



Full length article

The effects of metronome frequency differentially affects gait on a treadmill and overground in people with Parkinson disease^{*}

Madelon Hoppe^a, Guneet Chawla^a, Nina Browner^b, Michael D. Lewek^{a,*}

^a Division of Physical Therapy, Department of Allied Health Sciences, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

^b Department of Neurology University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

ARTICLE INFO

Keywords:

Gait
Parkinson disease
Exercise therapy
Spatiotemporal analysis
Cueing

ABSTRACT

Background: Treadmills and rhythmic auditory cueing can influence stepping rhythm for individuals with Parkinson disease (PD). Of concern, however, is that auditory cueing directly addresses the temporal features of gait, whereas adjusting step length may be more important for people with PD. Stepping to a faster cadence when walking overground may increase gait speed, but without requiring an increased step length. Furthermore, given the potentially valuable role of walking on a treadmill for individuals with PD, we are concerned that increasing cadence with rhythmic auditory cueing while walking at a constant treadmill speed will induce even shorter steps.

Research question: What is the effect of different metronome cue frequencies on spatiotemporal gait parameters when walking overground compared to walking on a treadmill in people with PD?

Methods: Using a repeated-measures design, 21 people with PD (stage 1–3) walked overground and on a treadmill with and without metronome cues of 85 %, 100 %, and 115 % of their baseline cadence frequency for one minute each. We assessed step length, and cadence during all conditions. Gait speed was assessed during overground gait.

Results: An interaction effect between cue frequency and walking environment revealed that participants took longer steps during the 85 % condition on the treadmill only. When walking overground, metronome cues of 85 % and 115 % of baseline cadence yielded decreases and increases, respectively, in both cadence and gait speed with no associated change in step length.

Significance: These data suggest that people with PD are able to alter spatiotemporal gait parameters immediately when provided the appropriate metronome cue and walking environment. We propose to target shortened step lengths by stepping to the beat of slow frequency auditory cues while walking on a treadmill, whereas the use of fast frequency cues during overground walking can facilitate faster walking speeds.

1. Introduction

Common gait alterations for individuals with Parkinson disease (PD) include decreased stride length, increased variability of movement, freezing of gait, decreased gait speed, and increased cadence [1,2]. These gait abnormalities are associated with decreased motor automaticity, which begins to deteriorate in the early stages of PD [3]. In an effort to improve gait mechanics and quality of life for individuals with PD, physical therapy often targets gait rhythmicity [4].

Walking on a motorized treadmill can encourage more automatic gait for individuals with PD, due to the continuous belt movement compared to the self-generating gait pattern performed overground [5,6]. As a result, treadmill walking exhibits less gait variability

compared to overground gait [7]. Even a single session of treadmill walking can elicit longer steps for individuals with PD [8]. This may be because individuals with advanced PD, unlike unimpaired individuals, may take increased step lengths with decreased cadence when walking on a treadmill compared to overground [9]. These changes in gait following treadmill walking might be due to a combination of the proprioceptive input from the belt displacement of the limbs, visual cues of the distance from the front of the treadmill, or the constant velocity of the belt [7,9].

The use of rhythmic auditory cues has likewise successfully improved gait parameters in people with PD [10,11]. Rhythmic auditory cueing presumably serves as an external auditory stimulus to bypass the impaired internal timing present in PD [12]. Generally, the use of

^{*} These data were presented in abstract form at the Combined Sections Meeting of the APTA, Washington, DC, January 2019.

^{*} Corresponding author at: 3043 Bondurant Hall, CB#7135, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA.

E-mail address: mlewek@med.unc.edu (M.D. Lewek).

rhythmic auditory cues has contributed to increases in gait speed and step lengths [10,13,14], although this finding is inconsistent [2,15]. Importantly, however, the prescriptive literature has been narrowly focused on the use of *faster* tempos of rhythmic auditory cueing [11]. This is presumably because most investigators seek to increase gait velocity, and therefore suggest that cueing should be used only at frequencies or tempos that match or exceed the individual's baseline cadence [12,16]. Furthermore, the use of slower cueing frequencies has been suggested to increase falls risk [16].

Of concern is that auditory cueing is intended to impact the temporal features of gait, [17] but impacting step length may be more important for individuals with PD [2,18]. Gait speed is a function of both temporal (e.g., cadence) and spatial (e.g., step length) features [19]. When walking overground, however, auditory cue-induced changes in cadence may increase gait speed, but without obliging an individual to increase step length. Furthermore, given the potentially valuable role of treadmill walking for individuals with PD [5,7], we are concerned that increasing cadence with rhythmic auditory cueing while walking at a constant treadmill speed will induce even shorter steps. Clearly, the environmental context of rhythmic auditory cueing should matter. Therefore, the purpose of this study was to determine the effect of metronome cues on spatiotemporal gait parameters when walking overground compared to walking on a treadmill in people with PD. This information will be critical in order to determine the optimal training environment to achieve specific gait training goals. We hypothesize that individuals with PD will increase step length with *slow* tempo metronome cueing during treadmill walking due to the fixed treadmill speed, but will increase step length overground while stepping to *fast* tempo metronome cueing. In particular, we are aware of increased gait speeds with faster metronome cues during overground walking [11,15,17], that we attribute to increased cadence (prescribed by the metronome) and increased step lengths.

2. Methodology

2.1. Participants

We recruited participants diagnosed with PD by a neurologist with a Hoehn and Yahr (H&Y) Stage 1–3. Additional criteria included self-reported ability to walk > 10 m overground and on a treadmill for at least 14 min with rest breaks as needed. Exclusion criteria included uncontrolled cardiorespiratory/metabolic disease, other neurologic/orthopedic disorders that affect gait, and severe communication impairments that impeded understanding of study purpose and procedures. All participants signed an informed consent form approved by the UNC-Chapel Hill IRB. The project was listed on ClinicalTrials.gov (NCT03253965).

2.2. Procedures

Participants completed the Montreal Cognitive Assessment (MoCA) and the Unified Parkinson Disease Rating Scale (UPDRS) prior to testing. Participants initially walked over a 20 ft pressure mat (Zeno, Protokinetics, Havertown, PA, USA) with instructions to walk at their “comfortable speed.” From this baseline testing, PKMAS software calculated baseline gait speed and cadence for each participant, which was used to determine the treadmill speed and metronome frequencies.

Each participant performed four different walking conditions on both an instrumented treadmill and overground. These conditions consisted of a Control (no metronome) and three metronome conditions of 85 %, 100 %, and 115 % of the cadence frequency from the baseline overground testing. The Control (no cue) condition was always performed first and the order of the metronome conditions was randomized using a random number generator. The treadmill and overground tests were counterbalanced. We played a Google metronome through a speaker for all metronome conditions.

2.2.1. Overground testing

Each participant walked over the 20 ft pressure mat for four passes of continuous walking for each condition. No assistive devices were used. Instructions were given to “match each step to the beat of the metronome.” The initial steps of each trial and the turns between each pass were completed off the walkway and were not included in the data collection or analysis. Standing rest breaks were given as needed between conditions.

2.2.2. Treadmill testing

Participants walked on a dual-belt instrumented treadmill (Bertec, Columbus, OH, USA) for all treadmill conditions. The treadmill speed was set to the gait speed from the initial baseline overground test, and maintained for all conditions. For three subjects, the treadmill speed was reduced due to an inability to reach the intended treadmill speed safely. Participants were discouraged from using handrails, however, 12 participants required handrails for balance only. For those cases, handrail use was maintained across conditions. All participants wore a harness attached overhead, but no body weight support was provided, and the harness did not restrict limb motion. Oxygen saturation and heart rate were monitored for safety (Radical7, Masimo Corp, Irvine, CA). Rest breaks were provided as needed.

Instructions were given to “match each step to the beat of the metronome.” Participants were given ~15 s to synchronize with the metronome each time the frequency was changed, and data was then collected for one minute. As participants walked on the treadmill, the positions of the feet were tracked using retro-reflective markers placed on both heels by an 8-camera motion capture system (MX40+, Vicon, Los Angeles, CA, USA) at 120 Hz. Ground reaction force data were sampled simultaneously at 1200 Hz from the treadmill.

2.3. Data management

For all overground trials, we used the PKMAS software to remove partial steps and calculate average step length, cadence, and gait speed from all remaining steps. Data were processed separately for each condition. For all treadmill trials, data were analyzed with custom Labview programs (National Instruments, Austin, TX, USA). In particular, step length was measured as the anteroposterior distance between heel markers at initial contact. Step time was calculated as the time between successive heel strikes. Cadence was then calculated as the inverse of step time. Mean cadence accuracy was the difference between the actual cadence and the intended cadence (i.e., metronome frequency). Of note, the mean cadence accuracy does not provide any information about the stability of the cadence signal, and thus the coupling between the participant's cadence and the metronome can not be determined.

2.4. Data analysis

We used SPSS (ver 25, IBM, Chicago, IL, USA) to perform separate two-way repeated measures ANOVAs (repeated for metronome condition and walking environment) for step length, cadence, and mean cadence accuracy. If significant effects were found, one-way ANOVAs or paired sample *t*-tests were used, as appropriate. A Bonferroni correction was used to account for multiple comparisons. Because gait speed did not change on the treadmill, we used a one-way ANOVA to assess for changes in overground gait speed. We used an alpha of 0.05 for our statistical analysis. Prior to data collection, we performed a sample size estimate using G*Power. We were unaware of any work that has compared faster and slower cue frequencies across walking environments. However, we used an effect size ($f > 0.39$) based on differences in step length between treadmill and overground [20] and stride length differences between metronome cue conditions [17]. This assumption indicated that we would need 18 participants for an alpha of 0.05 and power of 0.80.

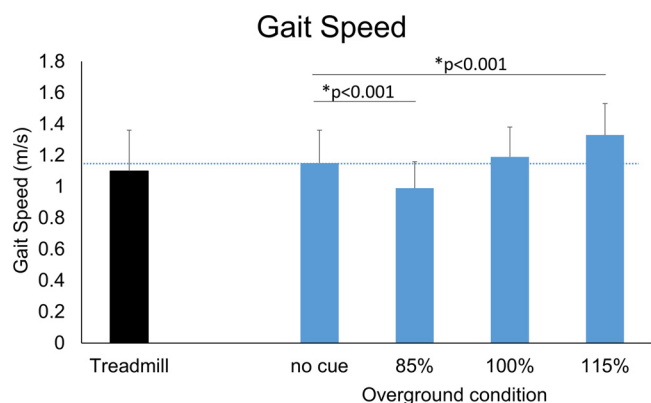


Fig. 1. Gait speed (m/s) during overground gait demonstrated dramatic alterations with the 85 % and 115 % metronome conditions compared to the no cue (Control) condition. The horizontal dashed line represents the no cue condition for easier visualization of relevant comparisons. The treadmill speed did not change between conditions and is indicated on the left for reference. Error bars indicate standard deviation.

3. Results

3.1. Participants

Twenty-one individuals with PD participated (13 male, 8 female; 69.8 ± 9.8 years old). The average MoCA score was 27 ± 2.9 and participants had experienced symptoms for 10.5 ± 7.7 years. Five of the participants were classified as H&Y Stage 1, nine were classified as H&Y Stage 2, and seven were classified as H&Y Stage 3. The average UPDRS score was 19.4 ± 13.7 with the average motor axial subscore of 4.8 ± 3.5 . Nine participants were classified as axial rigid and 12 as tremor predominant.

3.2. Gait speed

The treadmill speed was kept constant for all conditions (1.10 ± 0.26 m/s), however, overground gait speed changed when stepping with different metronome frequencies ($p < 0.001$, $\eta_p^2 = 0.764$, Fig. 1). Specifically, overground gait speed increased for the 115 % metronome condition (1.33 ± 0.20 m/s; $p < 0.001$; Cohen's d : 1.39) and decreased for the 85 % metronome condition to 0.99 ± 0.17 m/s ($p = 0.001$; Cohen's d : 1.07) compared to Control (no cue) walking (1.15 ± 0.21 m/s). We did not observe any change in gait speed at the 100 % metronome condition (1.19 ± 0.19 m/s; $p = 0.512$; Cohen's d : 0.34).

3.3. Step length

We observed an interaction effect between walking environment (treadmill vs overground) and metronome frequency ($p < 0.001$, $\eta_p^2 = 0.554$; Fig. 2). We therefore assessed the effect of metronome frequency on step length separately for the treadmill and overground environments. Here, we observed that step lengths were affected by the metronome frequency on the treadmill only ($p < 0.001$, $\eta_p^2 = 0.761$), but not during overground walking ($p = 0.163$, $\eta_p^2 = 0.087$). Post hoc testing of treadmill walking revealed that the slower (i.e., 85 %) metronome frequencies yielded an 11 % larger step length (0.61 ± 0.13 m; $p < 0.001$; Cohen's d : 1.72), whereas the faster (i.e., 115 %) frequencies induced 11 % smaller step lengths (0.49 ± 0.10 m; $p < 0.001$; Cohen's d : 1.30) compared to treadmill walking without a metronome (0.55 ± 0.12 m).

3.4. Cadence

Participants demonstrated their ability to modulate cadence ($p < 0.001$, $\eta_p^2 = 0.896$), by slowing their cadence in the 85 % condition ($p < 0.001$; $\eta_p^2 = 0.904$) and increasing their cadence in the 115 % condition ($p < 0.001$; $\eta_p^2 = 0.856$) compared to Control walking (Fig. 3). However, we observed an overall higher cadence on the treadmill compared to walking overground ($p = 0.026$, $\eta_p^2 = 0.223$). This difference was primarily due to the 85 % condition, in which higher cadence during treadmill walking was observed compared to overground walking ($p = 0.006$; Cohen's d : 0.67), whereas all other frequencies yielded comparable cadences between walking environments (all $p > 0.256$).

We likewise observed an interaction effect between walking environment and metronome frequency for mean cadence accuracy ($p = 0.014$, $\eta_p^2 = 0.224$). Post-hoc evaluation revealed that participants had less mean accuracy on the treadmill at slower (85 %) tempos compared to overground ($p = 0.006$; Cohen's d : 0.67). Participants exhibited only small cadence errors for the 100 % and 115 % conditions while walking on both the treadmill and overground ($p > 0.256$).

4. Discussion

The purpose of this study was to determine the effect of metronome cue frequency on spatiotemporal gait parameters when walking overground and walking on a treadmill for individuals with PD. We had hypothesized that step length would be differentially affected by metronome frequency based on the walking environment. Indeed, we observed that step lengths were longer when walking with slow tempo cues on the treadmill only, whereas step length was unaltered during overground walking. Instead, the induced change in cadence during overground walking resulted in different walking speeds without the expected alterations in step length.

Although it was already known that people with PD have the ability to immediately alter gait in response to metronome cues, our results extend this finding to both overground and treadmill environments, with a particular emphasis on the specific alterations associated with different cueing frequencies. Our findings likely arise from a mix of biomechanical and neuroanatomic mechanisms. In particular, as noted by others, the ability to accept external regulation of rhythmic timing may be critical [12]. Importantly, functional magnetic resonance imaging (fMRI) studies have demonstrated diminished activation in many locomotor areas of the brain in people with PD [21]. This altered activation, in part, impairs the ability to independently modify gait mechanics through internal regulation [22]. Use of external cues, such as the metronome and treadmill used here, places less demand on internal regulation of gait timing. Since the motor circuits for synchronization remain intact for people with PD, the combined use of a treadmill and rhythmic auditory cues may improve gait mechanics in ways the person would not be able to change and maintain independently [9,16,17,23].

Walking speed arises directly from spatial (e.g., step length) and temporal (e.g., cadence) measures [19,24]. As such, when gait speed is fixed (e.g., on a treadmill) and cadence is manipulated, the step length must change. The same is not true for overground walking, where gait speed is free to fluctuate. Indeed, we observed predictable changes to step length on the treadmill with manipulations to cadence, but the step lengths remained unaltered during overground walking, despite substantial alterations to cadence. These findings suggest that stepping to a *reduced* cadence tempo should reliably *increase* step lengths during treadmill walking. This approach runs counter to conventional approaches to rhythmic auditory cueing, which promote the use of faster cadences during overground walking [12,16]. Although some have noted that step lengths will increase during overground walking with faster cadences [11], this finding is not ubiquitous [15,25,26]. We can speculate that participant instructions may have contributed to this finding [27]. Importantly, we did not provide our participants with any

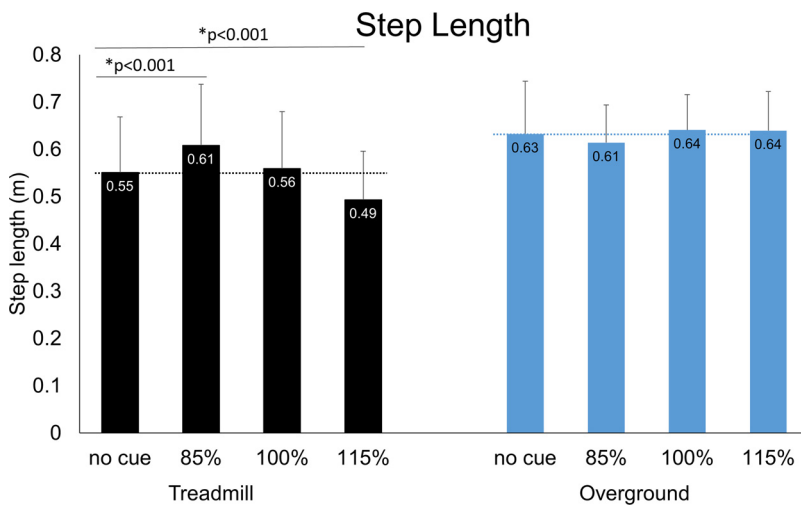


Fig. 2. Step length (m) during treadmill gait (black) and overground gait (blue/gray). Despite no difference between conditions during overground gait, we observed significant changes during treadmill walking. Of note, the 85 % condition elicited longer steps, whereas the 115 % condition produced shorter steps compared to the no cue condition. The horizontal dashed line represents the respective no cue conditions for easier visualization of relevant comparisons. Error bars indicate standard deviation.

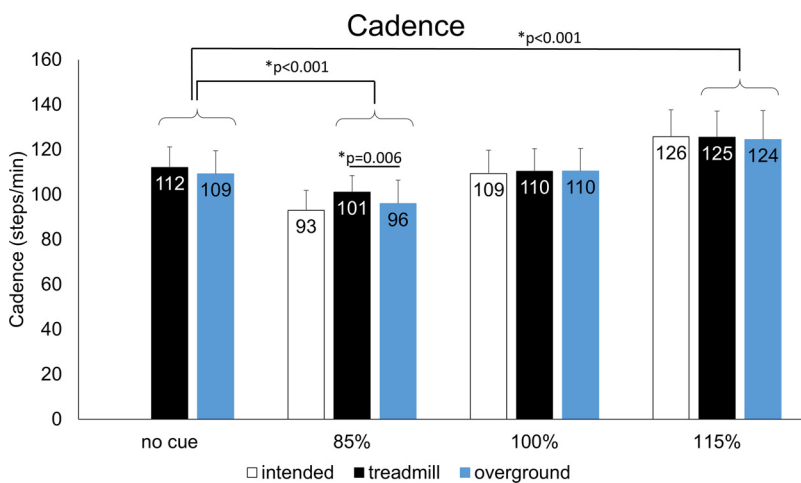


Fig. 3. Cadence (steps/min) was influenced by the walking environment (treadmill: black; overground: blue/gray), due to the inability to match intended cadence on the treadmill during the 85 % condition. Slower metronome cues reduced cadence overall, whereas faster metronome cues generated higher cadence. Examining the difference between the intended cadence and treadmill/overground values indicates the mean cadence accuracy. Error bars indicate standard deviation.

particular instruction related to altering their step length, but rather told them to simply “step with the beat”. We can speculate that if we had instructed participants to increase their step length during overground gait, that we would have seen that alteration as well [27]. Clearly, however, the ability to modulate gait speed plays a critical role in the spatial response to cue-induced stepping.

Participants in this study were able to match stepping cadence to the 100 % and 115 % metronome cues both overground and on the treadmill but exhibited larger mean errors with the 85 % metronome cue (particularly during treadmill walking). Despite the mean cadence errors associated with the 85 % cues, we still observed large changes in step length on the treadmill. Thus, even when participants did not match the cue accurately, the desired gait change was still observed.

We can use these results to guide treatment selection based on specific goals. In particular, treatment goals for individuals with PD are typically aimed at addressing common gait abnormalities, such as decreased gait speed, decreased step length, and increased cadence [9,22,23]. Based on our results, an immediate increase in gait speed can be realized by walking overground with the 115 % metronome cue. If the treatment goal is to increase step length, we propose that walking on a treadmill with 85 % metronome cues can immediately produce a larger step length. Finally, cadence is directly manipulated both on the treadmill and overground with a corresponding change to the cueing frequency. Given the specificity of the various cueing frequencies and their impact on both overground and treadmill walking, we propose a novel pairing of cue frequencies to elicit immediate changes to all relevant parameters. Initially, treadmill walking with slow metronome

cues will elicit large step lengths. We propose that immediately following this “priming” stepping practice with overground walking using fast metronome cues will allow for faster walking with long step lengths. Our preliminary work in this area is encouraging [28]. Importantly, there seem to be no detrimental effects on standard clinical measures of balance in that small cohort [28].

4.1. Study limitations

There were several limitations to this study. First, we did not use a measure of postural stability during gait. Given the concern that walking with slower cadence can impair stability [16], this may be an important factor to consider in future work [28]. Additionally, some participants walked slower on the treadmill compared to overground (N = 3). As a result, the step lengths appeared somewhat shorter during treadmill walking compared to overground walking. Furthermore, the procedure for computing step length was different for treadmill and overground gait. In short, the step lengths from the treadmill likely underestimates the true step length due to trailing limb heel rise prior to leading limb heel strike. Although our procedure allows for valid within-environment comparisons, our between-environment comparisons of step length should be interpreted with caution. Because we were primarily concerned with within-subject effects, we chose not to recruit an unimpaired group. Additionally, some participants used the handrails on the treadmill and some did not. This is likely because handrails provide support for improved balance and mobility [7]. In healthy adults, there is no difference in step length between holding or

not holding handrails on a treadmill [29]. Although gait variability was not one of the outcomes assessed in this study, there is potential for differences in gait mechanics depending on use of handrails. There was also potential for fatigue-related changes in gait since rest breaks were only provided if requested, or unless heart rate or gait quality indicated the need for one. Lower extremity fatigue in PD can affect gait parameters, including step length and gait speed [30]. Finally, we tested slightly more people with H&Y stage 2 and 3 than stage 1, suggesting that our results may be more heavily influenced by more advanced PD.

5. Conclusions

In conclusion, we observed a relationship between the frequency of metronome cues and walking environment for gait mechanics in people with PD. The desired gait change (i.e. gait speed, step length, or cadence) influences the type of cue and environment required to achieve that particular goal. People with PD are able to change spatiotemporal measures in response to various cue frequencies during both overground and treadmill walking; however, further exploration is needed to determine if these results can be used as a gait training technique that carries over to long-term gait changes.

Declaration of Competing Interest

Nina Browner has received travel and speaker fees from Parkinson Foundation and a grant for Parkinson Foundation Center of Excellence at University of North Carolina at Chapel Hill. For the remaining authors none are declared.

References

- [1] E. Knutsson, An analysis of Parkinsonian gait, *Brain* 95 (3) (1972) 475–486 http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=4655275.
- [2] M.E. Morris, R. Ianssek, T.A. Matyas, J.J. Summers, The pathogenesis of gait hypokinesia in Parkinson's disease, *Brain* 117 (Pt 5) (1994) 1169–1181 <https://www.ncbi.nlm.nih.gov/pubmed/7953597>.
- [3] T. Wu, M. Hallett, P. Chan, Motor automaticity in Parkinson's disease, *Neurobiol. Dis.* 82 (2015) 226–234 <https://www.ncbi.nlm.nih.gov/pubmed/26102020>.
- [4] S.H. Keus, B.R. Bloem, E.J. Hendriks, A.B. Bredero-Cohen, M. Munneke, G. Practice Recommendations Development, Evidence-based analysis of physical therapy in Parkinson's disease with recommendations for practice and research, *Mov. Disord.* 22 (4) (2007) 451–460 quiz 600 <https://www.ncbi.nlm.nih.gov/pubmed/17133526>.
- [5] S. Frenkel-Toledo, N. Giladi, C. Peretz, T. Herman, L. Gruendlinger, J.M. Hausdorff, Treadmill walking as an external pacemaker to improve gait rhythm and stability in Parkinson's disease, *Mov. Disord.* 20 (9) (2005) 1109–1114 <https://www.ncbi.nlm.nih.gov/pubmed/15929090>.
- [6] O. Bello, J.A. Sanchez, M. Fernandez-del-Olmo, Treadmill walking in Parkinson's disease patients: adaptation and generalization effect, *Mov. Disord.* 23 (9) (2008) 1243–1249 <http://www.ncbi.nlm.nih.gov/pubmed/18464281>.
- [7] O. Bello, M. Fernandez-Del-Olmo, How does the treadmill affect gait in Parkinson's disease? *Curr. Aging Sci.* 5 (1) (2012) 28–34 <https://www.ncbi.nlm.nih.gov/pubmed/21762092>.
- [8] M. Pohl, G. Rockstroh, S. Ruckriem, G. Mrass, J. Mehrholz, Immediate effects of speed-dependent treadmill training on gait parameters in early Parkinson's disease, *Arch. Phys. Med. Rehabil.* 84 (12) (2003) 1760–1766 <https://www.ncbi.nlm.nih.gov/pubmed/14669180>.
- [9] O. Bello, G. Marquez, M. Cambor, M. Fernandez-Del-Olmo, Mechanisms involved in treadmill walking improvements in Parkinson's disease, *Gait Posture* 32 (1) (2010) 118–123 <https://www.ncbi.nlm.nih.gov/pubmed/20452773>.
- [10] M.H. Thaut, G.C. McIntosh, R.R. Rice, R.A. Miller, J. Rathbun, J.M. Brault, Rhythmic auditory stimulation in gait training for Parkinson's disease patients, *Mov. Disord.* 11 (2) (1996) 193–200 <http://www.ncbi.nlm.nih.gov/pubmed/8684391>.
- [11] G.C. McIntosh, S.H. Brown, R.R. Rice, M.H. Thaut, Rhythmic auditory-motor facilitation of gait patterns in patients with Parkinson's disease, *J. Neurol. Neurosurg. Psychiatry* 62 (1) (1997) 22–26 <http://www.ncbi.nlm.nih.gov/pubmed/9010395>.
- [12] A. Ashoori, D.M. Eagleman, J. Jankovic, Effects of auditory rhythm and music on gait disturbances in parkinson's disease, *Front. Neurol.* 6 (2015) 234 <http://www.ncbi.nlm.nih.gov/pubmed/26617566>.
- [13] A. Nieuwboer, G. Kwakkel, L. Rochester, D. Jones, E. van Wegen, A.M. Willems, et al., Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial, *J. Neurol. Neurosurg. Psychiatry* 78 (2) (2007) 134–140 <https://www.ncbi.nlm.nih.gov/pubmed/17229744>.
- [14] M. Murgia, R. Pili, F. Corona, F. Sors, T.A. Agostini, P. Bernardis, et al., The use of footstep sounds as rhythmic auditory stimulation for gait rehabilitation in parkinson's disease: a randomized controlled trial, *Front. Neurol.* 9 (2018) 348 <http://www.ncbi.nlm.nih.gov/pubmed/29910764>.
- [15] T.E. Howe, B. Lovgreen, F.W. Cody, V.J. Ashton, J.A. Oldham, Auditory cues can modify the gait of persons with early-stage Parkinson's disease: a method for enhancing parkinsonian walking performance? *Clin. Rehabil.* 17 (4) (2003) 363–367 <https://www.ncbi.nlm.nih.gov/pubmed/12785243>.
- [16] P. Arias, J. Cudeiro, Effects of rhythmic sensory stimulation (auditory, visual) on gait in Parkinson's disease patients, *Exp. Brain Res.* 186 (4) (2008) 589–601 <http://www.ncbi.nlm.nih.gov/pubmed/18214453>.
- [17] A.M. Willems, A. Nieuwboer, F. Chavret, K. Desloovere, R. Dom, L. Rochester, et al., The use of rhythmic auditory cues to influence gait in patients with Parkinson's disease, the differential effect for freezers and non-freezers, an explorative study, *Disabil. Rehabil.* 28 (11) (2006) 721–728 <https://www.ncbi.nlm.nih.gov/pubmed/16809215>.
- [18] M.E. Morris, R. Ianssek, T.A. Matyas, J.J. Summers, Stride length regulation in Parkinson's disease. Normalization strategies and underlying mechanisms, *Brain* 119 (Pt 2) (1996) 551–568 <https://www.ncbi.nlm.nih.gov/pubmed/8800948>.
- [19] M.D. Lewek, The influence of body weight support on ankle mechanics during treadmill walking, *J. Biomech.* 44 (1) (2011) 128–133 <http://www.ncbi.nlm.nih.gov/pubmed/20855074>.
- [20] O. Bello, J.A. Sanchez, C. Vazquez-Santos, M. Fernandez-Del-Olmo, Spatiotemporal parameters of gait during treadmill and overground walking in Parkinson's disease, *J. Parkinsons Dis.* 4 (1) (2014) 33–36 <https://www.ncbi.nlm.nih.gov/pubmed/24496097>.
- [21] D.S. Peterson, K.A. Pickett, R.P. Duncan, J.S. Perlmutter, G.M. Earhart, Brain activity during complex imagined gait tasks in Parkinson disease, *Clin. Neurophysiol.* 125 (5) (2014) 995–1005 <https://www.ncbi.nlm.nih.gov/pubmed/24210997>.
- [22] M.W. Rodger, C.M. Craig, Beyond the metronome: auditory events and music may afford more than just interval durations as gait cues in parkinson's disease, *Front. Neurosci.* 10 (2016) 272 <https://www.ncbi.nlm.nih.gov/pubmed/27378841>.
- [23] C. Nombela, L.E. Hughes, A.M. Owen, J.A. Grahn, Into the groove: can rhythm influence Parkinson's disease? *Neurosci. Biobehav. Rev.* 37 (10 Pt 2) (2013) 2564–2570 <https://www.ncbi.nlm.nih.gov/pubmed/24012774>.
- [24] M.P. Murray, R.C. Kory, B.H. Clarkson, S.B. Sepic, Comparison of free and fast speed walking patterns of normal men, *Am. J. Phys. Med.* 45 (1) (1966) 8–23 <https://www.ncbi.nlm.nih.gov/pubmed/5903893>.
- [25] R.L. Freedland, C. Festa, M. Sealy, A. McBean, P. Elghazaly, A. Capan, et al., The effects of pulsed auditory stimulation on various gait measurements in persons with Parkinson's Disease, *NeuroRehabilitation* 17 (1) (2002) 81–87 <https://www.ncbi.nlm.nih.gov/pubmed/12016350>.
- [26] J.M. Hausdorff, J. Lowenthal, T. Herman, L. Gruendlinger, C. Peretz, N. Giladi, Rhythmic auditory stimulation modulates gait variability in Parkinson's disease, *Eur. J. Neurosci.* 26 (8) (2007) 2369–2375 <https://www.ncbi.nlm.nih.gov/pubmed/17953624>.
- [27] K. Baker, L. Rochester, A. Nieuwboer, The immediate effect of attentional, auditory, and a combined cue strategy on gait during single and dual tasks in Parkinson's disease, *Arch. Phys. Med. Rehabil.* 88 (12) (2007) 1593–1600 <https://www.ncbi.nlm.nih.gov/pubmed/18047873>.
- [28] M.A. Sherron, S.A. Stevenson, N. Browner, M.D. Lewek, Targeted Rhythmic Auditory Cueing During Treadmill and Overground Gait for Individuals with Parkinson disease: A Case Series *J Neurol Phys Ther* (in press).
- [29] W.L. Siler, A.L. Jorgensen, R.A. Norris, Grasping the handrails during treadmill walking does not alter sagittal plane kinematics of walking, *Arch. Phys. Med. Rehabil.* 78 (4) (1997) 393–398 <https://www.ncbi.nlm.nih.gov/pubmed/9111459>.
- [30] P.C. Santos, L.T. Gobbi, D. Orციולי-Silva, L. Simieli, J.H. van Dieen, F.A. Barbieri, Effects of leg muscle fatigue on gait in patients with Parkinson's disease and controls with high and low levels of daily physical activity, *Gait Posture* 47 (2016) 86–91 <https://www.ncbi.nlm.nih.gov/pubmed/27264409>.