Targeted Rhythmic Auditory Cueing During Treadmill and Overground Gait for Individuals With Parkinson Disease: A Case Series

Margaret A. Sherron, PT, DPT, Sarah A. Stevenson, PT, DPT, Nina M. Browner, MD, and Michael D. Lewek, PT, PhD

Background and Purpose: Rhythmic auditory cueing and treadmill walking can improve spatiotemporal gait parameters through entrainment of movement patterns. Careful selection of cue frequencies is necessary if treadmill walking is to be employed, because cadence and step length are differentially affected by walking on a treadmill and overground. The purpose of this study was to describe the treatment of gait impairments for individuals with Parkinson disease, using strategically selected rhythmic auditory cue frequencies on both a treadmill and overground.
Case Description: Three individuals with Hoehn & Yahr stage 2 Parkinson disease participated in this case series.
Intervention: All participants completed 6 weeks of gait training, in which each session employed rhythmic auditory cueing during treadmill-based gait training followed by overground gait training. We provided targeted rhythmic auditory cueing with a metronome set to 85% and 115% of their self-selected cadence for treadmill and overground training, respectively. We performed clinical tests of gait and balance prior to, midway, and following training, and at a 3-month follow-up.
Outcomes: All participants improved overground gait speed (participant 1: +0.27 m/s; participant 2: +0.20 m/s; and participant 3: +0.18 m/s) and stride length (15.7 ± 4.17 cm) with small changes to cadence. Likewise, there were only small changes in balance.
Discussion: We hypothesize that the large improvements in gait speed are due to the concomitant increases in stride length. Further research is needed to test the effect of targeted rhythmic auditory cueing during treadmill and overground gait.
Video Abstract available for more insights from the authors (see the Video, Supplemental Digital Content 1, available at: http://links.lww.com/JNPT/A309).

Key words: *feedback, human movement system, locomotor, rehabilitation, walking*

(*JNPT* 2020;00: 1–7)

Division of Physical Therapy, Department of Allied Health Sciences, University of North Carolina at Chapel Hill (M.A.S., S.A.S., M.D.L.); and Department of Neurology, University of North Carolina at Chapel Hill (N.M.B.).

Margaret A. Sherron and Sarah A. Stevenson are co-first authors.

Nina M. 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.

The authors declare no conflict of interest.

ClinicalTrials.gov registration number: NCT03660605.

Supplemental digital content is available for this article. Direct URL citation appears in the printed text and is provided in the HTML and PDF versions of this article on the journal's Web site (www.jnpt.org).

Correspondence: Michael D. Lewek, PT, PhD, University of North Carolina at Chapel Hill, Chapel Hill, 3043 Bondurant Hall, CB#7135, NC 27599 (mlewek@med.unc.edu).

ISSN: 1557-0576/20/00000-0001

DOI: 10.1097/NPT.0000000000000315

INTRODUCTION

Individuals with Parkinson disease (PD) commonly exhibit distinctive gait features such as bradykinesia, decreased arm swing, decreased stride length, and increased cadence, resulting in shuffled steps.[1,2] The lack of movement automaticity may also contribute to freezing of gait, inducing dynamic balance deficits and increasing the risk of falls.[3] Pharmacological management is often a primary component of treatment, given its ability to increase dopamine stores and reduce disease symptoms; however, medications can be ineffective at improving gait deficits.[4,5] Therefore, intensive gait rehabilitation is warranted as an adjunct to drug therapy for individuals with PD.

The use of external cues is commonly employed during rehabilitation for individuals with PD,[6,7] who have impaired internal pacing but are able to use external timing cues to improve the rhythmicity of gait.[8-10] For example, walking on a treadmill provides external somatosensory cues (ie, speed of the treadmill belt) to drive the stepping pattern.[11] Furthermore, treadmill walking appears to reduce the elevated prefrontal cortex activity for people with PD,[12] which may promote greater gait automaticity.

Auditory cues, such as musical beats, metronomes, and rhythmic clapping, can also present external cues that can aid gait training for individuals with PD.[13,14] Walking with auditory cues can have a positive impact on gait initiation, and reduce freezing episodes and falls for individuals with PD.[10,15] More specifically, metronomes offer an effective, clinically feasible strategy to improve gait speed, stride length, and cadence.[13,14] Authors often advocate for higher (ie, faster) cue frequencies in the overground environment to elicit increased gait speed,[8,14,16,17] although the use of external (eg, auditory) cues on a treadmill may enhance clinical outcomes.[18] Recently, it was suggested that slower metronome frequencies, when employed during treadmill walking, will increase step lengths for individuals with PD.[19] During overground walking, however, faster tempo metronomes can increase cadence and gait speed, but do not alter step length.[20] Therefore, we propose that coupling slow cadence cues on a treadmill (to enhance stride length), followed immediately by faster cadence cues overground (to enhance cadence and gait speed), will elicit positive spatiotemporal gait features for individuals with PD.

Increasing stride length has the potential to increase the time spent in single-limb stance. Such a change may affect dynamic balance, although there is limited evidence regarding the effects of gait training with auditory cueing on balance outcomes.[21] It is possible, however, that gait training with auditory cueing can improve motor control and anticipatory postural control, leading to improved balance.[21]

The carryover from the treadmill environment to the overground environment is critical for correcting multiple aspects of disordered walking in individuals with PD. Therefore, the purpose of this case series was to describe the use of a novel pairing of both big, slow movements (obtained with *slow* tempo rhythmic auditory cueing on a *treadmill*) followed by high-intensity rapid movements (obtained during *fast* tempo rhythmic auditory cueing during *overground walking*) during gait training for individuals with PD. We believe that this novel pairing of training conditions will address both the affected spatial and temporal aspects of gait. Furthermore, we hypothesize that improving gait mechanics will improve overall balance in individuals with PD. Each of the 3 participants signed an informed consent form approved by the institutional review board of the University of North Carolina at Chapel Hill.

CASE DESCRIPTIONS

All participants completed an evaluation prior to training. During this initial evaluation, they completed the Mini-Balance Evaluation Systems Test (Mini-BESTest),[22] the Freezing of Gait Questionnaire (FOGQ),[23] the Montreal Cognitive Assessment (MoCA),[24] the Four Square Step Test (FSST),[25] and the Step Test.[26] To evaluate gait, all participants performed a 6-minute walk test (6MWT) along a 100-ft hallway with a GaitRite mat (CIR Systems, Franklin, New Jersey) placed in the middle of the hallway. While ambulating across the GaitRite mat, PKMAS software (Protokinetics, Havertown, Pennsylvania) calculated gait speed, cadence, and stride length for each pass to determine an average value for the test. To eliminate any effect of repeated testing, all participants performed a practice 6MWT 1 week prior to the actual pretest.

Participant 1

History and Systems Review

The first participant (P1) was diagnosed with PD by his neurologist 4 years before our evaluation (Table 1), although he had right hand resting tremor and bradykinesia 2 years prior to his official PD diagnosis. He was started on dopaminergic therapy at the time of his diagnosis 4 years ago although his levodopa therapy started only 2 years prior to our evaluation. His medical history was otherwise unremarkable. Prior to his diagnosis, he was very physically active and enjoyed going to the gym several times per week. After his diagnosis, he continued going to the gym but noticed a decrease in his ability to ambulate safely on the treadmill and began using the stationary bike. Upon his initial evaluation with us, he expressed an interest to increase his walking speed to improve his ability to keep up with his grandchildren and reduce freezing episodes.

Table 1. Participant Demographics

	P1	P2	P3
Age, y	72	66	75
Sex	Male	Female	Female
Handedness	Left	Right	Right
MoCA (max: 30)	29	30	29
MDS-UPDRS part III	11 (on meds)	10 (on meds)	14
Hoehn & Yahr	2	2	2
Current medications	Carbidopa/levodopa 300 mg/d and pramipexole 3 mg/day	Levodopa therapy at 300 mg/d, amantadine at 300 mg/d, and ropinirole 6 mg/d	None

Abbreviations: MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment.

Clinical Impression and Examination

Due to his diagnosis of PD, we were concerned about the possibility of decreased stride length, gait speed, and balance and the effects these could have on safety when ambulating in the community and his risk of falls. His pretest clinical outcome measures are listed in Table 2. Observationally, he appeared to ambulate at a slightly slower than normal speed, without the use of an assistive device, with slightly decreased arm swing bilaterally and decreased stride lengths. The decrease in stride length and gait speed was hypothesized to be due, in part, to the subtle deficits in balance (eg, Step Test). He appeared to be a good candidate for gait training with rhythmic auditory cueing, given his high level of motivation, desire to improve his walking, and his self-reported progression of symptoms.

Participant 2

History and Systems Review

The second participant (P2) was diagnosed with PD 8 years ago with initial symptoms of rigidity and bradykinesia affecting her right arm and leg. Besides the diagnosis of PD, she also had an unremarkable medical history. Prior to her diagnosis, she was very physically active, participating in dance recitals and going for walks around her neighborhood. After her diagnosis, she continued to work as a dance teacher, and walked in her neighborhood with her husband frequently, but she reported a decrease in her rhythm and coordination during dancing. Her goals were to improve her coordination and rhythm when walking and dancing.

Table 2. Participant 1 Outcome Measures

Measure	Practice	Pretest	Midtest	Posttest	Follow-up
6MWT distance, m	444.7	436.2	529.4	533.1	528.8
Gait speed, m/s	1.24	1.21	1.47	1.48	1.47
Cadence, steps/min		105	112	114.7	114.8
Stride length, cm		144	163	164.5	160.2
Mini-BESTest		27		27	28
Step Test, reps		25 (L: 12; R:13)		38 (L: 19; R: 19)	37 (L: 19; R: 18)
Four Square Step Test, s		11.87		7.9	7.18
Freezing of Gait Questionnaire		7		4	4

Abbreviations: Mini-BESTest, Mini-Balance Evaluation Systems Test; 6MWT, 6-minute walk test.

Clinical Impression and Examination

As with P1, we were concerned about the possibility of deficits in spatiotemporal measures of gait due to her diagnosis of PD. Her outcome measures from the pretest are found in Table 3. Visually, we observed decreased stride lengths and a quickened cadence. She ambulated without an assistive device but had a wide base of support. We attributed her decreased stride length and increased base of support to her reported feelings of being unstable, although we noted that her clinical balance measures were good. Given her findings, we believed that she had a good chance of improving her gait with gait training with rhythmic auditory cueing.

Participant 3

History and Systems Review

The third participant (P3) presented with a left hand resting tremor and generalized slowness of movements about 2 years before our initial evaluation. She was diagnosed with PD within a few months after development of her symptoms, but because she continued to be active she was not started on dopaminergic therapy by the time of our evaluation. Her medical history was significant for a stroke in 2003, prior to her diagnosis of PD, which left her with residual left-sided weakness. She reported walking on the treadmill at the gym prior to her PD diagnosis, but stated that she always had to use the handrail due to her fear of falling. After her diagnosis, she became more sedentary, participating mainly in seated activities such as tutoring and sewing and only occasionally exercised by walking around her neighborhood. At the time of her initial evaluation with us, she stated her goal was to improve her balance and ability to walk in her neighborhood.

Clinical Impression and Examination

Given the dual diagnosis of PD and a prior stroke, we were concerned that deficits in her gait and balance were contributing to her inability to be as active in the community as she wanted. The history of stroke also caused us to consider the extent of residual hemiparesis as well as the presence of any gait and balance asymmetries. All of her clinical outcome measures from the pretest evaluation are found in Table 4. We observed that her gait had a decreased step length on the left side and she ambulated with a wide base of support. Additionally, she ambulated with decreased gait speed, a decreased step length, and decreased arm swing on the left side. We hypothesized that the wide base of support and decreased stride length were due to impairments in balance, while the decreased step length and arm swing on the left were likely due to residual weakness (not tested) from her previous stroke and/or asymmetric symptoms associated with her PD progression.

INTERVENTION

We implemented intensive gait training, with a combination of treadmill-based and overground walking to improve mobility for all 3 participants. To address issues with spatiotemporal aspects of gait, we incorporated a novel pairing of rhythmic auditory cueing. We expected that improved spatiotemporal gait parameters would contribute to enhanced balance and balance perception.

Over 6 weeks, P1 and P3 completed 15 sessions and P2 completed 16 sessions. Each session lasted approximately an hour. During each session, participants began with treadmill-based gait training and ended with indoor overground walking, which was performed on a level surface through hallways and doorways, to enhance transfer and generalizability. We used a metronome during both treadmill and overground walking to

Table 3. Participant 2 Outcome Measures

Measure	Practice	Pretest	Midtest	Posttest	Follow-up
6MWT distance, m	451.4	472.1	517.6	543.8	557.5
Gait speed, m/s	1.25	1.31	1.44	1.51	1.55
Cadence, steps/min		132.8	134	136.4	139.6
Stride length, cm		124	133.7	137.6	138.2
Mini-BESTest		25		28	28
Step Test, reps		41 (L: 21; R: 20)		52 (L: 26; R: 26)	52 (L: 26; R: 26)
Four Square Step Test, s		6.35		5.13	4.94
Freezing of Gait Questionnaire		3		2	2

Abbreviations: Mini-BESTest, Mini-Balance Evaluation Systems Test; 6MWT, 6-minute walk test.

Table 4. Participant 3 Outcome Measures

Measure	Practice	Pretest	Midtest	Posttest	Follow-up
6MWT distance, m	354.5	346.3	395.3	411.5	438.9
Gait speed, m/s	0.98	0.96	1.10	1.14	1.22
Cadence, steps/min		102	106.5	109	111
Stride length, cm		118	134.3	131	140
Mini-BESTest		19		22	23
Step Test, reps		30 (L: 15; R: 15)		28 (L: 13; R: 15)	34 (L: 17; R: 17)
Four Square Step Test, s		11.08		11.1	9.29
Freezing of Gait Questionnaire		10		10	9

Abbreviations: Mini-BESTest, Mini-Balance Evaluation Systems Test; 6MWT, 6-minute walk test.

encourage improvements in both gait speed and step length. Importantly, however, we used different frequencies during treadmill and overground walking. Specifically, when participants walked on the treadmill, we set the metronome to 85% of the comfortable overground cadence to encourage increased step lengths.[19] After priming for longer step lengths, participants then walked overground as they stepped to the beat of the metronome set to 115% of pretest overground cadence. This overground portion was intended to promote increased gait speed with greater cadence and greater step lengths. The frequency set by the metronome was maintained throughout the 6 weeks of training despite changes in treadmill speed.

We set a goal to reach 20 minutes of walking during both overground and treadmill training, which was consistent with past work.[27] However, all participants began with varying times and gradually increased the duration of training. During the initial training session, P1 and P2 both completed 15 minutes of walking on the treadmill with 1 rest break, but were able to complete 20 minutes without a break by the end of the 6 weeks. P3 completed 10 minutes with 1 rest break on the treadmill during the initial session and ended the 6 weeks completing 20 minutes with 1 break. Initially, P1 completed 15 minutes of overground walking with 1 rest break but progressed to 20 minutes without a break by the last session. P2 walked for 10 minutes overground with 1 rest break during the initial session but was able to walk 20 minutes without a break by the final training session. P3 completed 10 minutes of walking with 1 break at the beginning of the 6 weeks and was able to ambulate a total of 13 minutes without a rest break by the last session.

We assessed blood pressure and heart rate at the beginning and end of each session, as well as during each rest break. The intensity of the training was determined by the participants' physiologic response to exercise (ie, heart rate), as well as their subjective reports given on the Borg Scale (goal: 13-17 on the 6- to 20-point scale) measuring their rate of perceived exertion.[28] All participants started walking on the treadmill at their comfortable overground speed. Over the course of the 6 weeks of training, we increased the treadmill speed, as needed, with the goal of selecting the highest speed that participants could attain while appearing to maintain the correct stepping frequency and keeping the physiologic cardiovascular response below 75% of heart rate reserve. P1 began with a treadmill speed of 1.2 m/s and completed training at a speed of 1.4 m/s during the final session. P2 began at 1.3 m/s and was walking at 1.5 m/s at the end of the 6 weeks. P3 began with a treadmill speed of 0.95 m/s but only progressed to a speed of 1.0 m/s by the final session. Although we attempted 1.05 m/s after 3 weeks of training, we reduced back to 1.0 m/s due to her inability to step with the metronome at that speed. All participants wore a safety harness that was attached overhead; however, no unweighting was used with any participants throughout the course of training.

While walking, each participant also received occasional verbal feedback regarding the spatiotemporal measures of gait.[29] P1 and P2 both received feedback regarding decreased step length bilaterally, whereas P3 received feedback more specifically about her decreased step length on the left. Additionally, feedback was provided to P1 and P3 regarding maintenance of an upright posture, due to their tendency to lean forward during ambulation on the treadmill. Each participant was also provided with verbal feedback to achieve heel strike on beat with the metronome.

At the beginning of training, all participants held onto the handrails while walking on the treadmill, although we discouraged use of the handrails for all participants to challenge balance. P1 and P2 progressed to no handrail use by the end of the 6 weeks; however, P3 continued to use both handrails throughout the training program.

During week 4, P3 reported a feeling of lightheadedness after completing the treadmill walking and exhibited a drop in blood pressure to 86/62 mm Hg. After 10 to 15 minutes of rest, her blood pressure improved; however, the session was stopped early and no overground training was completed for that session. In addition, each participant reported at some point throughout training that they had forgot to take their medication prior to the training session. In these instances, the participants reported the treadmill training was more difficult; however, there were no noticeable differences in their performance.

OUTCOMES

All participants repeated testing after 3 weeks of training (midtest), within 1 week after the last training session (posttest), as well as 3 months after completing training (follow-up). All clinical outcome measures are shown in Tables 2 to 4.

All 3 participants improved their gait speed by the midtest, and maintained or exceeded that improvement at the posttest and 3-month follow-up. For each participant, the improvement in gait speed also yielded an increase in 6MWT distance, cadence, and stride length. The minimum detectable change (MDC) is 0.18 m/s for gait speed,[30] 82 m for the 6MWT,[30] and 15 steps/min for cadence[31] for people with PD. All participants met or exceeded the MDC for gait speed by the posttest and exceeded it by follow-up. P1 and P3 exceeded the MDC for the 6MWT by posttest, with P2 exceeding the MDC by follow-up. Although we are unaware of an established MDC for stride length, we observed that none of the participants exceeded the MDC for cadence, suggesting that each participant's primary means of increasing gait speed was through the large observed change in stride length.

The changes in balance measures were not as dramatic as the gait outcomes. P1 demonstrated score improvements in the Step Test, FSST, and FOGQ (see Table 2). P2 improved in the Mini-BESTest, Step Test, FSST, and FOGQ (see Table 3). Finally, P3 improved on the Mini-BESTest (see Table 4).

At the completion of training, all of the participants noted improvements in their community mobility. P1 reported that instead of ambulating slower than his wife and grandkids, he now often found himself walking slightly ahead of them. P2 reported that she noticed improvements in her stability while walking outside with her husband and in her coordination during dance. She also reported that she noticed she was ambulating with a much quicker pace after the training. P3 reported improvements in self-perceived gait speed and stated that she noticed an improved ability to ambulate further distances when walking in her neighborhood.

DISCUSSION

Our purpose was to perform an exploratory analysis of the effect of gait training with targeted rhythmic auditory cueing on gait speed, cadence, stride length, and static and dynamic balance. Ultimately, we found that after participants trained both on the treadmill and overground with targeted rhythmic auditory cueing, all participants demonstrated improvements in spatiotemporal gait parameters. Indeed, after 6 weeks of training we observed improvements in gait speed and stride length compared with pretest. These improvements persisted or further increased at the 3-month follow-up. In addition, we noted some small improvements in balance for each participant. These findings suggest that greater testing is warranted in a more heterogeneous sample of people with PD to determine the efficacy of this intervention paradigm on balance and mobility outcomes.

The use of rhythmic auditory cueing during gait training is not a novel intervention, as it has been examined in prior studies both overground[13,32] and on a treadmill.[18,21] However, the use of different metronome frequencies to specifically target key components of gait had not been previously reported. Here, the frequency of the metronome was intentionally set slower than the participant's baseline cadence during treadmill walking and faster during overground walking.[20] In contrast, previous research has promoted the use of a higher frequency metronome exclusively.[13] We propose that our incorporation of the slow frequency metronome during treadmill walking likely contributed to the large improvements in stride length in our participants.

At the end of training, all 3 participants demonstrated improvements in their comfortable gait speed that met or exceeded the MDC. Although these large changes in gait speed exceed those reported in previous studies,[13,14,32] we were particularly struck by the subjective reports from each participant, as they reported noticing an increase in gait speed when ambulating in the community. As an example, P2 reported that her husband no longer walks with her because he complains that she now walks too far ahead of him. It is likely that the progressive nature of the training, coupled with the targeted approach to enhance both stride length (via slow-tempo rhythmic auditory cueing on the treadmill) and cadence (via fast-tempo rhythmic auditory cueing overground), contributed to these improvements in gait speed.

Additionally, all participants increased stride length at the end of 6 weeks of training, with the improvements exceeding prior evaluations of auditory cueing within the same treatment duration.[13,14,32,33] In fact, our participant's improvements were nearly double the stride length improvements reported by others.[13,32] In addition, the observed changes persisted at a 3-month follow-up, which exceeds the findings reported by others.[34] We believe that the biggest contributor to these robust increases in stride length was the slowing of the metronome tempo during the treadmill training. As the treadmill continued to move at the same fast speed, participants took fewer steps to match the metronome, thus requiring them to increase their stride length to stay centered on the treadmill. We cannot discount the role of the concomitant verbal cues provided during training, however. As a clinical intervention, we provided occasional verbal encouragement to maintain synchronization with the metronome and maintain increased step lengths. These verbal cues may also have had a role in the improved spatiotemporal parameters that we observed.[35]

Although our primary purpose was to ascertain how targeted gait training would affect particular gait parameters, we also sought to determine whether there were any improvements in balance following training. Prior work has suggested a carryover of gait training with cueing resulting in improved balance scores.[21,36] Our results suggest that there were small improvements in balance for all participants; however, the improvements may not be clinically meaningful. It is important to note that our participants were high functioning, so ceiling effects of the selected tests may have masked any potential improvements in balance. The psychometric properties of the FSST are only available for individuals with Huntington's disease,[37] but if applied to our participants, then only P1 exceeded the MDC. The MDC for the Mini-BESTest is 5.5 points for people with PD,[22] which was not feasible for 2 of our participants due to a ceiling effect. Although there is a lack of published psychometrics of the Step Test, we noted that P1 and P2 both improved by 13 and 11 total repetitions, respectively, which our clinical judgment suggests may be a considerable improvement.

The small sample size of our case series clearly limits the ability to generalize these results to other individuals with PD. Furthermore, all of the participants had the same stage of disease; therefore, the results cannot be generalized to other stages of disease progression.[38] It is also important to note that the training involved three 1-hour sessions each week for 6 weeks, which may prove challenging in an outpatient setting. Finally, the lack of controls means that we cannot determine causation with our study design. It is possible that participants would have improved their gait with training that did not include rhythmic cueing targeted to key gait parameters. In particular, treadmill walking alone is known to facilitate small improvements in certain outcome measures of gait for individuals with PD.[39] When high-intensity training is employed, gait endurance (ie, 6MWT) can also be improved.[40] Therefore, it is unknown which component parts (rhythmic cueing, occasional verbal cueing, treadmill/overground walking, and high-intensity training) are critical to the outcomes we observed with our participants. We can speculate that each of these components represents an "active ingredient," given the independent success of rhythmic cueing, treadmill walking, transfer to overground walking, verbal cues, and the progressive high-intensity cardiovascular training. Further research, however, will ascertain the contributing factors to the observed gait improvements.

SUMMARY

This case series describes the novel use of targeted rhythmic auditory cueing to improve gait and balance in individuals with PD. All 3 participants demonstrated improvements in gait speed and stride length by the end of 6 weeks of training, with these changes persisting for at least 3 months. We observed only small changes in balance, however, presumably due to the high functioning status of our participants at pretest. The outcomes demonstrated by these participants are encouraging for future research.

REFERENCES

1. Morris ME, Iansek R, Matyas TA, Summers JJ. The pathogenesis of gait hypokinesia in Parkinson's disease. *Brain*. 1994;117(pt 5):1169-1181.
2. Lewek MD, Poole R, Johnson J, Halawa O, Huang X. Arm swing magnitude and asymmetry during gait in the early stages of Parkinson's disease. *Gait Posture*. 2010;31(2):256-260.
3. Hallett M. The intrinsic and extrinsic aspects of freezing of gait. *Mov Disord*. 2008;23(suppl 2):S439-S443.
4. Sethi K. Levodopa unresponsive symptoms in Parkinson disease. *Mov Disord*. 2008;23(suppl 3):S521-S533.
5. Curtze C, Nutt JG, Carlson-Kuhta P, Mancini M, Horak FB. Levodopa is a double-edged sword for balance and gait in people with Parkinson's disease. *Mov Disord*. 2015;30(10):1361-1370.
6. Rocha PA, Porfirio GM, Ferraz HB, Trevisani VF. Effects of external cues on gait parameters of Parkinson's disease patients: a systematic review. *Clin Neurol Neurosurg*. 2014;124:127-134.
7. Keus SH, Bloem BR, Hendriks EJ, Bredero-Cohen AB, Munneke M; Practice Recommendations Development Group. Evidence-based analysis of physical therapy in Parkinson's disease with recommendations for practice and research. *Mov Disord*. 2007;22(4):451-460; quiz 600.
8. Ashoori A, Eagleman DM, Jankovic J. Effects of auditory rhythm and music on gait disturbances in Parkinson's disease. *Front Neurol*. 2015; 6:234.
9. Peterson DS, Smulders K. Cues and attention in Parkinsonian gait: potential mechanisms and future directions. *Front Neurol*. 2015;6:255.
10. Gomez-Gonzalez J, Martin-Casas P, Cano-de-la-Cuerda R. Effects of auditory cues on gait initiation and turning in patients with Parkinson's disease. *Neurologia*. 2019;34(6):396-407. [In English, Spanish].
11. Frenkel-Toledo S, Giladi N, Peretz C, Herman T, Gruendlinger L, Hausdorff JM. Treadmill walking as an external pacemaker to improve gait rhythm and stability in Parkinson's disease. *Mov Disord*. 2005;20(9):1109-1114.
12. Thumm PC, Maidan I, Brozgol M, et al. Treadmill walking reduces prefrontal activation in patients with Parkinson's disease. *Gait & posture*. 2018;62:384-387.
13. Thaut MH, McIntosh GC, Rice RR, Miller RA, Rathbun J, Brault JM. Rhythmic auditory stimulation in gait training for Parkinson's disease patients. *Mov Disord*. 1996;11(2):193-200.
14. Ford MP, Malone LA, Nyikos I, Yelisetty R, Bickel CS. Gait training with progressive external auditory cueing in persons with Parkinson's disease. *Arch Phys Med Rehabil*. 2010;91(8):1255-1261.
15. Thaut MH, Rice RR, Braun Janzen T, Hurt-Thaut CP, McIntosh GC. Rhythmic auditory stimulation for reduction of falls in Parkinson's disease: a randomized controlled study. *Clin Rehabil*. 2019;33(1):34-43.
16. McIntosh GC, Brown SH, Rice RR, Thaut MH. Rhythmic auditory-motor facilitation of gait patterns in patients with Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 1997;62(1):22-26.
17. Arias P, Cudeiro J. Effects of rhythmic sensory stimulation (auditory, visual) on gait in Parkinson's disease patients. *Exp Brain Res*. 2008;186(4):589-601.
18. Frazzitta G, Maestri R, Uccellini D, Bertotti G, Abelli P. Rehabilitation treatment of gait in patients with Parkinson's disease with freezing: a comparison between two physical therapy protocols using visual and auditory cues with or without treadmill training. *Mov Disord*. 2009;24(8):1139-1143.
19. Chawla G, Wygand M, Browner N, Lewek MD. Individuals with Parkinson's disease retain spatiotemporal gait control with music and metronome cues [published online ahead of print July 30, 2019]. *medRxiv*. doi:10.1101/19003269.
20. Hoppe M, Chawla G, Browner N, Lewek MD. The effects of metronome frequency differentially affects gait on a treadmill and overground in people with Parkinson disease. *Gait Posture*. 2020;79:41-45.
21. Harro CC, Shoemaker MJ, Frey O, et al. The effects of speed-dependent treadmill training and rhythmic auditory-cued overground walking on balance function, fall incidence, and quality of life in individuals with idiopathic Parkinson's disease: a randomized controlled trial. *NeuroRehabilitation*. 2014;34(3):541-556.
22. Leddy AL, Crowner BE, Earhart GM. Utility of the Mini-BESTest, BESTest, and BESTest sections for balance assessments in individuals with Parkinson disease. *J Neurol Phys Ther*. 2011;35(2): 90-97.
23. Giladi N, Shabtai H, Simon ES, Biran S, Tal J, Korczyn AD. Construction of freezing of gait questionnaire for patients with Parkinsonism. *Parkinsonism Relat Disord*. 2000;6(3):165-170.
24. Gill DJ, Freshman A, Blender JA, Ravina B. The Montreal cognitive assessment as a screening tool for cognitive impairment in Parkinson's disease. *Mov Disord*. 2008;23(7):1043-1046.
25. Duncan RP, Earhart GM. Four square step test performance in people with Parkinson disease. *J Neurol Phys Ther*. 2013;37(1):2-8.
26. Mercer VS, Freburger JK, Chang SH, Purser JL. Step Test scores are related to measures of activity and participation in the first 6 months after stroke. *Phys Ther*. 2009;89(10):1061-1071.
27. Herman T, Giladi N, Hausdorff JM. Treadmill training for the treatment of gait disturbances in people with Parkinson's disease: a mini-review. *J Neural Transm (Vienna)*. 2009;116(3):307-318.
28. Penko AL, Barkley JE, Koop MM, Alberts JL. Borg scale is valid for ratings of perceived exertion for individuals with Parkinson's disease. *Int J Exerc Sci*. 2017;10(1):76-86.
29. Lewek MD, Braun CH, Wutzke C, Giuliani C. The role of movement errors in modifying spatiotemporal gait asymmetry post stroke: a randomized controlled trial. *Clin Rehabil*. 2018;32(2):161-172.
30. Steffen T, Seney M. Test-retest reliability and minimal detectable change on balance and ambulation tests, the 36-item short-form health survey, and the unified Parkinson disease rating scale in people with parkinsonism. *Phys Ther*. 2008;88(6):733-746.
31. Lang JT, Kassan TO, Devaney LL, Colon-Semenza C, Joseph MF. Test-retest reliability and minimal detectable change for the 10-meter walk test in older adults with Parkinson's disease. *J Geriatr Phys Ther*. 2016;39(4):165-170.
32. Murgia M, Pili R, Corona F, et al. The use of footstep sounds as rhythmic auditory stimulation for gait rehabilitation in Parkinson's disease: a randomized controlled trial. *Front Neurol*. 2018;9:348.
33. Bella SD, Benoit CE, Farrugia N, et al. Gait improvement via rhythmic stimulation in Parkinson's disease is linked to rhythmic skills. *Sci Rep*. 2017;7:42005.

34. Nieuwboer A, Kwakkel G, Rochester L, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. *J Neurol Neurosurg Psychiatry*. 2007;78(2):134-140.
35. Behrman AL, Teitelbaum P, Cauraugh JH. Verbal instructional sets to normalise the temporal and spatial gait variables in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 1998;65(4):580-582.
36. Song JH, Zhou PY, Cao ZH, Ding ZG, Chen HX, Zhang GB. Rhythmic auditory stimulation with visual stimuli on motor and balance function of patients with Parkinson's disease. *Eur Rev Med Pharmacol Sci*. 2015;19(11):2001-2007.
37. Kloos AD, Fritz NE, Kostyk SK, Young GS, Kegelmeyer DA. Clinimetric properties of the Tinetti Mobility Test, Four Square Step Test, Activities-specific Balance Confidence Scale, and spatiotemporal gait measures in individuals with Huntington's disease. *Gait Posture*. 2014;40(4):647-651.
38. Lirani-Silva E, Lord S, Moat D, Rochester L, Morris R. Auditory cueing for gait impairment in persons with Parkinson disease: a pilot study of changes in response with disease progression. *J Neurol Phys Ther*. 2019;43(1):50-55.
39. Mehrholz J, Kugler J, Storch A, Pohl M, Hirsch K, Elsner B. Treadmill training for patients with Parkinson's disease. *Cochrane Database Systematic Rev*. 2015(9):CD007830.
40. Lamotte G, Rafferty MR, Prodoehl J, et al. Effects of endurance exercise training on the motor and non-motor features of Parkinson's disease: a review. *J Parkinsons Dis*. 2015;5(1):21-41.