroke (Rodriguez-Fornells et al., 2012). Cueing and feedback was researched in a study by Corzani and colleagues (2019) on individuals with Parkinson's disease. When patients walked slower or faster than their target cadence, cueing or feedback was used to restore the normal cadence. According to this study's findings, motor adaptations appear to be more successful when receiving feedback (Corzani et al., 2019). A study about PwMS from Moumdjian and colleagues (2019) showed that motivation was increased when walking to music compared to metronomes, caused by the experience of musical 'agency', or the feeling of being in control. PwMS were able to synchronize their steps to music and metronomes at various tempi during a three-minute walking task (Moumdjian et al., 2019b). This synchronization is also observed when PwMS walked for 12 minutes, especially when walking to music (Moumdjian et al., 2019a). The role of auditory-motor coupling in the treatment of neurological disorders has already been extensively studied. Moens and colleagues (2014) examined four distinct adaptation strategies to align music with movement in healthy controls (HC). The alignment strategy that continuously adapted the music to the participants' walking pattern showed the best results in terms of synchronization (Moens et al., 2014). Therefore, the current study aims to investigate the effects of music and metronomes on spatiotemporal gait parameters minute-by-minute between HC and PwMS. This study proposes that the process of synchronization will improve the gait parameters of PwMS during prolonged walking when assistive adaptations in auditory stimuli are implemented to bring the participant's steps back in accordance with the beat.

## 2. Methods

### 2.1 Participants

This observational non-blinded case-control study focuses on PwMS with progressive subtypes. Patients were recruited through the Rehabilitation and MS center in Pelt and Melsbroek, as well as through flyers. Once recruited, they were screened for inclusion criteria. Patients were included if they had been diagnosed with progressive MS with an Expanded Disability Status Scale (EDSS) score below 6.5 and could walk for 12 minutes at a speed of 0.8-1.2 meters per second (mps). Patients were excluded if they suffered from amusia, deafness, or cognitive impairment that interfered with understanding the study instructions, or if the patient was pregnant. The study's objectives were to include ten patients with a progressive subtype of MS and ten healthy aged-matched controls starting at 35 years old (**Table 1**). Testing occurred at the Rehabilitation and MS center in Pelt and Melsbroek and the Hasselt University campus in Diepenbeek. This study with the code B1152020000019 was approved by the Committee on Medical Ethics of UHasselt on January 20, 2021.

**Table 1**

*Baseline Characteristics of the Participants.*

Characteristics	Healthy controls (n = 10)	Patients (n = 10)
Mean age (years)	57 (SD 6.8)	49 (SD 9.9)
Mean level of education	8 (2.7)	8 (1.7)
Males (N)	6	5
Females (N)	4	5
Median EDSS (range) <sup>a</sup>	/	4.4 (2.5 – 6.0)
Baseline gait speed (mps) <sup>b</sup>	1.3 (0.1)	0.84 (0.2)
Baseline cadence (spm) <sup>c</sup>	119.4 (9.5)	98.3 (13.6)
Baseline stride length (m)	1.20 (0.03)	1.00 (0.03)
Median MSWS-12 score (60) <sup>d</sup>	/	43
Median MFIS Total (84) <sup>e</sup>	/	52
Median MFIS Physical (36)	/	23
Median MFIS Cognitive (40)	/	20
Median MFIS Psychological (8)	/	4
Median Dual-Tasking Questionnaire	/	2.8
Median PASAT (60) <sup>f</sup>	/	38.5

<sup>a</sup> EDSS: Expanded Disability Status Scale. <sup>b</sup> mps: meters per second. <sup>c</sup> spm: steps per minute.

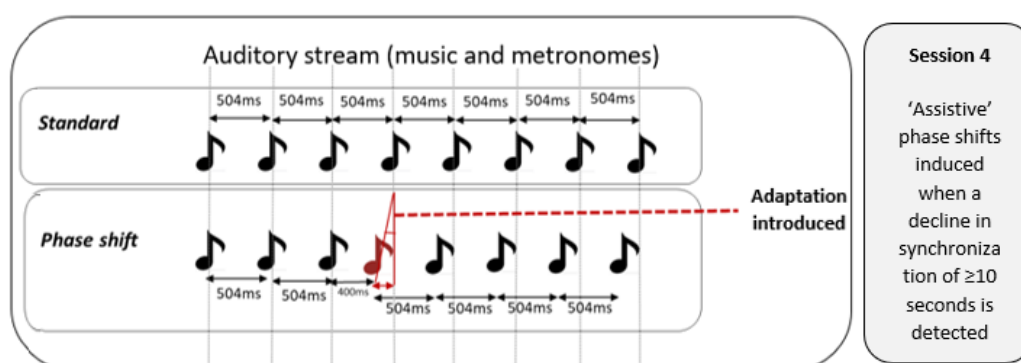
<sup>d</sup> MSWS-12: Multiple Sclerosis Walking Scale 12 items. <sup>e</sup> MFIS: Modified Fatigue Impact Scale 21 items. <sup>f</sup> PASAT: Paced Auditory Serial Addition Test.

## 2.2 Experimental procedure

The study consisted of a clinical descriptive testing session and a beat perception testing and finger tapping session, followed by two experimental walking sessions, all performed on different testing days. This study reports on results obtained during the first and fourth sessions. The second session, tapping at different tempi, and the third session, three-minute walking on standard and adaptive beats in music and metronomes at different tempi, will be discussed elsewhere.

### 2.2.1 Session 1: descriptive clinical evaluation

The first session consisted of a descriptive clinical examination and lasted two hours, with rest time included. During this testing session, general data (demographic and disease information such as EDSS-score, MS type and duration, and medications), data about motor functions (walking speed, muscle strength, spasticity, dynamic and static balance), cognitive functions, motor fatigue, cognitive fatigue, self-reported outcomes for fatigue, the experience of music reward, mood, self-reported outcomes for activity and balance, walking (Multiple Sclerosis Walking Scale-12) and a dual task battery (Dual-tasking Questionnaire) were gathered. Of particular interest for this study are general characteristics and motor function. Additionally, participants had accomplished a one-minute tapping test on a 100 beats per minute (bpm) metronome to appraise tapping skills. Lastly, a habituation task with music was assessed. Based on previously conducted studies on walking on metronomes and music in patients with MS (Moumdjian et al., 2019a; Moumdjian et al., 2019b; Moumdjian et al., 2020), the song 'Sanctum' by the artist 'Shades of the Abyss' was used to instruct participants to synchronize by stepping to the beat.



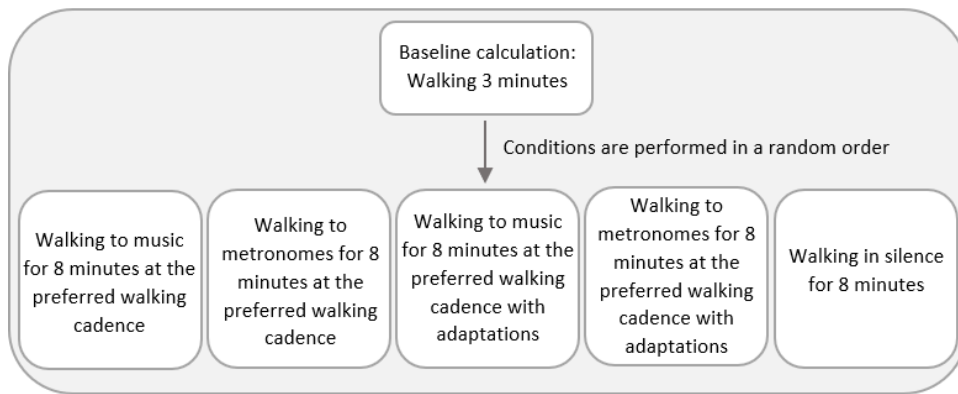
**Figure 1** - Illustration of Standard Inter-beat-intervals and the introduction of Adaptations to the standard auditory stream using a Phase Shift in Session 4.

### *2.2.2 Session 4: walking in silence and to standard and adaptive beats*

The fourth session examined walking to standard and supporting adaptive beats in music and metronomes throughout an eight-minute walking test. Given the hypothesized presence of reduced walking performance over time, the aim is to gain insight into the natural behavior of a dynamic system during prolonged walking. Furthermore, it is examined whether sustaining a high synchronization throughout the eight-minute duration can be ameliorated with the induction of subconsciously perceived assistive adaptations in the auditory stream. The D-jogger, an interactive music player, continuously monitored the participant's synchronization level (Moens et al., 2014). When a decline in synchronization consistency was ascertained within a ten-second time window, the software offered a phase shift of the sequential beat (**Figure 1**), bringing the beat closer to the step. The person was therefore facilitated to 'catch up' with the beat, which made it feasible to resume synchronization. This is also referred to as the 'adaptive strategy', which states that when someone's pace slows down, the beat of the music or metronomes similarly slows down as well to match the patients' steps and reestablish synchronization. The assignment of walking for eight minutes was chosen since it represents walking in everyday life. Especially for PwMS, this can be challenging.

#### *2.2.2.1 Procedure*

In order to establish their preferred walking cadence (baseline), participants first walked silently for three minutes. Participants then randomly performed five experimental walking conditions, including one condition in silence. Participants were instructed to walk for eight minutes while listening to music twice and metronomes twice, in two different conditions. The non-adaptive condition was characterized by walking on auditory stimuli following the preferred walking cadence, predetermined by their baseline measurement. During the second condition, the adaptive condition, participants also walked at their desired, predetermined walking cadence, but once changes in cadence were detected the participant heard assistive adaptations in the auditory stimuli, which caused them to be brought back to their desired cadence. Between each condition, the participants could rest for 15 minutes. In total, there were five different situations. Therefore, this session lasted roughly two hours and is illustrated in **Figure 2**. The research questions and outcome measures relevant to this session are shown in **Table 2**.



**Figure 2** - Visual Illustration of Session 4.

**Table 1**

*Research Questions and Outcome Measures of Session 4.*

Research questions	Primary outcome measures	Secondary outcome measured
<b>Session 4: walking for eight minutes under different conditions</b>		
1. How do assistive adaptations in music and metronomes impact gait parameters and synchronization in progressive MS during a prolonged walking task, and does the adaptive strategy work?	Spatiotemporal gait parameters (cadence, speed, stride length)	Synchronization (RVL)
2. Are there any differences in walking to adaptive auditory stimuli, non-adaptive auditory stimuli, and silence?		
3. How do these effects differ between HC and PwMS?		

### 2.2.3 Equipment

During the fourth session, participants were asked to listen to auditory stimuli through an interactive music player called The D-jogger (Moens et al., 2014), consisting of headphones, two sensors secured to the ankles, and a laptop with custom-made software. Similar to previous studies, an existing music database was used to elect the music (Van Geel et al., 2020; Moundjian et al., 2019b; Moundjian et al., 2020). The D-jogger conveyed auditory stimuli at any given tempo by altering the beat frequency of the music and metronomes and computed the synchronization between gait and music and the gait dynamics. The adaptation was presented by employing phase shifts in the inter-beat intervals, as illustrated in **Figure 1**. To measure gait, participants were equipped with four portable APDM sensors to determine spatiotemporal gait parameters, including cadence, stride length, and walking speed

(Washabaugh et al., 2017) as in previous research (Moumdjian et al., 2019a; Moumdjian et al., 2019b; Moumdjian et al., 2019c). A sensor was attached to each ankle and wrist.

Finally, two laptops were used. With one laptop, data was analyzed using the program 'Mobility Lab'. With the other laptop, the D-jogger, synchronization was established, and it was determined which music or metronomes the participant would hear. All this was set up to prevent the participants from viewing the laptop screens. Without distracting stimuli, such as other patients or people, therapists, radio music, traffic noise, etc., they walked in a square of approximately four meters by four meters.

#### *2.2.4 Outcome measures*

##### *2.2.4.1 Primary outcome measures*

Spatiotemporal gait parameters. The APDM sensors measured the cadence (steps per minute), speed (meters per second), and stride length of the left and right foot together (meters).

##### *2.2.4.2 Secondary outcome measures*

Synchronization. Synchronization of the steps to the auditory beat was assessed using the resultant vector length (RVL), which indicates the consistency of timing differences between two periodic signals. In this study, the timing difference of individual steps relative to their nearest beats was determined, also known as the phase angle. By averaging the sine and cosine coordinates of each phase angle, RVL was calculated. RVL represents how well participants aligned their steps in time to the beats, indicated by a value ranging from zero to one. Higher values illustrate more consistent synchronization, whereas lower values indicate inconsistent synchronization. (Moumdjian et al., 2020)

### 2.3 Data-analysis

The collected data were computationally modeled. Data modeling attempted to develop the most straightforward algorithm to forecast participants' synchronization behavior. To frame this model, a stepwise model construction was applied to predict participants' synchronization behavior.

A mixed model analysis of variance (ANOVA) was applied to the spatiotemporal gait parameters (cadence, stride length, and speed) with group (HC vs. PwMS) as a between-

subjects factor and condition (adaptive, non-adaptive, and silence) and minute (minute one through eight) as within-subjects factors. These analyses were performed for both the music and metronome conditions. The same model was used for the RVL, but with group (HC vs. PwMS) as a between-subjects factor and condition (adaptive vs. non-adaptive) and stimuli (music vs. metronome) as within-subjects factors. When interactions were present, a multiple comparisons Tukey's test was further performed as a post hoc test for pairwise comparisons. Missing data were manually removed from the datasheet. JMP 17 (trial) was used to conduct all of the analyses. The cut-off level for significance was chosen at  $P < 0.05$ .

### 3. Results

#### 3.1 Participants

Of the 20 participants (ten HC and ten PwMS) included in the study, data were retained from nine PwMS and nine HC. One subject was removed from the study by visual inspection of the data due to the presence of manifest outliers. This patient walked very slowly, preventing the sensors from calculating all gait parameters. One HC was also completely excluded from the study since data was only collected for the non-adaptive music and silence condition, and there was a substantial amount of missing data.

#### 3.2 Outcome measures

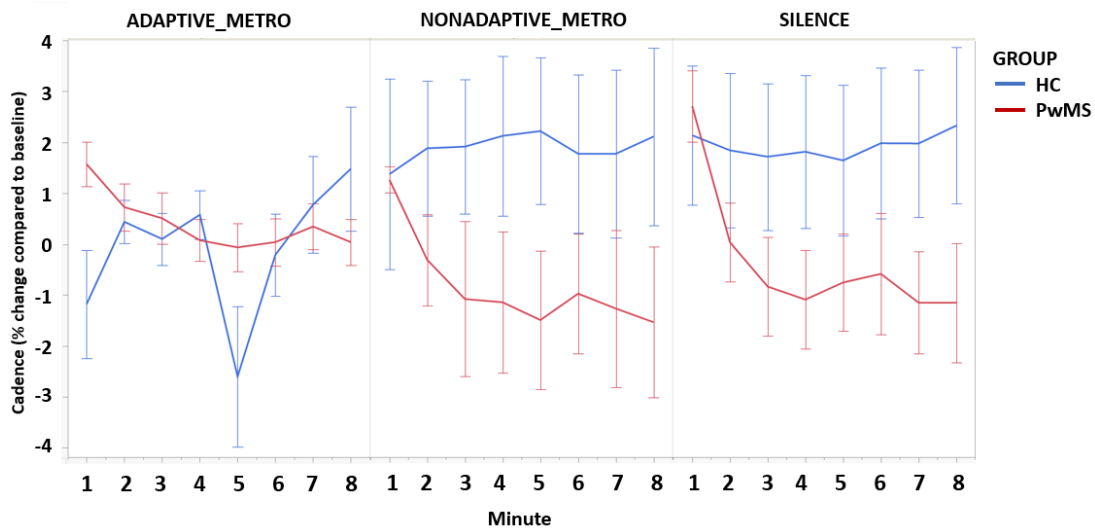
All data from spatiotemporal gait parameters were normalized relative to that participant's mean baseline. This signifies the percentage of difference in the gait parameter compared to the gait parameter during baseline. For cadence, a negative value implies that the participant took x % fewer steps per minute compared to their baseline measurement, and a positive value implies that the participant took x % more steps per minute. For speed and stride length, these values represent that the person walked x % slower or faster and took x % shorter or longer steps, respectively, compared to the baseline measurement.

##### *3.2.1 Cadence*

###### *3.2.1.1 Walking to metronomes*

Significant main effects were found for group,  $F(11, 384) = 21.6023$ ,  $p < 0.0001$ . Significant interactions were discovered for group\*minute  $F(11, 384) = 6.6334$ ,  $p = 0.0104$ , and group\*condition  $F(11, 384) = 8.0920$ ,  $p = 0.0004$ . The post hoc test indicated that HC had a significantly lower cadence while walking to adaptive metronomes compared to non-adaptive metronomes and silence ( $t = -3.21, -3.29$ ,  $p = 0.0182, 0.0138$ , respectively). It also showed that HC who walked to non-adaptive metronomes had a significantly higher cadence than PwMS in the non-adaptive metronome and silence condition ( $t = 4.66, 3.88$ ,  $p = <0.0001, 0.0017$ , respectively). This post hoc test further indicated that HC who walked in silence had a significantly higher cadence compared to PwMS in the non-adaptive and silence condition ( $t = 4.76, 3.98$ ,  $p = <0.0001, 0.0012$ , respectively). This is shown in **Figure 3**.

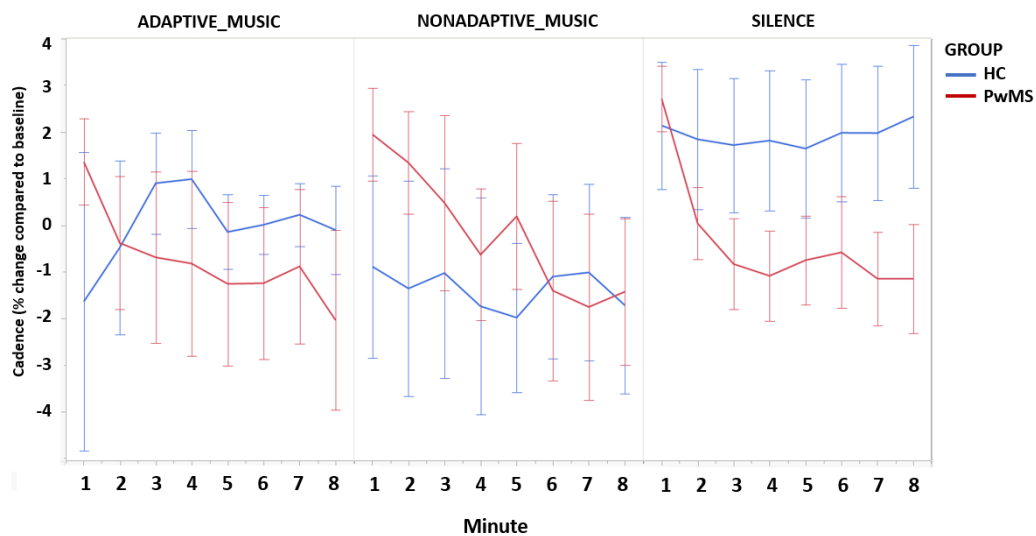




**Figure 3** – Reports the results for Mean Cadence (steps per minute) between healthy controls (HC) and people with MS (PwMS) walking to Metronomes in the adaptive, non-adaptive, and silence condition, minute-by-minute.

### 3.2.1.2 Walking to music

Significant main effects were found for condition,  $F(11, 379) = 4.4993$ ,  $p = 0.0117$ . Significant interactions were established for group\*minute  $F(11, 379) = 5.3772$ ,  $p = 0.0209$ , and group\*condition  $F(11, 379) = 5.2903$ ,  $p = 0.0054$ . The post hoc test indicated that HC had a significantly lower cadence while walking to non-adaptive music compared to silence ( $t = -4.49$ ,  $p = 0.0001$ ). It also showed that HC who walked in silence had a significantly higher cadence compared to PwMS in the adaptive music and silence condition ( $t = 3.52, 3.01$ ,  $p = 0.0063, 0.0329$ , respectively). This is depicted in **Figure 4**.

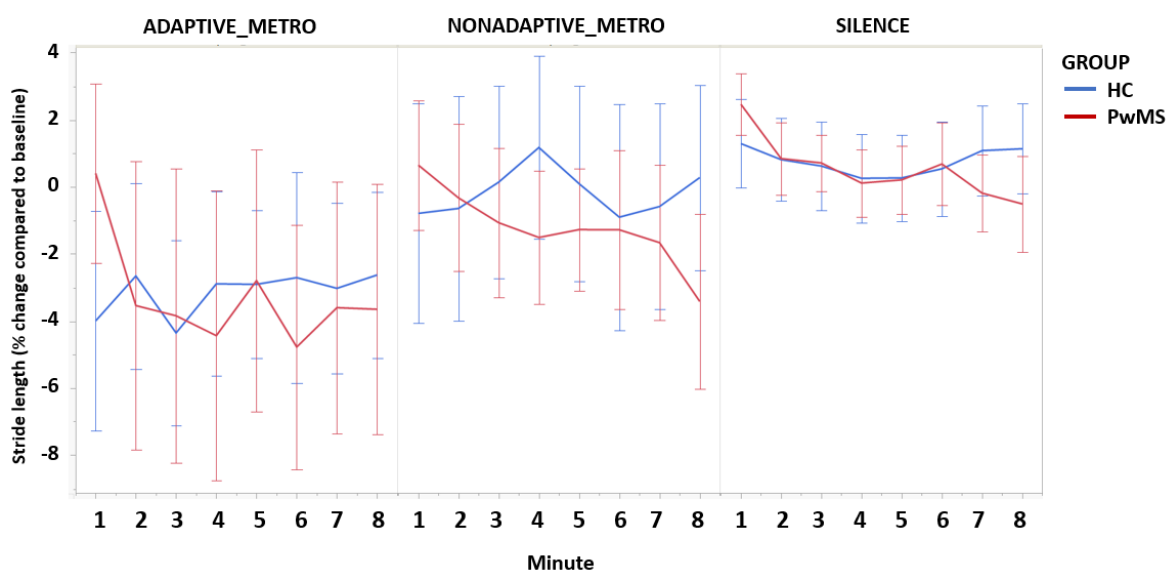


**Figure 4** – Reports the results for Mean Cadence (steps per minute) between healthy controls (HC) and people with MS (PwMS) walking to Music in the adaptive, non-adaptive, and silence condition, minute-by-minute.

### 3.2.2 Stride length

#### 3.2.2.1 Walking to metronomes

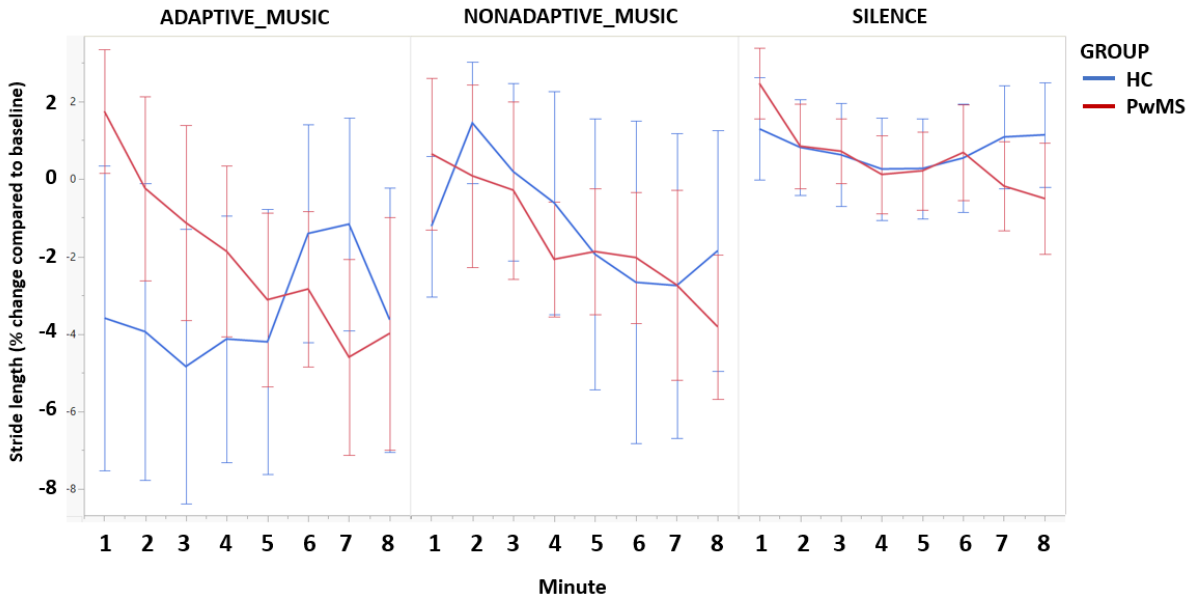
Significant main effects were found for condition  $F(11,384) = 9.5181$ ,  $p < 0.0001$ . The post hoc test indicated that both HC and PwMS had a significantly shorter stride length while walking to adaptive metronomes compared to silence ( $t = -3.01$ ,  $-3.10$   $p = 0.0333$ ,  $0.0255$ , respectively). It also showed that HC in the silence condition had a significantly longer stride length compared to PwMS in the adaptive metronome condition ( $t = 3.35$ ,  $p = 0.0113$ ). This is illustrated in **Figure 5**.



**Figure 5** - The results for Mean Stride Length (meters) between healthy controls (HC) and people with MS (PwMS) walking to Metronomes in the adaptive, non-adaptive, and silence condition, minute-by-minute.

#### 3.2.2.2 Walking to music

Significant main effects were found for minute  $F(11,379) = 4.8505$ ,  $p = 0.0282$ , and condition  $F(11,379) = 9.0161$ ,  $p = 0.0001$ . The post hoc test indicated that HC who walked to adaptive music had a significantly shorter stride length compared to both HC and PwMS who walked in silence ( $t = -3.74$ ,  $-3.46$ ,  $p = 0.0029$ ,  $0.0078$ , respectively). This is shown in **Figure 6**.

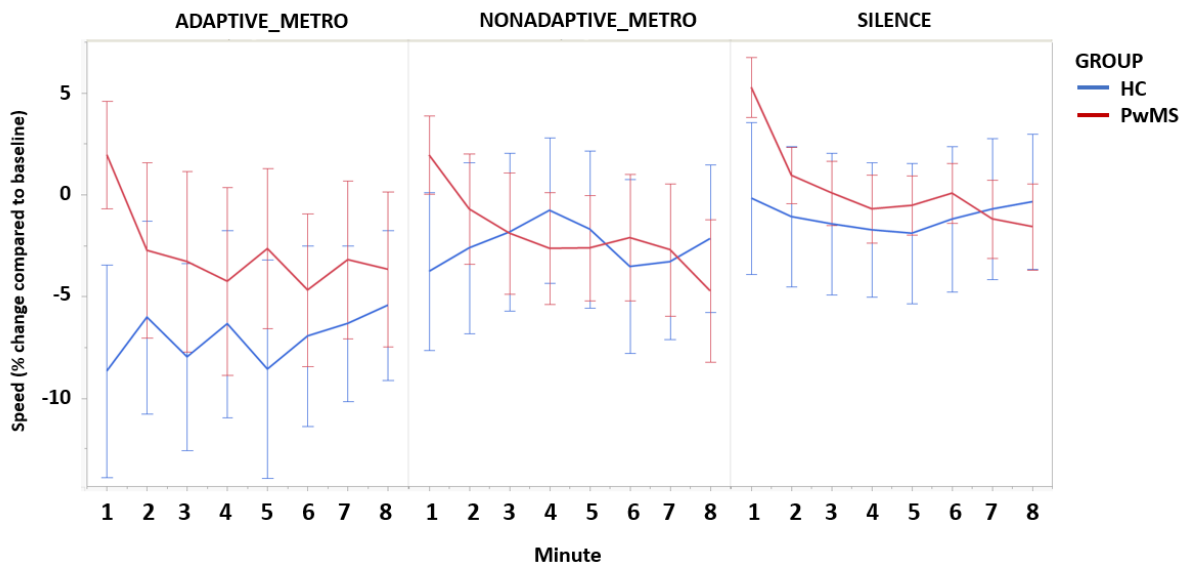


**Figure 6** - Reports the results for mean stride length (meters) between healthy controls (HC) and people with MS (PwMS) walking to music in the adaptive, non-adaptive, and silence condition, minute-by-minute.

### 3.2.3 Speed

#### 3.2.3.1 Walking to metronomes

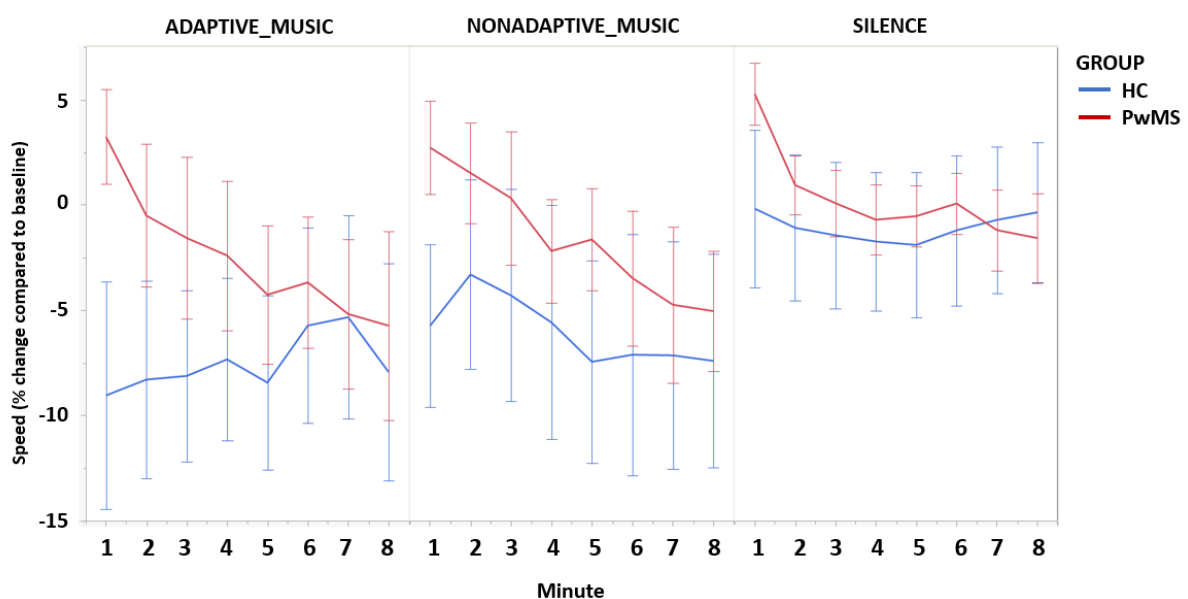
Significant main effects were found for condition  $F(11,384) = 6.1936$ ,  $p = 0.0023$ . The post hoc test indicated that HC who walked to adaptive metronomes had a significantly lower speed than HC and PwMS who walked in silence ( $t = -3.19, -3.91$ ,  $p = 0.0191, 0.0015$ , respectively). This is depicted in **Figure 7**.



**Figure 7** – Reports the results for mean speed (meters per second) between healthy controls (HC) and people with MS (PwMS) walking to metronomes in the adaptive, non-adaptive, and silence condition, minute-by-minute.

### 3.2.3.2 Walking to music

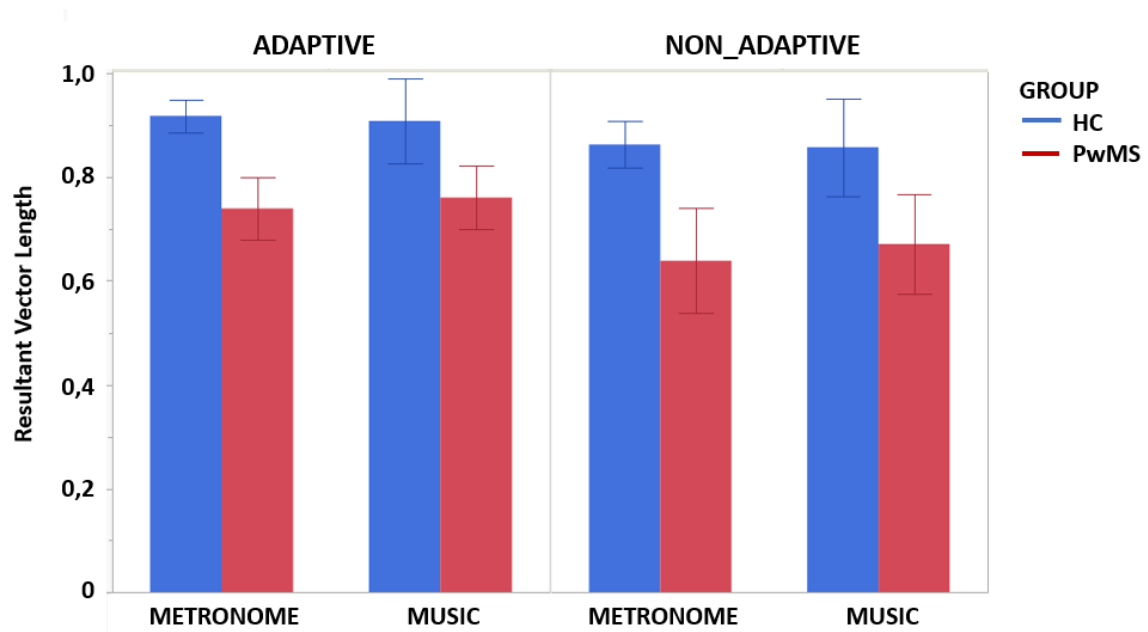
Significant main effects were found for group  $F(11,379) = 12.5438$ ,  $p = 0.0004$ , minute  $F(11,379) = 5.2421$ ,  $p = 0.0226$ , and condition  $F(11,379) = 7.2636$ ,  $p = 0.0008$ . Significant interactions were found for group\*minute  $F(11,379) = 4.3623$ ,  $p = 0.0374$ . The post hoc test indicated that HC who walked to adaptive music had a significantly lower speed compared to HC who walked in silence and PwMS who walked in non-adaptive music and silence conditions ( $t = -3.66, -3.27, -4.33$ ,  $p = 0.0040, 0.0150, 0.0003$ , respectively). It also showed that HC who walked to non-adaptive music had a significantly lower speed compared to both HC and PwMS who walked in silence ( $t = -2.88, -3.59$ ,  $p = 0.0482, 0.0049$ ). This is illustrated in **Figure 8**.



**Figure 8** - Reports the results for mean speed (meters per second) between healthy controls (HC) and people with MS (PwMS) walking to music in the adaptive, non-adaptive, and silence condition, minute-by-minute.

### 3.2.4 RVL

Significant main effects were found for group  $F(7,73) = 1.7306$ ,  $p = 0.0022$ . When the post hoc test was performed, no significant results were obtained. A graph (**Figure 9**) was compiled to examine visual trends. It can then be observed that both groups show better values in the adaptive condition, but overall, HC established higher RVL.



**Figure 9** - Reports the results for mean resultant vector length between healthy controls (HC) and people with MS (PwMS) walking to music and metronomes in the adaptive and non-adaptive condition.

## 4. Discussion

### 4.1 Main results

This observational study investigated the effects of different conditions (adaptive, non-adaptive, and silence) in music and metronomes on spatiotemporal gait parameters in an eight-minute walking task and how they differ between HC and PwMS. Additionally, auditory-motor coupling by means of synchronization was reviewed. This study hypothesized that the use of auditory stimuli would improve the gait parameters of PwMS due to the process of synchronization. Results demonstrated a decrease in all gait parameters for PwMS over the eight-minute period. The decline in cadence was best inhibited when the patients walked on metronomes with the adaptive strategy. The effects of auditory stimuli on cadence were more evident than the effects on stride length. This is not groundless given that auditory-motor coupling focuses primarily on cadence and rhythm. The auditory stimuli, both in the condition with assistive adaptations and without adaptations, even administered to slower walking speed in PwMS. However, the adaptive strategy accomplished a beneficial effect on synchronization, as all groups better aligned their steps with the beats when they heard assistive adaptations. Walking to metronomes also allured to higher synchronizations than walking to music, this can be explained by the simple and predictable rhythm of the metronome as opposed to the complex rhythm in music.

In the analysis of cadence, significant effects were observed for both walking to metronomes and walking to music. The results for walking to metronomes revealed a significant difference in cadence between HC and PwMS. The significant interaction effects indicated that the impact of both the duration of the walking task and the condition on cadence varies depending on the group. HC took fewer steps when walking on adaptive metronomes but exhibited an increased cadence when walking to non-adaptive metronomes and silence, compared to PwMS. According to **Figure 3**, a slight decrease in cadence over time can be noticed for PwMS in all conditions, ending at or even below their baseline cadence. This decrease in cadence may result from motor disorders, fatigue, or balance problems. Contrarily, HC maintained a steady cadence in the non-adaptive and silence condition, resulting in a higher cadence than their baseline tempo. It can be perceived that a sudden decrease in steps per minute taken by the HC appears in minute five in the adaptive metronome condition. When visually inspecting the data, several HC showed a remarkably

lower cadence for the fifth minute in this condition. It is possible that the HC participated with less motivation to complete the session successfully and eventually lost focus on the task, which can account for the abrupt drop in the graph. It should be highlighted that these findings were obtained solely from visual inferences and were not supported by statistical analysis.

Significant differences in cadence across the various conditions were identified while people walked to music. Significant interaction effects suggested that the duration of the task, as well as the condition, differs between HC and PwMS. The presence of non-adaptive music significantly reduced the cadence of HC, whereas the silence condition increased the number of steps per minute taken compared to PwMS. When inspecting **Figure 4**, it can be noticed that the data for music is far less stable compared to the metronome condition. PwMS showed a gradual decline in their steps per minute taken across all conditions, eventually reaching a cadence below their baseline. The HC completed an irregular eight-minute walking task in the adaptive and non-adaptive music conditions, even walking continuously below their baseline cadence during the non-adaptive condition. Given that these walking tasks were effortless for HC, this negative effect could be explained by the fact that they may experience some degree of boredom or lack of challenge. These factors could affect motivation and concentration, potentially impacting their performance. During walking in silence, on the other hand, the number of steps per minute remained adequately stable and was even higher than their baseline cadence. Again, these results were not statistically proven and were based entirely on visual assumptions.

Generally speaking, it can be stated that HC benefit more from walking in non-adaptive metronome conditions and in silence since this increases their cadence. These findings are not entirely consistent with previous research, which discovered an increase in cadence for all participants during walking to both auditory stimuli (Moumdjian et al., 2020). However, the previous study examined walking to different tempi in music and metronomes in HC and PwMS, whereas this study examines the effects of different conditions in music and metronomes. Therefore, direct comparisons cannot be made. In all conditions, PwMS started their eight-minute walking task greatly but declined as they neared the end. The adaptive strategy seems to work better with metronomes compared to music to stop the decrease in cadence over eight minutes in PwMS. They also walked persistently above or at their baseline

cadence in this condition. Prior research reveals consistent results regarding the decrease in cadence found with PwMS toward the end of the walking task (Moumdjian et al., 2019a).

In the analysis of stride length, significant main effects were observed for walking to both metronomes and music. When measuring stride length while walking to metronomes, it was discovered that the presence of adaptive metronomes shortened the distance of the steps in both HC and PwMS. On the contrary, walking in silence resulted in a longer stride length in HC compared to PwMS in the adaptive condition and, consequently, had a favorable impact. These results were also graphed, although no statistically significant information can be extracted from them. **Figure 5** presents a reduction in stride length throughout the time in all conditions for PwMS. It is noteworthy that when walking in silence, the stride length of both groups differed only slightly, and PwMS even walked above their baseline until a few minutes before the end.

Significant main effects when walking to music indicated that stride length was influenced by both the walking duration and the auditory condition. Compared to walking in silence, HC's stride length was shortened when adaptive music was present. According to **Figure 6**, a decrease in stride length throughout the time is seen in all conditions in PwMS and in the non-adaptive music condition in HC. In the non-adaptive condition, HC and PwMS exhibit nearly the same pattern of attenuation of step length. As previously stated, walking in silence increases the length of the steps taken by PwMS. However, these results were only obtained visually and were not statistically significant.

Overall, both the adaptive music and metronome condition resulted in shortened stride length in both groups, in contrast to walking in silence, which showed superior results for stride length. These findings are not entirely inconsequential. Since the participants were instructed to walk artificially to the beat, their steps may sometimes not have followed their natural gait pattern, resulting in shorter steps. Previous research established a decrease in stride length for both HC and PwMS in music and metronomes, but since this study investigated the effect of different tempi and not different conditions, the findings cannot be directly translated to this study (Moumdjian et al., 2019b).



The analysis of speed revealed significant main effects for both walking to metronomes and walking to music. Walking to adaptive metronomes particularly resulted in a slower walking speed for HC than walking in silence. **Figure 7** demonstrated that while HC did not gradually slow down, they did walk slower than their baseline speed in every condition, indicating that walking to metronomes negatively impacted their walking speed. PwMS, on the other hand, experienced a slowdown in speed yet walked faster than the HC in every condition. Once again, these graphical results were acquired by visual assessment only and were not proven statistically significant.

When walking to music, it was discovered that HC walked slower when listening to adaptive music compared to walking in silence in both HC and PwMS. Visual inferences could be drawn from **Figure 8**, where it is apparent that walking to music has a negative effect on HC's walking speed. In both the adaptive and non-adaptive conditions, HC walked far more slowly than their standard walking speed, although their pace did not diminish throughout the eight minutes. PwMS did show a decrease in speed over time but almost never walked slower than the HC. As mentioned above, walking in silence seemed the most beneficial for their speed since it was closest to baseline in this condition.

Overall, walking to music and metronomes in both the adaptive and non-adaptive conditions leads to a slower walking speed in both groups and even a decrease in speed in PwMS. Furthermore, walking in silence does not benefit HC, but this effect seems lesser. PwMS fluctuate around their baseline speed when walking in silence. Previous research confirms a reduced walking speed in HC and PwMS for music and metronomes (Moumdjian et al., 2019b). However, it should be kept in mind that this study focused on walking at different tempi rather than in different conditions, hence these findings cannot be merely compared.

When analyzing RVL, a synchronization difference between HC and PwMS can be observed. No significant interaction effects were ascertained, which could be explained by the relatively small sample size. The limited statistical findings led to the creation of a graph from which visual implications could be deduced. **Figure 9** demonstrated that both HC and PwMS were able to synchronize to all auditory stimuli in all conditions. However, walking to adaptive conditions showed higher RVL values and therefore higher synchronization, demonstrating the effectiveness of the adaptive strategy. The fact that PwMS could hear and respond to changes in rhythm confirmed the hypothesis that synchronization with assistive adaptations

would help PwMS align their steps back with the beat. When looking at the results from the Paced Auditory Serial Addition Test (PASAT), it is seen that PwMS achieve a median score of 38.5 on 60. A higher score denotes faster and more flexible processing of auditory information (Paced Auditory Serial Addition Test (PASAT), 2023). The patients demonstrate a favorable performance on this task, which supports the synchronization hypothesis. It is evident that HC synchronized better in all conditions, meaning they could better align their steps to the auditory beat than PwMS. A small difference between synchronizing to music and metronomes can be observed. HC have slightly higher synchronization values when walking on metronomes, whereas PwMS show slightly higher synchronization while walking on music. Previous research on walking to music and metronomes at different tempi indicated that both HC and PwMS exhibited higher synchronization when walking to metronomes. However, HC did synchronize at higher values than PwMS (Moumdjian et al., 2019b). This is consistent with the results of the current study, aside from the part that PwMS synchronize better to metronomes and keeping in mind that those findings result from walking to different tempi. In turn, another study by Moumdjian and colleagues (2019), where participants had to walk for 12 minutes to music and metronomes at different tempi, showed that PwMS synchronized better to music, which is more compatible with the findings of this current research (Moumdjian et al., 2019a). The reason that HC synchronize better with metronomes has actually been proven before (McKinney & Moelants, 2006). This is because metronomes have pulses that are more straightforward to forecast since they are stable and unambiguous, unlike music which is rhythmically more complex. (Moumdjian et al., 2019b). This is depicted in the graph but, as previously stated, is not statistically supported due to the small sample size. A feasible explanation for the patients' poorer achievement may be that the dual task of walking combined with adjusting the steps with the auditory stimuli was cognitively highly demanding for the PwMS, primarily since their disease is characterized, among other things, by cognitive impairment (Moumdjian et al., 2019a). When looking at the results from PwMS of the Dual-Tasking Questionnaire, a median score of 2.8 out of 5 is observed. A score of 1 indicates that participants never experience dual-task-related problems, whereas a score of 5 indicates that people experience this problem frequently (Evans et al., 2009). The score of the patients suggests that they occasionally encounter difficulties with dual tasks, which could be a contributing factor to their inadequate performance. PwMS achieved a score of less than

half on the cognitive component of the Modified Fatigue Impact Scale-12 items (MFIS-12), further indicating their challenges with cognitive tasks (Kos et al., 2003).

Although it is not statistically proven, visual data demonstrates that both groups benefit from the adaptive strategy. Walking to metronomes is slightly more advantageous for HC, whereas PwMS benefit more from walking to music.

#### 4.2 Limitations and future research

When evaluating the findings, it is essential to consider the current study's limitations. One of the crucial limitations of this study is its small sample size ( $n = 20$ ), as has been mentioned before. Furthermore, the participant's cognitive level was not considered, which could have indirectly interfered with the results. Likewise, the results may have been affected by the how active the person is and how much and far they walk in daily life, genre of the music, e.g., rock vs. jazz, fatigue, age, and gender, although these factors were not taken into consideration. The size of the walking space can also be seen as a limitation. The track of four meters by four meters caused participants to make numerous turns. However, since all sessions were conducted under identical circumstances, this ensured that all participants walked the same standardized path, which may not have affected the outcomes. A strength of this research is that this rehabilitation modality is accessible to implement in practice, recognizing that only music-playing equipment is required.

Future research should include the reciprocal relationship between cognition and synchronization ability, as well as the effects of how active the participant is in daily life, music genre, fatigue, age, and gender on outcome measures. This study did not examine the effects of multiple sessions over an extended period of time. However, in the context of auditory-motor coupling in the rehabilitation of PwMS, they may be an interesting finding.

## **5. Conclusion**

The present study provides insight into how various auditory stimuli affect gait parameters in PwMS compared to HC. It can be concluded that PwMS, in all conditions, performed well at the beginning of their eight-minute walking activity. However, their gait parameters deteriorated relative to their baseline as the task progressed. Nonetheless, they walked at or above their baseline cadence when listening to metronomes with assistive adaptations. PwMS benefited from walking in silence in terms of stride length and had reasonably excellent outcomes in terms of speed.

Visually, it was seen that PwMS overall did not perform better with assistive adaptations in the auditory stimuli, compared to music and metronomes without adaptations, as their gait parameters were below baseline each time. It can be determined that both groups were able to synchronize, yet HC synchronizes better than PwMS in all conditions. The latter benefit most from walking to music with assistive adaptations, demonstrating that the adaptive strategy for synchronization is effective.



## Reference list

1. Corzani, M., Ferrari, A. U., Ginis, P., Nieuwboer, A., & Chiari, L. (2019). Motor Adaptation in Parkinson's Disease During Prolonged Walking in Response to Corrective Acoustic Messages. *Frontiers in Aging Neuroscience*, 11. <https://doi.org/10.3389/fnagi.2019.00265>
2. Evans, J., Greenfield, E., Wilson, B. A., & Bateman, A. (2009). Walking and talking therapy: Improving cognitive–motor dual-tasking in neurological illness. *Journal of the International Neuropsychological Society*, 15(1), 112–120. <https://doi.org/10.1017/s1355617708090152>
3. Ginis, P., Heremans, E., Ferrari, A. U., Dockx, K., Canning, C. G., & Nieuwboer, A. (2017). Prolonged Walking with a Wearable System Providing Intelligent Auditory Input in People with Parkinson's Disease. *Frontiers in Neurology*, 8. <https://doi.org/10.3389/fneur.2017.00128>
4. Goldman, M. D., Marrie, R. A., & Cohen, J. A. (2008). Evaluation of the six-minute walk in multiple sclerosis subjects and healthy controls. *Multiple Sclerosis Journal*, 14(3), 383–390. <https://doi.org/10.1177/1352458507082607>
5. Kos, D., Kerckhofs, E., Nagels, G., D'Hooghe, B. D., Duquet, W., Duportail, M., & Ketelaer, P. (2003). Assessing fatigue in multiple sclerosis: Dutch modified fatigue impact scale. *PubMed*, 103(4), 185–191. <https://pubmed.ncbi.nlm.nih.gov/15008502>
6. Leone, C., Severijns, D., Doležalová, V., Baert, I., Dalgas, U., Romberg, A., Bethoux, F., Gebara, B., Medina, C. S., Maamâgi, H., Rasova, K., De Noordhout, B. M., Knuts, K., Skjerbæk, A. G., Jensen, E. C., Wagner, J. M., & Feys, P. (2016). Prevalence of Walking-Related Motor Fatigue in Persons With Multiple Sclerosis. *Neurorehabilitation and Neural Repair*, 30(4), 373–383. <https://doi.org/10.1177/1545968315597070>
7. McKinney, M. F., & Moelants, D. (2006). Ambiguity in Tempo Perception: What Draws Listeners to Different Metrical Levels? *Music Perception*, 24(2), 155–166. <https://doi.org/10.1525/mp.2006.24.2.155>
8. Moens, B., Muller, C. J., Van Noorden, L., Franěk, M., Celie, B., Boone, J., Bourgois, J., & Leman, M. (2014). Encouraging Spontaneous Synchronisation with D-Jogger, an Adaptive Music Player That Aligns Movement and Music. *PLOS ONE*, 9(12), e114234. <https://doi.org/10.1371/journal.pone.0114234>

9. Moumdjian, L., Maes, P., Bella, S. D., Decker, L. M., Moens, B., Feys, P., & Leman, M. (2020). Detrended fluctuation analysis of gait dynamics when entraining to music and metronomes at different tempi in persons with multiple sclerosis. *Scientific Reports*, 10(1). <https://doi.org/10.1038/s41598-020-69667-8>
10. Moumdjian, L., Moens, B., Maes, P., Van Geel, F., Ilsbroukx, S., Borgers, S., Leman, M., & Feys, P. (2019). Continuous 12 min walking to music, metronomes and in silence: Auditory-motor coupling and its effects on perceived fatigue, motivation and gait in persons with multiple sclerosis. *Multiple Sclerosis and Related Disorders*, 35, 92–99. <https://doi.org/10.1016/j.msard.2019.07.014>
11. Moumdjian, L., Moens, B., Maes, P., Van Nieuwenhoven, J., Van Wijmeersch, B., Leman, M., & Feys, P. (2019). Walking to Music and Metronome at Various Tempi in Persons With Multiple Sclerosis: A Basis for Rehabilitation. *Neurorehabilitation and Neural Repair*, 33(6), 464–475. <https://doi.org/10.1177/1545968319847962>
12. Moumdjian, L., Moens, B., Vanzeir, E., De Klerck, B., Feys, P., & Leman, M. (2019). A model of different cognitive processes during spontaneous and intentional coupling to music in multiple sclerosis. *Annals of the New York Academy of Sciences*, 1445(1), 27–38. <https://doi.org/10.1111/nyas.14023>
13. MS Symptoms. (n.d.). National Multiple Sclerosis Society. <https://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms>
14. Paced Auditory Serial Addition Test (PASAT). (n.d.). National Multiple Sclerosis Society. [https://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-MS-Researchers/Research-Tools/Clinical-Study-Measures/Paced-Auditory-Serial-Addition-Test-\(PASAT\)](https://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-MS-Researchers/Research-Tools/Clinical-Study-Measures/Paced-Auditory-Serial-Addition-Test-(PASAT))
15. Rehabilitation. (n.d.). National Multiple Sclerosis Society. <https://www.nationalmssociety.org/For-Professionals/Clinical-Care/Managing-MS/Rehabilitation>
16. Rodríguez-Fornells, A., Rojo, N., Amengual, J. L., Ripollés, P., Altenmüller, E., & Münte, T. F. (2012). The involvement of audio-motor coupling in the music-supported therapy applied to stroke patients. *Annals of the New York Academy of Sciences*, 1252(1), 282–293. <https://doi.org/10.1111/j.1749-6632.2011.06425.x>

17. Schaefer, R. (2014). Auditory rhythmic cueing in movement rehabilitation: findings and possible mechanisms. *Philosophical Transactions of the Royal Society B*, 369(1658), 20130402. <https://doi.org/10.1098/rstb.2013.0402>
18. Shema-Shiratzky, S., Gazit, E., Sun, R., Regev, K., Karni, A., Sosnoff, J. J., Herman, T., Mirelman, A., & Hausdorff, J. M. (2019). Deterioration of specific aspects of gait during the instrumented 6-min walk test among people with multiple sclerosis. *Journal of Neurology*, 266(12), 3022–3030. <https://doi.org/10.1007/s00415-019-09500-z>
19. Test, J. (2023). Soorten MS. MS Vereniging. [https://msvereniging.nl/over-ms/soorten-ms/?gad=1&gclid=CjwKCAjw36GjBhAkEiwAKwIWYV3t0Xbfb0f92wjt8tJp6OGicBWtFcYCbfkhUTddRoGjeGWtQihxghoCxGoQAvD\\_BwE](https://msvereniging.nl/over-ms/soorten-ms/?gad=1&gclid=CjwKCAjw36GjBhAkEiwAKwIWYV3t0Xbfb0f92wjt8tJp6OGicBWtFcYCbfkhUTddRoGjeGWtQihxghoCxGoQAvD_BwE)
20. Van Geel, F., Veldkamp, R., Severijns, D., Dalgas, U., & Feys, P. (2020). Day-to-day reliability, agreement and discriminative validity of measuring walking-related performance fatigability in persons with multiple sclerosis. *Multiple Sclerosis Journal*, 26(13), 1785–1789. <https://doi.org/10.1177/1352458519872465>
21. Washabaugh, E. P., Kalyanaraman, T., Adamczyk, P. G., Claffin, E. S., & Krishnan, C. (2017). Validity and repeatability of inertial measurement units for measuring gait parameters. *Gait & Posture*, 55, 87–93. <https://doi.org/10.1016/j.gaitpost.2017.04.013>