The Effects of Treadmill Walking on Gait Parameters in Individuals with Dementia with Lewy Bodies

Honors Research Thesis

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Abstract

Background: Individuals with dementia with Lewy Bodies (DLB) exhibit motor impairments similar to those seen in Parkinson's disease (PD), including gait disturbances, thus increasing their risk for falls. While research suggests that treadmill training is a successful treatment modality in PD, our current study is the first to investigate its effects in the DLB population. The purpose of this study was to investigate the safety, feasibility, and effects on gait of a single 20 minute session of treadmill walking (TW) in individuals with DLB. We hypothesized that TW would improve gait velocity, and spatial and temporal gait parameters. **Methods:** This study utilized a one group pre-test/post-test design with ANOVA analysis. Eight individuals with a diagnosis of DLB underwent the 20 minute TW intervention. Spatiotemporal gait parameters in forward, forward fast, and backward walking were assessed with GAITRite before and after the intervention. **Results:** No abnormal HR or BP responses were observed during the intervention or testing. No adverse events occurred. Seven of eight (87.5%) participants were able to complete the TW and testing; 4 participants achieved their comfortable overground walking speed on the treadmill. There were significant improvements in temporal gait measures of comfortable walking post-TW. For example, we found an increase in stride velocity (71.22 ± 19.45 cm/s to 79.68 ± 23.43 cm/s; P = 0.028), a decrease in stance time (0.83 ± 0.04 s to 0.78 ±0.04 s; P = 0.006), and a decrease in double support time (0.47 ±0.05 to 0.43 ± 0.06; P = 0.012) post-intervention. There were no significant changes in spatiotemporal measures of backwards and fast walking gait parameters. **Conclusions:** This study demonstrates that TW is safe and feasible in individuals with DLB. All subjects improved on velocity and the majority of temporal parameters of gait exclusively in comfortable walking, suggesting that the benefits of TW may be task specific. Pace training on a treadmill with multiple sessions may be a beneficial intervention for individuals with DLB.

Background

Dementia is a general term for a decline in mental ability that is severe enough to interfere with an individual's daily life. Dementia is not a single disease; rather it encompasses a wide range of symptoms associated with impairments in mental function such as losses in memory, communication and language, ability to focus, reasoning and judgment, and visual perception. Alzheimer's disease (AD) is the most common form of dementia, accounting for 60 to 80 percent of all cases. Other forms of dementia include vascular dementia, dementia with Lewy Bodies, Huntington's disease, Parkinson's disease (PD) dementia, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, Wernicke-Korsakoff Syndrome, frontotemporal dementia, and mixed dementia. Although these dementias are associated with different mechanisms of brain cell damage, they have many overlapping symptoms making it difficult for doctors to differentiate their diagnoses. While some symptoms of dementia can be reversed by correcting the cause of the problems, most dementias are progressive neurodegenerative diseases with no cure and no treatments to slow or stop progression. Treatment is instead focused on temporarily relieving symptoms so that the affected individual can function to their greatest ability.[1]

Dementia with Lewy Bodies, hereafter referred to as DLB, is the third most common subtype of dementia accounting for 10 to 25 percent of all cases, and is characterized by the presence of protein deposits in the brain.[1] DLB is a progressive neurological disease and will lead to deteriorating motor function, severe memory disturbance, neuroleptic reactions, disproportionate visuospatial deficits, and global functioning deterioration in late stages.[2,3] The protein deposits in DLB, termed Lewy bodies after their discovery by Frederick Lewy in the early 1900s, are composed of alpha-synuclein protein and have been found to deplete

cholinergic and dopaminergic markers in varying areas of the brain.[2] Lewy bodies are also found in other types of dementia, most commonly PD dementia and AD, suggesting that these 3 diseases may be related to the same underlying abnormalities in how the brain processes alpha-synuclein.[4] Although causes of these processing abnormalities are not known, a case-control study of individuals with DLB has shown that a history of anxiety, depression, stroke, and a family history of PD are risk factors for the development of DLB, and that those with DLB are significantly less likely to have had cancer or use caffeine compared to controls.[5] DLB typically presents between the ages of 50 and 85 with the mean age of onset at 68 years.[3] DLB is associated with a greater risk of mortality and institutionalization than AD.[3,6]

DLB presents with many non-specific, cognitive, and motor manifestations. A majority of DLB patients will experience fluctuations in cognition that resemble signs of delirium. These fluctuations include excessive daytime sleepiness and transient confusion, and varying levels of attention and alertness that can last over minutes, hours, or days. Other non-specific manifestations include syncope, delusions, transient loss of consciousness, multimodal hallucinations, and visual hallucinations in 13-80% of all patients. Cognitive manifestations of DLB include severe memory impairment, attentional deficits, visuospatial dysfunction, difficulty with recognizing faces (prosopagnosia) and colors (color agnosia), and problems with assembling/drawing objects (constructional apraxia) and initiating hand movements (ideomotor apraxia). Language skills are negatively impacted by spoken false memories (confabulation), incoherence, involuntary repetition (perseveration), difficulty naming common objects, and a reduction in verbal fluency. Changes in brain and cardiovascular structures are also present in DLB and can help distinguish this disease from other dementias.[3] The rate of cognitive decline in DLB is similar to that seen in AD, but with less memory loss in the early stages than AD.[2,3]

Motor manifestations include akinetic-rigid syndrome, tremor, slowness of movement (bradykinesia), and postural instability.[3]

DLB, PD, and PD dementia share many common symptoms, therefore it is pertinent to note these as well as their differences. Non-motor symptoms that are common in both DLB and PD dementia are depression, visual hallucination, delusion, trouble interpreting visual information, malfunctions of the autonomic nervous system, and a condition known as rapid eye movement sleep behavior disorder in which the individual physically acts out while dreaming.[4] Movement impairments in individuals with DLB are very similar to those seen in PD. Overlapping motor manifestations between the two diseases include hunched posture, balance problems, falls, rigid muscles, shuffling walk, trouble initiating movement, bradykinesia, and facial masking.[2,4] Unlike PD, motor symptoms of DLB are usually bilateral instead of unilateral and no rest tremor is present. The onset and severity of parkinsonian symptoms in DLB are highly variable.[2]

It may be difficult to clinically diagnose DLB as this disease shares many features with other dementias. Definitive diagnosis of DLB is made only after a brain autopsy upon death.[2] The first consensus guidelines for the clinical diagnosis of DLB were made in 1996 and revised in 2005, but the accuracy of clinical diagnosis has still been relatively low.[2,3,7] Because of these accuracy issues, more than 50% of DLB cases are missed, possibly leading to ineffective treatment strategies and severe adverse effects of treatment.[8] DLB diagnosis is made when 2 of the following 3 core diagnostic features are present in addition to dementia; 1.) fluctuating cognition, 2.) visual hallucinations, and 3.) movement disorder. The presence of suggestive features such as REM sleep behavior disorder, severe neuroleptic sensitivity, and low dopamine transporter uptake can also aid in diagnosis. Similar to the diagnostic procedures for other

dementias, history taking, physical and mental examinations, and lab tests are used in the diagnosis of DLB.[3] Because DLB, PD dementia, and AD present with similar symptoms, the timing of symptom onset is key in diagnosing the correct disorder. The main difference between DLB and PD dementia is the presence of movement symptoms before dementia symptoms. The diagnosis of DLB is made when dementia symptoms associated with DLB develop first, when both dementia symptoms and movement symptoms are present at the time of diagnosis, or when movement symptoms present within a year after DLB diagnosis. On the other hand, if only movement symptoms are present at the time of original PD diagnosis and dementia symptoms appear a year or more later, then the diagnosis is PD dementia.[4] DLB is most commonly misdiagnosed as AD, but is increasingly differentiated from AD through the use of biomarkers tests, such as those that measure alpha synuclein and oxidized alpha-helical form of amyloid β_{40} in the cerebrospinal fluid.[3,4]

There are currently no treatments that can stop or slow the progression of brain cell damage in DLB. Rather, treatments are focused on relieving symptoms of DLB to improve quality of life for affected individuals.[4] Pharmacologic management may include the use of cholinesterase inhibitors, psychostimulants, atypical neuroleptics, and selective serotonin reuptake inhibitors.[9] Cholinesterase inhibitors work to improve the cholinergic deficit seen in DLB and aim to treat cognitive symptoms and improve consciousness. Rivastigmine is the most commonly used cholinesterase inhibitor, with one study showing significant improvement in 50% of patients.[3] Psychostimulants, such as levodopa, are used to improve extrapyramidal signs and motor symptoms.[3] Levodopa has shown to be tolerable and beneficial in managing motor symptoms in small trials of DLB patients, but has not been shown to be as effective in DLB as it has in individuals with PD and PD dementia.[2,3] Atypical neuroleptics may help relieve symptoms

of delusions and agitation but their use should be closely monitored.[9,10] Finally, selective serotonin uptake inhibitors can be used to treat symptoms of depression and anxiety.[9]

For the purpose of this study, we chose to focus our efforts on the management of motor manifestations of DLB, specifically disorders of gait. Gait is defined by the Merriam-Webster dictionary as a manner of walking or moving on foot.[11] Gait impairments in individuals with DLB include decreased velocity, shorter step lengths, decreased arm swing, stooped posture, and shuffling gait.[12] Gait and balance disorders have been shown to be prevalent in 40 percent of individuals with mild dementia, 87 percent with moderate dementia, and 100 percent with severe dementia.[12] This is a cause for concern since disorders of gait are one of the major determinants of a patient's independence and quality of life.[13] Additionally, these gait impairments lead to an increased risk of falls as demonstrated by the finding that 37 percent of patients with DLB experienced multiple falls (> 5) over a 3 month period.[14] In another study, 77% of the DLB subjects (N = 30) experienced at least one fall over the course of a year.[15]

Based on reports that up to 70 percent of DLB patients have parkinsonian symptoms, including gait impairments, we reason that the DLB population may benefit from treatments typically utilized in the PD population.[12] One relatively new mode of therapy that has been implemented in the treatment of PD is treadmill training.[16] In this form of therapy, an individual is subjected to a single session or multiple sessions of walking on a treadmill. The results from post-treadmill overground walking tests are then compared to the subject's pre-treadmill test results to examine changes in various gait parameters.

There have been several studies that have investigated the effects of a treadmill walking (TW) intervention on gait parameters in individuals with PD. These studies have shown that

treadmill training may have the ability to reduce gait disturbances in those affected by PD, suggesting that this may be used as a complementary or alternative option to traditional therapy.[13,17-20] While most of these studies have implemented interventions consisting of multiple walking sessions over an extended period of time, three studies have investigated the immediate effects of a single session of treadmill training for individuals with PD. To better examine the effects of our intervention in relation to the current research, we will be focusing on the three studies that utilized a single session of TW to improve gait parameters. These studies are discussed in more detail below. In all three studies, the participants wore an overhead safety harness while on the treadmill to protect against falls. No adverse events were reported as a result of treadmill training.[13,19,20]

In a study by Pohl et al., seventeen individuals with early PD (Hoehn and Yahr scale stages I through III; i.e. motor symptoms ranging from mild to moderately severe[21]) and gait disturbances participated in 3 gait training interventions and one control intervention. One intervention was given per day for 4 consecutive days. The interventions had varying methodologies: 1.) structured speed-dependent treadmill training (STT), 2.) limited progressive treadmill training (LTT), 3.) conventional gait therapy (CGT), and 4.) a control intervention. In the STT intervention, participants walked on a treadmill for a total of 30 minutes with at least 5 incremental 10% increases in training speed depending on the participant's ability to walk safely. For the LTT intervention, participants walked at their pre-tested overground walking speed for 30 minutes with no increases in training speed. Brief rests were given in both STT and LTT interventions as needed. The CGT intervention consisted of physiotherapeutic gait therapy for 30 minutes administered by two skilled therapists trained in gait therapy (i.e. proprioceptive neuromuscular fascicultation (PNF)) techniques. For the control intervention, participants did not

receive any therapeutic treatment and instead rested in a recumbent or comfortable sitting position for 30 minutes. The results of the interventions showed no significant changes in any gait parameters after CGT and the control intervention. There were significant improvements in speed, stride length, and double-stance duration after STT and LTT interventions, and a significant gain in de-loading rate after STT with no significant changes in symmetry parameters or other vertical forces across all interventions.[19]

Frenkel-Toledo et al. conducted a study comparing gait measures across three walking conditions: usual walking, walking with the assistance of a wheeled walker, and walking on a treadmill. Thirty-six individuals with early stage PD and 30 control subjects participated. Participants were required to perform each intervention for two minutes; treadmill speed was set to their walker-assisted gait speed. Gait parameter measures in the treadmill intervention were compared to measures of the walker-assisted intervention. The treadmill was shown to significantly reduce stride time variability and swing time variability in both PD and control subjects, significantly reduce the swing time of PD subjects but not controls, and significantly reduce the fractal index (i.e., indicating a less ordered, more random stride time series) of the controls but not the PD subjects. No significant treadmill effect was found on stride length or average stride time, due to the same gait speeds between the two interventions. These results indicate that a treadmill acts as an external pacemaker to significantly reduce gait variability and enhance gait stability.[20]

In a study conducted by Bello et al., 16 individuals with PD (8 moderate PD and 8 advanced PD participants as determined by the Hoehn and Yahr scale) and 8 healthy controls participated in a TW session. The treadmill intervention consisted of five 4 minute blocks of TW with 3 minute rest periods in between blocks. The target speed of the treadmill belt was the

participant's pre-intervention overground walking speed. All participants were able to reach their target speed by the 5th 4-minute block, thus measurements from this block were used to compare pre- and post-intervention measurements. Post-intervention measurements were taken immediately after the intervention as well as 5 and 10 minutes after. For all participants, the three post-treadmill measurements of gait speed and step length were significantly higher than pre-intervention values. There was a significant increase in gait cadence in the immediate post-intervention measurement of the control and moderate PD groups when compared to their pre-intervention cadence. Cadence remained significantly high for the control and advanced PD groups in the second and third post-intervention tests. These results suggest that a single session of treadmill training improves overground gait and the effects last for at least 15 minutes.[13]

Based on the positive results of a single session of treadmill training seen in individuals with PD and the similarities in movement and gait disturbances between PD and DLB, we chose to investigate the effects of providing a TW intervention to individuals with DLB. To our knowledge, no studies to date have assessed the effects of TW to improve gait parameters in individuals with DLB. The primary purpose of this study was to investigate the safety, feasibility, and possible effects on gait in individuals with DLB. We hypothesized that a single 20 minute session of TW would improve gait velocity, and spatial and temporal gait parameters in individuals diagnosed with DLB.

Methods

Population and Sample

Eight individuals with a diagnosis of DLB were recruited from the Movement Disorders

Clinic and the Memory Disorders Clinic at The Ohio State University Wexner Medical Center to participate in the study. These individuals met the inclusion criteria of being able to walk 80 feet without assistance, to provide informed consent and assent, and to understand directions. Participants were required to have their Legally Authorized Representative (LAR) sign the consent form and the participant gave assent. Individuals were excluded from the study if they had any clinically significant musculoskeletal or neurological disease, other than DLB, that would affect gait. Institutional Review Board approval was obtained.

Study Design

The investigation utilized a one group pre-test/post-test design with control for learning effects within subjects to compare changes in gait parameters. Data was collected in the form of two pre-test measures and one post-test measure. Measurements were taken using the GAITRite system (an electronic sensitized carpet) and the Timed "Up and Go" (TUG) Test which are discussed in more detail below.

Outcome Measures

Spatiotemporal gait parameters were measured using the GAITRite system. This system consists of a 4.88 meter electronic carpet with sensors that record footfalls to a computer software program. The GAITRite system has been shown to have a strong concurrent validity with a more commonly used system, the Clinical Stride Analyzer, for the measurement of footfall patterns in adults and has been found to have a high test-retest reliability in both healthy adults and those suffering from a neurological disorder.[22,23]

The TUG Test was used to measure mobility and fall risk. This test requires participants to stand up from a chair, walk 3 meters, turn around and return to the chair.[24] It has been found that adults with PD who took more than 11.5 seconds to complete the TUG test were at a risk for

falls (sensitivity = 0.66, specificity = 0.62).[25] The TUG test has been shown to be a reliable and valid measure for quantifying functional mobility.[24]

Procedures

Participants began pre-test 1 by walking on the GAITRite carpet to complete 4 trials each of forward walking at a comfortable speed, forward walking at a fast speed, and backward walking at a comfortable speed for a total of 12 trials. They then completed TUG testing to obtain outcome measures for pre-test 1. After pre-test 1, participants sat in a chair and rested for 20 minutes before being retested on all measures (pre-test 2) to control for learning effects. Participants were then placed in a harness over the treadmill that acted solely as a safety measure and did not support their weight. After familiarization with the treadmill, participants completed a total of 20 minutes of TW. The treadmill protocol aimed to set the treadmill speed to each participant's comfortable overground walking speed, as determined by GAITRite data, for the first five minutes provided that they could walk at this speed safely (i.e. no abnormal vital signs, excessive effort, or loss of balance). Speed would then be incrementally increased by 10% at each 5 minute period (3 times total) thereafter. If the participant could not walk safely after a speed increase, the speed was decreased to their previous comfortable speed and maintained at that level for the remainder of the training session. Participants were asked to report their Rated Perceived Exertion (RPE) on a 0 – 10 scale, where 0 indicates no effort at all and 10 indicates maximum effort, at each five minute interval. Rest breaks were given as needed during the TW intervention, with the participants returning to their last comfortable speed after resting. Immediately after the completion of the 20 minute treadmill session, participants were retested on all outcome measures (post-test).

Data Analysis

Statistical analysis was completed using SPSS Version 22. Results from the GAITRite testing were analyzed using the average of three trials of each walking condition (comfortable speed, fast speed, backward walking) to assess differences in gait measures in all three conditions. Data from the GAITRite and TUG testing was analyzed using an Analysis of Variance (ANOVA) to discern any significant changes in the outcome measures of gait parameters after the treadmill training.

Facilities and Resources

Research was conducted in the Mobility and Exercise in Neurological Disorders (MEND) laboratory. The laboratory is located at The Ohio State University main campus in Atwell Hall, room 236. Equipment used, other than the measurement tools discussed previously, included the Biodex Gait Trainer 3 treadmill (950 model with extended handrails) and the Biodex Medical unweighing system. Aside from our patient recruitment from the OSU Movement Disorders Clinic or the OSU Memory Disorders Clinic, no other departments or outside agencies cooperated with the research project.

Results

Participant Characteristics

Participant characteristics are presented in Table 1. Values are displayed as mean ± standard deviation. The study population consisted of eight individuals, 4 males and 4 females, with a mean age of 75.88 ± 6.36 years (range = 68 – 86). Years since diagnosis ranged from 0.17 to 10 years (3.17 ± 3.35) while years since onset of symptoms ranged from 2 to 10 years (5.43 ± 2.57). One participant reported experiencing two falls within the past week, two participants

reported at least one fall in the past 6 weeks, and three reported at least one fall in the past 6 months. Two participants occasionally used a cane as an assistive device and one participant used a two-wheeled walker. Mean Mini-Mental State Examination (MMSE) scores for our study population (19.14 ± 9.14) indicated a positive screen for dementia (scores ≤ 24).[26]

Intervention

Seven of eight participants (87.5%) were able to complete the 20 minute TW intervention and subsequent testing. The participant who could not complete the intervention was only able to walk for 6 minutes and reported being "too tired" to perform post-intervention assessments. This participant also reported the longest time since symptom onset (10 years). Participants' comfortable overground walking speeds were recorded using GAITRite. One participant's overground walking speed was not obtained due to equipment malfunction. Although no participants were able to begin TW at their comfortable overground walking speed, four participants were able to attain their comfortable overground walking speed during the 20 minutes on the treadmill. Additionally, three participants were able to follow the intervention protocol of 10% increases in speed at each 5 minute interval (Table 2). Participants were permitted to take as many rest breaks as needed throughout the 20 minutes of TW. Aside from the one participant who stopped after 6 minutes, one participant reported being very tired and took a total of four rest breaks for 5 minutes each and another participant took two breaks for a total time of 16 minutes. One participant needed constant cueing to walk with big steps and another reported that she had to think about stepping.

The four participants who were able to attain their comfortable overground walking speed on the treadmill had higher MMSE scores (i.e., less cognitive impairment) than those who did not (Figure 1). After running a Spearman's correlation we found that the ability to reach

comfortable walking speed on the treadmill during this 20 minute session had a strong positive correlation to MMSE scores ($R_S = 0.874$; $P = 0.01$).

Heart rate and blood pressure values were both taken prior to the TW intervention and after the intervention. Heart rate values were also taken at each 5 minute interval on the treadmill. Maximum heart rate values were calculated according to the Haskell and Fox (220 minus age) equation. No participant reached their maximum heart rate and blood pressure responses were normal per ACSM guidelines (Table 3; Table 4).[27]

Participants were asked to rate their perceived exertion (RPE) during the intervention. Mean reported RPE values on a 0 – 10 scale indicated low perceived exertion. The highest reported RPE value was a 7 in the 15 – 20 minute interval of TW (Figure 2).

Gait Parameters

Measurements of gait parameters were obtained using the GAITRite system and TUG testing. Operational definitions of gait parameters and a diagram of the gait cycle are included in appendices B and C for reference. There were no significant differences in gait measures from pre-test 1 to pre-test 2, ruling out a learning effect of the testing. Therefore only the data comparing pre-test 1 to post-test measures are reported, as the pre-test 1 values were thought to better represent the participants' natural gait patterns at pretesting.

GAITRite data showed significant differences in gait parameters from pre-intervention to post-intervention (Table 4). All significant changes were seen in comfortable walking. Additionally, all of these differences were in velocity and temporal measures of gait. Specifically, participants showed statistically significant increases in gait velocity, cadence, and stride velocity and decreases in stance time and double support time ($P < 0.05$). Step time was

approaching significance while there were no significant differences in swing time or spatial parameters of comfortable forward walking. Gait parameters of fast and backward walking did not change after a one-time 20 minute TW session. No subjects had markedly worse outcomes across gait measures after the TW intervention.

Mean TUG scores improved post-intervention (25.78 ± 12.47 s and 18.87 ± 13.57 s, respectively), but this difference was not significant (P = 0.282).

Table 1. Participant characteristics

	Mean ± SD (Range)
Age (years)	75.88 ± 6.36 (68 – 86)
Gender	4 Male 4 Female
Years Post Diagnosis (N = 7)	3.17 ± 3.35 (0.17 – 10)
Years since onset of symptoms	5.43 ± 2.57 (2 – 10)
MMSE scores (N = 7)	19.14 ± 9.14 (0 – 27)

MMSE = Mini-mental state examination

Table 2. Treadmill speed

Participant	Comfortable Walking speed (mph)	Speed (mph) 0-5 mins	Speed (mph) 5-10 mins	Speed (mph) 10-15 mins	Speed (mph) 15-20 mins
1	1.68	1.4	1.5	1.6	1.7
2	1.07	0.3	NR	NR	NR
3	1.01	0.2	0.4	0.4	0.3
4	1.3	1.0	1.0	1.0	1.0
5	1.28	1.0	1.1	1.2	1.3
6	1.92	1.1	1.2	1.4	1.5
7	1.76	1.4	1.4	1.5	1.8
8	NR	1.7	1.8	1.9	2.0

mph = miles per hour; mins = minutes; NR = not recorded

Table 3. Heart Rate values

Participant	Calculated HR Max	Initial HR	HR (0-5 min)	HR (5-10 min)	HR (10-15 min)	HR (15-20 min)	HR (Post-test)
1	151	56	70	75	76	75	81
2	144	60	NR	NR	NR	NR	NR
3	145	97	80	85	79	85	85
4	138	64	68	78	80	82	74
5	134	54	53	63	84	80	100
6	141	64	85	97	91	95	80
7	149	80	100	105	109	112	100
8	152	80	88	82	92	98	80

HR = heart rate; HR max = maximum heart rate; NR = not recorded

Table 4. Blood pressure values

Participant	Initial BP	BP (Post-test)
1	110/78	120/82
2	100/64	NR
3	108/60	118/80
4	128/52	128/64
5	100/60	110/67
6	130/80	142/76
7	135/78	118/80
8	160/98	158/96

BP = blood pressure; NR = not recorded

Table 5. GAITRite			
Gait Parameters (N=6)	Pre-test Mean ± SD	Post-test Mean ± SD	Significance P-value
	Temporal measures		
Velocity (m/s)	0.70 ± 0.19	0.79 ± 0.23	**P = 0.035**
Cadence (steps/minute)	99.05 ± 5.62	104.67 ± 4.67	**P = 0.033**
Step Time (s)	0.62 ± 0.03	0.58 ± 0.02	P = 0.055
Stance Time (s)	0.83 ± 0.04	0.78 ± 0.04	**P = 0.006**
Stride Velocity (cm/s)	71.22 ± 19.45	79.68 ± 23.43	**P = 0.028**
Double Support Time (s)	0.47 ± 0.05	0.43 ± 0.06	**P = 0.012**
Swing Time (s)	0.38 ± 0.03	0.36 ± 0.04	P = 0.246
	Spatial measures		
Stride Length (cm)	85.66 ± 22.55	91.24 ± 27.22	P = 0.115
Step Length (cm)	42.52 ± 11.37	46.09 ± 14.35	P = 0.145
Swing Percentage Average (%)	30.68 ± 2.22	31.34 ± 2.74	P = 0.267
Double Support Percentage Average (%)	38.59 ± 4.78	37.16 ± 5.62	P = 0.238
HH Average (cm)	11.69 ± 4.75	10.91 ± 5.22	P = 0.118

m/s = meters per second; cm/s = centimeters per second; HH: Heel-to-heel

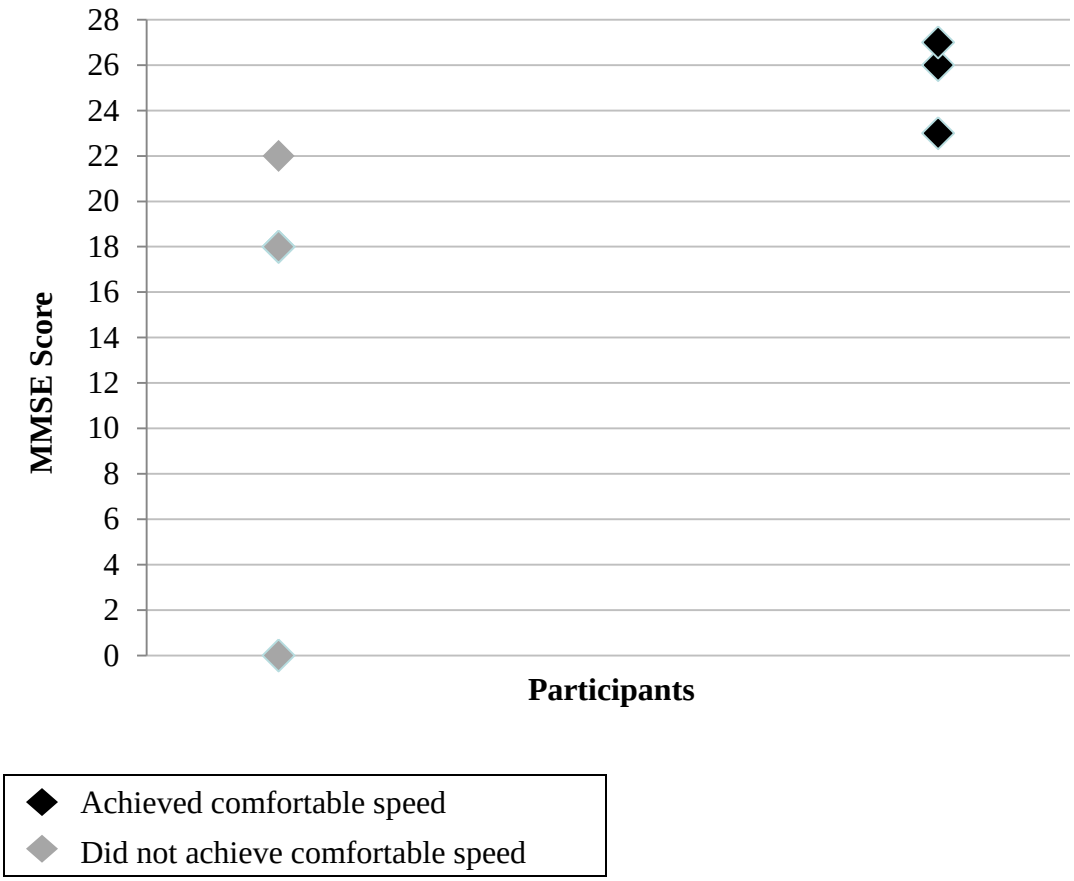

Figure 1. Correlation between Mini-mental state examination (MMSE) score and treadmill speed

The ability to achieve comfortable overground walking speeds on the treadmill had a strong positive correlation to MMSE scores in our population ($R_S = 0.874$; $P = 0.01$). Those with higher MMSE scores (i.e. less cognitive impairment) were significantly more likely to reach their comfortable overground walking speed than individuals with lower scores.

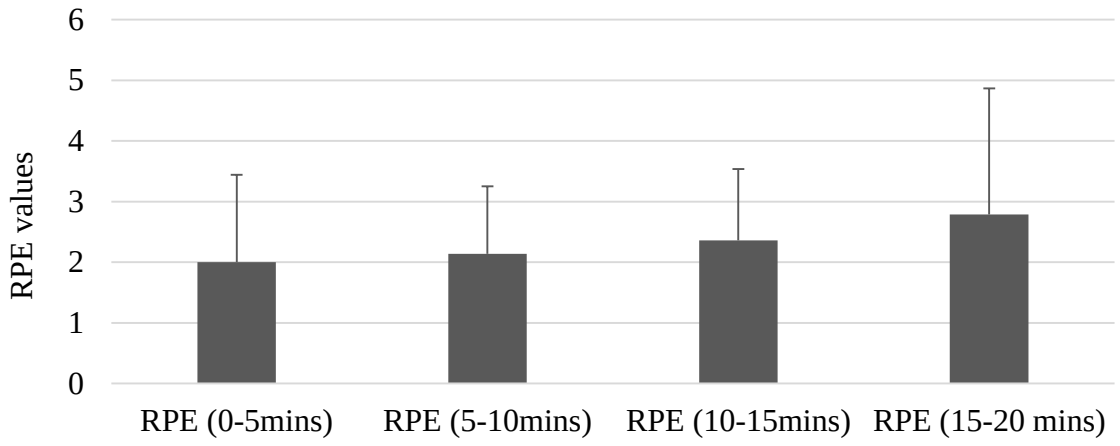

Figure 2. Rated Perceived Exertion (RPE) during TW
Mean reported RPE values on a 0 – 10 scale indicated low perceived exertion.

Discussion

To our knowledge, this is the first study to examine the safety, feasibility, and effects on gait of a treadmill-based intervention in individuals with DLB. Key findings of this study suggest that a single 20 minute TW intervention is safe and feasible for individuals with DLB, and that improvements in gait parameters may be task specific.

Safety and Feasibility

Similar to outcomes in the PD population, acceptability of the treadmill intervention was good and no adverse events occurred.[28] Heart rate and blood pressure responses were normal in our participants during TW, agreeing with the finding that treadmill training poses relatively low cardiovascular risks in individuals with PD.[18] Combined, these results suggest that our intervention was safe for these individuals with DLB. The majority of participants were able to complete the full 20 minutes of TW and RPE values indicated low perceived exertion, suggesting that this was a tolerable intervention. Aside from the participant who did not complete training, only two other participants needed to take rest breaks during the intervention and did so for an average of 18 minutes total each. The one participant who could not complete the TW had the longest duration of disease and greatest cognitive impairment, possibly indicating that this participant was severely deconditioned.

No participant was able to follow our proposed intervention procedure of starting at their comfortable overground walking speed. However, we did have participants who were able to increase their treadmill speed as described in our procedures. The participants who were able to reach their comfortable overground walking speed during TW had higher levels of functioning, per MMSE scores, than those who did not. After further investigation, we found the variables of

MMSE score and ability to reach comfortable overground walking speed during TW to have a strong positive correlation. These findings indicate that a single 20 minute session of TW is safe and feasible in individuals with DLB, although the standard protocol for treadmill training interventions may need to be modified to better accommodate differences in cognitive functioning and the orientation to TW.

Effects on Gait Parameters and Fall Risk (TUG scores)

We found a single 20 minute session of TW to have significant improvements on gait parameters in our participants, specifically in velocity and temporal measures of comfortable forward walking. Similar to previous findings in the PD population, participants significantly increased their gait speed post-TW.[13,18,28] Participants also significantly increased their cadence and stride velocity and decreased their stance time and double support time, all of which could indicate more fluid movement while walking. No participant had markedly worse gait outcomes after the TW intervention and the majority of the gait parameters were trending toward improvement. Although these improvements are promising, it is unclear whether these results were clinically meaningful. The difference in velocity did not meet the threshold to be clinically meaningful.[29]

There were no significant differences in spatial parameters of comfortable walking, nor in any gait measures of backward and fast walking. It is unclear why we only saw improvements in temporal measures of gait, but this finding may be explained by participants increasing their cadence rather than stride length to walk faster, which is an adjustment not typically seen in other populations.[28] All significant improvements were seen in comfortable walking, suggesting

that TW is task-specific and improvements may be the result of practice. Participants may need more training over an extended period of time to see clinically meaningful improvements in gait.

There was not a significant difference between pre-test and post-test mean TUG scores (25.78 s and 18.87 s; P = 0.282). Our participants' average times to complete the TUG testing could indicate that they are at an increased risk of falls. However, TUG testing has been shown to be unreliable for individuals with cognitive impairments and therefore our findings should not be taken as conclusive evidence of increased fall risk for the participants in our study.[30]

The small sample size and inclusion criteria of this study preclude generalization of our findings to the entire DLB population. Other limitations of our study include a lack of a definitive diagnosis of DLB since this can only be made upon autopsy and a lack of a measure for motor disease severity (Unified Parkinson's Disease Rating Scale). Our study only measured immediate effects of TW and therefore it should not be assumed that these improvements were retained over a longer period of time.

Conclusion

In conclusion, our study is the first to demonstrate that TW is a safe and feasible intervention in individuals with DLB. Additionally, we found a single 20 minute TW session to have favorable effects on gait parameters, suggesting that pace training on a treadmill with multiple sessions may be a beneficial intervention for individuals with DLB. Due to our small sample size we cannot confirm that the improvements in gait that we found are clinically meaningful, but we believe that our results are promising and warrant further investigation. Future studies of treadmill training for individuals with DLB should focus on implementing treadmill training programs with multiple sessions over extended periods of time, with an

emphasis on investigating the long term effects of training that may improve health-related quality of life.

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Appendix A. List of abbreviations

AD = Alzheimer's Disease

DLB = Dementia with Lewy Bodies

PD = Parkinson's Disease

TUG = Timed "Up and Go"

TW = Treadmill Walking

Appendix B. Operational definitions of gait parameters

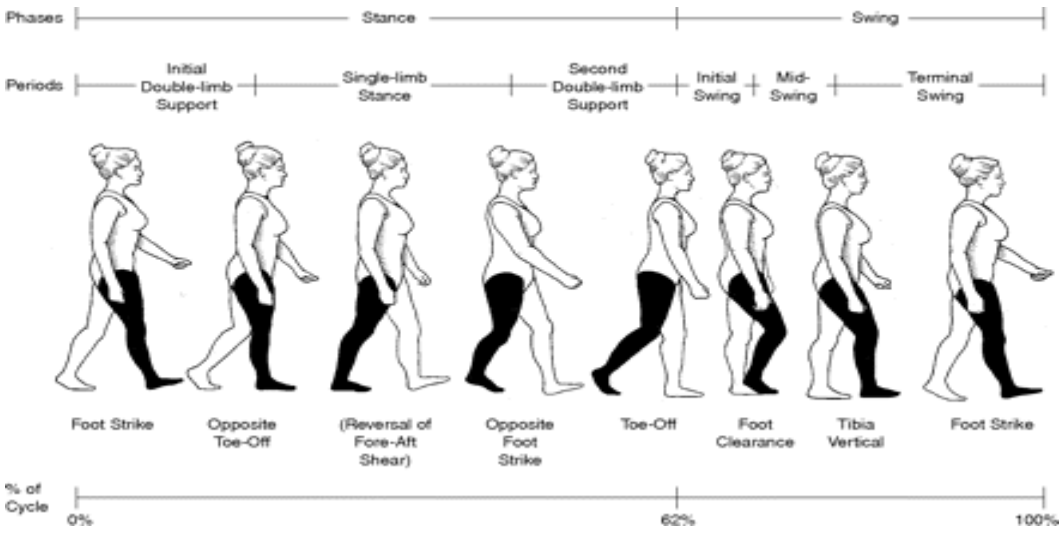
Gait parameter	Operational definition
Spatial parameters	
Step length (cm)	Anterior-posterior distance from the heel of one footprint to the heel of the opposite footprint
Stride length (cm)	Anterior-posterior distance between heels of two consecutive footprints of the same foot (left to left, right to right); two steps (e.g., a right step followed by a left step) comprise one stride or one gait cycle
Step width (cm)	Lateral distance from heel center of one footprint to the line of progression formed by two consecutive footprints of the opposite foot
Temporal parameters	
Cadence (steps/min)	Number of steps per minute, sometimes referred to as step rate
Step time (s)	Time elapsed from initial contact of one foot to initial contact of the opposite foot
Stride time (s)	Time elapsed between the initial contacts of two consecutive footfalls of the same foot
Stance time (s)	The stance phase is the weight bearing portion of each gait cycle initiated at heel contact and ending at toe off of the same foot; stance time is the time elapsed between the initial contact and the last contact of a single footfall
Swing time (s)	The swing phase is initiated with toe off and ends with initial contact of the same foot; swing time is the time elapsed between the last contact of the current footfall to the initial contact of the next footfall of the same foot
Single support time (s)	Single support occurs when only one foot is in contact with the ground; single support time is the time elapsed between the last contact of the opposite footfall to the initial contact of the next footfall of the same foot
Double support time (s)	Double support occurs when both feet are in contact with the ground simultaneously; double support time is the sum of the time elapsed during two periods of double support in the gait cycle
Temporophasic parameters	
Stance time (%GC)	Stance time normalized to stride time
Swing time (%GC)	Swing time normalized to stride time

Gait parameter	Operational definition
Single support time (%GC)	Single support time normalized to stride time
Double support time (%GC)	Double support time normalized to stride time
Spatiotemporal parameters	
Gait speed (cm/s)	Calculated by dividing the distance walked by the ambulation time
Stride speed (cm/s)	Calculated by dividing stride length by the stride time

cm = centimeters; s = seconds; %GC = % gait cycle.

Courtesy of: Hollman J, McDade E, Petersen R. Normative spatiotemporal gait parameters in older adults. *Gait & Posture*. May 2011; 34(1): 111-118. doi:10.1016/j.gaitpost.2011.03.024

Appendix C. Diagram of normal gait cycle



Courtesy of: Lim M, Huang R, Wu A, Girardi F, Cammisa F. Evaluation of the elderly patient with an abnormal gait. *The Journal Of The American Academy Of Orthopaedic Surgeons*. February 2007;15(2):107-117.