World Journal of Methodology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.5662/wjm.v4.i3.133

World J Methodol 2014 September 26; 4(3): 133-143
ISSN 2222-0682 (online)

EDITORIAL

Effects of physical activity in Parkinson's disease: A new tool for rehabilitation

Paolo Borrione, Eliana Tranchita, Pierpaolo Sansone, Attilio Parisi

Paolo Borrione, Eliana Tranchita, Pierpaolo Sansone, Attilio Parisi, Department of Movement, Human and Health Sciences, University of Rome "Foro Italico", 00194 Rome, Italy
Author contributions: Sansone P and Tranchita E contributed equally in writing the article and in reviewing the literature; Borrione P and Parisi A contributed in the conception, design, writing and final approval of the article.
Correspondence to: Paolo Borrione, MD, Department of Movement, Human and Health Sciences, University of Rome "Foro Italico", Piazza Lauro de Bosis 15, 00194 Rome, Italy. paolo.borrione@uniroma4.it
Telephone: +39-06-36733569 **Fax:** +39-06-36733344
Received: March 20, 2014 **Revised:** May 28, 2014
Accepted: July 25, 2014
Published online: September 26, 2014

Abstract

Parkinson's disease (PD) is a common neurodegenerative disease characterized by bradykinesia, tremor, rigidity, and postural instability. Motor disorders are composite and combined, adversely affecting the patient's health. Tremor and rigidity are correlated with worsening manual dexterity as well as postural changes such as akinesia and camptocormia. Moreover, gait alteration as well as postural instability, with consequent impairment in balance, increase the risk of falls. It is well known that these symptoms respond poorly to pharmacologic therapy in PD patients. Physical therapy is the most effective non-pharmacological aid to PD patients. Available data in the literature indicate that any rehabilitation protocol has to focus on: cognitive movement strategies, cueing strategies, and improved physical capacity and balance. Different training programs for PD patients have been designed and evaluated but only specific training strategies, tailored and individualized for each patient, may produce improvements in gait speed and stride length, decrease motor and balance symptoms and improve quality of life. Furthermore, aerobic training may improve muscle trophism, strength and mobility. It seems reasonable to state that tailored physical activity is a valid tool to be included in the therapeutic program of PD patients, considering that this approach may ameliorate the symptoms as well as the overall physical incapacity, reduce the risk of falls and injuries, and ultimately improve quality of life.

Key words: Parkinson's disease; Motor disorders; Postural instability; Physical exercise; Training

Core tip: A review of the literature underlines the importance of tailored physical activity in patients with Parkinson disease. Several studies demonstrated the key role that specific training strategies may have on motor disorders and postural instability affecting patients with Parkinson disease. Since it has been clearly demonstrated that these symptoms respond poorly to pharmacologic therapy, it seems necessary to combine the traditional treatment of Parkinson disease with a specific exercise training strategy in order to reduce motor disorders as well as postural instability, with the aim of improving quality of life of the patients affected by this neurologic disease.

Borrione P, Tranchita E, Sansone P, Parisi A. Effects of physical activity in Parkinson's disease: A new tool for rehabilitation. *World J Methodol* 2014; 4(3): 133-143 Available from: URL: http://www.wjgnet.com/2222-0682/full/v4/i3/133.htm DOI: http://dx.doi.org/10.5662/wjm.v4.i3.133

PARKINSON'S DISEASE

Parkinson's disease (PD) is the second most common neurodegenerative disorder, after Alzheimer's disease. PD affects 1% of the population over 60 years of age, and the risk increases proportionally with age.

The primary symptoms of PD are bradykinesia, tremor, rigidity, and postural instability. Bradykinesia refers to the slowness of the patient's movements[1] and affects every single patient[2]; it is evident especially when evaluating gait, but it affects every voluntary movement. Patients also manifest a global reduction in spontaneous movements (*e.g.*, gestures, winking) and deliberate movements (*e.g.*, arm swing), defined as akinesia[1]. PD's tremor affects 75% of the diagnosed subjects[3]. This "resting tremor" differs from essential tremor since it manifests when the body part affected is not involved in voluntary movements. Rigidity affects 90%-99% of PD patients[4] and it is caused by muscular hypertonia; the typical posture of PD patients, camptocormia*,* is in fact due to excessive activation of flexor muscles in the trunk and limbs[4]. Postural instability is "the impairment in balance that compromises the ability to maintain or change posture such as standing and walking"[5]. This condition does not usually affect the early stages of the illness, and is one of the most difficult symptoms to be treated[6].

For many reasons, it is essential to describe the impaired Parkinsonian gait. In chronological order, patients experience difficulties when starting to walk, a condition called "start hesitation"[7]; walking speed and stride length are abnormally reduced; lower limb joints excursion is reduced due to rigidity; timing of steps is extremely irregular and asymmetric; and arm swing is decreased or absent. Moreover, 2 typical features are also present: festinating gait or festination is characterized by the patient's sudden acceleration as an attempt to keep their center of gravity between their feet in order to compensate for their flexed posture[8]. Freezing of gait (FoG) is defined as a sudden stop in the patient's gait, often with legs trembling in place and the sensation of being "glued" to the floor. This symptom manifests more frequently while turning, when the path changes or gets more narrow, in a diagonal direction, when dealing with obstacles and other stressful situations or just before reaching the destination[8-11].

Subjects affected by PD also experience several non-motor symptoms, such as autonomic dysfunctions (dysphagia, constipation, urinary incontinence, sexual dysfunction, orthostatic hypotension) cognitive impairment, dementia, depression (which affects 30%-40% of patients)[12], anxiety, sleep disorders and decreased olfactory sense.

PD motor disorders are very complex and interconnected, and their adverse consequences for both patient's health and quality of life are very well known. Tremor and rigidity significantly reduce the quality of life since they worsen manual dexterity, thus affecting simple everyday activities such as cutting food pill-taking and posture[13]. Moreover, gait impairments (especially FoG and stride variability) as well as postural instability (and the consequent reduced balance) represents harmful conditions of PD since they increase the risk of falls[11,14,15]. According to statistics, almost 70% of patients experience falls at least once per year[16] and 25% of subjects in the first 10 years of disease suffer a hip fracture[11], an injury correlated with high morbidity and mortality in PD patients[17]. Furthermore, falls can trigger a vicious circle that aggravates even more the patient's condition: fear of other falls and injuries reduce the subjects' mobilization, which in turn causes sarcopenia, decreased fitness, osteoporosis, loss of independence, social isolation, and reduced participation in simple daily activities[11,18-20]. In extreme cases of these impairments there is a condition which is sometimes referred as "malignant parkinsonism", in which rapid disease progression, premature home nursing, depression and cognitive decline, increase the mortality risks[11].

There is no cure for PD and pharmacological treatment (of which levodopa is the long-term gold standard) still lacks significant effects on the previously described harmful symptoms. Indeed, postural instability, balance problems and gait disorders such as FoG and stride variability respond poorly to medication[9-11,21-24]. Even worse, many authors describe a "paradoxal effect" of medication[11,21,25] since two-thirds of falls occur when patients are under the effect of medication ("on" phase)[21]. This condition may be explained by the fact that dopaminergic treatment improves gait speed and general mobility (thus stimulating the patients to move), but not balance and postural instability[21,25]. Finally, some adverse effects of long-term pharmacological treatment, such as levodopa-induced dyskinesia and orthostatic hypotension, are very well known causes of falls[18,25,26].

Therefore, it is evident that the study of new approaches aimed to improve the motor aspects of PD patients is necessary. Nowadays, besides optimal medication, it is evident that physical therapy is the most effective non-pharmacological aid for patients with PD. It is not the aim of this paper to describe in detail the pathophysiology underlying each symptom, but putative mechanisms for each exercise protocol will be discussed in detail in the ensuing paragraphs.

EXERCISE GUIDELINES FOR PD

The most relevant guidelines for physical exercise in PD have been designed by Morris[27] and Keus *et al*[28] (Table 1).

External cues represent effective interventions aimed to improve motor performance, especially gait. Cognitive movement strategies refer to those mental techniques taught to patients in order to improve their everyday motor tasks. The key intervention is to teach the patient to subdivide complex and automated motor sequences in series of single, simple movements that must be performed in the correct, fixed order. This strategy is aimed to render motor performance as a conscious activity, thus avoiding dual-tasking[27,28] as well as bypassing the defective basal ganglia[28]. Balance training is another crucial point of the model, since it can prevent falls. Furthermore, improving physical capacity with aerobic training, strength and flexibility exercises may reduce symptoms as well as improve the patient's general well-being and quality of life.

In this setting, the individualization of training represents a crucial approach. Indeed, PD symptoms change, often with fluctuations, with the progression of the dis-

Table 1 Essential points in Parkinson's disease exercise therapy

	Effects
Cueing strategies	Improve motor performance (especially gait)
Cognitive movement strategies	Improve everyday motor tasks (walking, standing up, sitting down, dressing, *etc.*), and quality of life
Balance training	Prevent risk of falls, improve postural stability
Aerobic training	Improve physical capacity
Strength and flexibility	Improve general well-being and quality of life

ease. Therefore, physical therapists, in conjunction with the caregivers and neurologists, should adapt, modify and tailor the exercise program to the patient's specific needs. Regular assessments[28] should be performed in order to analyze the effects of both medications and physical therapy, and consequently adapt them to the patient's actual condition.

To achieve feasible improvements, a physical therapy protocol should be at least 8-10 wk long. Ideally, patients should train 3 d per week, 60-75 min per session. Moreover, it is also recommended to perform stretching exercises daily in order to reduce rigidity. Obviously, choosing an enjoyable and stimulating exercise protocol, thus promoting adherence and long-term compliance is of major importance when considering both the patient's prognosis and quality of life.

TRAINING STRATEGIES

Different training programs for patients with PD have been designed and evaluated.

Treadmill

Treadmill training is probably the most examined form of exercise for patients with PD.

Single-pulse Transcranial Magnetic Stimulation studies have shown abnormalities of the Cortical Silent Period (CSP duration) and other corticomotor excitability measures in patients with PD, reflecting greater corticomotor excitability in these patients. It is known that CSP is mainly mediated by gamma-aminobutyric acid (GABA)-B receptors, and abnormalities of GABAergic transmission are key points of the pathophysiology of movement disorders involving the basal ganglia. In addition, voluntary exercise may increase brain-derived neurotrophic factor (BDNF) levels thus enhancing neuronal function by promoting synaptogenesis and neurogenesis. Indeed, BDNF modulates the level of functional inhibition in an activity-dependent manner by regulating the number of GABAergic interneurons. While the role of BDNF in modulating GABA-mediated inhibitory transmission is not fully understood, conceivably the lengthening of CSP, related to high intensity exercise, may be related to an exercise-induced increase in BDNF[29].

The rationale behind the use of a treadmill in PD patients, proposes that the device works as an external cue[9,30-33] which bypasses the defective basal ganglia. In this setting patients do not need to pay attention to triggering[31,34,35], selecting and maintaining a motor sequence[35], and they can focus only on the motor action of walking[35]. Furthermore, as stated by Cakit *et al*[21], "a guiding principle in neurologic rehabilitation is that a skill will be improved if it is practiced"; therefore, walking on a treadmill can improve Parkinsonian gait since, as described by several authors[33,36,37], it can also generate motor learning. The need for improving gait and walking in people affected by PD is related to the achievement of performance improvement. In addition, gait training is necessary to reduce gait disorders (such as FoG, gait variability and festination) which directly cause reduced mobility, falls and injuries that can severely worsen the patient's health and quality of life. As described by Frenkel-Toledo *et al*[31], the rhythm imposed by the machine regularizes the patient's gait, with steps becoming longer and less variable. Considering that stride variability represents the main risk indicator of falls in the elderly[38], this improvement acquires even more significance. Indeed, different studies[21,36,39] show that treadmill training directly decreases risk and actual falls in subjects affected by PD.

As proven by 2 studies, even a single session of treadmill training generates improvements in the gait of PD patients. In the study of Pohl *et al*[32], patients tried 3 different interventions for gait treatment: Speed-Dependent Treadmill Training (SDTT, in which the patient walks 10 s at his/her maximum safe speed, and if that speed was sustainable it would have been increased after a short rest), Limited Progressive Treadmill Training (in which the belt speed was never increased over walking speed reported at baseline) and Conventional Gait Therapy (CGT, based on Proprioceptive Neuromuscular Fasciculation concepts). After just a 30-min training session, both of the treadmill protocols showed significant improvements in gait speed and stride length; also, double stance duration was decreased. Similarly, Bello *et al*[40] described improvements in gait speed and stride length after a single, 20-min treadmill session.

Several studies focused on the effects of a longer-term protocol in Parkinson's patients. Miyai *et al*[41] demonstrated that, in comparison with traditional physical therapy, a 4-wk body weight-supported treadmill training (BWSTT) program was effective on symptoms]as shown by the unified parkinson's disease rating scale (UPDRS)] as well as on gait speed. In another study of Miyai *et al*[37], patients received a 45-min BWSTT training 3 times a week for 1 mo, with belt speed progressively increased over the training period. Results showed higher gait speed and decreased number of steps over a 10 m distance, and effects lasted, respectively, at the 1- and 4-mo-follow up. Herman *et al*[36] demonstrated that an intensive treadmill protocol, with patients training 30 min, 4 times per week over a 6-wk period (with belt speed progressively increased), could generate improvements not only in gait parameters (speed, swing time variability), but also in balance, motor symptoms (as showed by the values of UPDRS-Ⅲ) and quality of life (assessed with Parkinson's Disease Questionnaire-39). Four studies evalu-

Table 2 Results of treadmill training

Pohl *et al*[32]	Single session 10 s at maximum safe speed	After 30 min training	Improvement in gait speed and stride length
Bello *et al*[40]	Single 20 min session		Improvement in gait speed and stride length
Miyai *et al*[41]	Body weight supported treadmill training	45-min session, 3 times/wk, for 4 wk	Decrease of symptoms (UPDRS scale) and improvements in gait speed
Miyai *et al*[37]	Body weight supported treadmill training	45-min session, 3 times/wk, for 4 wk with progressive increasing of belt speed	Improvement in gait speed, decreasing of steps number over a 10 m distance. The effects lasted over 1 and 4 mo of follow up
Herman *et al*[36]	Intensive treadmill protocol	30 min session, 4 times/wk, for 6 wk with progressive increasing of belt speed	Improvement in gait parameters (speed, swing time variability), balance, motor symptoms (UPDRS scale) and in quality of life
Cakit *et al*[21]	Speed dependent treadmill training	30 ± 5 min session, 8 wk	Improvement in tolerated speed and distance walked, in balance and reduction in fear of falls
Fisher *et al*[29]	Body weight supported treadmill training	3.0 metabolic equivalents session, 3 times/wk for 8 wk	Improvement in gait speed, step and stride length, hip and ankle joint excursion, and decrease cortico-motor excitability
Protas *et al*[39]	Walking in all 4 directions and step training	1 h session, 3 times/wk for 8 wk	Reduction of falls, improvement in gait speed and stride length, improvement in dynamic balance
Rose *et al*[42]	Skipping, sprinting, walking, running and jumping on a lower body positive-pressure antigravity treadmill + spatial cues	1 h session, 3 times/wk for 8 wk	Improvement in gait and functional capacity, better quality of life, improvement in motor symptoms (UPDRS scale)

UPDRS: Unified Parkinson's Disease Rating Scale.

ated the treadmill training protocol carried out over 8 wk. Cakit *et al*[21] trained their patients with a SDTT protocol and described improvements in tolerated speed and distance walked, improved balance and reduced fear of falls. Fisher *et al*[29] demonstrated that high-intensity BWSTT 3 times a week over an 8-wk period improved: gait speed, step and stride length, hip and ankle joint excursion, body weight distribution, and, as pointed by the authors, "importantly" in CSP length, which in fact translates into decreased corticomotor excitability. Protas *et al*[39] designed a specific treadmill protocol, in which patients walked in all 4 directions at a speed higher than normal gait; "step training" was also included, as the treadmill belt was suddenly switched off during the exercise. Results showed a substantial reduction in falls, increased gait speed and stride length as well as improved dynamic balance. In the latest study[42], different tasks were performed by patients, such as skipping, sprinting, walking, running, jumping, and also spatial cues where used, with the patient working on a lower body positive-pressure antigravity treadmill. The study by Rose *et al*[42] showed significant and promising results for this brand new, high intensity protocol: improvements affected the score for Movement Disorders Society- UPDR Scale, better quality of life (32% improvement at Parkinson's Disease Questionnaire-39), and increased gait and functional capacity [assessed with the 6-minute walk test (6MWT)].

Finally, it is mandatory to note that treadmill training may generate positive effects also on the central nervous system, namely, dopamine availability and corticomotor excitability, 2 central elements which are impaired by PD and cause motor disorders. Different interventions of treadmill training are shown in Table 2.

Cueing strategies

It is known that the normal footstep pattern is not lost in PD, rather there is a problem in activating the correct stepping response for a given context. Several studies demonstrated that the interaction between the basal ganglia and supplementary motor area (SMA) is disrupted during movement performance. The SMA normally prepares for a forthcoming predictable movement with a steady increase in neuronal activity during the premovement period. Once the external signal to move occurs, the neuronal activity in the SMA abruptly ceases. The basal ganglia discharge with brief bursts of phasic activity at the end of submovements performed in a sequence. This activity represents an internal cue which triggers the rapid drop in SMA neuronal activity. If the basal ganglia cue was absent or disturbed, as in PD, then it is possible that the SMA preparatory activity would be disturbed, leading to an abnormally executed movement[43].

As a consequence of the dopaminergic neuronal defection, the basal ganglia do not provide the correct cues for motor sequences to cortical motor areas (primary motor cortex, premotor cortex and supplementary motor area). This defect justifies the patient's inability to prepare and maintain the execution of complex and well-learned movements, *e.g.*, walking[9,22,34,43-45]. Specific gait impairments like FoG and festination are probably caused by an internal lack of rhythmic cues[9,14,46].

Conceivably, physical therapy should aim to compensate the physiologic defections at the base of the motor impairments[14,32,47]. In this setting, adapted exercise should be planned with the aim of reaching the cortical motor areas and bypassing the affected basal ganglia, in order to improve motor performance. External cues seem to be an effective method[14,27,28], and many authors demonstrated their efficacy. There are 3 types of cues which have been mainly studied: visual (transverse stripes placed on the walk path), auditory (music or simple beeps and sounds) and somatosensory (vibrations). Visual cues seems to facilitate Parkinsonian gait since they focus patient's concentration during the act of walking, thus making it a vol-

Table 3 Results of cueing training

Thaut *et al*[49]	Rhythmic auditory cues	Walking, stop-and-go, stair stepping listening to music	30 min/d for 3 wk	Improvement in gait speed, stride length and cadence
McIntosh *et al*[50]	Rhythmic auditory cues	Walking and stop-and-go listening to music	Single session	Improvement in gait speed, stride length and cadence
del Olmo *et al*[34]	Rhythmic auditory cues	Walking in different condition (with or without metronome cadence)	1 h/d, for 5 times/wk for 4 wk	Improvement in gait temporal stability
Azulay *et al*[48]	Dynamic and static visual cues	Walking on a 12-m walkway with parallel transversal white stripes with normal/stroboscopic lights	Single session	Increased velocity and stride length in the normal lights condition, suggesting the role of a specific visuo-motor pathway elicited by the moving cues
Rochester *et al*[35]	Auditory + visual cues	Little itinerary performed at home	Single session	Auditory cues improved performance (stride length) in the functional task, and a tendency for increased walking speed was noticed with both types of cue
Nieuwboer *et al*[23]	Visual, auditory or somato-sensory cues	Home-based cueing training program	30 mine session, 3 d/wk for 3 wk	Improvement in posture, gait speed, step length, reduction of FoG episodes and increased confidence in gait tasks
Frazzitta *et al*[9]	Treadmill + external cues	Progressive treadmill training with auditory (musical beats) and visual cues	20 min every day for 4 wk	Improvement in UPDRSIII, 6MWT, gait speed, stride cycle, FoG questionnaire

FoG: Freezing of Gait; 6MWT: 6-Minute walk test; UPDRS: Unified Parkinson's Disease Rating Scale.

untary task[11,48]. Auditory cues provide an external rhythm that bypasses the affected basal ganglia, thus improving gait performance, timing and cadence[9,7,33,49]. No information is given for the putative mechanism of somatosensory cues efficacy but the explanation may rationally be very similar to the auditory cues.

McIntosh and colleagues studied the effect of rhythmic auditory cues on the gait of PD patients. Their first study[49] was a 3-wk home-based gait training program: patients trained 30 min/d, with walking, stop-and-go and stair stepping performed while patients listened to music in a headset (music tempo was progressively increased during the experiment). There were significant improvements regarding gait speed, stride length and cadence. In the second protocol[50], auditory cues again facilitated subjects' gait, with significant improvements in gait speed (patients were able to walk at a speed higher than their maximal one), stride length and cadence. del Olmo *et al*[34] also assessed the effect of auditory cues on PD gait. Fifteen patients underwent gait training (which also included manual dual-tasking) with rhythmic sounds, 1 h per day, 5 d a month: auditory cues increased gait temporal stability, especially in those patients with greater impairment at baseline (a discovery that gains even more significance given that the level of gait impairment is proportional to PD severity).

Azulay *et al*[48] analyzed the effect of both dynamic and static visual cues on PD gait. Participants in the study session walked on a 12-m walkway with parallel transversal white stripes (visual cue) spaced at 45 cm intervals; patients walked first with normal lights on, and then with stroboscopic lights (used to suppress the perception of movement of the stripes). While performance significantly decreased due to the absence of dynamic cues (stroboscopic lights), patients increased velocity and stride length in the normal lights, suggesting the role of a specific visual-motor pathway elicited by the moving cues.

Most of the studies available in the literature compared the different type of cues. Rochester *et al*[35] examined the effect of both visual and auditory cues on a gait dual task performed at home: patients simply had to stand up, go to their kitchen, put 2 cups on a tray, walk back, leave the tray on a near table and sit down again. Auditory cues improved performance in the functional task (stride length), and a tendency for increased walking speed was noticed with both kinds of cue. The most complete study on external cues for PD is the RESCUE trial designed by Nieuwboer *et al*[23]. One hundred and fifty-three patients participated in this home-based cueing training program, in which patients had to perform gait tasks while receiving visual, auditory or somatosensory cues; training sessions lasted 30 min, 3 d per week, for 3 wk. The program generated many significant improvements in: posture and gait, gait speed, step length, reduction of FoG episodes (assessed through the FoG Questionnaire), and increased confidence in gait tasks (assessed with the Falls Efficacy Scale); importantly, 67% of patients preferred auditory cues, while the remaining 33% favored somatosensory cues.

Frazzitta *et al*[9] designed an experimental study, in which 40 patients who suffered FoG were divided into 2 groups: the first underwent progressive treadmill training with auditory (musical beats) and visual cues, while the second group followed a traditional protocol combining visual and auditory cues. Improvements were found in both groups for all the measured parameters (UPDRS-Ⅲ, 6MWT, gait speed, stride cycle, FoG questionnaire), showing the positive effect of both cues on motor performance. Table 3 summarizes the cueing strategies.

Improving physical capacity: Resistance training

Due to both central and peripheral causes, PD patients suffer muscle weakness (sarcopenia). Weakness in the lower limbs particularly affects basic daily tasks such as standing up from a chair and walking. Moreover, sarcopenia is considered a secondary cause of bradykinesia[51]. Muscle weakness is also strongly related to impaired balance, since it reduces the ability to respond to postural and balance modifications[51]. When considering this observation, its association with the risk of falls is straightforward. Moreover, the consequences of balance loss (falls, injuries, immobilization) may adversely contribute to the maintenance of bone mass density in the hip[52], increasing the risk of hip fracture.

In PD, the nigral dopaminergic deficit results in an increase in tonic inhibition of the thalamus and reduction in the excitatory drive to the motor cortex leading to disruption of cortical activation of the muscle. Conceivably, this disorder may result in impaired motor unit recruitment and could contribute both to bradykinesia and muscle weakness.

When considering these impairments, resistance training has been proposed as an efficient intervention aimed at reducing muscle weakness, bradykinesia, balance problems, as well as improving bone parameters, physical functioning, ADLs and the quality of life[52-54].

Several observations suggest that resistance training may facilitate functional plasticity in the cortex and muscle activation patterns. For this reason, in PD patients, this kind of training could be therapeutic to modify the activity in the cortex and basal ganglia, as well as the connectivity between and within these structures. Indeed, several studies showed that resistance training resulted in an increase in electromyographic activation, possibly explained by improved motor unit recruitment, increased firing rate, and better synchronization[54].

The first resistance training intervention for PD was evaluated by Scandalis *et al*[55] in 2001. Their protocol included exercises for quadriceps, hamstring, calves and abdominal muscles. Training sessions took place twice a week for 8 wk. The authors described improvements in strength, gait speed and stride length.

Several studies assessed the effects of progressive resistance exercise (PRE), which uses a high resistance load progressively increasing during the period of training. In the study of Schilling *et al*[56], patients performed resistance training for lower limb muscles twice a week for 8 wk: as expected, leg strength was significantly improved. Hirsch *et al*[57] evaluated the efficacy of PRE for balance parameters. Patients were assigned to 2 different groups: while group 2 simply performed balance exercises, group 1 trained balance plus high-intensity PRE for knee and ankle muscles. Sessions took place 3 times per week on non consecutive days for 10 wk. Both groups improved balance, strength and reduced falls, but the group treated with PRE and balance training performed better and their results were greater. PRE, as shown by the study of Hass *et al*[53], may also improve typical walking impairment of PD such as gait initiation. Their 10-wk PRE program, which focused mainly on lower limb muscles, generated improvements both in postural adjustment and spatiotemporal parameters during gait initiation, and consequently muscle strength. O'Brien *et al*[58] focused more on the patient's perception of a PRE protocol. After 20 sessions (performed twice weekly), the researchers interviewed the participants. Patients reported physical and psychological benefits from the PRE program and expressed positive feedback as well as the intention to attend future programs.

Another very efficient strengthening method is eccentric training. The advantage of this type of conditioning lies in the fact that eccentric contraction can generate high forces and perform more work (and thus increase strength quicker) while requiring less energy when compared with concentric contraction, thus reducing fatigue. Dibble and colleagues rightly speculated on this assumption, and after having assessed the safety and feasibility of high-intensity eccentric training for PD patients, they evaluated its benefits. The protocol was the same for their 2 studies[59,60]: 2 groups (experimental and control) underwent the same exercise program, which included calisthenics, treadmill, balance training and conditioning 3 times per week for 12 wk; the only difference regarded lower muscle conditioning, for which the experimental group performed high-intensity eccentric exercise, while the control group underwent traditional strength exercises. Convincingly, in both studies, the experimental group results showed significant improvement in all tested parameters, namely: muscle hypertrophy, strength, mobility, bradykinesia, quality of life and UPDRS score (Table 4).

Balance training

Degeneration of the basal ganglia involves several physiological systems essential for balance control. Dysfunction of the basal ganglia influences the ability of central nervous system to translate sensory information (somatosensory, visual and vestibular) into a single reference frame, which is important for assessment of limb and body position in relation to the environment. Deficient motor regulation in PD manifests as poor inter-segmental coordination, difficulties adopting postural synergies and delayed adjustment in motor commands when moving from one task to another. To be specific, balance training needs to target functions, or impairments, of balance control associated with PD symptoms[61].

As already discussed, postural instability is probably the symptom with the lower response to pharmacotherapy[10,11,24]. A reduced ability to adapt to balance changes and perturbations automatically increases the risk of falling as well as the consequent injuries such as hip fracture[11]. The need for an integrative therapy that would ameliorate the PD patient's response is evident. With this aim, exercise interventions focused specifically on balance have been developed and evaluated.

Tai Chi, a Chinese martial arts discipline, has been proposed as a useful exercise program for PD patients since it encompasses techniques such as weight shifting, slow and controlled movement, trunk rotations, different stances, multidirectional stepping, and maintenance of postures that directly target PD balance and gait[62,63]. Many authors evaluated the effect of a Tai Chi program in PD patients (Table 5).

Table 4 Effects of resistance training

Scandalis *et al*[55]	Exercises for quadriceps, hamstring, calves and also abdominal muscles	2 times/wk for 8 wk	Improved strength, gait speed and stride length
Schilling *et al*[56]	PRE for lower limbs muscles	2 times/wk for 8 wk	Improved leg strength
Hirsch *et al*[57]	Balance exercise plus high-intensity PRE for knee and ankle muscles	3 times/wk for 10 wk	Improved balance, strength and reduced falls
Hass *et al*[53]	PRE program, focused mainly on lower limbs muscles	2 times/wk for 10 wk	Improvement in both postural adjustment and spatiotemporal parameters during gait initiation (protective effect on falls), and improved muscle strength
O'Brien *et al*[58]	PRE	2 times/wk for 10 wk	Physical and psychological benefits
Dibble *et al*[59,60]	High Intensity eccentric training exercise program for lower muscles which included calisthenics, treadmill, balance training and conditioning	3 times/wk for 12 wk	Improvement in muscle hypertrophy, strength, mobility, bradykinesia, Quality of life and UPDRS score

PRE: Progressive resistance exercise; UPDRS: Unified Parkinson's Disease Rating Scale.

Table 5 Effects of balance training

Li *et al*[62]	Tai Chi *vs* resistance training and stretching	60 min sessions 2 times/wk for 24 wk	Tai Chi group improved their postural stability significantly more than both the other groups; stride length and velocity, strength, timed up-and-go test, functional reaching and UPDRS-Ⅲ score were significantly higher in the Tai Chi group when compared with stretching; Tai Chi improved stride length, reduced rate of falls at follow up and, as shown by the posturography, there was a reduction of deviations of movement, which the authors suggest to be a reduction of dyskinesia
Hackney *et al*[63]	Tai Chi program	60 min session for 10-13 wk (total 20 session)	Improved global and motor symptoms (UPDRS and UPDRS-Ⅲ), balance, tandem stance, one leg stance, backward walking, and gait endurance (6MWT)
Schmitz-Hubsch *et al*[24]	Qi Gong program	90 min weekly training for 2 mo	Intervention showed a "stabilizing effect on PD symptoms": specifically, postural instability improved, as well as UPDRS-Ⅲ score. Also, autonomic dysfunction (constipation and pain) decreased, and during physiotherapy sleep disturbances and daytime sleepiness diminished

6MWT: 6-Minute Walk Test; UPDRS: Unified Parkinson's Disease Rating Scale.

Li *et al*[62] compared the effect of a Tai Chi program with resistance training and stretching (used as control). Subjects in each group trained twice a week for 6 mo. The Tai Chi training program was particularly designed for balance and gait training. Results showed that the Tai Chi group improved their postural stability significantly more than either of the other groups. Stride length and velocity, strength, timed up-and-go test (which evaluates static and dynamic balance and gait), functional reaching and UPDRS-Ⅲ score were significantly higher in the Tai Chi group when compared to stretching. Furthermore, 2 findings are of particular significance: the rate of falls at follow-up was lower in Tai Chi group, and, as shown by posturography, there was a reduction in deviations of movement as a result of reduced dyskinesia. Hackney and Earhart[63] evaluated the effect of 20 lessons (over 13 wk) of Tai Chi. Patients improved their global and motor symptomatology (UPDRS and UPDRS-Ⅲ), balance, tandem stance, one leg stance, backward walking, and gait endurance (6MWT). In addition, "patients reported enjoyment in the protocol and physical and psychological improvements".

Schmitz-Hübsch *et al*[24] determined the effect of another Chinese exercise therapy, Qi Gong (which includes posture, breathing techniques and attention strategies). Their 2-mo intervention showed a "stabilizing effect on PD symptoms": specifically, postural instability improved, as well as UPDRS-Ⅲ score. Moreover, autonomic dysfunction (constipation and pain) decreased, and during physiotherapy sleep disturbances and daytime sleepiness diminished.

Finally, worthy of mention is the innovative, balance-specific program designed and assessed by Esculier *et al*[64]. The researchers submitted PD patients to a home-based program using Nintendo Wii Fit with balance board. The device focuses on balance tasks and visual feedback of movements is constantly provided, together with auditory and proprioceptive cues. Additionally, the console and the games seemed to be very enjoyable and motivating for the patient. In this study, patients trained for 40 min, 3 d a week, for 6 wk. Results were meaningful, with improvements in static and dynamic balance, gait, functional strength of the lower limbs, one-leg stance time and reduced fear of falling.

Dance

Due to its nature, dance appears to be one of the most effective exercise protocols for PD patients. Indeed, as discussed by Dr. Earhart, all the recommended key areas[28] for physical therapy in PD are met[65]. Music serves as an

Table 6 Results of dance training

Hackney *et al*[66,69]	Tango	60 min session, 2 d/wk for 10 wk (total 20 sessions)	Decreased UPDRS score, improved balance, reduced fear of falling. Trends of improvement for FoG and at Timed Up and Go test
Hackney *et al*[67]	Tango *vs* Foxtrot	60 min session, 2 d/wk for 13 wk (total 20 session)	Both types of dance improved gait speed, balance, backward stride length, cardiovascular function and symptoms (UPDRS); only Tango generated improvements for FoG
Duncan *et al*[70]	Tango in patients "off medication"	60 min session, 2 d/wk for 12 mo	Bradykinesia and motor symptoms severity (assessed with MDS-UPDRS-Ⅲ) were reduced; gait speed, balance, dual task walking speed and upper extremity function all improved; rigidity, FoG and gait endurance remained stable, but in the control group they progressively worsened, ("braking" effect on PD progression)

PD: Parkinson's disease; UPDRS: Unified Parkinson's Disease Rating Scale.

external cue, thus facilitating motor performance; specific movement strategies are taught; balance is trained, especially in its dynamic form. Although not directly addressed, dance may improve strength and flexibility. Finally, when trained at the right intensity, dance promotes cardiovascular functioning as an optimal form of aerobic exercise. This discipline may be considered an ideal choice among all adapted physiotherapy programs, since it addresses specific Parkinsonian impairments such as walking backward, turning and multitasking. Furthermore, the Tango appears to be the most Parkinson-specific discipline, since the basic step used is walking; frequent stops and starts are common (thus challenging the patient's start hesitation); directional changes and turning are included, and dancing at different rhythms and speeds addresses bradykinesia. Furthermore, some techniques like stepping or tapping the partner's feet, crossing feet, and shifting the body weight from one leg to another, are very similar to strategies used in rehabilitation of FoG[65-68].

Researchers have evaluated 2 dance discipline so far: waltz/foxtrot and, of course, Tango. In 2 studies, Hackney *et al*[66,67] reported that 20 Tango sessions diminished symptoms, improved balance, and reduced fear of falling. Moreover, trends of improvement in FoG and the Timed Up and Go test (which measures static and dynamic balance) were found. Significantly, in both studies, half of the patients decided to participate in additional Tango sessions; an unequivocal sign of the patients' enjoyment of the protocol. Hackney and Earhart[68,69] also tried to evaluate the difference between partnered and non-partnered dance, since "the partner's importance and influence remains equivocal". Again, 20 Tango sessions generated improvements in gait, balance and functional mobility. No difference were found between the 2 groups, but the authors suggested that, for safety reasons, a partner may be useful for patients in the later stages of PD since the partner acts as a balance support. Duncan and Earhart[70] reported a 12-mo study, in which 52 patients assigned to a Tango group trained twice a week for 1 h. In this study, patients were tested only off medication "to ultimately determine whether exercise may be disease modifying". Significantly, patients benefitted greatly from the long-term protocol: motor symptom severity (assessed with MDS-UPDRS-Ⅲ) was reduced, as well as bradykinesia. Gait speed, balance, dual task walking speed and upper extremity function all improved. Rigidity, FoG and gait endurance remained stable, but in the control group they progressively worsened. These results confirm how exercise can have a "braking" effect on PD progression (Table 6).

CONCLUSION

With the exception of tremors, tailored physical activity has shown to improve all the prominent motor symptoms of PD patients including those harmful disturbances such as FoG, stride variability and balance impairments. Furthermore, it has been clearly demonstrated that each of the different types of physical activity resulted in a better quality of life. It is therefore reasonable to state that tailored physical activity could be considered as a valid intervention to be included in the therapeutic program of PD patients.

Each training protocol has specific technical characteristics targeting different PD deficiencies. Studies applying treadmill training described improvements in patient gait in quick FoG, festinating gait and balance loss. Moreover, in several studies researchers reported improvements in UPDRS, functional capacity and quality of life.

The use of external cues to bypass the affected basal ganglia also showed promising results. Most of the spatiotemporal walking parameters, such as gait speed, stride variability, cadence, and step length improved after the use of external cues. Nieuwboer *et al*[23] also reported that external cues reduced FoG events and improved patient confidence when considering the risk of falls.

Dancing is an alternative program which seems promising and efficient for the treatment of PD symptoms. Specific Parkinsonian patterns such as bradykinesia, dynamic balance, backward walking, turning and multitasking are directly targeted with dance. In addition, the Argentinian Tango can be labeled as a "Parkinson-specific discipline". The effect of the dance relies on its social and enjoyable nature, which stimulates patient compliance for longer periods, thus potentially enhancing the positive effects of the program and expanding its beneficial effect to the emotional and psychological sphere.

The beneficial effects of resistance training are not limited to muscle hypertrophy and improved strength. Indeed, significant improvements have been described when considering balance, bradykinesia, gait, mobility and quality of life. Balance-specific protocols, mainly Tai Chi, resulted in significant improvements when considering gait, balance and posture, finally leading to a reduced risk of falls.

As discussed by most of the authors cited, the main limit of adapted physical therapy in PD patients relies in the lack of a standardized therapeutic protocol for common use. Even if future investigations should address this issue, we strongly support the adoption of an individualized approach. Indeed, PD is a very complex disease, with different and fluctuating symptoms which affect the patients almost uniquely. Consequently, a physical therapy protocol should not be standardized, but tailored and individualized to the patient's personal condition in order to target his/her precise motor impairments.

Consequently, it seems crucial to educate the patient early about the benefit of an active lifestyle, including regular participation in an specific physiotherapy program, in order to promote independence, physical functionality and quality of life. Patients should choose an enjoyable program in order to promote adherence. Based on the available experience, training sessions should last 60-75 min at least 3 times per week, especially in the earlier stages. It seems to be useful to perform stretching exercises daily in order to reduce rigidity and improve joint and muscular capability.

REFERENCES

1 **Berardelli A**, Rothwell JC, Thompson PD, Hallett M. Pathophysiology of bradykinesia in Parkinson's disease. *Brain* 2001; **124**: 2131-2146 [PMID: 11673316 DOI: 10.1093/brain/124.11.2131]

2 UKPDSBB Clinical Diagnostic Criteria, United Kingdom Parkinson's Disease Society Brain Bank

3 **Helmich RC**, Hallett M, Deuschl G, Toni I, Bloem BR. Cerebral causes and consequences of parkinsonian resting tremor: a tale of two circuits? *Brain* 2012; **135**: 3206-3226 [PMID: 22382359 DOI: 10.1093/brain/aws023]

4 European Parkinson's Disease Association [no date] 'Rigidity and Parkinson's' [online]. Available from: URL: http://www.epda.eu.com/en/parkinsons/in-depth/pdsymptoms/rigidity/rigidity-and-parkinsons/

5 **Kim SD**, Allen NE, Canning CG, Fung VS. Postural instability in patients with Parkinson's disease. Epidemiology, pathophysiology and management. *CNS Drugs* 2013; **27**: 97-112 [PMID: 23076544 DOI: 10.1007/s40263-012-0012-3]

6 National Parkinson Foundation [no date] 'Parkinson's Toolkit: Postural Instability' [online]. Available from: URL: http://www.toolkit.parkinson.org/content/postural-instability

7 **Jiang Y**, Norman KE. Effects of visual and auditory cues on gait initiation in people with Parkinson's disease. *Clin Rehabil* 2006; **20**: 36-45 [PMID: 16502748 DOI: 10.1191/0269215506cr925oa]

8 **Grabli D**, Karachi C, Welter ML, Lau B, Hirsch EC, Vidailhet M, François C. Normal and pathological gait: what we learn from Parkinson's disease. *J Neurol Neurosurg Psychiatry* 2012; **83**: 979-985 [PMID: 22752693 DOI: 10.1136/jnnp-2012-302263]

9 **Frazzitta G**, Maestri R, Uccellini D, Bertotti G, Abelli P. Rehabilitation treatment of gait in patients with Parkinson's disease with freezing: a comparison between two physical therapy protocols using visual and auditory cues with or without treadmill training. *Mov Disord* 2009; **24**: 1139-1143 [PMID: 19370729 DOI: 10.1002/mds.22491]

10 **Grimbergen YA**, Munneke M, Bloem BR. Falls in Parkinson's disease. *Curr Opin Neurol* 2004; **17**: 405-415 [PMID: 15247535 DOI: 10.1097/01.wco.0000137530.68867.93]

11 **Bloem BR**, Hausdorff JM, Visser JE, Giladi N. Falls and freezing of gait in Parkinson's disease: a review of two interconnected, episodic phenomena. *Mov Disord* 2004; **19**: 871-884 [PMID: 15300651 DOI: 10.1002/mds.20115]

12 **Blonder LX**, Slevin JT. Emotional dysfunction in Parkinson's disease. *Behav Neurol* 2011; **24**: 201-217 [PMID: 21876260 DOI: 10.3233/BEN-2011-0329]

13 **Rahman S**, Griffin HJ, Quinn NP, Jahanshahi M. Quality of life in Parkinson's disease: the relative importance of the symptoms. *Mov Disord* 2008; **23**: 1428-1434 [PMID: 18543333 DOI: 10.1002/mds.21667]

14 **Rubinstein TC**, Giladi N, Hausdorff JM. The power of cueing to circumvent dopamine deficits: a review of physical therapy treatment of gait disturbances in Parkinson's disease. *Mov Disord* 2002; **17**: 1148-1160 [PMID: 12465051 DOI: 10.1002/mds.10259]

15 **Hausdorff JM**. Gait variability: methods, modeling and meaning. *J Neuroeng Rehabil* 2005; **2**: 19 [PMID: 16033650 DOI: 10.1186/1743-0003-2-19]

16 **Bloem BR,** Steijns JAG, Smits-Engelsman BCM. An update on falls. *Curr Opin Neurol* 2003; **16:** 15–26 [DOI: 10.1097/00019052-200302000-00003]

17 **Coughlin L**, Templeton J. Hip fractures in patients with Parkinson's disease. *Clin Orthop Relat Res* 1980; **(148)**: 192-195 [PMID: 7379394]

18 **Michałowska M**, Fiszer U, Krygowska-Wajs A, Owczarek K. Falls in Parkinson's disease. Causes and impact on patients' quality of life. *Funct Neurol* 2005; **20**: 163-168 [PMID: 16483454]

19 **Morris ME**. Locomotor training in people with Parkinson disease. *Phys Ther* 2006; **86**: 1426-1435 [PMID: 17012646 DOI: 10.2522/ptj.20050277]

20 **Wielinski CL**, Erickson-Davis C, Wichmann R, Walde-Douglas M, Parashos SA. Falls and injuries resulting from falls among patients with Parkinson's disease and other parkinsonian syndromes. *Mov Disord* 2005; **20**: 410-415 [PMID: 15580552 DOI: 10.1002/mds.20347]

21 **Cakit BD**, Saracoglu M, Genc H, Erdem HR, Inan L. The effects of incremental speed-dependent treadmill training on postural instability and fear of falling in Parkinson's disease. *Clin Rehabil* 2007; **21**: 698-705 [PMID: 17846069 DOI: 10.1177/0269215507077269]

22 **Hausdorff JM**, Cudkowicz ME, Firtion R, Wei JY, Goldberger AL. Gait variability and basal ganglia disorders: stride-to-stride variations of gait cycle timing in Parkinson's disease and Huntington's disease. *Mov Disord* 1998; **13**: 428-437 [PMID: 9613733]

23 **Nieuwboer A**, Kwakkel G, Rochester L, Jones D, van Wegen E, Willems AM, Chavret F, Hetherington V, Baker K, Lim I. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. *J Neurol Neurosurg Psychiatry* 2007; **78**: 134-140 [PMID: 17229744 DOI: 10.1136/jnnp.200X.097923]

24 **Schmitz-Hübsch T**, Pyfer D, Kielwein K, Fimmers R, Klockgether T, Wüllner U. Qigong exercise for the symptoms of Parkinson's disease: a randomized, controlled pilot study. *Mov Disord* 2006; **21**: 543-548 [PMID: 16229022 DOI: 10.1002/mds.20705]

25 **Bloem BR**, Grimbergen YA, Cramer M, Willemsen M, Zwinderman AH. Prospective assessment of falls in Parkinson's disease. *J Neurol* 2001; **248**: 950-958 [PMID: 11757958 DOI: 10.1007/s004150170047]

26 **Earhart GM**, Falvo MJ. Parkinson disease and exercise. *Compr Physiol* 2013; **3**: 833-848 [PMID: 23720332 DOI: 10.1002/cphy.c100047]

27 **Morris ME**. Movement disorders in people with Parkinson disease: a model for physical therapy. *Phys Ther* 2000; **80**: 578-597 [PMID: 10842411]

28 **Keus SH**, Bloem BR, Hendriks EJ, Bredero-Cohen AB, Munneke M. Evidence-based analysis of physical therapy in Parkinson's disease with recommendations for practice and research. *Mov Disord* 2007; **22**: 451-460; quiz 600 [PMID: 17133526 DOI: 10.1002/mds.21244]
29 **Fisher BE**, Wu AD, Salem GJ, Song J, Lin CH, Yip J, Cen S, Gordon J, Jakowec M, Petzinger G. The effect of exercise training in improving motor performance and corticomotor excitability in people with early Parkinson's disease. *Arch Phys Med Rehabil* 2008; **89**: 1221-1229 [PMID: 18534554 DOI: 10.1016/j.apmr.2008.01.013]
30 **Filippin NT**, da Costa PH, Mattioli R. Effects of treadmill-walking training with additional body load on quality of life in subjects with Parkinson's disease. *Rev Bras Fisioter* 2010; **14**: 344-350 [PMID: 20949235 DOI: 10.1590/S1413-35552010005000016]
31 **Frenkel-Toledo S**, Giladi N, Peretz C, Herman T, Gruendlinger L, Hausdorff JM. Treadmill walking as an external pacemaker to improve gait rhythm and stability in Parkinson's disease. *Mov Disord* 2005; **20**: 1109-1114 [PMID: 15929090 DOI: 10.1002/mds.20507]
32 **Pohl M**, Rockstroh G, Rückriem S, Mrass G, Mehrholz J. Immediate effects of speed-dependent treadmill training on gait parameters in early Parkinson's disease. *Arch Phys Med Rehabil* 2003; **84**: 1760-1766 [PMID: 14669180 DOI: 10.1016/S0003-9993(03)00433-7]
33 **Herman T**, Giladi N, Hausdorff JM. Treadmill training for the treatment of gait disturbances in people with Parkinson's disease: a mini-review. *J Neural Transm* 2009; **116**: 307-318 [PMID: 18982238 DOI: 10.1007/s00702-008-0139-z]
34 **del Olmo MF**, Cudeiro J. Temporal variability of gait in Parkinson disease: effects of a rehabilitation programme based on rhythmic sound cues. *Parkinsonism Relat Disord* 2005; **11**: 25-33 [PMID: 15619459 DOI: 10.1016/j.parkreldis.2004.09.002]
35 **Rochester L**, Hetherington V, Jones D, Nieuwboer A, Willems AM, Kwakkel G, Van Wegen E. The effect of external rhythmic cues (auditory and visual) on walking during a functional task in homes of people with Parkinson's disease. *Arch Phys Med Rehabil* 2005; **86**: 999-1006 [PMID: 15895348 DOI: 10.1016/j.apmr.2004.10.040]
36 **Herman T**, Giladi N, Gruendlinger L, Hausdorff JM. Six weeks of intensive treadmill training improves gait and quality of life in patients with Parkinson's disease: a pilot study. *Arch Phys Med Rehabil* 2007; **88**: 1154-1158 [PMID: 17826461 DOI: 10.1016/j.apmr.2007.05.015]
37 **Miyai I**, Fujimoto Y, Yamamoto H, Ueda Y, Saito T, Nozaki S, Kang J. Long-term effect of body weight-supported treadmill training in Parkinson's disease: a randomized controlled trial. *Arch Phys Med Rehabil* 2002; **83**: 1370-1373 [PMID: 12370870 DOI: 10.1053/apmr.2002.34603]
38 **Maki BE**. Gait changes in older adults: predictors of falls or indicators of fear. *J Am Geriatr Soc* 1997; **45**: 313-320 [PMID: 9063277]
39 **Protas EJ**, Mitchell K, Williams A, Qureshy H, Caroline K, Lai EC. Gait and step training to reduce falls in Parkinson's disease. *NeuroRehabilitation* 2005; **20**: 183-190 [PMID: 16340099]
40 **Bello O**, Sanchez JA, Fernandez-del-Olmo M. Treadmill walking in Parkinson's disease patients: adaptation and generalization effect. *Mov Disord* 2008; **23**: 1243-1249 [PMID: 18464281 DOI: 10.1002/mds.22069]
41 **Miyai I**, Fujimoto Y, Ueda Y, Yamamoto H, Nozaki S, Saito T, Kang J. Treadmill training with body weight support: its effect on Parkinson's disease. *Arch Phys Med Rehabil* 2000; **81**: 849-852 [PMID: 10895994 DOI: 10.1053/apmr.2000.4439]
42 **Rose MH**, Løkkegaard A, Sonne-Holm S, Jensen BR. Improved clinical status, quality of life, and walking capacity in Parkinson's disease after body weight-supported high-intensity locomotor training. *Arch Phys Med Rehabil* 2013; **94**: 687-692 [PMID: 23187043 DOI: 10.1016/j.apmr.2012.11.025]
43 **Morris ME**, Iansek R, Matyas TA, Summers JJ. Stride length regulation in Parkinson's disease. Normalization strategies and underlying mechanisms. *Brain* 1996; **119** (Pt 2): 551-568 [PMID: 8800948 DOI: 10.1093/brain/119.2.551]
44 **Cunnington R**, Iansek R, Bradshaw JL, Phillips JG. Movement-related potentials in Parkinson's disease. Presence and predictability of temporal and spatial cues. *Brain* 1995; **118** (Pt 4): 935-950 [PMID: 7655889 DOI: 10.1093/brain/118.4.935]
45 **Robertson C**, Flowers KA. Motor set in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1990; **53**: 583-592 [PMID: 2391523]
46 **Giladi N**, McDermott MP, Fahn S, Przedborski S, Jankovic J, Stern M, Tanner C. Freezing of gait in PD: prospective assessment in the DATATOP cohort. *Neurology* 2001; **56**: 1712-1721 [PMID: 11425939 DOI: 10.1212/WNL.56.12.1712]
47 **Marchese R**, Diverio M, Zucchi F, Lentino C, Abbruzzese G. The role of sensory cues in the rehabilitation of parkinsonian patients: a comparison of two physical therapy protocols. *Mov Disord* 2000; **15**: 879-883 [PMID: 11009194]
48 **Azulay JP**, Mesure S, Amblard B, Blin O, Sangla I, Pouget J. Visual control of locomotion in Parkinson's disease. *Brain* 1999; **122** (Pt 1): 111-120 [PMID: 10050899 DOI: 10.1093/brain/122.1.111]
49 **Thaut MH**, McIntosh GC, Rice RR, Miller RA, Rathbun J, Brault JM. Rhythmic auditory stimulation in gait training for Parkinson's disease patients. *Mov Disord* 1996; **11**: 193-200 [PMID: 8684391]
50 **McIntosh GC**, Brown SH, Rice RR, Thaut MH. Rhythmic auditory-motor facilitation of gait patterns in patients with Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1997; **62**: 22-26 [PMID: 9010395 DOI: 10.1136/jnnp.62.1.22]
51 **Toole T**, Park S, Hirsch MA, Lehman DA, Maitland CG. The multicomponent nature of equilibrium in persons with parkinsonism: a regression approach. *J Neural Transm* 1996; **103**: 561-580 [PMID: 8811502]
52 **Falvo MJ**, Schilling BK, Earhart GM. Parkinson's disease and resistive exercise: rationale, review, and recommendations. *Mov Disord* 2008; **23**: 1-11 [PMID: 17894327 DOI: 10.1002/mds.21690]
53 **Hass CJ**, Buckley TA, Pitsikoulis C, Barthelemy EJ. Progressive resistance training improves gait initiation in individuals with Parkinson's disease. *Gait Posture* 2012; **35**: 669-673 [PMID: 22266107 DOI: 10.1016/j.gaitpost.2011.12.022]
54 **David FJ**, Rafferty MR, Robichaud JA, Prodoehl J, Kohrt WM, Vaillancourt DE, Corcos DM. Progressive resistance exercise and Parkinson's disease: a review of potential mechanisms. *Parkinsons Dis* 2012; **2012**: 124527 [PMID: 22191068 DOI: 10.1155/2012/124527]
55 **Scandalis TA**, Bosak A, Berliner JC, Helman LL, Wells MR. Resistance training and gait function in patients with Parkinson's disease. *Am J Phys Med Rehabil* 2001; **80**: 38-43; quiz 44-46 [PMID: 11138953]
56 **Schilling BK**, Pfeiffer RF, Ledoux MS, Karlage RE, Bloomer RJ, Falvo MJ. Effects of moderate-volume, high-load lower-body resistance training on strength and function in persons with Parkinson's disease: a pilot study. *Parkinsons Dis* 2010; **2010**: 824734 [PMID: 20976096 DOI: 10.4061/2010/824734]
57 **Hirsch MA**, Toole T, Maitland CG, Rider RA. The effects of balance training and high-intensity resistance training on persons with idiopathic Parkinson's disease. *Arch Phys Med Rehabil* 2003; **84**: 1109-1117 [PMID: 12917847 DOI: 10.1016/S0003-9993(03)00046-7]
58 **O'Brien M**, Dodd KJ, Bilney B. A qualitative analysis of a progressive resistance exercise programme for people with Parkinson's disease. *Disabil Rehabil* 2008; **30**: 1350-1357 [PMID: 18850350 DOI: 10.1080/09638280701614546]
59 **Dibble LE**, Hale TF, Marcus RL, Droge J, Gerber JP, LaStayo PC. High-intensity resistance training amplifies muscle hypertrophy and functional gains in persons with Parkinson' s disease. *Mov Disord* 2006; **21**: 1444-1452 [PMID: 16773643 DOI: 10.1002/mds.20997]
60 **Dibble LE**, Hale T, Marcus RL, Gerber JP, Lastayo PC. The safety and feasibility of high-force eccentric resistance ex-

ercise in persons with Parkinson's disease. *Arch Phys Med Rehabil* 2006; **87**: 1280-1282 [PMID: 16935068 DOI: 10.1016/j.apmr.2006.05.016]

61 **Conradsson D**, Löfgren N, Ståhle A, Hagströmer M, Franzén E. A novel conceptual framework for balance training in Parkinson's disease-study protocol for a randomised controlled trial. *BMC Neurol* 2012; **12**: 111 [PMID: 23017069 DOI: 10.1186/1471-2377-12-111]

62 **Li F**, Harmer P, Fitzgerald K, Eckstrom E, Stock R, Galver J, Maddalozzo G, Batya SS. Tai chi and postural stability in patients with Parkinson's disease. *N Engl J Med* 2012; **366**: 511-519 [PMID: 22316445 DOI: 10.1056/NEJMoa1107911]

63 **Hackney ME**, Earhart GM. Tai Chi improves balance and mobility in people with Parkinson disease. *Gait Posture* 2008; **28**: 456-460 [PMID: 18378456 DOI: 10.1016/j.gaitpost.2008.02.005]

64 **Esculier JF**, Vaudrin J, Bériault P, Gagnon K, Tremblay LE. Home-based balance training programme using Wii Fit with balance board for Parkinsons's disease: a pilot study. *J Rehabil Med* 2012; **44**: 144-150 [PMID: 22266676 DOI: 10.2340/16501977-0922]

65 **Earhart GM**. Dance as Therapy in Individuals with Parkinson Disease. *Eur J Phys Rehab Med* 2009; **45**: 231–238

66 **Hackney ME**, Kantorovich S, Levin R, Earhart GM. Effects of tango on functional mobility in Parkinson's disease: a preliminary study. *J Neurol Phys Ther* 2007; **31**: 173-179 [PMID: 18172414 DOI: 10.1097/NPT.0b013e31815ce78b]

67 **Hackney ME**, Earhart GM. Effects of dance on movement control in Parkinson's disease: a comparison of Argentine tango and American ballroom. *J Rehabil Med* 2009; **41**: 475-481 [PMID: 19479161 DOI: 10.2340/16501977-0362]

68 **Hackney ME**, Earhart GM. Effects of dance on gait and balance in Parkinson's disease: a comparison of partnered and nonpartnered dance movement. *Neurorehabil Neural Repair* 2010; **24**: 384-392 [PMID: 20008820 DOI: 10.1177/1545968309353329]

69 **Hackney ME**, Kantorovich S, Earhart GM. A Study on the Effects of Argentine Tango as a Form of Partnered Dance for those with Parkinson Disease and the Healthy Elderly. *Am J Dance Ther* 2007; **29**: 109-127 [DOI: 10.1007/s10465-007-9039-2]

70 **Duncan RP**, Earhart GM. Randomized controlled trial of community-based dancing to modify disease progression in Parkinson disease. *Neurorehabil Neural Repair* 2012; **26**: 132-143 [PMID: 21959675 DOI: 10.1177/1545968311421614]

P- Reviewer: Fang Q, Puntel RL **S- Editor**: Song XX
L- Editor: Cant MR **E- Editor**: Wu HL

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com