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Caroline Kim March 26, 2024

Three Months of Partnered Dance Aerobic Exercise May Reduce OFF-time and Enhance Quality of Life in Older Adults with Parkinson's Disease

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Abstract

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Objective: To determine if a three-month program of partnered dance aerobic exercise (PDAE) and walking aerobic exercise (WALK) are effective in reducing OFF-time and enhancing QOL and independence, and if PDAE is superior to WALK at reducing OFF-time.

Methods: Participants were randomized into 30 hours of PDAE or WALK over 3 months. Psychosocial questionnaires, MDS-UPDRS, and 3-day OFF-state diaries were administered at baseline and after three months to measure reported OFF-time, QOL, independence, and disease severity. Within-group comparisons were analyzed using paired *t*-tests, and between-group comparisons were analyzed using independent t-tests and a linear mixed-effects model.

Results: After three months, PDAE reduced OFF-time and improved motor symptoms. Compared to WALK, PDAE reduced OFF-time, improved motor symptoms, and enhanced the experience of daily living.

Conclusion: PDAE is superior to WALK and is an effective adjunctive therapy to help improve OFF-time and QOL in individuals with PD after three months. Further studies are needed to determine the relationship between improving OFF-time and quality of life.

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Abstract

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Introduction and Background

Parkinson's Disease

Parkinson's Disease (PD) is an intractable condition that severely impairs motor and cognitive function as well as quality of life and overall wellbeing (Kowal et al., 2013; Muslimovic et al., 2008). As the most common movement-related disorder and second most common neurodegenerative disease, PD affects up to 2% of adults over 65 years of age and is characterized by a loss of dopaminergic nerve cells in the basal ganglia (Samii et al., 2004). Motor symptoms are central to diagnosing PD, but non-motor symptoms are common and can dominate clinical presentations (Postuma et al., 2015). Common symptoms of PD include tremors in the hand, arm, leg, jaw, or head, muscle stiffness, bradykinesia, impaired balance and coordination, depression, difficulty swallowing, chewing, and speaking, and urinary and skin problems (Sveinbjornsdottir, 2016). OFF-time is one of the most concerting features of PD because of its impacts on the individual's quality of life (Politis et al., 2010).

Diagnostic criteria for PD

To be diagnosed with PD, patients must express three of four cardinal motor impairments: bradykinesia, tremor, rigidity, and postural instability. Progressive bradykinesia (the gradual worsening of slow, halting movements) is often the first-observed symptom of PD, and can be complicated by rigidity, resting tremor, or both. Diagnosis also requires that patients have unilateral presentation at onset and respond positively to levodopa, a dopamine-replacement therapy (Kempster et al., 2007). The overall collection of symptoms, also referred to as parkinsonism, can be attributed to PD following Movement Disorder Society (MDS) criteria

(Postuma et al., 2015). MDS guidelines for PD diagnoses require clinicians to confirm the patients has the absence of any exclusion criteria presenting within the first five years of the disease, at least two supporting criteria, and no red flags. MDS diagnosis criterion are summarized in Table 1.

Table 1

Movement Disorder Society Diagnosis Criteria for Parkinson's Disease

Criteria	**Characteristics**
Absence of exclusion criteria	Unequivocal cerebellar abnormalities Downward supranuclear gaze palsy Diagnosis of probably behavioral variant frontotemporal dementia or primary progressive aphasia
At least two supportive criteria	Clear, strong, and positive response to dopamine treatment (such as levodopa) Presence of levodopa-induced dyskinesia Rest tremor of a limb during clinical evaluation Positive results from one ancillary diagnostic test: Olfactory loss Clear cardiac sympathetic denervation from metaiodobenzylguanidine (a noradrenaline analog) scintigraphy
No red flags	Rapid decline of gait mobility resulting in dependency on a wheelchair within five years Complete absence or progression of motor symptoms after five years or more (unless stable from treatment) Early bulbar dysfunction Inspiratory reparatory dysfunction Severe autonomic dysfunction within the first five years of the disease Recurrent falls because of impaired balance within three years of disease onset

	Presence of disproportionate anterocollis Absence of common non-motor features after five years of disease Unexplained pyramidal tract signs Bilateral symmetric parkinsonism

Neurologically, PD is characterized by a severe loss of dopaminergic neurons in the pigmented pars compacta of the substantia nigra in the midbrain (Kalia & Lang, 2016). This loss of dopaminergic neurons in the midbrain affects the nigrostriatal pathway that connects the substantia nigra to the dorsal striatum, part of the basal ganglia, leading to denervation of the striatum and loss of dopaminergic input to the basal ganglia (Gordián-Vélez et al., 2021). Dopamine is an essential neurotransmitter for the function of basal ganglia and the initiation of voluntary movement (Lanciego et al., 2012). Loss of function in the basal ganglia leads to trouble initiating movement, and loss of output from the basal ganglia to the primary motor cortex is thought to be responsible for one of the hallmark signs of PD: bradykinesia (Bologna et al., 2020; Young et al., 2023). Another hallmark of PD is the accumulation of Lewy bodies, which contain misfolded α-synuclein proteins. These proteins also accumulate in similar disorders like multiple system atrophy and dementia with Lewy bodies. Such disorders are commonly called "synucleinopathies" (Goedert et al., 2017). Loss of dopaminergic neurons has been shown to precede the accumulation of Lewy bodies in the substantia nigra (Dijkstra et al., 2014).

Common functional impairments in PD

Common functional problems of people with PD affect motor, cognitive, and psychosocial domains. Motor issues include akinesia (difficulty initiating movements), bradykinesia (slow movements), rigidity, and tremor (Moustafa et al., 2016). Roughly 70% of PD

patients experience tremor (Helmich et al., 2012), the most common form of which is resting tremor, though kinetic tremor (during voluntary movements) and postural tremor (inability to maintain a stable posture against gravity) may also be present (Toth et al., 2004; Bhidayarsiri, 2005). Another common motor impairment is postural instability, which can be one of the most disabling features of PD by predisposing patients to injurious falls (Blaszczyk et al., 2007).

Cognitive problems are one of the more significant nonmotor symptoms of PD with insidious onset (Fang et al., 2020). Cognitive deficits in PD significantly impact executive function, speech dysfunction, visual-spatial ability, and memory impairment (Riedel et al., 2010). Mild-moderate cognitive impairment can be seen in early stages in around 40% of patients (Pfieffer et al., 2014). Previous epidemiological studies suggest that Parkinson's Disease Dementia (PDD) within eight years of the onset of PD may be as high as 78.2% (Aarsland et al., 2003).

Psychosocially, PD may also lead to depression, anxiety, and apathy (Pfieffer, 2015). Occurring at any time during PD progression, depression can be an early prodromal sign of PD and precede the onset of motor symptoms. Over time, depression is correlated with more significant motor impairment and disability (Pfieffer, 2015). Comorbidity rates of depressive conditions in PD patients suggest that as many as 17% also suffer from major depressive disorder, 22% from minor depression, and 13% with dysthymia (Reijnders et al., 2008). Similarly, anxiety can occur at any time during disease progression and prevails around 25-40% of the time (Simuni & Fernandez, 2013). Apathy has a prevalence of around 40% in PD, and there is a strong association between apathy and declinations of executive function (den Brok et al., 2015). In this way, PD affects all domains of living through both deleterious motor and nonmotor symptoms.

PD severely impacts the individual's quality of life and independence. Quality of life refers to one or more patient-reported outcomes. This definition lacks consistent terminology, leading to misunderstanding and misusing those measures (Den Oudsten et al., 2007). In a clinical context, therefore, health-related quality of life (QOL) is widely accepted, and it assesses the three domains of physical, psychological, and social well-being and satisfaction related to health. It combines objective functioning and subjective perceptions and judgments (Martinez-Martin et al., 2011). Nonmotor symptoms of PD, like depression, dementia, and psychosis, have a substantial impact on QoL (Martinez-Martin et al., 2011; Soh et al., 2011; Lawson et al., 2016). A study done by the Veterans Health Administration with over 15,000 participants with PD found that through the 36-item Short Form Health Survey, compared to patients with depression, congestive heart failure, stroke, chronic low back pain, arthritis, diabetes, and angina/coronary heart disease, patients with PD have a greater physical impairment dimension of QOL. Additionally, patients with PD had more significant mental health impairment in comparison to all other diseases except depression (Gage et al., 2003).

PD also impacts independence and the ability to carry out activities of daily living (ADL) (Santos García et al., 2021). The loss of functional independence leads to higher caregiver burden, higher resource use, greater risk for institutionalization, increased risk of death and comorbid complications, and a worse QOL (Covinsky et al., 2003; Macleod et al., 2016). Older age, higher severity of rigidity and bradykinesia, more severe axial symptoms, dyskinesia, cognitive impairment, and more advanced disease are all suggested predictors of functional dependency in PD (Alves et al., 2005; Muslimovic et al., 2008; Bjornestad et al., 2016; Macleod et al., 2016).

Common treatments for PD: levodopa

Given that PD is marked by reductions of dopamine in the brain, exogenous dopaminergic agonists often reverse PD symptoms, especially motor impairments. These pharmacotherapeutics directly stimulate postsynaptic dopamine receptors to temporarily restore striatal dopaminergic function. Directly administering dopamine is ineffective because dopamine cannot cross the blood-brain barrier (Hornykiewecz, 2002). However, select dopaminergic precursors, such as levodopa, can readily enter the brain. Because levodopa is a naturally occurring amino acid, it can be orally ingested where the small intestine absorbs it into the circulatory system. After levodopa reaches the brain, it is actively diffused across the blood-brain barrier and is converted into dopamine since it is an intermediate in the dopamine synthesis pathway (Nutt & Fellman, 1984). Levodopa may also have direct neuromodulatory and neurotransmitter effects that may aid its antiparkinsonian outcome (Misu et al., 2003). Currently, levodopa is the standard pharmaceutical treatment for PD and effectively improves motor symptoms in many patients within 15 to 30 minutes (LeWitt, 2008).

Downsides of levodopa: OFF-time

Despite its ease and speed of acting within the brain, levodopa is not a perfect PD treatment. On one hand, levodopa also has a short half-life of 90 minutes, which impacts the efficacy of the drug (Nutt, 1987). Moreover, levodopa can lose its efficacy over time. Generally, after several years of treatment, up to 75% of levodopa-treated PD patients experience medication-related motor fluctuations (Tsugawa et al., 2015), which is also known as “OFF-time”: the wearing-off of levodopa and reoccurrence of troubling motor and non-motor symptoms (Mantri et al., 2021). The prevalence of OFF-time is concerning due to its adverse

impact on independence and quality of life and is one of the most troublesome symptoms frequently reported by patients (Politis et al., 2010). OFF-time impacts mobility, activities of daily living, emotional well-being, cognition, communication, and bodily discomfort. Therefore, individuals who experience OFF-time report worse QOL and independence (Souza et al., 2007; Martinez-Martin et al., 2011; Leentjens et al., 2012; Stocchi et al., 2014; Kerr et al., 2016; Zhu et al., 2016).

The presence of OFF-time also impacts non-motor symptoms. PDQ-39 emotional well-being scores were significantly lower in patients who experienced OFF-time (Souza et al., 2007). Anxiety disorder, depression, and apathy are found to be more common in PD patients with OFF-time than those without (Kummer et al., 2010; Leentjens et al., 2012; Pontone et al., 2009; Yamanishi et al., 2013). Daily living experiences are also affected by OFF-time. PD patients who experience OFF-time are less likely to leave their homes as often, and motor fluctuations can cause patients to schedule their days around medication timing and make social situations less comfortable and more challenging to plan (Haahr et al., 2011; Kerr et al., 2016). The negative impact of OFF-time on mobility is described as a significant component of experiencing OFF-time. Off-time impacts activities like dressing, hygiene, getting around the house, communicating effectively, walking short distances, looking after the home, moving in bed, cutting food, getting around public places, and writing (Kerr et al., 2016).

While there are many possible explanations and factors that impact the development and severity of OFF-time, some issues relate to gastric uptake. Inconsistent and poor absorption and uptake of levodopa in the gastrointestinal tract impacts some individuals' experience of OFF-time. Everyday changes to gastric function can dramatically impact the absorption of levodopa, e.g., changes in pH due to antacids or proton pump inhibitors, intake of iron or other divalent

metals, and dietary factors like fat and L-neutral amino acid content (Nutt et al., 1984; Nyholm et al., 2002).

Once ingested, levodopa is moved into the gastrointestinal tract by the large nucleic amino acid transport system. Then, the enzyme aromatic L-amino acid decarboxylase heavily decarboxylates levdopa to dopamine. Levodopa uptake is further complicated by its competition with other L-neutral amino acids, for example those consumed as proteins and other dietary sources of amino acids (Virmani et al., 2016). Only 30% of levodopa reaches systemic circulation unchanged (Contin & Martinelli, 2010; Freitas et al., 2016). Peripheral tissue continues to decarboxylate levodopa, and less than 1% of ingested levodopa maintains bioavailability once it reaches the brain (Di Stefano et al., 2011). Although these inconsistencies with levodopa reaching the brain are the simplest explanation for "OFF-time", changes to the central pharmacokinetics through the loss of nigrostriatal pathway capacity and pharmacodynamic response to levodopa are thought to truly underlie the progression of OFF-time related to levodopa (Stocchi, 2006). Although the mechanisms underlying OFF-time are still being understood, response to the medication can change over time, often within two years after the start of treatment, and about half of the patients see unfavorable motor changes and/or dyskinesia after five years of being on levodopa (Nutt, 2001). A 9-month trial of levodopa also revealed that 29.7% of patients taking 600 mg/day, a high dosage, still experienced motor fluctuations (Fahn et al., 2004).

The onset of motor fluctuations is often seen in a predictable and time-dependent pattern from the last levodopa intake (initially 4 hours after intake). Motor fluctuation and presentation of PD symptoms in the morning before the first dose of levodopa (morning akinesia) is typical and occurs in 54-70% of PD patients (Aquino & Fox, 2015). A related but somewhat distinct

phenomenon, nocturnal hypokinesia, is also seen in almost 70% of mid-stage PD patients. It is associated with worse sleep quality, decreased mobility in bed, and worse quality of life (Bhidayasiri & Trenkwalkder, 2018). As the disorder progresses and time on medication increases, motor fluctuations can become more intense and less predictable. Other complications can then be observed like on-off phenomenon (rapid switching between on and off states), sudden-off (off state with no relationship to levodopa dosing), delayed-on (increased latency after levodopa dose), or no-on (no response to levodopa) (Aquino & Fox, 2015).

Additional pharmacological approaches

Levodopa is commonly taken with aromatic L-amino acid decarboxylase (AADC) inhibitors like carbidopa or benserazide to improve bioavailability and reduce peripheral side effects like cardiac arrhythmias, hypotension, nausea, and vomiting (Seeberger & Hauser, 2015). However, when AADC is inhibited, the main metabolic pathway for levodopa changes. Instead of being converted to dopamine, 3-O-methylation catalyzed by catechol-O-methyltransferase (COMT) breaks down levodopa into the metabolite 3-O-methyldopa (3-OMD), causing smaller amounts of levodopa to enter the brain. 3-OMD then accumulates in peripheral and central tissues, and high plasma levels of 3-O-methyldopa are associated with a poorer response to levodopa (Nutt & Fellman, 1984; Tohgi et al., 1991). 3-OMD also competes with levodopa to cross the blood-brain barrier. Therefore, COMT inhibitors are commonly used with levodopa to treat PD.

Currently, three common COMT inhibitors are on the market used as adjunctive therapy to levodopa/carbidopa in adults with PD who have motor complications: tolcapone, entacapone, and opicapone. Tolcapone was approved for use in the United States in 1997. However, shortly

after its approval, it was taken off the market for several instances of acute liver failure. It was eventually reintroduced under the condition that liver function in patients taking tolcapone is heavily monitored (Olanow et al., 2007). Entacapone was approved for use in the United States in 2003. Although tolcapone may be more effective than entacapone, the hepatotoxicity of tolcapone has limited its clinical use (Factor et al., 2001). Opicapone is a third generation COMT inhibitor that was authorized in the United States in 2020. It overcomes the limitations of tolcapone because of its low hepatotoxicity and high safety rating, and it overcomes limitations of the entacapone because it is a once-daily oral pill (Fabbri et al., 2018; Greenwood et al., 2021). Despite these pharmacological options there remain issues with each one, and patients still experience considerable OFF-time, which costs patients' and families' quality of life. Therefore, alternative, or adjunctive therapies are necessary to help address OFF-time in individuals with Parkinson's Disease.

Exercise, Dance, and PD: An alternative and engaging intervention strategy

Exercise has many benefits for patients with PD (Xu et al., 2019). Studies that determine the relationship between exercise and PD have shown that physical activity can delay disease onset and slow the progression of PD (Cheng et al., 2016; Mak et al., 2017). Patients who engage in moderate to intense exercise have a reduced risk of developing PD, and a study showed that males who participate in intensive exercise have a 60% reduction in developing PD (LaHue et al., 2016; Logroscino et al., 2006). However, some studies have indicated that physical activity may have a gender bias on PD, and the preventative effects of exercise on PD are more pronounced in males than females (LaHue et al., 2016; Logroscino et al., 2006; Yang et al., 2015).

Exercise is increasingly promoted as helpful for motor and cognitive symptom relief and may be neuroprotective (Ahlskog, 2011; Reynolds et al., 2016). Exercise improves motor impairment, slows cognitive decline, and enhances quality of life. Uc et al. (2014) demonstrated improved executive function, higher-level cognitive skills involved in the cognitive control of behavior, in 43 PD patients after aerobic exercise (Uc et al., 2014). Duchesne et al. (2015) reported improved inhibition and motor skill learning following aerobic exercise in early PD (Duchesne et al., 2015). David et al. (2016) showed that in 38 mild-to-moderate PD participants, resistance training improved attention and working memory (David et al., 2016). Additionally, continuous exercise can improve the performance of daily activities during the early stages of PD, like bradykinesia, balance, and turning (Corcos et al., 2012; Mak et al., 2017). Consistent with animal literature, dual cognitive/physical challenges may be the most effective in creating beneficial, durable effects on the brain's structure and function (Kempermann, 2008).

Exercise also grossly affects organ tissue and function, which may influence the pharmacokinetics of drugs (Reuters et al., 2000). A mice model study found that exercise can partially prevent the development of levodopa-induced dyskinesia and attenuate the side effects of levodopa (Aguiar. et al., 2013; Speck et al., 2019). Exercise can also improve dopamine efficiency and increase the expression of D2 receptors (Fisher et al., 2013; Petzinger et al., 2015). Therefore, exercise may significantly impact the patient's experience of OFF-time by increasing levodopa efficiency.

Dance could be a promising form of exercise for older adults, including those with PD. In general, dance has been proven to be beneficial for individuals with PD, especially for improving quality of life and motor impairment, specifically balance, gait, and motor symptom severity (Carapellotti et al., 2020; Emmanouilidis et al., 2021). Decreased fall rates were seen in nursing

home residents participating in a ballroom dancing program (da Silva Borges et al., 2014). An adapted form of the Argentine tango (adapted tango) has also proven to be beneficial for adults with PD. It has improved mobility and decreased gait deficits in older adults with PD (Hackney & Earhart, 2009a). Adapted tango also improved spatial cognition in PD patients (McKee & Hackney, 2013).

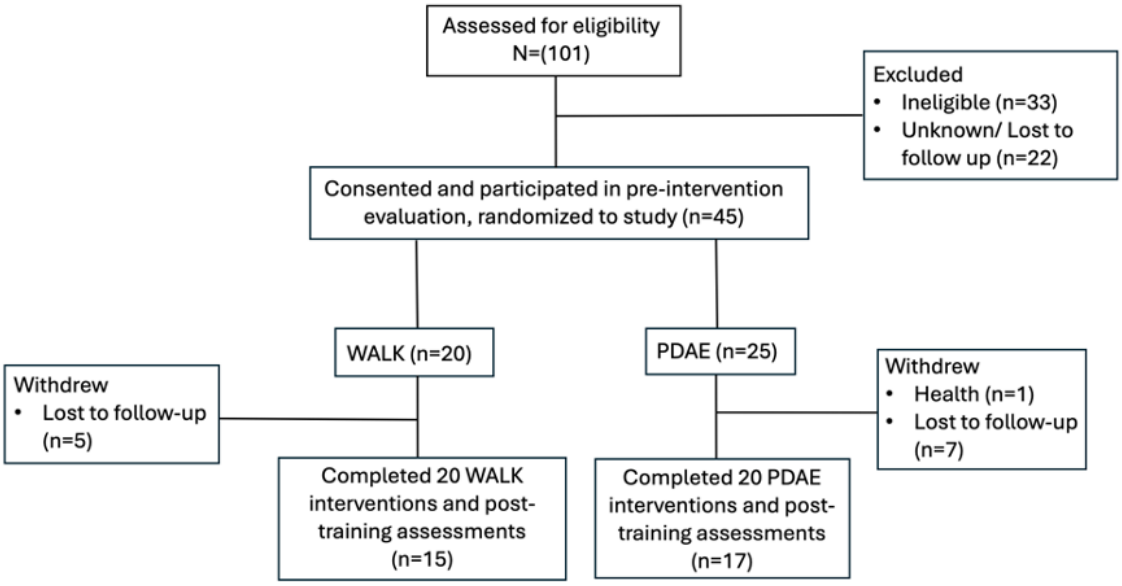
In the current study, we aim to investigate the effects of three months of cognitively engaging social dance, Partnered Dance Aerobic Exercise (PDAE), and walking aerobic exercise (WALK) on the impact of OFF-time and perceived QOL and independence factors in older adults with PD (Hackney et al., 2020). We look to determine if a three-month program of aerobic exercise in general affects OFF-time and QOL and independence factors, or if PDAE is a superior form of aerobic exercise to WALK. OFF-time symptoms and their impact on the patient's quality of life and independence factors are often associated. However, few studies examine how exercise-based interventions, specifically social dance, impact OFF-time symptoms and, consequently, quality of life and independence factors. Improving OFF-time symptoms in PD patients could be a valuable key to improving their quality of life and independence.

Methods

This study was approved by the Institutional Review Board of Emory University and the Review Committee for the Atlanta Veterans Affairs Medical Center (VAMC). The trial is described in full in the clinicaltrials.gov registry item NCT04122690 and in the protocol report by Hackney et al. (2020). All participants gave informed consent prior to participation in this study. Figure 1 describes participation throughout the study.

Figure 1

Consort Diagram of Participation



Participants

We recruited 45 participants with PD for this study. For group assignment, we recruited PD patients (age ≥ 40, Hoehn & Yahr stage I-III) who report OFF-time, indicated by score >=1 on UPDRS-IV item 4.3 i.e., time spent in the OFF state. Participants could walk 10 feet or more with or without an assistive device. Their PD diagnosis (ICD-10 G20) was based on established criteria (Hughes et al., 1992) and determined by a board-certified neurologist in training with movement disorders. In short, these diagnostic criteria state that individuals must present unilateral symptoms that include at least 3 of the cardinal signs of PD (rigidity, bradykinesia, tremor, postural instability), and must show clear symptomatic benefits from antiparkinsonian medications (Kempster et al., 2007). At initial assessment, participants were evaluated for

general health, ability to perform ADLs, fall risk, age, and education. The Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) was administered to determine cognitive status. Participants were excluded from the study if the score was less than 17 (Table 1).

Participants were recruited from the Atlanta VAMC Movement Disorders clinic using the VA Informatics and Computing Infrastructure (VINCI) databases to identify patients in the Atlanta VA Health Care System eligible for the study. Participants were also recruited from the Emory University Movement Disorders clinic, at local Parkinson-related support groups, educational meetings, and community events.

Table 2

Participant's Demographic and Clinical Characteristics at Baseline

	Total (n=45)	**PDAE (n=25)**	**WALK (n=20)**
Age (y)	70.1±7.27	69.68±7.38	70.65±7.30
Years w PD	7.57±5.64	6±4.29	9.52±6.58*
Hoehn & Yahr stage	2.30±0.61	2.36±0.59	2.23±0.64
Number of comorbidities	3.89±2.26	4±1.9	3.75±2.63
Sex			
Male	33 (73.33)	18 (50)	15 (75)
Female	12 (26.67)	7 (28)	5 (25)
Ethnic Background			
Black/African American	11 (24.44)	5 (20)	6 (30)
Asian	1 (2.22)	1 (4)	0 (0)
Hispanic or Latino	1 (2.22)	1 (4)	0 (0)
Native American	0 (0)	0 (0)	0 (0)
White/Caucasian	30 (66.67)	17 (68)	13 (65)
Multiracial	1 (2.22)	0 (0)	1 (5)

Other	1 (2.22)	1 (4)	0 (0)
Years of Education	16.4±2.41	16.64±2.69	16.2 (2.04)
Marital Status			
Single	4 (8.89)	2 (8)	2 (10)
Married/Partner	34 (75.56)	21 (84)	13 (65)
Separated/Divorced	5 (11.11)	2 (8)	3 (15)

Note. Values presented as Mean ± Standard Deviation for continuous variables or n (%) for categorical variables.

*p<0.0.5

Interventions

Fidelity was monitored by the investigators via weekly reports from interventionists and monthly class visits of both investigators. The dose for intervention was measured by the time spent in the class, e.g., one class is a dose of 90 minutes. The volume of the intervention is defined as frequency times duration, and therefore the volume per week was approximately 180 minutes/week for the Training Phase, which is the phase being considered in this work. The Maintenance phase of the trial is 90 minutes per week. The Maintenance phase is not presented in this paper and will be considered in a future publication. The intensity of the exercise for PDAE and WALK participants was measured with heart rate monitors.

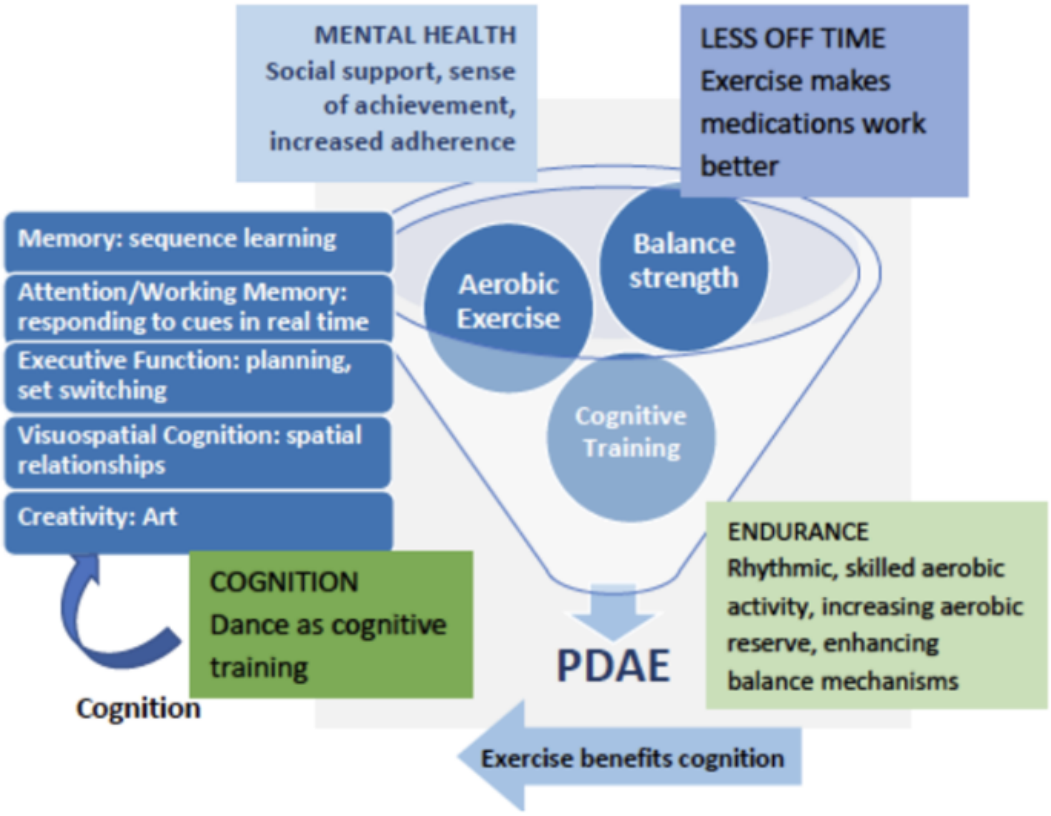
Intervention dose determinants: In the 3-month Training phase, participants were assigned to 12 weeks of 20 biweekly (90-minute) lessons. Fall incidence has been extremely rare over the past ten years, but fall prevention was a critical concern. All assistants for both PDAE and WALK were trained in PD-related posture problems, monitoring balance, and anticipating and preventing falls with a 2-hour experiential workshop.

Partnered Dance-Aerobic Exercise (PDAE)

PDAE is an adapted form of Argentine tango, aka adapted tango, and has been shown to improve motor function as measured by motor symptoms, balance, preferred, backward and fast gait, mobility, endurance, and QOL (Hackney & Earhart, 2009a, 2009b, 2010a, 2010b; Hackney et al., 2007; McKay et al., 2016; McKee & Hackney, 2013). During PDAE, people with PD partnered with an individual without PD, e.g., a trained caregiver, friend, or university student. The instructor and several trained assistants carefully monitored all participants. Class sizes consisted of 6 or fewer pairs of participants with PD and partners to maximize safety. Participants with PD danced both the follower and leader roles alternatingly, as has been done for several prior studies (Hackney et al., 2007; Hackney & Earhart, 2009a; Hackney & Earhart 2010a; Hackney & Earhart, 2010b). They also danced with new partners (individuals without PD) every 15 minutes; a widely practiced method considered by the dance teaching community to enhance learning. Participants engaged in partnering exercises concerning how to interpret motor goals through touch, exercises to develop understanding temporal relationship of movement to music, novel step introduction, connecting previously learned and novel step elements. Participants were not required to memorize specific step patterns but learned new steps in each class.

Figure 2

Hypothesized Beneficial Outcomes of Partnered Dance Aerobic Exercise



Note. Hypothesized beneficial outcomes of Partnered Dance Aerobic Exercise. From "Rationale and Design of the PAIRED Trial: Partnered Dance Aerobic Exercise as a Neuroprotective, Motor, and Cognitive Intervention in Parkinson's Disease," by M. Hackney et al., Frontiers in Neurology, 2020. Reprinted with permission.

Walking Aerobic Exercise (WALK)

Participants in WALK received the equivalent dose, volume, frequency, intensity, and duration of exercise to the PDAE group. Participants received equal contact and monitoring from study staff. WALK participants reported to the same facility and interacted with the same interventionist and assistants. Participants began the classes with a 25-minute warm-up followed by a 45-minute walking session and a 10-minute cool down, with breaks in between for transitions. The WALK is well described in Wells et al., 2023. Participants walked outside primarily overground, except when it rained or weather was otherwise inclement, and then participants would walk inside down long hallways at the center where the studies took place. WALK also took place in groups, with research volunteers and assistants, to ensure that PDAE and WALK participants received a socially engaging intervention.

Evaluations

Disease Severity and OFF-time

A blinded MDS-certified rater administered the MDS-UPDRS-I-IV at all evaluations. The MDS-UPDRS has 4 parts. I: non-motor experiences of daily living, II: motor experiences of daily living, III: motor examination, and IV: motor complications. The primary outcome, the MDS-UPDRS-IV score, measures MRMF, including dyskinesia, OFF-time, functional impact and complexity of fluctuations, and dystonia. MDS-UPDRS-IV item 3 measures the time spent in the OFF state, and item 4 measures the functional impact of the motor fluctuations. Each question is scored on a 5-point scale: (0) normal, (1) slight, (2) mild, (3) moderate, and (4) severe. A higher total score corresponds to more severe impairment (Goetz et al., 2008). We

administered a monthly 3-day OFF-state diary for corroboration (Hauser et al., 2004). OFF-state diaries were sent out via email to participants at the beginning of each month, and reminders texts and calls were sent out each week to ensure completion. Participants were first educated about the different states (asleep, on, on with troubling dyskinesia, or off) and then filled out the diary half-hourly over three consecutive days. Percent waking hours spent in each state were calculated. Percent waking hours spent in the OFF-state was determined as percent waking hours spent in the OFF-state plus percent waking hours spent in the on with troubling dyskinesia state.

While OFF-state diaries are a valid assessment of motor fluctuations and provide an in-depth look at the temporal dynamics of the experience of OFF-time without clinician interpretation and bias, it still has its limitations (Papapetropolous, 2012; Löhel et al., 2022). Using the MDS-UPDRS-IV in conjunction with 3-day OFF-state diaries provides a more complete look at the individual's experience of OFF-time. The MDS-UPDRS-IV helps overcome challenges of the 3-day OFF-state diary, like patient compliance and recall bias. The MDS-UPDRS-IV also provides a more comprehensive view of OFF-time because it rates the complexity and severity of OFF-time (Papapetropolous, 2012).

Self-Administered Psychosocial Questionnaires – QOL and Independence Measures

To measure the psychosocial impact of the social support/human touch interactions inherent to partnered dance exercise, participants completed several questionnaires within the week before each visit to complete questionnaires i.e., Beck Depression inventory–II (BDI-II), the Physical Activity Scale for the Elderly (PASE), the PD Questionnaire-39 (PDQ-39), the

Short Form 12 Health Survey (SF-12), Freezing of Gait questionnaire (FOGQ), and Gait and Falls questionnaire.

Beck Depression Inventory-II. The Beck Depression inventory-II (BDI-II) is a 21-item questionnaire that measures the severity of depression in adolescents and adults on a 63-point scale. Each question is rated on a 4-point scale ranging from 0 to 3 (Beck et al., 2011). A total score of 0-13 is considered minimal range, 14-19 is mild, 20-28 is moderate, and 29-63 is severe.

Physical Activity Scale for the Elderly (PASE) and Paffenbarger Physical Activity. The Physical Activity Scale for the Elderly (PASE) is an 11-item survey that measures the level of self-reported physical activity in individuals aged 65 years or older during the previous 7-day period (Washburn et al., 1993). Participation in activities were recorded as (1) no and (2) yes and scored as (0) never, (1), seldom (1-2 days/week), (2) sometimes (3-4 days/week), and (4) often (5-7 days/week). Duration was scored as (1) less than 1 hour, (2) more than 1 hour but less than 2 hours, (3) 2-4 hours, (4) more than 4 hours. A total score of 0 to 40 indicated a sedentary lifestyle, 41 to 90 light physical activity, and more than 90 as moderate to intense activity. The Paffenbarger Physical Activity Questionnaire is used with the PASE to assess physical activity in adults by quantifying the amount of exercise performed in the past week (Paffenbarger et al., 1993).

The 39-item Parkinson's Disease Questionnaire. The 39-item PD Questionnaire (PDQ-39) is a 39-item questionnaire that assesses 8 PD specific QOL dimensions (Hagell & Nilsson, 2009). Each question is rated on a 5-point Likert scale. For each question, participants indicated

the frequency of their feelings with the following scale: (0) never, (1) occasionally, (2) sometimes, (3) often, and (4) always or cannot do at all. Items are grouped into eight scales: Mobility, Activities of Daily Living (ADL), Emotional Wellbeing, Stigma, Social Support, Cognitive Impairment, Communication, and Bodily Discomfort that express the summed item scores as a percentage score ranging from 0 to 100, and an overall summary score is calculated by the sum of the eight PDQ-39 scale scores divided by eight (the number of scales) to yield a score between 0 and 100. Patients have previously improved on this test because of PDAE (Hackney & Earhart, 2009b).

Short Form 12 Health Survey. The Short Form 12 Health Survey (SF-12) is derived from the Short Form 36 Health Survey and is a 12-item questionnaire that assesses the impact of physical and mental health on everyday life (Ware et al., 1996). Each question is rated on a 5-point scale with a higher score indicating better health. Physical and Mental Component summary scores are calculated and standardized to have a mean of 50 in the general population, with a standard deviation of 10. A score above 50 indicates better compared to the average population, and a score below 50 indicates poorer QOL.

Freezing of Gait. The Freezing of Gait (FOG) questionnaire is a 6-item survey that measures freezing of gait severity on a 24-point scale (Giladi et al., 2009). Each question is rated on a 5-point scale ranging from 0 to 4. A higher total score corresponds to more severe freezing of gait.

Gait and Falls. The Gait and Falls questionnaire is a 16-item survey that measures fall risk on a 64-point scale. Each question is rated on a 5-point scale ranging from 0 to 4. A higher total score corresponds to a more severe fall risk.

Statistical Analysis

Descriptive statistics for all demographic, clinical, and outcome measures were calculated and reviewed visually. Independent-sample *t*-tests were used to compare baseline continuous measures of the groups. Chi-squared tests were used to compare categorical variables of the groups. Because all data were approximately normally distributed, independent t-tests were conducted to determine the change in outcome performance overtime (post-training minus baseline) between groups (PDAE and WALK). Paired t-tests were conducted to determine the change in outcome performance within groups (PDAE or WALK) between timepoints (baseline to post-training). A Pearson correlation coefficient was computed to assess the linear relationship between the percent change in percentage of waking hours spent in OFF-state and QOL and independence measures. Descriptive stats, within-group and between-group analyses, and Pearson correlations were performed using STATA version 18 (StataCorp, College Station, Texas, USA). Each outcome variable was further analyzed with a separate linear mixed model with a fixed effect for Time and Group, an interaction between Time and Group, and a random effect for participant. Linear mixed models were implemented in lmertest::lmer in RStudio version 2023.06.0 (RStudio, Boston, Massachussets, USA). *P* values less than 0.05 were considered significant.

Results

Forty-five participants (73.33% male) were enrolled and randomized (PDAE, n = 25; WALK, n = 20). Of the initial randomized participants, thirty-two completed the study through post-training (PDAE, n = 17; WALK, n =15). Descriptive and demographic statistics of the sample are summarized in Table 1. At baseline, participants did not differ significantly in age, number of comorbidities, sex, ethnic background, years of education, marital status, Hoeh and Yahr stage, or MoCA score. Participants did significantly differ at baseline in years with PD (p = .047); however, because participants were randomized into groups, and the significance was small, we consider this difference due to chance. At baseline, there was no statistically significant difference between PDAE and WALK for any QOL and independence or OFF-time measures. QOL and independence outcome measures are summarized in Table 2. OFF-time outcome measures are summarized in Table 3.

Table 3

WALK versus PDAE Baseline, Post-training, and Δ in QOL/Independence Outcome Measures

	WALK		PDAE	
	n	Mean ± SD	n	Mean ± SD
Freezing of Gait (/24)				
Baseline	18	8.50 ± 6.2	20	6.15 ± 6.0
Post-training	10	7.10 ± 7.43	13	5.54 ± 6.9
Δ		-1 ± 1.5		-0.09 ± -0.1
Gait and Falls (/64)				
Baseline	19	16.32 ± 15.5	23	15.04 ± 13.23
Post-training	15	17.13 ± 14.4	17	13.00 ± 13.6
Δ		-0.07 ± 6.6		0.25 ± 0.3

PDQ-39 (/100)				
Mobility				
Baseline	19	18.95 ± 20.7	22	23.41 ± 28.3
Post-training	15	25.17 ± 18.9	16	20 ± 26.3
Δ		4.64 ± 14.0		-2.00 ± -2.0
Activities of Daily Living				
Baseline	19	22.81 ± 23.3	22	22.35 ± 21.8
Post-training	15	27.78 ± 19.3	15	21.11 ± 24.0
Δ		4.46 ± 7.6		-1.79 ± -1.9
Emotional Wellbeing				
Baseline	19	11.84 ± 18.0	22	22.35 ± 17.2
Post-training	15	13.61 ± 18.3	15	16.11 ± 13.0
Δ		0.56 ± 13.9		-7.14 ± -7.7
Stigma				
Baseline	19	12.17 ± 17.9	22	13.35 ± 17.2
Post-training	15	10.42 ± 12.4	15	11.25 ± 17.2
Δ		0.89 ± 8.8		0 ± 0
Social Support				
Baseline	19	17.32 ± 36.0	22	15.34 ± 21.0
Post-training	15	13.33 ± 18.1	14	8.93 ± 14.3
Δ		5.06 ± 14.5		-0.96 ± -2.1
Cognitive Impairment				
Baseline	19	26.64 ± 21.7	22	27.27 ± 21.1
Post-training	15	28.33 ± 21.2	15	18.33 ± 14.7
Δ		0 ± 7.4		-7.59 ± -8.2
Communication				
Baseline	19	21.49 ± 26.3	22	24.62 ± 20.5
Post-training	15	26.67 ± 28.9	15	18.89 ± 20.0
Δ		7.74 ± 21.5		-4.17 ± -4.5
Bodily Discomfort				
Baseline	19	26.75 ± 21.8	22	28.79 ± 18.7
Post-training	15	35.56 ± 24.7	15	28.89 ± 17.2
Δ		6.55 ± 16.4		1.19 ± 0.6
Summary Index				
Baseline	19	19.75 ± 19.7	22	22.19 ± 14.9
Post-training	15	22.61 ± 17.0	16	16.90 ± 12.4
Δ		3.74 ± 7.2		-5.55 ± -6.1*
PASE				
Baseline	18	99.06 ± 77.0	23	125.72 ± 105.0
Post-training	15	129.78 ± 83.6	17	138.87 ± 99.1
Δ		19.32 ± 59.0		3.93 ± 4.1
Paffenbarger				

Baseline	19	2483.94 ± 4313.5	23	4319 ± 6184.3
Post-training	15	3216.63 ± 5137.8	17	5123.84 ± 6178.2
Δ		426.78 ± 3950.1		-267.731 ± -271.58
BDI-II (/63)				
Baseline	19	11.11 ± 8.6	23	10.61 ± 7.2
Post-training	15	9 ± 5.8	17	10.17 ± 6.6
Δ		-2.5 ± 6.0		0.75 ± 0.9
SF-12 (/100)				
Physical Component Summary				
Baseline	20	43.58 ± 11.8	22	44.51 ± 11.9
Post-training	15	43.54 ± 9.7	15	46.62 ± 13.1
Δ		0.63 ± 5.9		0.80 ± 0.8
Mental Component Summary				
Baseline	20	41.43 ± 7.1	22	40.64 ± 6.4
Post-training	15	39.25 ± 7.9	15	41.08 ± 4.3
Δ		-1.50 ± 5.9		1.64 ± 1.8
MDS-UPDRS				
Part 1 (/16)				
Baseline	20	10.35±6.3	25	12.04±7.2
Post-training	15	8.80±5.3	17	10.29±6.7
Δ		-1.80±3.4		-0.24±-0.44
Part 2 (/52)				
Baseline	20	14.2±8.9	23	12.87±8.2
Post-training	15	14.07±8.8	17	12.41±8.4
Δ		-1.2±4.5		-0.5±-0.47
Part 3 (/108)				
Baseline	20	36.35±15.3	25	40.24±13.3
Post-training	15	38.13±16.8	17	31.35±10.2*
Δ		-0.67±8.8		-9.82±-10.0**

Note. WALK versus PDAE baseline, post-training, and change in quality of life (QOL) and independence outcome measures. PDQ-39 is out of 100 points – all scales and subscales. SF-12 is out of 100 points and normalized to 50 with a standard deviation of 10.

*p<0.05, **p<0.01

Table 4

WALK versus PDAE Baseline, Post-training, and Δ in OFF-time Outcome Measures

	WALK		PDAE	
	n	Mean ± SD	n	Mean ± SD
MDS-UPDRS-IV				
Item 3				
Baseline	20	1.15 ± 0.8	25	1.6 ± 1
Post-training	14	1.07 ± 0.7	17	0.88 ± 0.9*
Δ		-0.07 ± 0.9		-0.82 ± -0.9*
Item 4				
Baseline	20	1.4 ± 1.5	25	1.48 ± 1.2
Post-training	14	1.00 ± 1.2	17	0.65 ± 1.0*
Δ		-0.43 ± 1.3		-0.71 ± 0.8
Total score (/23)				
Baseline	20	6 ± 4.4	25	6.48 ± 3.7
Post-training	14	5.71 ± 3.15	17	3.59 ± 3.5*
Δ		-0.12 ± 2.8		-2.47 ± -2.8*
3-Day OFF-state Diary				
% ON				
Baseline	14	70.45 ± 27.4	13	71.25 ± 27.3
Post-training	12	78.62 ± 24.2	9	58.17 ± 33.1
Δ		0.84 ± 17.9		-21.89 ± -24.6
% OFF				
Baseline	14	22.98 ± 19.5	13	26.26 ± 23.3
Post-training	12	21.06 ± 23.8	9	41.44 ± 22.1
Δ		-0.69 ± 18.3		-2.20 ± -2.5

Note. WALK versus PDAE baseline, post-training, and change in OFF-time scores.

*$p<0.05$

Baseline to post-training

In the PDAE group, there was a significant change in MDS-UPDRS-III score from baseline to post-training ($p = 0.02$). The PDAE group also had a significant change in MDS-UPDRS-IV item 3 score from baseline to post-training ($p = 0.02$), and a significant change in MDS-UPDRS Part IV item 4 score from baseline to post-training ($p = 0.02$). For the PDAE group, there was also a significant change in MDS-UPDRS Part IV total score from baseline to post-training ($p = 0.02$). No changes were noted in the QOL and independence measures. No changes were noted in the WALK group.

PDAE versus WALK

The PDAE group had a significant reduction in MDS-UPDRS-III score compared to the WALK group ($p = 0.002$). The PDAE group had a significant reduction in MDS-UPDRS-IV item 3 score compared to the WALK group from baseline to post-training, ($p = 0.02$). The PDAE group also had a significant reduction in MDS-UPDRS-IV total score compared to the WALK group ($p = 0.03$). Further analysis by a linear mixed-effects model revealed that the interaction between group and time had a significant effect on the change in the MDS-UPDRS-III score ($p = 0.001$), MDS-UPDRS-IV item 3 ($p = 0.02$), and MDS-UPDRS-IV total score ($p = 0.02$), but fixed effects of time and group did not have significant impact on the change in MDS-UPDRS-IV item 3 and total score.

The PDAE group also had a significant reduction in PDQ-39 summary index score compared to WALK group from baseline to post-training ($p = 0.02$). Further analysis by a linear mixed-effects model revealed that the interaction between group and time had a significant effect

on the change in PDQ-39 summary index score (p = 0.02), but fixed effects of time and group did not have significant impact on the change in PDQ-39 summary index score.

There was no significant change in scores (post-training minus baseline) between groups for the BDI-II survey, PDQ-39 subscales, PASE survey, Paffenbarger survey, SF-12 survey, FOG questionnaire, or Gait and Falls questionnaire. There was also no significant change in the percentage of waking hours spent in the on or OFF-state as reported by the 3-day OFF-state diary or MDS-UPDRS-IV item 4 score from baseline to post-training between the WALK and PDAE groups. Fixed effects of group, time, and interaction between group and time did not significantly impact the change of these QOL, independence, and OFF-time measures between groups.

Whole study correlations

Pearson correlation (r) and p values between the overall percent change in percentage of waking hours spent in the OFF-state against the percent change in all other QOL and independence variables are summarized in Table 4. There was a strong correlation with the PDQ-39 social support subscale (r = 0.90, p=0.005), suggesting that those who experienced a decrease in time spent in the OFF-state also demonstrated a decreased need for social support in their everyday lives. There was a moderate correlation with percent change in the Paffenbarger survey (r=0.56, p=0.03), suggesting that those who experience a decrease in time spent in the OFF-state also demonstrated a decrease in physical activity. All other measures showed no significant correlations with the percent change in percentage of waking hours spent in the OFF-state.

Table 5

Pearson Correlations between the percent change of the percentage of waking hours spent in the OFF-state and percent change in QOL and independence measures for both groups

	r	***p***
PASE	-0.39	0.29
Paffenbarger	0.56*	0.03
PDQ-39		
Mobility	-0.23	0.47
ADL	0.14	0.14
Emotional Wellbeing	0.19	0.19
Stigma	0.14	0.14
Social Support	0.90**	0.005
Cognitive Impairment	-0.01	0.97
Bodily Discomfort	-0.17	0.55
Summary Index	0.05	0.85
BDI-II	0.07	0.81
SF-12		
Physical Component Summary	0.09	0.72
Mental Component Summary	0.09	0.73

Note. Pearson Correlation between the percent change of the percentage waking hours spent in the OFF-state and percent change in QOL and independence measures for both groups.

*$p<0.05$, **$p<0.01$

Discussion

This study demonstrated improved motor function and OFF-time among 17 individuals with PD who completed 36 hours of adapted Argentine tango in comparison to 15 individuals with PD who completed WALK training for the same total duration. With the noted within-

group changes, this study demonstrated improved burden of PD to QOL from the PDQ-39 survey, motor function from the MDS-UPDRS-III, and motor complications from the MDS-UPDRS-IV in the PDAE group compared to the WALK group. Overall, a decrease in OFF-time was correlated to a decreased need for social support. Interestingly, a decrease in OFF-time was correlated with less physical activity through the Paffenbarger survey. Whether this correlation is directly attributable to the changes seen after a short program of PDAE or WALK or a third factor is unclear and certainly warrants further investigation. Aside from this one surprising finding, we believe that these findings generally support that an adapted Argentine tango program is a feasible and effective form of aerobic exercise for individuals with PD to serve as an adjunctive therapy to current pharmacological methods to improve OFF-time symptoms and motor function, which may impact their perceived QOL and independence. Walking aerobic exercise, while inferior to PDAE, may also provide benefits; however, a longer and more robust study is necessary to determine the potential impact of walking aerobic exercise on individuals with PD. Fortunately, we will be able to evaluate these same patients for effects at 10 months and at 16 months after beginning treatment with PDAE or WALK.

Improvement in MDS-UPDRS-III and IV

PDAE's improvement on the MDS-UPDRS-III and IV may suggest that PDAE helps slow disease progression, reduce the severity of motor impairment, and help the experience of motor complications. Typically, functional independence decreases throughout the disease progression. A Japanese study found that Hoehn and Yahr Stage II or below patients can engage in social and daily activities without much restriction. In Stage III (mild to moderate bilateral involvement, some postural instability but physically independent), they can live independently

but may have some restrictions on activities. Independent life becomes complicated in Stage IV (severe disability, unable to walk and stand unassisted) and beyond (Sato et al., 2006). MDS-UPDRS scores have been shown to relate to QOL. One study found that higher MDS-UPDRS-III scores were correlated to higher PDQ-39 summary index scores as well as mobility, ADL, and communication subscales, indicating a worse quality of life (Skorvanek et al., 2015). Another study found that MDS-UPDRS-III and IV were moderately correlated with QOL through the PDQ-8 (short version of PDQ-39) and EuroQOL-5D (five-item generic health status measure) (Martínez-Martín et al., 2014). Therefore, preventing advancements in the Hoehn and Yahr stage and increases MDS-UPDRS scores is an essential part of maintaining the QOL and independence of individuals with PD.

Improvement in PDQ-39

Because PDAE helped reduce the severity of motor complications, it is unsurprising that the PDQ-39 summary index score also improved through PDAE. Studies have correlated OFF-time and QOL through the PDQ-39 survey (Souza et al., 2007; Martinez-Martin, 2011; Leentjens et al., 2012; Stocchi et al., 2014; Zhu et al., 2016; Dowell et al., 2017). Previous work from our lab has shown improvements in PDQ-39 after 20 hours of adapted tango offered over 3 months (Hackney & Earhart, 2009b). In a study with 722 patients with PD, 44% experienced OFF-time with an average of 2.9 hours spent off-state per day. The patients who experienced OFF-time were correlated with high scores on most PDQ-39 subscales and the overall summary index, indicating worse QOL (Thach et al., 2021). Another study showed that patients who experienced OFF-time had significantly higher scores on the PDQ-39 survey for mobility, activities of daily living, emotional well-being, cognition, and communication; however, OFF-time did not impact

stigma, social support, and bodily discomfort. The impact on QOL and health status was directly related to the number of hours spent in the OFF-state (Martinez-Martin et al., 2011). Another study found that PDQ-39 subscales of ADL, emotional well-being, stigma, and bodily discomfort were worse in patients who experienced OFF-time versus those who did not. Furthermore, the number of hours spent in the OFF-state was directly correlated with PDQ-39 subscales of mobility, ADL, emotional well-being, stigma, communication, cognition, and bodily discomfort (Dowell et al., 2017). PDQ-39 bodily discomfort scores were also found to be worse in patients who experience OFF-time impacting specific manifestations influencing bodily comfort, including pain, aching, cramps, sweating or hot flashes/chills, dizziness, palpitations, shortness of breath, chest pain, nausea, abdominal distress, and numbness and tingling (Souza et al., 2007; Leentjens et al., 2012; Stocchi et al., 2014; Zhu et l., 2016). This study suggests that improving OFF-time may help enhance the individual's perception of their QOL by improving all aspects of the PDQ-39 overall, not just specific subscales. However, further studies are needed to better associate the relationship between improving OFF-time and its effects on QOL after PDAE and WALK.

Neither significant improvements nor declines were noted in other QOL or independence measures. As such, the program did lead to maintenance of these measures, which typically worsen due to the neurodegenerative nature of PD (Candel-Parra et al., 2021). Further, longer studies are needed to truly understand the impact of improving OFF-time on QOL and independence in individuals with PD. In older adults, more consistent findings of structural changes (increase in white and gray matter and volumetric increases) in the brain are seen after at least 6 months of consistent aerobic exercise (Cabral et al., 2019). Although benefits of exercise on QOL can be seen after three months, typically, studies on PD look at changes in QOL and

structural and functional changes in the brain after six to twelve months. (Eggers et al., 2018; Chen et al., 2020; Johansson et al., 2022). Greater QOL, specifically physical health QOL, as it relates to self-reported activities of daily living and self-perceived pain and discomfort, are associated with greater brain integrity in older adults (Ourry et al., 2021).

Possible mechanisms for improvement through PDAE

Adapted tango incorporates several aspects of movement that are possibly relevant for individuals with PD and may explain its superiority to walking aerobic exercise. Tango requires the participants to multitask and requires dynamic balance, turning, initiation of movement, moving at a variety of speeds, and often backward while close to a partner (Hackney et al., 2007). PDAE can also be considered light-moderate exercise because participants are stepping at 60-120 beats/minute (the typical tempo of tango music) and expending three metabolic equivalent of task per minute during typical tango dancing (Heyward, 2010). Using auditory cues, like in PDAE, to help facilitate movement has been proven to be beneficial for individuals with PD. Auditory cues can help increase gait initiation, walking speed, and cadence in laboratory settings, while performing functional tasks at home, and has been shown to reduce the severity of freezing (Howe et al., 2003; Dibble et al., 2004; Rochester et al., 2005; Nieuwboer et al., 2007). Auditory cues are particularly beneficial for individuals with PD since they may be able to bypass the defective look from the basal ganglia to the supplementary motor area via the thalamus that is normally used for internally cued movements (Nieuwboer et al., 1997). Evidence also suggests that auditory cues may access the premotor cortex via the cerebellum (Chuma et al., 2006). Therefore, the use of rhythmic cues from music, and guidance from their partners may be an important feature of tango as an effective intervention for individuals with PD.

Prior work has demonstrated adapted tango's improvement on mobility and QOL in PD versus other partnered dances (Hackney & Earhart, 2010a), non-partnered dance (Hackney & Earhart, 2010a), and generalized exercise (Hackney et al., 2007). Along with improving motor symptoms in individuals with PD, dance, in general, may help improve QOL because it reduces social isolation and increases participation in life situations (Hackney & Bennet, 2014). After a yearlong program of tango, participants recovered lost activities, began new ones, and gained the ability to engage in more complex activities, all of which enhanced their QOL (Foster et al., 2014). In-person dance classes aid in the improvement of QOL more than a self-guided exercise program because a supportive instructor is involved (Dereli & Yaliman, 2010).

Additionally, exercise has been found to influence the pharmacokinetics of levodopa. A mice model study found that exercise can partially prevent the development of levodopa-induced dyskinesia. It also attenuates the side effects of levodopa through normalization of the striatopallidal dopaminergic signaling without affecting the anti-parkinsonian effects of levodopa (Aguiar. et al., 2013; Speck et al., 2019). Exercise can also improve dopamine efficiency. A study found that exercising animals possessed less dopamine transporter, so dopamine stayed in their synapses longer. As a result, the cells receiving the dopamine signal had more D2 receptor binding sites and could receive a stronger signal (Petzinger et al., 2015). Additionally, positron emission tomography (PET) scans of a cohort of naïve PD patients showed that within one year of diagnosis and prior to medication use showed that exercise increased expression of D2 receptors (Fisher et al., 2013). Therefore, exercise, specifically dance because of its unique factors, might influence the experience of OFF-time by impacting levodopa efficiency.

Although PDAE and WALK both require balance and attention to movement control, tango differs from walking aerobic exercise because it is performed in close relationship to a

partner and in a setting that fosters community involvement, it is progressive in nature and the participant is always learning, and it is performed to music which may further engage the participant in addition to serving as an auditory cue (Hackney et al., 2007). Thus, adapted tango elements, including light-moderate intensity, and structured motor components that engage a memory of steps and directions while encouraging a keen awareness of spatial relationship and rhythm could contribute to some currently undetermined mechanisms to improvements in OFF-time. Further study into the application of therapies such as adapted tango for improving OFF-time is warranted and needed, given the prevalence of OFF-time in PD, which affects QOL and independence.

Limitations and future directions

Although this study was the first of its kind to demonstrate improved OFF-time measures in addition to the experience of daily living and motor function in individuals with PD who participated in a 3-month program of adapted tango and compared to individuals with PD who participated in walking aerobic exercise, it is not without its limitations. Due to the relatively small sample size and notable attrition rates (32% for PDAE, 25% for WALK), many of the whole study correlations between QOL and independence outcome measures and OFF-time showed no relationship and were not significant, and we are unable to determine if there is an association or correlation within each group. Additionally, since this study is only the first three months of a longer 16-month study, we are unable to determine how the change in OFF-time can predict the change in QOL and independence outcome measures. However, this study is a preliminary report about the first three months of a longer 16-months study. Larger studies are necessary to make more definitive conclusions. Future studies looking at the effect of the full

program of 16-months of PDAE versus WALK on individuals with PD will be able to overcome these limitations.

Conclusion

OFF-time is one of the most disconcerting features of PD and severely impacts the individual's QOL and independence. This novel study demonstrates that a short program of adapted tango improves motor function, OFF-time, and the experience of daily living in older adults with PD compared to a short program of walking aerobic exercise. This work may ultimately lead to further implementation of therapeutic movement and dance therapy as an effective and enjoyable non-pharmacological strategy for addressing OFF-time in individuals with PD to help improve their QOL and independence.

Author Contributions:

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