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# Do patients with PD benefit from music assisted therapy plus treadmill-based gait training? An exploratory study focused on behavioral outcomes

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## ABSTRACT

**Purpose:** Parkinson's disease (PD) is the second most common age-related neurodegenerative disorder, presenting not only with motor symptoms (resting tremor, bradykinesia, and muscular rigidity), but also with cognitive and behavioral problems that need to be addressed in a rehabilitation setting. Aim of the study was to evaluate the effects of a combined rehabilitative approach, using gait training coupled to music-based therapy, on cognitive and behavioral function in a sample of patients with PD.

**Materials and Methods:** Forty patients, meeting the inclusion criteria, were enrolled in this study and were randomly divided into two groups. The control group (CG) underwent traditional over ground gait training, whilst the experimental group (EG) underwent gait training with the Biodex Gait Trainer 3 (a treadmill integrated with music therapy). Each subject was evaluated at baseline (T0) and after the training (T1), using specific neuropsychological and motor function tests.

**Results:** The EG presented higher outcomes scores concerning mood and quality of life in all subscales of Psychological General Well-Being Index (i.e. anxiety, depression, health, vitality and positivity) and subscales of Brief-COPE, with regard to behavioral disengagement, positive reframing, planning, acceptance and use of emotional support, as compared to the CG. Moreover, a significant improvement in motor functioning, with regard to static and dynamic balance, was found in the EG.

**Conclusion:** Music-based gait training rehabilitation may be considered an effective strategy to improve behavioral performances, coping strategies and rehabilitation outcomes in patients with PD.

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## Introduction

Parkinson's disease (PD) is a neurodegenerative condition that is associated with the depletion of dopamine-containing neurons in specific brain regions. PD is the second most common age-related neurodegenerative disorder (after Alzheimer's disease), affecting nearly 1% of the population over 60 years and 5% in subjects up to 85 years [1], with a high health, social, and economic impact [2]. PD has traditionally been considered primarily as a motor disorder [3]; however, the burden of the non-motor symptomatology has often a high impact on both patients' and caregivers' burden and quality of life (QoL) [3, 4]. The motor symptoms of PD are attributed to the loss of striatal dopaminergic neurons, although non-motor symptoms are related to both dopaminergic and non-dopaminergic areas. The motor features of PD include resting

tremor, bradykinesia, and muscular rigidity [5]. Behavioural (impulse control disorders, depression, anxiety, apathy, and psychosis) and cognitive symptoms (including dementia) in PD are more common than expected, and their cumulative prevalence increases with the disease progression [6], with a consequent inability to participate in social and community life [7, 8]. The main behavioral symptoms (i.e. depression and anxiety) often negatively affect patients' QoL, coping strategies [9] and caregiver burden [3]. PD is increasingly recognized as a heterogeneous multisystem disorder involving other neurotransmitter systems, such as the serotonergic, noradrenergic and cholinergic circuits [10]. Levodopa, which is considered the gold standard therapy drug for PD since 1960, reduces rigidity and bradykinesia of striated muscles [11], whereas cholinesterase inhibitors,

with regard to rivastigmine and donepezil, may positively affect cognitive functions, behavioural disturbances, and activities of daily living. [12–15] However, the rehabilitation of behavioural difficulties in individuals with PD is important to improve patient management [16]. Multidisciplinary care, engaging neurologists, psychologists, psychiatrists, functional neurosurgeons, nurse specialists, social workers, and occupational therapists, as well as careful and comprehensive counselling for patients and their caregivers, is needed [17]. Several non-pharmacologic therapies, such as music therapy (MT), have recently been developed in order to improve the clinical manifestations of this disease. It has been demonstrated that MT has beneficial effects for the non-pharmacologic treatment of motor and non-motor symptoms and QoL of people with PD, especially when combined with conventional therapies [18]. Auditory stimulation *via* rhythmic cues can be used successfully in the rehabilitation also of the psychological status in PD's patients [19]. In particular, training based on rhythmic auditory stimulation (RAS) can improve gait parameters and kinematics in such patients [20–22]. Notably, long-term positive effects on walking in everyday life (even in the absence of stimulation) are reported following RAS-based rehabilitation programs [23]. Murgia et al. [24] investigated if a PD rehabilitation program integrated with ecological RAS (i.e. footstep sounds) can be more effective than the same program integrated with artificial RAS (i.e. metronome sounds). The results indicate that independently of the type of sound, the rehabilitation programs integrated with RAS are effective. Bella et al. argued that the benefits from the stimulation are likely to depend on patients' perceptual and sensorimotor rhythmic abilities. These abilities are sustained by both residual activity of impaired neuronal circuitries (basal ganglia– thalamo–cortical networks) and by alternative functional pathways (cerebello– thalamo–cortical networks). It has been demonstrated that relatively spared abilities to track the beat favor a positive response to rhythmic cueing. This was shown by patients' spontaneous tendency to align their footsteps to the beat and by their ability to detect whether a metronome was aligned or not to the beat of music [19, 21, 22].

**Table 1.** Demographics characteristics at baseline for both groups.

	Experimental	Control	All	p-value
Participants	20	20	40	
Age	63.2 ± 8.4	66.5 ± 6.2	64.9 ± 7.5	0.16
Education	2.3 ± 0.6	2.2 ± 0.7	2.2 ± 0.7	0.51
Gender				0.35
<i>Male</i>	10 (50.0%)	7 (35%)	17 (42.5%)	
<i>Female</i>	10 (50.0%)	13 (65%)	23 (57.5%)	
Hoehn & Yahr Scale	1.5 ± 0.53	1.7 ± 0.59	1.62 ± 0.57	0.17

Quantitative variables were expressed as means ± standard deviations, categorical variables as frequencies and percentages.

Moreover, music elicits emotional responses, as moving to music activates endorphin-related brain's pleasure circuits, and the rhythm of dancing to music may promote that satisfactory patterning which in turn may distract from sensations, such as fatigue [25].

This study sought to evaluate the effect of a combined rehabilitative approach, using music-based therapy and a gait training technology, on non-motor symptoms in patients with PD.

## Materials and methods

### Study population

Forty patients with PD (mean ± SD age: 63.2 ± 8.4 years; 50.0% male), who attended our Robotic and Behavioural Neurorehabilitation Unit from March to November 2018, were enrolled in this study and gave an informed consent. In order of recruiting, the patients were randomly divided into two groups: 20 patients constituted the control group (CG), and 20 patients the experimental group (EG). A more detailed description of the sample is in Table 1.

Inclusion criteria were as follows: i) diagnosis of PD according to the Movement Disorder Society Clinical Diagnostic Criteria for Parkinson's disease [26]; ii) Hoehn & Yahr Scale [27] between II and III; iii) presence of mild cognitive impairment (Mini-Mental State Examination [28] [MMSE > 23]) with normal executive function; iv) absence of disabling sensory alterations (i.e. auditory and visual loss); and v) no changes in anti-parkinsonian drug treatment in the previous 6 months.

Exclusion criteria were as follows: i) age >80 years; ii) presence of severe medical and psychiatric illness potentially interfering with the MT; iii) personal history of neoplasms and other neurological conditions; and v) neurologic music therapy in the last 3 months.

### Outcomes measures

Each participant was evaluated by a neuropsychologist, neurologist and physiotherapist before (T0) and immediately after the end of the training (T1).

The neuropsychological battery included: the Psychological General Well-Being Index (PGWBI) to assess the QoL related to health (HRQoL) [29]; and the Brief-Coping Orientation to Problems Experiences (Brief-COPE) [30] to assess a broad range of coping strategies [30].

Motor evaluation consisted in: the Functional Independence Measure Motor (FIM), which is used to assess a patient's physical, psychological level of disability and social function [31, 32]; the Time Up and Go Test (TUG) that assess patient's mobility [33]; and the 10 m Walking Test (10mWT), used to register walking speed in meters/second (m/s) over a short distance.

### Procedures

We decided to use two different rehabilitative approaches in the 2 groups: the CG underwent traditional over ground gait training whilst the EG was submitted to gait training by means of the Biodex Gait Trainer 3. Gait training in both the groups was performed 3 times a week for 8 weeks, for a total of 24 sessions, each lasting about 30 min. Both the groups were also submitted to traditional physiotherapy by means of exercises aimed at improving postural stability, lower limb joint mobilization, muscle stretching and motor coordination.

Gait Trainer is a platform that integrates gait training *via* a treadmill and RAS. The device is indeed equipped with an instrumented deck that issues acoustic cues to determine the exact tempo and rhythm during gait training and visual real-time bio-feedback to prompt patients to follow their gait pattern. In fact, the device provides online feedback, including step length, speed, and symmetry, to encourage patient progress and monitor patient performance. Patient footfalls were compared in real-time to the desired footfalls step by step and documented in a histogram. Patients were required to walk along with the music "angel elsewhere", which reaches a target music tempo of ~120 bpm. The song was presented with the lyrics, and the beat of the song was emphasized with a superimposed salient high-pitch bell sound. The patients were first trained to synchronize their footsteps to the beat of the music, which was adapted to their baseline gait performance; that is, the beat frequency of the RAS (namely, the beat rate of the music) was individually adjusted for each patient starting from the patient's best cadence (gait frequency and stride length). Then, the beat frequency was progressively increased up to the target beat frequency (120 bpm) through the first three to five

sessions. This frequency was then implemented for the remaining part of the RAS training. We adopted this intermediate target frequency and RAS setup as it has been shown that using a beat frequency not based on the patient's baseline cadence can worsen step length and gait cadence, especially when the frequency is set too low (60–90 bpm) or too high (>150 bpm) [34].

### Statistical analysis

Data were analyzed using the SPSS 16.0 version, considering a  $p < 0.05$  as statistically significant. The descriptive statistics were analyzed and presented as a media + standard deviation (SD) for continuous variables and as frequencies (%) for categorical variables for the two groups (Table 1). Finally, to examine the association between rehabilitative therapy and clinical outcomes, we performed the analysis of variance (ANOVA) in order to assess the type of treatment affected by the clinical outcome. The model had the performance obtained in tests that evaluate different cognitive and motor functions as dependent variable, the categorical variable 'Group' (1 = experimental; 2 = control), the variable "Time" (factor within subject with two levels: T0 e T1) and the scales/test for evaluate neuropsychological and motor functions and mood as independent variable. Student t-tests, using the Bonferroni correction, were used for post-hoc testing of group differences in time and performance, scores are in median (first-third quartile) (Table 3).

### Results

All patients completed the training, and both the groups underwent the same training amount. No significant differences were found in age ( $p = 0.16$ ), education level ( $p = 0.51$ ) as well as in gender ( $p = 0.35$ ) between the EG and CG. At baseline, no significant differences emerged between the scores of the two groups. Post-hoc analysis results (Table 3) showed that all of the patients in both the groups achieved significant changes in many test scores from baseline to end of the training. However, we observed more significant improvements in the EG, concerning mood and quality of life in all subscales (PGWI- anxiety, depression, health, vitality and positivity), except for self-control (PGWBI – self-control), besides some subscales of Brief-COPE, i.e. behavioral disengagement (SD), venting (V), positive reframing (PR), planning (P), acceptance (A), religion (R), self-blame (SB) and use of emotional support (UES). Moreover, there was a

**Table 2.** ANOVA decomposition in Group\*Time for all tests/scales.

Clinical Assessment	Df	Mean Square	F	P-value
PGWBI A	1, 38	1394.4	22.2	<0.001
PGWBI DM	1, 38	952.2	15.5	<0.001
PGWBI H	1, 38	667.0	10.3	0.002
PGWBI V	1, 38	627.2	15.7	<0.001
PGWBI P	1, 38	911.2	18.3	<0.001
PGWBI SC	1, 38	44.0	1.3	0.260
BRIEF COPE SD	1, 38	48.0	73.7	<0.001
BRIEF COPE AC	1, 38	32.5	23.5	<0.001
BRIEF COPE D	1, 38	6.0	5.2	0.02
BRIEF COPE SU	1, 38	18.0	33.0	<0.001
BRIEF COPE UES	1, 38	36.4	49.2	<0.001
BRIEF COPE BD	1, 38	43.5	66.2	<0.001
BRIEF COPE UIS	1, 38	1.5	0.6	0.41
BRIEF COPE V	1, 38	1.0	0.6	0.43
BRIEF COPE PR	1, 38	12.8	14.2	0.43
BRIEF COPE P	1, 38	6.6	6.0	<0.002
BRIEF COPE H	1, 38	.8	0.4	<0.05
BRIEF COPE A	1, 38	10.5	5.3	0.53
BRIEF COPE R	1, 38	.0	.0	<0.05
BRIEF COPE SB	1, 38	.1	.0	0.78
FIM Total	1, 38	672.8	259.8	<0.001
FIM C	1, 38	.2	.0	0.87
FIM M	1, 38	15.3	2.1	0.14
TUG R	1, 38	6.8	13.6	<0.002
TUG L	1, 38	7.5	12.4	<0.002
10 MT Time 1	1, 38	5.8	14.8	<0.001
10 MT Time 2	1, 37	3.4	4.3	<0.05
10 MT Time 3	1, 38	2.2	3.3	0.07
10 MT Median	1, 38	4.4	7.6	<0.05

Significant p-value are in bold.

\*Psychological General Well Being Index Anxiety (PGWBI A); Psychological General Well Being Index Depressed Mood (PGWBI DM); Psychological General Well Being Index General Health (PGWBI H); Psychological General Well Being Index Vitality (PGWBI V); Psychological General Well Being Index Positivity Well-being (PGWBI P); Psychological General Well Being Index Self-Control (PGWBI SC); Brief Coping Orientation to Problems Experienced Self Distraction (BRIEF COPE SD); Brief Coping Orientation to Problems Experienced Active Coping (BRIEF COPE AC); Brief Coping Orientation to Problems Experienced Denial (BRIEF COPE D); Brief Coping Orientation to Problems Experienced Substance Use (BRIEF COPE SU); Brief Coping Orientation to Problems Experienced Use of Emotional Support (BRIEF COPE UES); Brief Coping Orientation to Problems Experienced Behavioral Disengagement (BRIEF COPE BD); Brief Coping Orientation to Problems Experienced Use of Instrumental Support (BRIEF COPE UIS); Brief Coping Orientation to Problems Experienced Venting (BRIEF COPE V); Brief Coping Orientation to Problems Experienced Positive Reframing (BRIEF COPE PR); Brief Coping Orientation to Problems Experienced Planning (BRIEF COPE P); Brief Coping Orientation to Problems Experienced Humor (BRIEF COPE H); Brief Coping Orientation to Problems Experienced Acceptance (BRIEF COPE A); Brief Coping Orientation to Problems Experienced Religion (BRIEF COPE R); Brief Coping Orientation to Problems Experienced Self-Blame (BRIEF COPE SB); Functional Independence Measure Total (FIM Total); Functional Independence Measure Cognitive (FIM C); Functional Independence Measure Motor (FIM M); Time Up and Go Right (TUG R); Time Up and Go Left (TUG L); 10 m Walking Test Time 1 (10MT Time 1); 10 m Walking Test Time 2 (10MT Time 2); 10 m Walking Test Time 3 (10MT Time 3); 10 m Walking Test Median (10MT Median).

significant improvement in motor functioning, in particular in static and dynamic balance (as per Time up and go) and in general motor function (10MT- FIM), in the EG. Except for the Time up and go test, these motor improvements were present also in the CG. The ANOVA analysis showed the triple interaction between Group\*Time\*Tests/Scales ( $F_{(9,162)} = 21,741, p < 0.001$ ). In particular, the ANOVA decomposition (Table 2)

underlined that the scores of all tests/scales were influenced by the type of treatment, demonstrating how the effect of the two treatments was significantly different. In fact, only in the EG, we observed a significant improvement in most of the scales administered, as compared to the CG (Table 3).

## Discussion

PD is traditionally related to motor symptoms like bradykinesia, resting tremors, rigidity, and postural instability although the clinical range of PD encompasses various non-motor features such as visuospatial function, cognitive deficits, anxiety, depression and other neurobehavioral manifestation [35]. Studies on people suffering from PD rarely include neurological, psychological and behaviour features that, together with the chronicity and neurodegenerative nature of the illness, might exacerbate the patient's burden and have consequences in physical and mental health, psychological well-being and quality of life (QoL).

Pharmacotherapy and physiotherapy usually focus on motor outcomes, as the disorder presents itself as a disease characterized by motor difficulties, but there is poor literature that explores behavioural outcomes.

Our study supports music-guided gait training using Gait Trainer 3 (Biodex) as an effective neurorehabilitation strategy to improve both motor and behavioural performances, and consequently quality of life. In the last decades, authors underlined the beneficial effect of MT on motor function (bradykinesia, gait, freezing of gait) and emotional and psychological functioning, coping strategies, quality of life and life satisfaction in PD patients [36–39]. In line with previous findings [39–40], our study revealed higher psychological and emotional well-being after the musical treadmill training, confirming that active involvement in movements and the ability to walk “normally” may lead to physical, psychological and emotional benefits, as shown by the EG improvement in all subscales of the PGWBI.

In this regard, the use of MT techniques (especially RAS) has recently been recommended as part of the multidimensional approach to improve gait and gait-related activities for patients with PD and other neurological disorders. [32, 41] Pacchetti et al. [36] used MT to improve motor and emotional functioning in a group of PD patients, with positive results. In line with these authors, our exploratory study highlighted not only the benefits on the motor outcomes, but also on emotional, and behavioural functioning. Moreover, coping strategies in the EG improved concerning

**Table 3.** Post-hoc analysis of clinical scores between baseline (T0) and follow-up (T1), for both Experimental Group (EG) and Control Group (CG).

Clinical assessment	EG			CG		
	T0	T1	p-value	T0	T1	p-value
PGWBI A	51.0 (42.0 – 74.2)	75.0 (52.7 – 85.2)	<b>&lt;0.001</b>	36.0 (32.0 - 64.0)	37.5 (31.7 - 52.7)	0.26
PGWBI DM	60.0 (38.2 – 86.0)	72.0 (59.5 – 91.2)	<b>&lt;0.001</b>	36.5 (26.0 - 48.2)	33.0 (25.7 - 42.0)	0.07
PGWBI H	55.0 (38.2 - 66.0)	66.0 (50.2– 82.7)	<b>&lt;0.001</b>	35.0 (32.0 - 47.0)	35.5 (29.5- 48.5)	0.45
PGWBI V	54.5 (30.5 – 65.0)	64.0 (44.5 – 78.7)	<b>&lt;0.001</b>	40.0 (34.2- 50.0)	38.0 (30.0 -52.7)	0.43
PGWBI P	45.0 (28.7 – 60.0)	60.0 (47.7 –71.0)	<b>&lt;0.001</b>	45.0 (39.0 - 53.5)	46.5 (38.2 - 55.0)	0.64
PGWBI SC	63.0 (51.5 – 80.2)	66.0 (58.2 – 80.0)	0.17	50.0 (37.0 - 66.0)	50.0 (37.0 - 66.2)	0.66
BRIEF COPE SD	2.0 (2.0 – 2.2)	6.0 (5.0 – 7.0)	<b>&lt;0.001</b>	2.0 (2.0 – 3.0)	3.0 (3.0 - 3.0)	<b>&lt;0.001</b>
BRIEF COPE AC	3.0 (3.0 - 5.0)	7.5 (5.0 – 8.0)	<b>&lt;0.001</b>	3.5 (3.0 - 5.0)	3.5 (3.0 - 5.0)	0.21
BRIEF COPE D	2.5 (2.0 - 3.2)	4.5 (2.7 - 5.0)	<b>&lt;0.001</b>	3.0 (2.0 – 3.0)	5.0 (4.5 - 6.0)	<b>&lt;0.001</b>
BRIEF COPE SU	2.0 (2.0 – 2.0)	4.0 (3.0 – 5.0)	<b>&lt;0.001</b>	2.0 (2.0 – 3.0)	2.0 (2.0 – 2.0)	0.72
BRIEF COPE UES	3.5 (2.0 – 4.0)	6.0 (5.7 – 8.0)	<b>&lt;0.001</b>	3.5 (2.0 – 4.0)	4.0 (2.0 - 5.0)	0.25
BRIEF COPE BD	3.0 (2.0 - 5.0)	6.0 (5.0 - 7.0)	<b>&lt;0.001</b>	5.0 (3.0 - 5.0)	4.0 (3.0 - 5.0)	0.05
BRIEF COPE UIS	4.0 (4.0 - 5.2)	6.0 (3.0 - 7.0)	0.12	3.0 (2.0 - 4.0)	4.0 (3.0 - 6.0)	<b>0.01</b>
BRIEF COPE V	4.5 (2.0 - 6.0)	7.0 (5.0 - 7.2)	<b>&lt;0.001</b>	4.0 (2.7 - 4.0)	4.5 (2.7 - 7.0)	<b>0.01</b>
BRIEF COPE PR	5.5 (3.0 - 6.0)	7.0 (6.0 - 7.2)	<b>&lt;0.001</b>	5.0 (5.0 - 6.0)	5.0 (5.0 - 6.2)	0.26
BRIEF COPE P	5.0 (4.0 - 6.0)	7.0 (5.0 - 7.0)	<b>0.02</b>	5.0 (3.7 - 5.2 )	5.0 (3.0 - 5.2)	0.72
BRIEF COPE H	4.0 (2.7 - 6.0)	4.5 (4.0 - 6.0)	0.08	4.0 (3.0 - 5.2)	5.0 (4.0 - 6.0)	0.04
BRIEF COPE A	3.0 (3.0 - 4.0)	8.0 (7.7 - 8.0)	<b>&lt;0.001</b>	4.0 (2.7 - 4.2)	7.0 (5.0 - 8.0)	<b>&lt;0.001</b>
BRIEF COPE R	4.0 (3.0 - 4.0)	6.0 (4.7 - 7.2)	<b>&lt;0.001</b>	3.5 (3.0 - 4.0)	7.0 (4.0 - 7.2)	<b>&lt;0.001</b>
BRIEF COPE SB	4.0 (2.0 - 5.0)	5.0 (4.0 - 6.0)	<b>&lt;0.001</b>	4.0 (3.0 - 4.2)	5.0 (4.0 - 6.2)	<b>&lt;0.001</b>
FIM Total	80.0 (76.7 - 84.5)	92.0 (88.0 - 99.0)	<b>&lt;0.001</b>	80.5 (78.0 - 85.2)	82.0 (79.0 - 85.2)	<b>&lt;0.001</b>
FIM C	28.5 (22.7 - 30.0)	31.0 (26.7 - 33.0)	<b>&lt;0.001</b>	31.0 (30.0 - 32.0)	34.5 (31.5 - 36.0)	<b>&lt;0.001</b>
FIM M	50.0 (50.0 - 56.0)	58.0 (52.0 - 58.2)	<b>&lt;0.001</b>	55.0 (50.0 - 60.0)	60.0 (59.0 - 62.0)	<b>0.02</b>
TUG R	10.2 (8.0 - 12.3)	8.8 (7.3 - 11.1)	<b>&lt;0.001</b>	7.0 (6.2 - 8.1)	6.2 (6.1 - 7.6)	0.14
TUG L	11.3 (8.3 - 13.1)	9.2 (7.4 - 11.8)	<b>&lt;0.001</b>	6.0 (5.3 - 7.2)	5.4 (5.3 - 7.3)	0.19
10 MT Time 1	5.6 (4.7 - 6.0)	4.9 (4.2 - 5.3)	<b>&lt;0.001</b>	10.6 (8.3 - 12.1)	9.3 (7.2 - 10.6)	<b>&lt;0.001</b>
10 MT Time 2	4.9 (4.4 - 6.1)	4.3 (4.1 - 5.2)	<b>0.01</b>	10.4 (8.1 - 11.4)	9.3 (7.1 - 10.2)	<b>&lt;0.001</b>
10 MT Time 3	5.1 (4.6 - 6.3)	4.1 (4.0 - 5.4)	<b>&lt;0.001</b>	10.1 (7.9 - 11.0)	9.5 (7.1 - 10.0)	<b>&lt;0.001</b>
10 MT Median	5.6 (4.6 - 6.1)	4.4 (4.1 - 5.3)	<b>0.01</b>	10.4 (8.0 - 11.6)	9.4 (7.1 - 10.2)	<b>&lt;0.001</b>

Scores are in median (first-third quartile); significant differences are in bold.

\*Psychological General Well Being Index Anxiety (PGWBI A); Psychological General Well Being Index Depressed Mood (PGWBI DM); Psychological General Well Being Index General Health (PGWBI H); Psychological General Well Being Index Vitality (PGWBI V); Psychological General Well Being Index Positivity Well-being (PGWBI P); Psychological General Well Being Index Self-Control (PGWBI SC); Brief Coping Orientation to Problems Experienced Self Distraction (BRIEF COPE SD); Brief Coping Orientation to Problems Experienced Active Coping (BRIEF COPE AC); Brief Coping Orientation to Problems Experienced Denial (BRIEF COPE D); Brief Coping Orientation to Problems Experienced Substance Use (BRIEF COPE SU); Brief Coping Orientation to Problems Experienced Use of Emotional Support (BRIEF COPE UES); Brief Coping Orientation to Problems Experienced Behavioural Disengagement (BRIEF COPE BD); Brief Coping Orientation to Problems Experienced Use of Instrumental Support (BRIEF COPE UIS); Brief Coping Orientation to Problems Experienced Venting (BRIEF COPE V); Brief Coping Orientation to Problems Experienced Positive Reframing (BRIEF COPE PR); Brief Coping Orientation to Problems Experienced Planning (BRIEF COPE P); Brief Coping Orientation to Problems Experienced Humour (BRIEF COPE H); Brief Coping Orientation to Problems Experienced Acceptance (BRIEF COPE A); Brief Coping Orientation to Problems Experienced Religion (BRIEF COPE R); Brief Coping Orientation to Problems Experienced Self-Blame (BRIEF COPE SB); Functional Independence Measure Total (FIM Total); Functional Independence Measure Cognitive (FIM C); Functional Independence Measure Motor (FIM M); Time Up and Go Right (TUG R); Time Up and Go Left (TUG L); 10 m Walking Test Time 1 (10 MT Time 1); 10 m Walking Test Time 2 (10 MT Time 2); 10 m Walking Test Time 3 (10 MT Time 3); 10 m Walking Test Median (10 MT Median).

active coping, use of emotional support, positive reframing and planning abilities, and decreased in behavioural disengagement.

We may argue that MT applied to the Biodex treadmill may be related to the creation of an external time-keeper that supports the weakened role of the basal ganglia [42], perhaps through the involvement of compensatory networks involving the cerebellum [43]. Regarding the motor outcomes of our exploratory study, we found better improvement in the EG (as per FIM scores and 10mWT). Rochester [44] demonstrated that a 3-week-training with RAS implied a learning effect that improved gait, freezing and movements fluidity. This was probably due to the “boosting” of brain plasticity within the internal time-keeping and rhythm formation process, known as entrainment mechanism. The latter can be enhanced by both a selected music [43] and

the use of technologies that utilize interactive computer-generated systems for improving brain-body interaction and sensory-motor integration.

In addition, the influence of emotional feelings on gait performance of the sit-to-walk task has been only recently investigated in healthy adults [45]. In PD patients, gait abnormalities and the continuous or episodic disturbance of movements changes [46] seems to be in relation to the dopaminergic system impairment and cholinergic dysfunction of locomotor structures, which are also involved in emotion, executive functioning and behaviour [47]. On such basis, we could hypothesize that the improvement in TUG only in the EG might be linked to the involvement of music in treadmill training, which evidences that responses to triggered musical-emotional stimuli can also affect attention and motor behaviour. Moreover, cognition

(in particular of the executive functions), cholinergic/dopaminergic activation and emotional control seems to play a pivotal role on motor behavior in PD patients [48, 49].

As gait speed is a significant predictor of performance of daily living activities, the effect of a music-based therapy may have important implications not only in gait-related activities but also in global functioning and independence in PD [50]. Furthermore, in line with Terrie Vann-Ward et al. [51], our results showed that being involved in activities that require motor engagement, such as psychophysical rehabilitation with an on-going acoustic feedback, requires planning abilities, coordination, and activated feelings, which are all together solicited during training.

Social identity, emotional well-being and behavioural integrity cover an important role in PD patients [40], and are strongly linked to gait abilities in a proportional way. As MT may involve the multidimensional aspects of PD patients, a consequent improvement of QoL after the training is expected. [52]

### Limitations and strengths

This pilot study has some limitations. First, the sample size is relatively small and does not let us to generalize the findings to the PD population. Second, we did not perform an assessment at 3 and/or 6 months follow-up. Further larger sample multicenter studies with short and long-term follow-up are needed to confirm our promising findings. Furthermore, future studies could include patients with greater disease severity, also using more specific outcome measures. Finally, the use of instrumental tests, including surface EMG, EEG and fMRI should be advisable, to better understand the neurophysiological basis underpinning both motor (as in our previous study) [53] and cognitive recovery after MT.

However, this study is the first to analyze the neurobehavioural aspects of patients with PD subjected to gait rehabilitation using Biodex Gait Trainer 3. Indeed, its major strength is that it focused not only on motor symptoms, but also on the psychological, cognitive and behavioral aspects of patients with PD, also assessing coping strategies.

### Conclusions

Music assisted gait training may be a complementary and valuable tool in improving not only motor symptoms in PD patients, but also behavioral and psychological status, with a consequent betterment of QoL.

Further larger sample studies with long-term follow up are need to confirm these promising findings.

### Disclosure statement

No potential conflict of interest was reported by the authors. Q1

### References

- [1] de Lau LM, Breteler MM. Epidemiology of Parkinson disease. *Lancet Neurol*. 2006;5(6):525–535.
- [2] Calne SM. The psychosocial impact of late-stage Parkinson's disease. *J Neurosci Nurs*. 2003;35(6):306–313.
- [3] Hiseman JP, Fackrell R. Caregiver burden and the non-motor symptoms of Parkinson's disease. *Int Rev Neurobiol*. 2017;133:479–497. [10.1016/bs.irn.2017.05.035](https://doi.org/10.1016/bs.irn.2017.05.035).
- [4] Benavides O, Albuquerque D, Chaná-Cuevas P. Burden among caregivers of patients with Parkinson disease. *Rev méd Chile*. 2013;141(3):320–326.
- [5] DeMaagd G, Philip A. Parkinson's disease and its management: part 1: disease entity, risk factors, pathophysiology, clinical presentation, and diagnosis. *Pharm Ther*. 2015;40(8):504–532. Aug
- [6] Prakash KM, Nadkarni NV, Lye WK, et al. The impact of non-motor symptoms on the quality of life of Parkinson's disease patients: a longitudinal study. *Eur J Neurol*. 2016;23(5):854–860.
- [7] O'Callaghan C, Lewis SJG. Cognition in Parkinson's Disease. *Int Rev Neurobiol*. 2017;133:557–583.
- [8] Papagno C, Trojano L. Cognitive and behavioral disorders in Parkinson's disease: an update. I: cognitive impairments. *Neurol Sci*. 2018;39(2):215–223.
- [9] Costa FP, Diaféria G, Behlau M. Communicative aspects and coping strategies in patients with Parkinson's disease. *Arq Neuropsiquiatr*. 2014;28(1):46–52.
- [10] Sauerbier A, Jenner P, Todorova A, et al. Non motor subtypes and Parkinson's disease. *Park Relat Disord*. 2016;22(Suppl 1):S41–S46.
- [11] Pinho P, Monteiro L, Soares Mf de P, et al. Impact of levodopa treatment in the voice pattern of Parkinson's disease patients: a systematic review and meta-analysis. *CoDAS*. 2018;30(5):e20170200.
- [12] Rolinski M, Fox C, Maidment I, et al. Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. *Cochrane Database Syst Rev*. 2012;14(3):CD006504.
- [13] Rektorova I. Current treatment of behavioral and cognitive symptoms of Parkinson's disease. *Parkinsonism Relat Disord*. 2019;59:65–73.
- [14] Emre M, Cummings JL, Lane RM. Rivastigmine in dementia associated with Parkinson's disease and Alzheimer's disease: similarities and differences. *J Alzheimer's Dis*. 2007;11(4):509–519.
- [15] Dubois B, Tolosa E, Katzschlager R, et al. Donepezil in Parkinson's disease dementia: a randomized, double-blind efficacy and safety study. *Mov Disord*. 2012;27(10):1230–1238.

- 637 [16] Witt K, Kalbe E, Erasmí R, et al. Nonpharmacological  
638 treatment procedures for Parkinson's disease. *Der*  
639 *Nervenarzt*. 2017;88(4):383–390.
- 640 [17] Van der Marck MA, Bloem BR. How to organize multi-  
641 specialty care for patients with Parkinson's disease.  
642 *Park Relat Disord*. 2014;20 Suppl 1:S167–S73.
- 643 [18] García-Casares N, Martín-Colom JE, García-Arnés JA.  
644 Music therapy in Parkinson's disease. *J Am Med Dir*  
645 *Assoc*. 2018;19(12):1054–1062.
- 646 [19] Bella SD, Benoit CE, Farrugia N, et al. Effects of music-  
647 ally cued gait training in Parkinson's disease: beyond  
648 a motor benefit. *Ann NY Acad Sci*. 2015;1337(1):  
649 77–85.
- 650 [20] Cancela J, Moreno EM, Arredondo MT, et al.  
651 Designing auditory cues for Parkinson's disease gait  
652 rehabilitation. 2014 36th Annual International  
653 Conference of the IEEE Engineering in Medicine and  
654 Biology Society; 2014. p. 5852–5855.
- Q2 [21] Bella SD, Benoit CE, Farrugia N, et al. Gait improve-  
655 ment via rhythmic stimulation in Parkinson's disease  
656 is linked to rhythmic skills. *Sci Rep*. 2017;7(1):42005.
- [22] Bella SD, Dotov D, Bardy B, et al. Individualization of  
657 music-based rhythmic auditory cueing in Parkinson's  
658 disease. *Ann N Y Acad Sci*. 2018;1423(1):308–317.
- [23] Dalla Bella S. Music and movement: towards a transla-  
659 tional approach. *Neurophysiol Clin*. 2018;48(6):  
660 377–386.
- [24] Murgia M, Pili R, Corona F, et al. The use of footstep  
661 sounds as rhythmic auditory stimulation for gait  
662 rehabilitation in Parkinson's disease: a randomized  
663 controlled trial. *Front Neurol*. 2018;9:348.
- [25] de Dreu MJ, van der Wilk AS, Poppe E, et al.  
664 Rehabilitation, exercise therapy and music in patients  
665 with Parkinson's disease: a meta-analysis of the  
666 effects of music-based movement therapy on walking  
667 ability, balance and quality of life. *Parkinsonism Relat*  
668 *Disord*. 2012;18(Suppl 1):S114–S119.
- [26] Postuma RB, Berg D, Stern M, et al. MDS clinical diag-  
669 nostic criteria for Parkinson's disease. *Mov Disord*.  
670 2015;30(12):1591–1601.
- [27] Hoehn M, Yahr M. Parkinsonism: onset, progression,  
671 and mortality. *Neurology*. 1967;17(5):427–442.
- [28] Folstein MF, Folstein SE, McHugh PR. Mini-mental  
672 state". A practical method for grading the cognitive  
673 state of patients for the clinician. *J Psychiatr Res*.  
674 1975;12(3):189–198.
- [29] Dupuy HJ. The psychological general well-being  
675 (PGWB) index. *Am J Cardiol*. 1984;54(7):908–913.
- [30] Carver CS. You want to measure coping but your pro-  
676 tocol's too long: consider the brief COPE. *Int J Behav*  
677 *Med*. 1997;4(1):92–100.
- [31] Granger CV, Hamilton BB, Linacre JM, et al.  
678 Performance profiles of the functional independence  
679 measure. *Am J Phys Med Rehabil*. 1993;72(2):84–89.
- [32] Ashoori A, Eagleman DM, Jankovic J. Effects of audi-  
680 tory rhythm and music on gait disturbances in  
681 Parkinson's disease. *Front Neurol*. 2015;6:234.
- [33] Richardson S. The timed "up & go": a test of basic  
682 functional mobility for frail elderly persons. *J Am*  
683 *Geriatr Soc*. 1991;39(2):142–148.
- [34] Leow L-A, Parrott T, Grahn JA. Individual differences  
684 in beat perception affect gait responses to low- and  
685 high-groove music. *Front Hum Neurosci*. 2014;8:811.
- [35] Kalia LV, Kalia SK, Lang AE. Disease-modifying strat-  
686 egies for Parkinson's disease. *Mov Disord*. 2015;30(11):  
687 1442–1450.
- [36] Pacchetti C, Mancini F, Aglieri R, et al. Active music  
688 therapy in Parkinson's disease: an integrative method  
689 for motor and emotional rehabilitation. *Psychosom*  
690 *Med*. 2000;62(3):386–393.
- [37] Rosengren L, Brogårdh C, Jacobsson L, et al. Life satis-  
691 faction and associated factors in persons with mild to  
692 moderate Parkinson's disease. *NeuroRehabilitation*.  
693 2016;39(2):285–294.
- [38] Pusswald G, Fleck M, Lehrner J, et al. The "sense of  
694 coherence" and the coping capacity of patients with  
695 Parkinson disease. *Int Psychogeriatr*. 2012;24(12):  
696 1972–1979.
- [39] Rosqvist K, Hagell P, Odin P, et al. Factors associated  
697 with life satisfaction in Parkinson's disease. *Acta*  
698 *Neurol Scand*. 2017;136(1):64–71.
- [40] Hammarlund CS, Andersson K, Andersson M, et al.  
699 The significance of walking from the perspective of  
700 people with Parkinson's disease. *J Parkinsons Dis*.  
701 2014;4(4):657–663.
- [41] Keus SHJ, Bloem BR, Hendriks EJM, et al. Evidence-  
702 based analysis of physical therapy in Parkinson's dis-  
703 ease with recommendations for practice and research.  
704 *Mov Disord*. 2007;22(4):451–460.
- [42] Rubinstein TC, Giladi N, Hausdorff JM. The power of  
705 cueing to circumvent dopamine deficits: a review of  
706 physical therapy treatment of gait disturbances in  
707 Parkinson's disease. *Mov Disord*. 2002;17(6):1148–1160.
- [43] Thaut MH. Neurologic music therapy techniques and  
708 definitions. In: *Rhythm, music and the brain*. New  
709 York (NY): Taylor and Francis Group; 2005.
- [44] Rochester L, Baker K, Hetherington V, et al. Evidence  
710 for motor learning in Parkinson's disease: acquisition,  
711 automaticity and retention of cued gait performance  
712 after training with external rhythmical cues. *Brain Res*.  
713 2010;1319:103–111.
- [45] Kang GE, Gross MM. Emotional influences on sit-to-walk  
714 in healthy young adults. *Hum Mov Sci*. 2015;40:  
715 341–351.
- [46] Giladi N, Horak FB, Hausdorff JM. Classification of gait  
716 disturbances: distinguishing between continuous and  
717 episodic changes. *Mov Disord*. 2013;28(11):1469–1473.
- [47] Galna B, Lord S, Burn DJ, et al. Progression of gait  
718 dysfunction in incident Parkinson's disease: impact of  
719 medication and phenotype. *Mov Disord*. 2015;30(3):  
720 359–367.
- [48] Rochester L, Yarnall AJ, Baker MR, et al. Cholinergic  
721 dysfunction contributes to gait disturbance in early  
722 Parkinson's disease. *Brain*. 2012;135(9):2779–2788.
- [49] Amboni M, Barone P, Hausdorff JM. Cognitive contri-  
723 butions to gait and falls: evidence and implications.  
724 *Mov Disord*. 2013;28(11):1520–1533.
- [50] Verghese J, Wang C, Holtzer R. Relationship of clinic-  
725 based gait speed measurement to limitations in com-  
726 munity-based activities in older adults. *Arch Phys*  
727 *Med Rehabil*. 2011;92(5):844–846.
- Q3



- [51] Vann-Ward T, Morse JM, Charmaz K. Preserving self: theorizing the social and psychological processes of living with Parkinson disease. *Qual Health Res.* 2017; 27(7):964–982.
- [52] Ellis T, Cavanaugh JT, Earhart GM, et al. Which measures of physical function and motor impairment best predict quality of life in Parkinson’s disease? *Park Relat Disord.* 2011;17(9):693–697.
- [53] Calabrò RS, Naro A, Filoni S, et al. Walking to your right music: a randomized controlled trial on the novel use of treadmill plus music in Parkinson’s disease. *J Neuroeng Rehabil.* 2019;16(1):68

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