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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

The effect of Disability, Different Tempi and Experience of Music on Tapping Performance in People with Progressive Multiple Sclerosis

Tiemen Aerts
Ruben Glassée

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

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Preface

We are pleased to present our Master's thesis titled "The Effect of Disability, Different Tempi, and Experience of Music on Tapping Performance in People with Progressive Multiple Sclerosis." This thesis represents the culmination of our studies in Rehabilitation Sciences and Physical Therapy at the University of Hasselt (UHasselt). It forms part of the broader research study, "Understanding the Effect of Variances on Precision in Predictive Coding when Walking to Music and Metronomes in Persons with Multiple Sclerosis with Progressive Subtypes", conducted by PhD student Nele Vanbilsen and supervised by Prof Dr. Peter Feys (UHasselt).

The study from PhD student Nele Vanbilsen focuses on the effect of motor, cognitive, and perceptual timing impairments on synchronisation precision when walking or tapping to music and metronomes in persons with progressive Multiple Sclerosis. Specifically, our thesis addresses the tapping component of this study. The data collection for this thesis was carried out at REVAL UHasselt, Noorderhart Rehabilitation & MS, the National MS Centre in Melsbroek, and the library 'De Krook' in Ghent. We began this work during our scientific internship in the first year of our Master's program and continued writing the thesis from September 2023 to August 2024.

Our research is situated within the research areas of 'Motor Control, Cognition & Brain' and 'Upper Limb Rehabilitation'. These areas are particularly relevant because finger tapping requires significant cognitive capacity and motor control. The results of our study may contribute to the development of rehabilitation strategies for the upper limb in people with progressive Multiple Sclerosis. To date, limited research has been conducted on the influence of music and metronomes on the synchronisation capacity of the upper limb of people with progressive Multiple Sclerosis. Our findings can potentially serve as a foundation for developing more targeted treatments for this population.

During our first Master's year, we were both involved in participant recruitment, data collection and data analysis. The writing of the thesis was divided equally and all sections were reviewed by both authors to ensure consistency and accuracy. The research questions were formulated in consultation with our co-promoters.

We extend our gratitude to our supervisors, PhD student Nele Vanbilsen and Dr. Lousin Moumdjian, for their support, patience, and invaluable feedback throughout this process. We also thank our promoter, Prof. Dr. Peter Feys, for his guidance and expertise. Finally, we express our heartfelt appreciation to our families for their trust and support during the writing of this thesis.

Tiemen Aerts and Ruben Glassée
Hoeselt and Diepenbeek, 19th of August 2024

Table of contents

Abstract

Background. Persons with Multiple Sclerosis (PwMS) often suffer from upper limb (UL) impairments. Auditory stimulation as a part of rehabilitation strategies, while some research has been done on the subject, is still a facet of physiotherapy that remains somewhat unexplored, especially in MS.

Objectives. To investigate the auditory sensorimotor synchronisation (SMS) ability of PwMS compared to healthy controls (HC), if any relations exist between this ability and UL impairment, disability, and cognition, and finally to look into the effects different auditory stimuli and tempi could have.

Methods. Participants were asked to tap on a tapping device while being presented with auditory stimuli at 5 different tempi (-8%, -4%, 0%, +4% and +8% of a baseline measurement tempo).

Results. A total of 21 PwMS and 16 HC completed all research sessions. Both PwMS and HC were able to consistently synchronise tapping to auditory stimuli, with better synchronisation being noted with metronome as opposed to music. All participants had a tendency to anticipate the beat, however taps of PwMS who are more sensitive to musical reward aligned more closely with presented musical stimuli.

Conclusion. Both PwMS and HC demonstrated the ability to synchronise to auditory stimuli. This ability is influenced by factors such as the type and tempo of the stimulus. While more research in this field is needed, auditory-motor coupling may have implications for certain rehabilitation strategies in PwMS

Keywords. Multiple Sclerosis; tapping; music; metronome; tempi; UL impairment; cognition; music experience

Introduction

Upper limb (UL) function is vital for daily life, and its impairment significantly affects people with Multiple Sclerosis (PwMS), particularly those with progressive forms (PMS). MS is a chronic, inflammatory disease of the central nervous system (CNS), characterised by demyelination and resulting in a gradual accumulation of disability (Lassmann et al., 2007). PMS, including primary progressive (PPMS) and secondary progressive (SPMS) forms, leads to a continuous worsening of neurological function independent of relapses (Ontaneda & Fox, 2015). This research focuses on PMS due to the limited treatment options currently available (Campbell et al., 2016).

Approximately 75% of PwMS experience some degree of UL dysfunction, which impacts their independence and quality of life (QOL) (Ingram et al., 2022). These dysfunctions arise from sensory, motor, and cognitive impairments, often affecting one or both sides of the body (Ingram et al., 2022; Bertoni et al., 2015). Many PwMS exhibit impaired manual dexterity, with 60%–75% showing reduced Nine-Hole Peg Test (NHPT) scores, often due to altered sensation, decreased strength, tremor, and reduced tactile sensitivity (Bertoni et al., 2015). As MS progresses, UL impairments such as muscle weakness, tremors, sensory deficits, and impaired motor control become more pronounced (Valè et al., 2020; Kahraman, 2018), with additional cognitive deficits such as impaired attention, visuospatial perception, executive function, and memory further exacerbating impairments in UL function (Stoquart-ElSankari et al., 2010; Valè et al., 2020).

Despite the critical need for effective interventions, research on UL rehabilitation in MS is limited, especially when compared to research on lower limb rehabilitation or UL rehabilitation in other neurological conditions like stroke (Lamers et al., 2016). This scarcity of research highlights the need for studies focused on UL rehabilitation in PMS, particularly because effective disease-modifying therapies are lacking for this group (Lamers et al., 2016). While some studies suggest that rehabilitation can promote brain plasticity, there is a need for more objective measures of its efficacy and a better understanding of the mechanisms underlying functional recovery (Donzé & Massot, 2021). Rhythmic auditory stimulation (RAS), such as finger-tapping to the rhythm of a metronome or music, is a promising strategy for promoting neuroplasticity.

Finger-tapping tasks are valuable tools for assessing UL function and tracking disease progression in MS (Gulde et al., 2021). These tasks measure central excitability and conductivity, revealing that PwMS generally have reduced tapping frequencies and impaired bimanual coordination compared to healthy controls (HC), indicating sensorimotor integration deficits (Bonzano et al., 2013). This research explores auditory sensorimotor synchronisation (SMS) difficulties in PwMS through finger-tapping tasks in response to auditory stimuli (Repp, 2005). Such tasks rely on the integrity of corticospinal, cerebellar, and proprioceptive pathways, often compromised in PwMS (Ingram et al., 2022; Guimarães & Sá, 2012). Additionally, damage to the basal ganglia and cerebellum, which are critical for timing processes, further exacerbates these difficulties (Bonzano et al., 2017; Repp, 2005).

Understanding auditory SMS challenges in PwMS and their impact on finger-tapping can guide the development of targeted treatments to improve fine motor skills. Research indicates that RAS, particularly music-based interventions, has the potential to facilitate neuroplastic changes and enhance motor performance through neural entrainment in PwMS (Della Bella et al., 2017; Gibson, 2021). In rehabilitation of people with neurological conditions, consistent movement is likely critical for establishing robust neural connections and improving motor impairments (Gibson, 2021). If these findings are validated, integrating RAS into rehabilitation programs for PwMS could lead to significant improvements in both QOL and UL function. Nevertheless, further evidence-based studies are needed to support these claims, as music-based therapy remains an emerging field (Gibson, 2021).

Previous studies indicate that in PwMS, sensorimotor integration deficits and reduced sensory input lead to altered motor strategies, such as increased contact time between the thumb and another finger (Signori et al., 2020). However, when it comes to rehabilitation, the literature lacks clear recommendations due to the wide range of tempi used in tests across various studies. Research in other neurological populations like Parkinson's Disease (PD) and Essential Tremor (ET) suggests that music enhances entrainment better than metronomes, especially at medium and fast tempi, and that patients with PD and ET exhibit greater variability in tapping accuracy, while no definitive guidance for PwMS has been established (Rose et al.,2019; Luft et al., 2019).

The primary objectives of this study are threefold: to evaluate whether PwMS can consistently synchronise during a standard tapping task compared to HC; to investigate the effects of type and tempo of the presented auditory stimuli may have on tapping performance; and to explore the relationships between clinical factors (UL impairment, musical experience, level of disability, cognition) and tapping performance, and how these relationships differ with different types and tempi of auditory stimuli. This study hypotheses that PwMS will face greater difficulty synchronising their tapping with auditory rhythms compared to healthy individuals and that higher EDSS scores and related UL impairment will correlate with greater difficulty in the finger-tapping task.

Methodology

A case-controlled observational study was conducted to gather data on the performance of tapping tasks, including both PwMS with progressive subtypes and (HC).
Testings were performed at either Noorderhart Rehabilitation & MS, National MS Centre Melsbroek, at the University of Hasselt in Diepenbeek or in Ghent.
This study was approved by the Medical Ethical Committees of Hasselt University, the National MS Centre Melsbroek, and the Noorderhart Rehabilitation and MS Centre on January 20, 2021. The study is registered in the clinicaltrials.gov website (registration number: NCT04856384) and carries Belgian number B1152020000019.

Participants

PwMS were recruited through two MS rehabilitation centres in Belgium, Noorderhart Rehabilitation & MS and National MS Centre Melsbroek.
HC were recruited through social media, flyers and in-person recruitment by researchers.

A list of inclusion and exclusion criteria for PwMS and HC is provided in **Table 1**.
Walking-related criteria were defined to be able to include participants in the broader study this research is part of, which also investigates auditory-motor coupling during walking.

Table 1

Inclusion and Exclusion Criteria

	PwMS	HC
Inclusion criteria	- Age between 30 - 70 years old - Diagnosis of progressive MS[a] - No relapses within the last month - Ability to walk for 12 minutes - Walking speed between 0.8 - 1.2m/s - Right-handed	- Age between 30 - 70 years old - Right-handed
Exclusion criteria	- Amusia - Deafness - Pregnancy - Cognitive impairment hindering understanding of study instructions and/or performing questionnaires	- Diagnosis of any neurological disease - Any condition that affects walking ability - Cognitive impairment hindering understanding of study instructions and/or performing questionnaires

Note. PwMS = People with Multiple Sclerosis; HC = Healthy Controls

[a]Diagnosis following the 2017 revisions of the McDonald Diagnostic Criteria (Thompson et al., 2018)

Procedure

Subjects participated in four sessions. **Figure 1** outlines a schematic overview of the study flow. The third and fourth sessions feature experiments regarding the ability of PwMS and HC to synchronise steps to music and metronome, however, as this study focuses on the tapping performance of the participants, a detailed description of these sessions will be omitted.

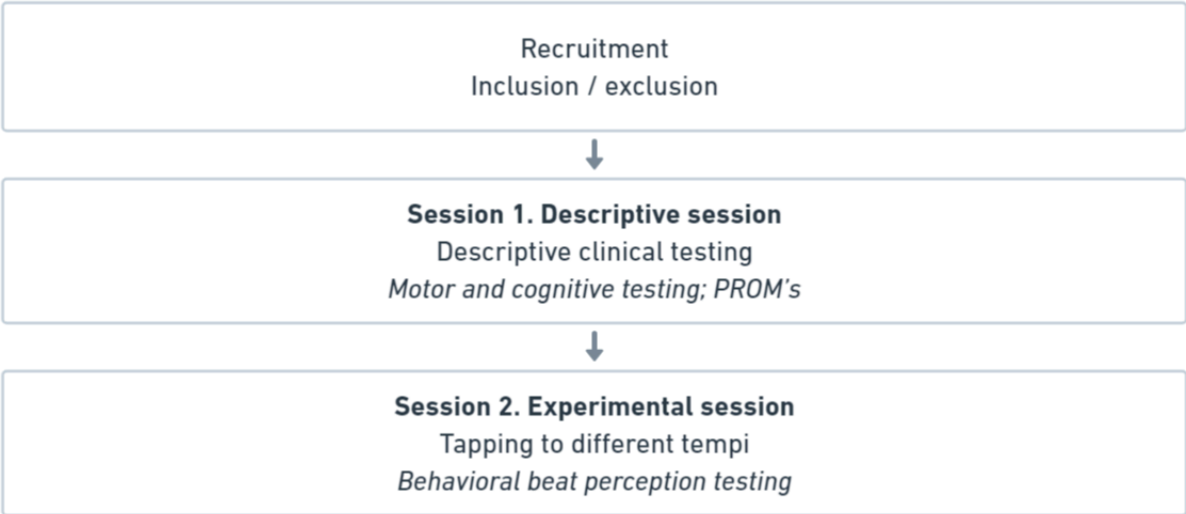
Each session was timed to be around two hours, including rest time and preparation of equipment.

Session 1. Descriptive session

During the first session, after recruitment and checking of the inclusion and exclusion criteria, descriptive data will be collected by the researcher.

Figure 1

Study Flow.



Session 2. Experimental session

In this second session, participants were sat at a table with a tapping device within reach. A baseline tapping measurement was carried out, where the participants were asked to tap on the device for one minute at a spontaneous tempo. Having completed the baseline measurement, participants were instructed to either sit still and listen to music or metronome, which was played through headphones, or to tap to the beat of the music or metronome. A total of five tempi (-8%, -4%, 0%, +4% and +8% of the baseline measurement) were tested, each for the duration of one minute.

The main experiment consists of two facets: a behavioural facet where outcome measures related to tapping performance were gathered and analysed, and a second part where data from an electroencephalogram (EEG) was taken and analysed. The scope of this study is limited to the behavioural facet of the experiment, and will not be looking into EEG-data. Data collected during the listening task was not analysed in this study, as this exceeds the scope of the behavioural facet of the experiment.

Descriptive measures

To investigate the effect of disability, UL impairment and experience of music on tapping performance in PwMS, a number of descriptive measures were used in this study.

Expanded Disability Status Scale (EDSS). The EDSS is currently the most used clinical tool for quantifying disability in PwMS (Kahraman, 2018). Scores range from 0 (normal neurological function) to 10 (death to MS), with higher scores indicating greater disability. It assesses eight functional systems, including motor and sensory functions, and is primarily used to monitor disease progression and treatment efficacy (Kurtzke, 1983). For all its merit, it is however not able to assess UL function or cognition (Kahraman, 2018), highlighting the need for other measures to evaluate these factors.

Nine Hole Peg Test (NHPT). UL impairment was quantified with the use of the NHPT, a standardised test regarded as the gold standard for measuring manual dexterity in PwMS (Ingram et al., 2022; Feys et al., 2017). During the test, individuals are required to place and remove pegs from a pegboard as quickly as possible, with separate assessments for each hand. In this study, only the score of the dominant right hand was used for all PwMS.

Symbol Digit Modalities Test (SDMT). The SDMT is a neuropsychological assessment that evaluates cognitive processing speed (Benedict et al., 2017), often used to detect cognitive impairments in PwMS (Strober et al., 2019). Participants were required to match symbols with corresponding numbers in a certain timeframe, providing a measure of cognitive function.

Barcelona Music Rewards Questionnaire (BMRQ). A somewhat obscure tool for those not versed in music-centred research, the BMRQ is a subjective evaluation of the impact of music on emotional and cognitive processes (Mas-Herrero et al., 2013). The BMRQ evaluates how music influences mood, motivation, and cognitive engagement, particularly in tasks requiring synchronisation to auditory stimuli. Higher scores indicate a greater sensitivity and responsiveness to the rewards associated with music (Mas-Herrero et al., 2013).

Outcome Measures

Besides the descriptive data collected in the first session, we also look at following objective outcome measures.

Primary outcome measures

Mean relative Phase Angle (rPA). The rPA describes the timing of taps relative to the closest beat as an angle (Rosso et al., 2021) . Taps synced in phase, i.e. perfectly to the beat, result in the rPA of 0°, tapping in period, i.e. exactly between two beats, results in an rPA of 180° (Rosso et al., 2021). Taps after the beat result in a positive rPA, taps before the beat result in a negative rPA (Rosso et al., 2021).

Mean Resultant Vector Length (RVL). To calculate the RVL we look at the distribution of the rPA over time. An even distribution points towards an unstable rPA, while a steep distribution tells us that all taps more or less coincide with the perceived beats of either music or metronome (Rosso et al., 2021). The value of the RVL can vary between 0 and 1, 0 indicating unstable synchronisation and 1 indicating perfect synchronisation between the beats and tapping of the participant (Rosso et al., 2021). A cut-off value of 0.75 was used to define the ability to synchronise, with scores <0.75 being considered not able to synchronise (Moumdjian et al., 2019b).

Mean Asynchrony. The Mean Asynchrony is measured in milliseconds and is calculated as the mean difference between the onset of the participant's tap and the onset of the closest beat, either from metronome or music (Rosso et al., 2021). Typically, the Mean Asynchrony is a negative value, indicating a slight tendency to anticipate the beat (Repp, 2005).

Secondary outcome measure

Mean Inter-Tap Interval (ITI). The ITI delineates the temporal gap between two successive taps and is typically measured in milliseconds. The larger the ITI, the greater the temporal span between taps; conversely, the smaller the ITI, the shorter the temporal gap between taps.

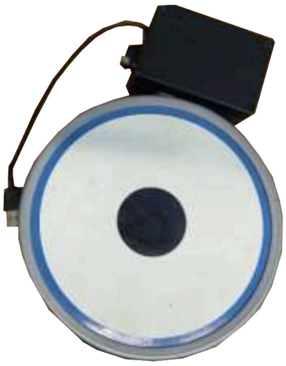
Equipment

For this research, several devices and softwares were used to collect the relevant data.

Tapping device. A round pad containing strain gauge pressure sensors connected to a Teensy 3.2 microcontroller (https://www.pjrc.com) was used to register the timing of taps (Moumdjian et al., 2022), as seen in **Figure 2**. Participants were seated in a chair, with the tapping device positioned centred in front of them within arms length. Participants were asked to perform the tapping tasks with their dominant hand.

Figure 2

Tapping device.



Software. The audio was provided through a custom made software based on the D-jogger (Moens et al., 2014), using a Max MSP Patch (https://docs.cycling74.com/max7/tutorials/03_msphowmspworks).

Headphones. The participants were asked to equip a pair of in-ear headphones provided by the researcher. Through these headphones the auditory stimuli, being either music or metronome, were provided. These stimuli were pulled from an existing music database already used in other studies (Moumdjian et al., 2019a), containing tracks with varying bpm categorised by music genre.

Data Analysis

To examine tapping data collected during this experiment, two methods were used.
First, a mixed model was built for each outcome measure (RVL, rPA, Mean Asynchrony and Mean ITI), incorporating group (HC vs PwMS) as between-subjects factors and stimuli (Music vs Metronome) and tempi (-4%, 0%, +4% and +8% of the baseline) as within-subjects factors. Post-hoc analyses were conducted using Tukey's multiple comparisons test when interactions were significant.
Simple linear regressions were performed with clinical factors (EDSS, NHPT, SDMT and BMRQ) as independent variables and outcome measures (RVL, rPA, Mean Asynchrony and Mean ITI) as dependent variables, with separate analyses also being ran per tempo and type of the administered auditory stimuli. PwMS were also divided into two categories based on EDSS score, being mild MS (EDSS score between 0 and 3.5) and moderate to severe MS (EDSS score between 4 and 9.5) (Conradsson et al., 2018), to investigate a possible difference in tapping performance between PwMS based on levels of impairment, using a 2-sample t-test.
Data analysis was performed using JMP Pro 17 (SAS Institute Inc., Cary, NC, USA). Missing data, which constituted a small portion of the dataset, were excluded from analysis by the software. A significance level of $p < .05$ was established for all statistical tests.

Results

Descriptive session

Descriptive characteristics

Of all potential participants screened, 39 passed both inclusion and exclusion criteria (21 PwMS and 18 HC). Later on, 2 HC were excluded (one drop-out and one participant due to poor quality of recorded data), leaving a dataset including 21 PwMS and 16 HC.
Table 2 shows the results of the descriptive analysis concerning demographic, motor and cognitive characteristics of both PwMS and HC.

Significant differences between both groups were found for the Buschke SRT, SDMT, PASAT and Stroop Color Tests (1, 2 and 3). All other descriptive outcome measures were either only administered in the PwMS-group, or displayed no significant difference between groups.

Experimental session

Synchronisation in PwMS compared to HC.

Table 3 relays the results related to synchronisation in tapping tasks to different stimuli and tempi. Mean data shows that, overall, patients were able to consistently synchronise to the beat at every tempo and with both stimuli, seeing as mean RVL scores consistently clear the .75 cut-off value.

Effect of type and tempo of auditory stimuli on synchronisation in PwMS and HC.

It should be noted that the normality of residuals was checked for all models. Seeing as no model exhibited normality according to the results of Shapiro-Wilk tests, the first inclination would be to reject all conclusions drawn from these models. However, according to Schielzeth et al. (2020) the models used show a remarkable robustness to data in violation of the normality assumptions that are usually in place. Using this research as a building block, conclusions can be drawn from the data provided by the models used, but should be examined carefully by any and all.
A visual summary of these results can be found in **Figure 3**.

Resultant Vector Length. Models show that for RVL, a significant interaction effect of stimuli*tempi ($F(4, 317) = 3.7$, $P = .0058$), with post-hoc tests showing that PwMS performed significantly worse with musical stimuli at a low tempo compared to metronomes at both fast ($t = 3.68$, $p = .0101$) and slow tempi ($t = 3.90$, $p = .0046$), as well as metronomes at baseline tempo ($t = 3.94$, $p = .0040$). Tapping to a slower (-8%) musical tempo also proved to be more difficult than tapping to a faster (+4%) musical tempo ($t = -3.26$, $p = .0399$).
Relative Phase Angle. For rPA, results show a significant effect of stimuli ($F(1, 325) = 18.1$, $P < .0001$), with post-hoc tests showing a significantly better ability to synchronise to metronome compared to musical stimuli ($t = -4.25$, $p < .0001$).

Table 2

Descriptive Analysis of Demographic, Motor and Cognitive Data of Study Participants

Descriptive Information	**PwMS** (n = 21)	**HC** (n = 16)	**t Test** (Prob > |t|)
Demographic Data			
Age *(years)*	51.48 ± 10.1	55.53 ± 6.75	ns
Gender *(M/F)*	14/7	7/9	ns[a]
Education *(years)*	7.38 ± 2.38	8.81 ± 2.56	ns[b]
EDSS *(0-10)*	4.19 ± 1.18	N/A	N/A
Motor Data			
NHPT/R avg *(s)*	26.11 ± 6.41	N/A	N/A
NHPT/L avg *(s)*	32.07 ± 33.15	N/A	N/A
Cognitive Data			
BMRQ *(a.u.)*	68.33 ± 9.22	N/A	N/A
Buschke SRT *(a.u.)*	35.52 ± 13.84	21.63 ± 4.56	.0002[b]
7/24 SRT *(a.u.)*	30.1 ± 4.35	31.38 ± 2.25	ns
COWAT *(a.u.)*	34.57 ± 11.02	34.5 ± 6.01	ns
SDMT *(N)*	35.81 ± 8.67	59.56 ± 8.92	.002[b]
PASAT *(N)*	49.95 ± 10.15	48.75 ± 1.29	>.0001[b]
Stroop Color Test 1	56.57 ± 8.09	50.81 ± 4.71	.0133[b]
Stroop Color Test 2	67.33 ± 7.61	62.31 ± 4.09	.0227
Stroop Color Test 3	98.38 ± 12.82	92.75 ± 4.39	.0075[b]

Abbreviations: PwMS = People with Multiple Sclerosis; HC = Healthy Controls; ns = not significant; M = Male; F = Female; EDSS = Expanded Disability Status Scale; N/A = not applicable; NHPT/Ravg = Nine Hole Peg Test/Right average; NHPT/Lavg = Nine Hole Peg Test/Left average; s = seconds; BMRQ = Barcelona Music Reward Questionnaire; a.u. = arbitrary unit; Buschke SRT = Buschke Selective Reminding Test; 7/24 SRT = Spatial Recall Test; COWAT = Controlled Oral Word Association Test; SDMT = Symbol Digit Modality Test; PASAT = Paced Auditory Serial Addition Test

[a]signifies the use of Pearson test for categorical data. [b]signifies the use of Wilcoxon rank-sum test for non-normally distributed data.

Mean Asynchrony. Similar results are shown for Mean Asynchrony, with a significant effect of stimuli ($F(1, 325) = 2.83$, $P < .0001$), favouring metronomic stimuli to musical stimuli as per post-hoc tests ($t = -4.56$, $p < .0001$).

Mean Inter-tap Interval. Finally, analysis of the Mean ITI-model yielded a significant interaction effect for group*stimuli ($F(1, 320) = 1.87$, $P = .0011$). Post hoc tests showed that tapping to negative tempi results in a greater Mean ITI in PwMS when compared to positive tempi ($t = 4.38$, $p = .0002$) and baseline tempo ($t = 2.75$, $p = .0492$). PwMS also exhibited a greater Mean ITI when tapping to metronomes when compared to a musical stimuli ($t = 5.13$, $p < .0001$).

Effect of clinical factors on synchronisation in PwMS.

To investigate the relationships between the different clinical measures (EDSS, NHPT, SDMT and BMRQ) and tapping performance, and the possible effects of type and tempo of the auditory stimuli on those relationships, separate simple linear regressions were analysed for each stimulus and tempo. The results presented in this section only include data from PwMS.

Looking at the linear regression including all PwMS, significant negative correlations were found between RVL and the NHPT ($R^2 = .03$, $F(1, 204) = 5.44$, $p = .0206$) and the EDSS ($R^2 = .02$, $F(1, 204) = 4.95$, $p = .0272$). Worse NHPT scores were also linked to higher negative Mean Asynchrony ($R^2 = .05$, $F(1, 204) = 11.22$, $p = .001$). A significant negative correlation was found between the SDMT and Mean ITI ($R^2 = .03$, $F(1, 204) = 5.39$, $p = .0212$).

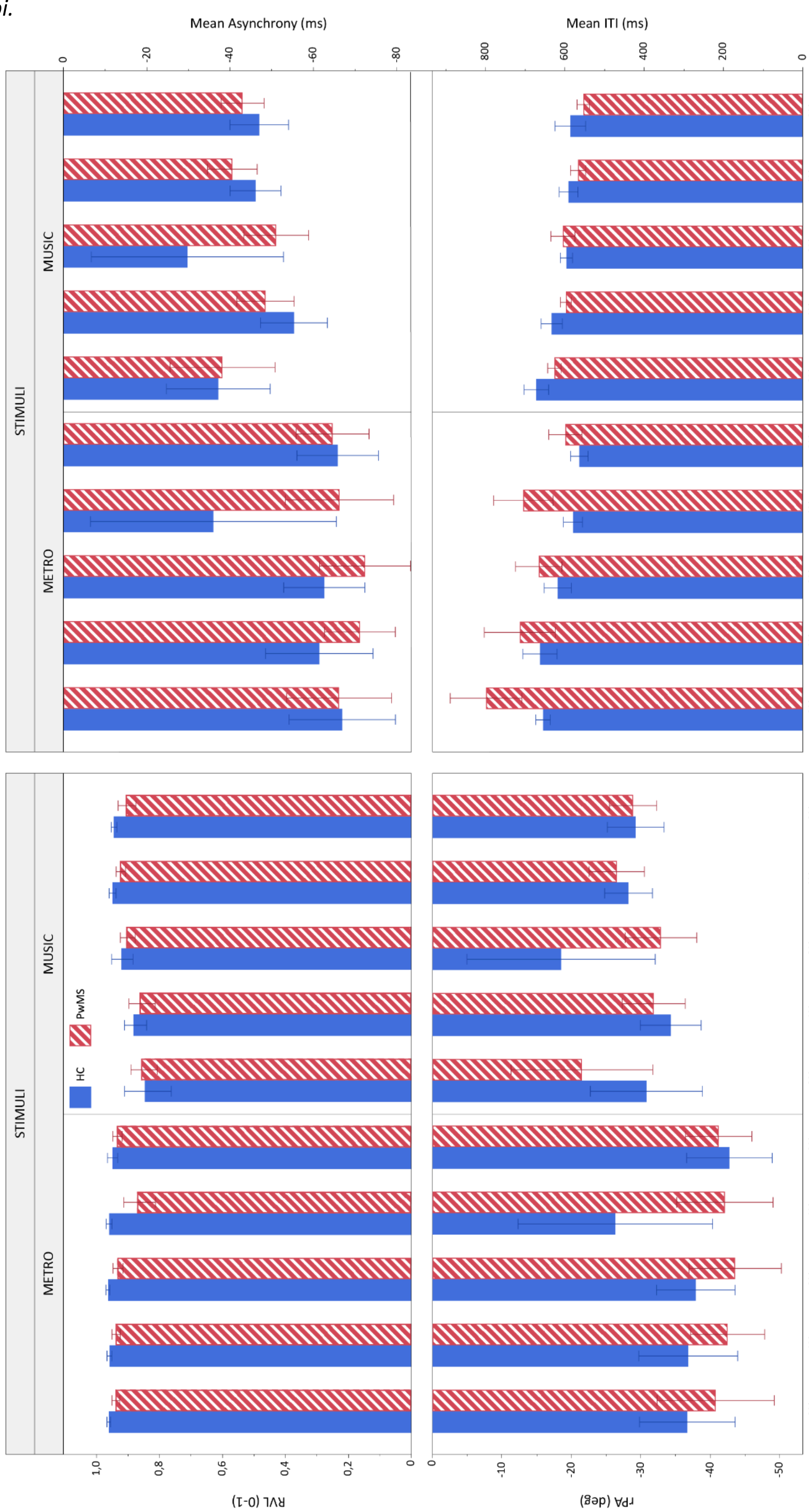
When comparing outcome measures between the mild impairment and moderate to severe impairment groups, a significant difference ($t = -2.96$, $p = .0017$) was found in RVL scores favouring PwMS suffering from mild impairments, who proved significantly better at synchronising their tapping to the beat.

The type of stimulus used proved to have an impact on these effects. When looking at the data of metronome trials, significant negative correlations were found between the NHPT and RVL ($R^2 = .14$, $F(1, 101) = 15.98$, $p = .0001$), rPA ($R^2 = .1$, $F(1, 101) = 11.51$, $p = .0001$) and Mean Asynchrony ($R^2 = .17$, $F(1, 101) = 21,16$, $p = .0001$). A visual representation of the correlations between the NHPT and RVL can be seen in **Figure 4**. When presented with musical stimuli, however, these correlations seem to disappear. Here, significant positive correlations were found between the BMRQ and rPA (R^2 = .04, F(1, 101) = 4.01, p = .0478) and Mean Asynchrony (R^2 = .07, F(1, 101) = 7.1, p = .009), while both the SDMT (R^2 = .04, F(1, 101) = 4.05, p = .0468) and NHPT (R^2 = .04, F(1, 101) = 4.49, p = .0366) showed a significant effect on the Mean ITI, with worse NHPT or SDMT scores correlating with greater intervals between two taps.

The tempo of the presented stimulus also influenced the relations between these clinical factors and the outcome measures. All significant effects disappear at a tempo of 8% below the baseline, while at 4% below baseline only one significant effect presents itself, being the negative correlation between the NHPT and Mean Asynchrony (R^2 = .12, F(1, 39) = 5.46, p = .0247). At baseline tempo, we see a similar negative correlation between the NHPT and both rPA (R^2 = .1, F(1, 40) = 4.29, p = .0448) and Mean Asynchrony (R^2 = .14, F(1, 40) = 6.74, p = .0131), as well as a positive correlation between the BMRQ and Mean ITI (R^2 = .1, F(1, 40) = 4.23, p = .0463). At 4% above baseline, the NHPT shows a significant negative correlation on the RVL (R^2 = .18, F(1, 38) = 8.09, p = .0071), while at 8% above baseline, a similar negative correlation can be seen between the NHPT and Mean Asynchrony (R^2 = .1, F(1, 39) = 4.51, p = .04).

Figure 3

Reports of mean results of secondary outcome measures of PwMS and HC tapping to music and metronome at different tempi.



Abbreviations: RVL = Resultant Vector Length; rPA = relative Phase Angle; HC = Healthy Controls; PwMS = People with Multiple Sclerosis; METRO = Metronome

Table 3

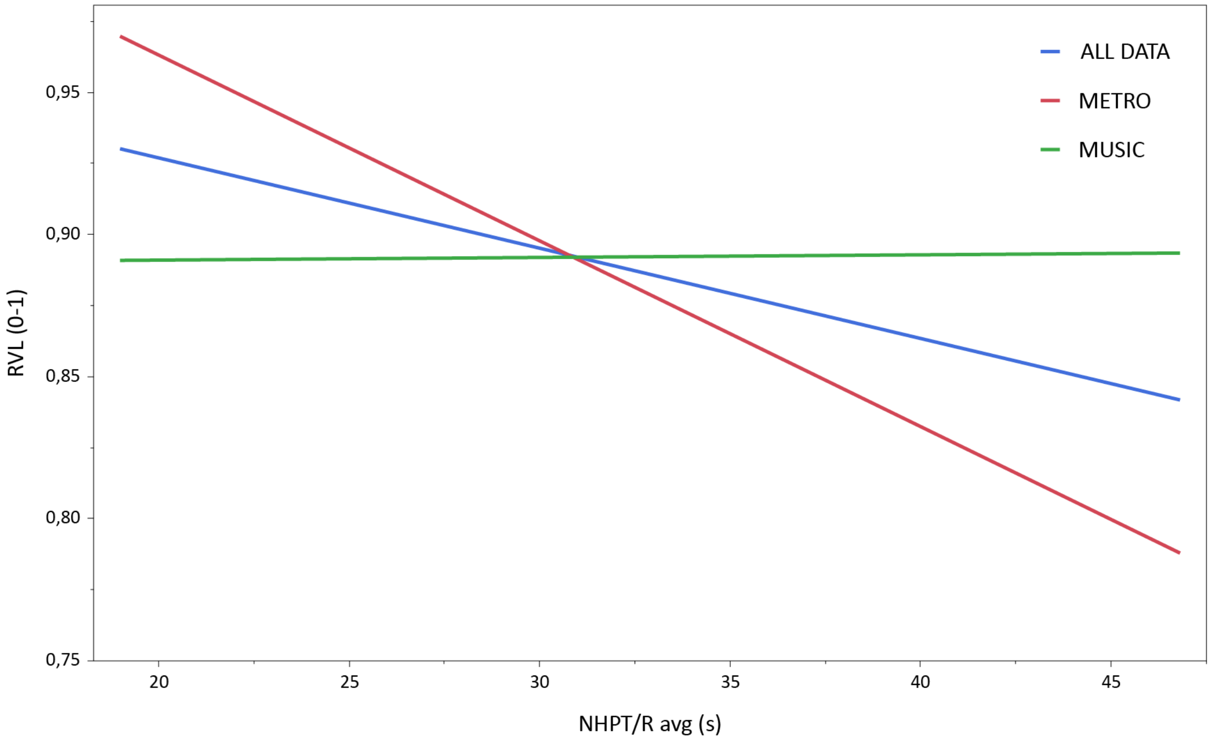
Descriptive Analysis of Outcome Measures of Tapping to Music and Metronome at Different Tempi on Auditory-Motor Coupling

		Tempi									
		-8%		-4%		0%		+4%		+8%	
OM	**Stimulus**	PwMS	HC	PwMS	HC	PwMS	HC	PwMS	HC	PwMS	HC
RVL *(0-1)* *Mean (±SD)*	Music	0.87 *(±0.02)*	0.9 *(±0.02)*	0.88 *(±0.02)*	0.9 *(±0.02)*	0.9 *(±0.02)*	0.93 *(±0.02)*	0.89 *(±0.02)*	0.92 *(±0.02)*	0.9 *(±0.02)*	0.93 *(±0.02)*
	Metronome	0.91 *(±0.02)*	0.93 *(±0.02)*	0.92 *(±0.02)*	0.94 *(±0.02)*	0.94 *(±0.02)*	0.96 *(±0.02)*	0.93 *(±0.02)*	0.95 *(±0.02)*	0.94 *(±0.02)*	0.97 *(±0.02)*
rPA *(deg.)* *Mean (±SD)*	Music	-27.91 *(±5.11)*	-24.66 *(±5.66)*	-32.43 *(±5.12)*	-29.17 *(±5.64)*	-29.94 *(±5.12)*	-26.69 *(±5.65)*	-27.61 *(±5.15)*	-24.36 *(±5.66)*	-31.39 *(±5.12)*	-28.14 *(±5.64)*
	Metronome	-38.76 *(±5.13)*	-35.5 *(±5.68)*	-43.27 *(±5.13)*	-40.02 *(±5.65)*	-40.79 *(±5.11)*	-37.53 *(±5.65)*	-38.46 *(±5.13)*	-35.2 *(±5.64)*	-42.24 *(±5.13)*	-38.98 *(±5.65)*
Mean Asynchrony *(ms)* *Mean (±SD)*	Music	-43.66 *(±8.42)*	-37.82 *(±9.28)*	-52.09 *(±8.43)*	-46.25 *(±9.24)*	-47.51 *(±8.44)*	-41.66 *(±9.28)*	-40.15 *(±8.49)*	-34.31 *(±9.28)*	-47.51 *(±8.43)*	-41.66 *(±9.24)*
	Metronome	-63.89 *(±8.45)*	-58.05 *(±9.32)*	-72.32 *(±8.45)*	-66.47 *(±9.26)*	-67.73 *(±8.41)*	-61.89 *(±9.27)*	-60.38 *(±8.45)*	-54.53 *(±9.25)*	-67.73 *(±8.45)*	-61.89 *(±9.26)*
Mean ITI *(ms)* *Mean (±SD)*	Music	675.42 *(±35.09)*	645.49 *(±38.99)*	635.6 *(±35.13)*	605.67 *(±38.85)*	603.32 *(±35.14)*	573.39 *(±38.96)*	598.09 *(±35.31)*	568.16 *(±38.97)*	561.38 *(±35.13)*	531.45 *(±38.85)*
	Metronome	739.23 *(±35.2)*	709.3 *(±39.11)*	699.4 *(±35.17)*	669.47 *(±38.92)*	667.13 *(±35.07)*	637.2 *(±38.93)*	661.9 *(±35.18)*	631.97 *(±38.88)*	625.19 *(±35.17)*	595.26 *(±38.92)*

Abbreviations: OM = Outcome Measures; PwMS = People with Multiple Sclerosis; HC = Healthy Controls; RVL = Resultant Vector Length; SD = Standard Deviation; rPA = relative Phase Angle; deg. = degrees; Mean ITI = Mean Inter-Tap Interval; ms = milliseconds

Figure 3

Reports of mean results of secondary outcome measures of PwMS and HC tapping to music and metronome at different tempi.



Abbreviations: PwMS = Persons with MS; HC = Healthy Controls; RVL = Resultant Vector Length; NHPT/R avg = Nine Hole Peg Test; METRO = Metronome

Discussion

This study offers insights into auditory-motor coupling in PwMS and HC when exposed to various auditory stimuli, including music and metronomes, at different tempi. Synchronisation abilities were assessed across five distinct tempi, with consideration of factors such as UL impairment (measured by the NHPT), disability (EDSS), cognition (SDMT), and musical experience (BMRQ).

The findings reveal that both PwMS and HC consistently and stably synchronised their taps during finger-tapping tasks, regardless of whether the stimuli were musical or metronomic. This answers the first research question and aligns with previous studies, such as those by Moumdjian (2019b), which demonstrated that both PwMS and HC participants could synchronise to music and metronomes across all tempi during walking tasks. These results suggest that this ability could extend to finger-tapping tasks as well. Furthermore, participants in both groups exhibited anticipatory tapping, consistently tapping slightly ahead of the beat across all tempi and stimulus types. This observation supports earlier findings that HC tend to anticipate beat onset and maintain stable synchronisation throughout tasks (Rosso et al., 2021). The presence of negative mean asynchrony (NMA) in all participants, where they anticipate the beat, is a well-documented phenomenon in auditory SMS studies (Repp, 2005). However, despite extensive research, the mechanisms underlying NMA remain only partially understood.

This study also reveals findings regarding the effects of auditory stimuli type (metronome or music) and tempo on finger-tapping performance in both PwMS and HC. It was observed that both groups experienced greater difficulty when tapping to a slow tempo (-8%) compared to a faster tempo (4%) when the auditory stimulus was music. Additionally, tapping to slow music (-8%) proved more challenging than tapping to a stimulus at any tempo provided by a metronome. Participants demonstrated closer synchronisation to the beat (i.e. rPA closer to 0° and Mean Asynchrony closer to 0ms) when tapping to a metronome than when tapping to music. Furthermore, this study found that PwMS exhibited an increased Mean ITI when tapping to a metronome compared to music, indicating that PwMS take more time between taps when following a metronomic rhythm.

Further analysis reveals that in PwMS, poorer performance on the NHPT is associated with a lower RVL and a more negative Mean Asynchrony, indicating reduced synchronisation and increased anticipation of the beat. Additionally, PwMS with higher EDSS scores experienced greater difficulties with synchronisation, with a significant difference between PwMS suffering from mild impairments compared to those suffering from moderate to severe impairments. Lastly, PwMS scoring higher on the SDMT exhibited shorter ITI compared to those with lower SDMT scores, suggesting that higher cognitive function is associated with less time between taps.

In the context of UL impairments in PwMS, previous research has shown that improving hand function, particularly manual dexterity, through music production on a keyboard can facilitate functional hand use, as evidenced by improved NHPT scores (Gatti et al., 2014). Multisensory stimulation, including auditory stimuli from active music-making, may play a crucial role in motor planning, which requires the integration of various sensory inputs (Gatti et al., 2014). This suggests that auditory-motor coupling can be effectively utilised in the rehabilitation of UL impairments in PwMS.

The study demonstrates that when participants tapped to the rhythm of a metronome, poorer performance on the NHPT correlated with a lower RVL, reduced rPA, and more NMA, indicating greater difficulty in synchronising with the beat and increased anticipation compared to those with better NHPT scores. Conversely, when tapping to the rhythm of music, participants with higher scores on the BMRQ showed better synchronisation than those with lower scores, implying a more refined alignment with musical rhythms in PwMS who are more sensitive to musical reward. This observation underscores the potential benefits of incorporating music into the rehabilitation of PwMS, as music-based interventions address multiple aspects of the disease holistically (Gibson, 2021). Engaging various brain systems through music during rehabilitation facilitates the formation of neural connections before the primary rehabilitation activity begins (Gibson, 2021). This is particularly relevant in treating neurodegenerative diseases, where forming new neural connections can compensate for lost functions, potentially aiding in the recovery of lost connections (Gibson, 2021). The rhythmic consistency of music-based interventions is likely to improve physical symptoms by strengthening neural connections through repeated electrical activity (Gibson, 2021). Keep in mind, not only people who are sensitive to musical reward may benefit from music-based therapy. However, the direct application of this concept to MS has yet to be fully established, necessitating further research to better understand its relevance to the specific characteristics of this condition.

When stimuli were presented at a very low tempo (-8%), no correlations were found between these clinical measures and outcome measures. At all other tempi, however, the results show that PwMS suffering less UL impairment (i.e. scoring better on the NHPT) tapped significantly closer to the beat than PwMS suffering from more UL impairment, again suggesting a link between UL impairment and tapping performance.
At baseline tempo, PwMS with high BMRQ scores, indicating a strong sensitivity to musical reward, showed a smaller interval between taps.

No research is without its limitations, and this study is no exception. A primary limitation is the small sample size, consisting of 21 PwMS and 16 HC. The limited sample size may have impacted the accuracy of the findings and may not adequately represent the broader population. Future research with a larger sample size could yield more reliable results and enhance the study's statistical power.

Another limitation is the variability in the musical stimuli used. Each tempo required a different song, introducing some variability that was not present in the metronome stimuli, which consisted of a monotonous, simple rhythmic tone. However, it should be noted that all songs were confined to a single genre chosen by the participant, somewhat limiting the variability of the music stimuli.

Future research should aim to expand on these findings by including larger and more diverse samples, which would enhance the generalisability of the results. Additionally, further investigations in the mechanisms underlying NMA in PwMS during finger-tapping tasks is necessary, particularly in relation to different types of auditory stimuli. Exploring the role of musical training in improving auditory-motor coupling and its potential benefits in rehabilitation programs for PwMS is another promising area for future research. Lastly, longitudinal studies examining the long-term effects of rhythm-based interventions on motor function and neural connectivity in PwMS would provide valuable insights into the potential for remyelination and the overall effectiveness of these interventions. The inclusion of PwMS with manifest UL impairment in these studies could provide additional insights relevant to the development of rhythm-based interventions.

Conclusion

This study demonstrates that even though both PwMS and HC are able to synchronise their tapping to certain stimuli, tempo and type of auditory stimuli have a certain effect on outcome parameters concerning tapping performance, with tapping to slow music proving to be a difficult task when compared to tapping to metronome. This study also shows that PwMS who experience higher UL impairment and/or disability have more trouble synchronising to both music and metronome at a variety of tempi, suggesting that integrating rhythm-based therapies could potentially enhance functional outcomes in these patients. These therapy-modalities may even be more useful in patients who have a strong sensitivity to musical reward, seeing as they are already more able to synchronise more closely to the beats of musical stimuli.

We conclude that tapping performance in PwMS can be influenced by both the tempo and type of auditory stimuli, and can be linked to UL impairment, disability and experience of music, with implications for rehabilitation using tapping tasks (e.g. music-based tapping therapy modalities).

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