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Lessons and challenges of trials involving ancillary therapies for Parkinson's disease

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Abstract
Progressive impairment, particularly related to gait, postural control and cognitive decline, are not effectively treated by the current pharmacological and surgical management of Parkinson's disease (PD). This has led many patients and treating physicians to explore concomitant therapeutic modalities such as aerobic exercise, resistance training, physical therapy, massage, dance and music therapy, tai chi and others to aid in reducing symptomatology and improving patient quality of life.

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Chapter 32

Lessons and challenges of trials involving ancillary therapies for the management of Parkinson's disease

Chris J. Hass, Elizabeth L. Stegemöller, Madeleine E. Hackney and Joe R. Nocera

Introduction

Progressive impairment, particularly related to gait, postural control and cognitive decline, are not effectively treated by the current pharmacological and surgical management of Parkinson's disease (PD). This has led many patients and treating physicians to explore concomitant therapeutic modalities such as aerobic exercise, resistance training, physical therapy, massage, dance and music therapy, tai chi and others to aid in reducing symptomatology and improving patient quality of life. Over the last 15 years, the research community has also experienced an explosion of efforts into studying the efficacy of these treatments on motor and nonmotor symptoms, as well as their ability to enhance patient well-being. For example, in the decade preceding 2004, there were roughly 10–15 papers published per year related to exercise in PD. From 2004 to 2013, this number skyrocketed to an average of 50 papers per year. With this progression of efforts, the quality and ingenuity of treatments have expanded from small pilot studies of walking and weight training to large multicenter trials investigating robotic-assisted cycling and exercises paired with brain-stimulation techniques. In general, many of the abovementioned accessory treatments have proven moderately effective. However, issues with study designs, small sample sizes and heterogeneous outcome measures coupled with the trials and tribulations of prescribing these treatments to the heterogeneous PD community have largely prevented a major contribution of these therapies to advances in the treatment of PD. Although the evidence from the animal literature is quite compelling with respect to neuroprotective and neuroplastic benefits of exercise, as well as the ability of different exercises to result in differential effects on the nervous system, these effects in humans have been more difficult to demonstrate. In this chapter, we will outline the effectiveness of the more popular movement and behavioral therapies on the treatment of motor and nonmotor features of PD.

Aerobic exercise

Aerobic exercise improves a wide range of functional outcomes in individuals with PD. Indeed, individuals with PD benefit from aerobic exercise as much as healthy older adults [1, 2]. In fact, aerobic exercise interventions may represent one of the best ways to prevent disability and secondary complications associated with PD [3]. For example, multiple studies examining 16-week aerobic exercise training regimens have reported improvements in oxygen consumption (VO_2) consistent with a healthier and more efficient cardiovascular system, improved scores on the Unified Parkinson's Disease Rating Scale (UPDRS), and improved performance on physical function performance tests and movement initiation [4]. Specifically, Bergen *et al.* [5] demonstrated a 26% improvement in peak VO_2 among PD patients follow aerobic training. Additionally, improved walking economy has been noted in individuals with PD who participated aerobic activity [6]. When compared with other forms of exercise, aerobic interventions have demonstrated a greater improvement on select facets of physical function. For example, when compared with a medical Chinese exercise (qigong), Burini *et al.* [7] demonstrated that aerobic training exerted a significant impact on moderately disabled PD patients in functional parameters

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including, the 6-min walk test, Borg scale and cardiorespiratory outcomes (peak VO_2).

Studies from animal models suggest that aerobic exercise may not only have effects on physical function – it may also interfere with the disease process itself. For example, treadmill or wheel running initiated soon after a unilateral 6-hydroxydopamine (6-OHDA) lesion reduced neurochemical loss, lessened forelimb motor deficits and reduced dopamine loss when compared with sedentary lesioned rats [8]. Forced-exercise paradigms, in which the animal has to maintain a running velocity that is greater than their preferred running speed, have also been studied. Results from forced-exercise paradigms in animals demonstrate short- and long-term improvements in forelimb akinesia, stride length and step length, as well as sparing of striatal dopamine compared with sedentary lesioned animals [8, 9]. Similarly, Poulton and Muir [10] reported that forced treadmill running ameliorated dopamine loss in 6-OHDA rats.

Forced aerobic exercise in the human PD condition has demonstrated equally intriguing results. Ridgel *et al.* [11] randomly assigned ten mild to moderate PD patients to either 8-weeks of forced exercise or voluntary exercise. Patients in the forced-exercise group pedaled on a stationary tandem bicycle with the assistance of a trainer at a rate 30% greater than their preferred voluntary rate. Patients randomized to the voluntary group pedaled at their preferred rate. The results demonstrated that the forced-exercise group improved their UPDRS motor score by 35%. Interestingly, improvements in coordination of grasping forces during the performance of a functional bimanual dexterity task improved significantly in the forced-exercise group, suggesting improved central motor function.

Another promising aerobic intervention for PD patients is treadmill/gait training. Patients with PD who have undergone gait training on a treadmill have shown improvements in UPDRS motor scores, increases in gait speed and cadence during walking, and reductions in the number of falls [12, 13]. Research examining progressive speed-dependent treadmill training showed an improvement in gait speed and stride length of walking in early PD when compared with conventional gait therapy [14].

Unfortunately, despite being classified as a movement disorder, cognitive deficits are present in a large percentage of PD patients and greatly impact on function and quality of life. Cognitive deficits in PD affect complex working memory (WM), the ability to store and manipulate information held in memory, and the ability to store information despite distraction [15]. In addition, a wide range of executive function abilities including planning, inhibitory processes and set-shifting, are impaired in PD [16–18]. Interestingly, recent work from the healthy older-adult literature [19, 20] suggests that aerobic exercise and/or cardiovascular fitness may reverse age-related cognitive decline and facilitate a healthy cortex. For example, Colcombe *et al.* [21] demonstrated that older adults with greater levels of cardiovascular fitness have significantly less atrophy of the gray matter in the frontal cortex, which typically shows the greatest age-related decline [22]. Furthermore, greater aerobic fitness is associated with sparing of age-related deterioration of the anterior and posterior white-matter tracts. Several other randomized controlled trials report that aerobic exercise has its greatest effects on improving the frontal cognitive processes, which are greatly impacted in PD.

While the above studies illustrate that aerobic exercise combats cognitive decline in healthy aging, the potential impact of aerobic exercise on cognitive changes in PD have not been studied thoroughly. Preliminary data are indeed encouraging, as results from a case study by Nocera *et al.* [23] demonstrated that a patient with PD improved on cognitive outcomes including executive and language processes following an aerobic exercise intervention. This work suggests improvements in brain health in PD similar to that of older adults who participate in aerobic exercise. However, larger randomized trials are warranted to evaluate the efficacy of aerobic exercise for ameliorating declines in cognitive performance in people with PD.

The work described above suggests that aerobic exercise can be an effective way to prevent disability in PD patients, as it targets critical functional areas impacted by the disease process. However, it appears critical that the type of aerobic exercise be tailored to the specific needs of the patient. Furthermore, care must be taken to have a complete understanding of the fall risk and cardiac symptomatology of the patient such that safe guards can be implemented and the risk lessened. Future studies need to address issues that currently plague the data in this arena including sample size, optimal state and timing of medication, as well as how more alternative, perhaps forced-exercise, models, can be implemented and have an impact on those further along in the disease process.

Resistance training

While improvements in cognitive and physical function are observed following traditional aerobic exercise (treadmill walking, cycling), recent reviews suggest that the most supportive evidence for therapeutic benefits are based on interventions incorporating strength training [24, 25]. Decrements in muscular strength have negative consequences on the performance of activities of daily living (ADLs) such as getting out of a chair or putting away groceries on a shelf above chest height. These decrements and others lead to reduced physical activity, deconditioning, increased frailty and dependence on the services of others. The quantity and quality of muscle mass and strength impacts numerous aspects of daily performance in older adults and people with PD such as walking speed, stair negotiation, avoiding obstacles, chair rise, and recovering from slips and trips. Recent comprehensive reviews suggest that the progression of these losses may be attenuated or at least slowed through regular resistance training exercise [24, 25]. We suggest that resistance training is a safe, effective and noninvasive way of reducing the symptoms of the disease that gives patients an active role in the management of their disease, yet we know little about the mechanisms by which such benefits are achieved.

Several of the neural consequences and symptoms of PD reinforce the rationale for providing resistance training to patients [26]. First, loss of muscle strength is frequently observed, particularly in the muscles surrounding the hip, knee and ankle in both the unmedicated and medicated state. Furthermore, loss of muscle strength contributes to bradykinesia and reduced balance capabilities during dynamic locomotor tasks. In addition to loss of strength, PD researchers observe a reduction in the ability to produce force rapidly, which is particularly important when trying to take a recovery step after a stumble or reaching out the arm to grab a handrail to prevent a fall. Torque production has also been shown to vary with movement velocity, with particular deficits between the more- and less-affected side becoming pronounced at fast movement speeds. Aberrant muscle activation patterns are frequently observed during single joint and functional movement tasks. These abnormal activation patterns are likely related to impairments in variability, intensity and frequency of the corticospinal activation of the muscle. It is unclear, however, if these changes that are seen in muscular performance are solely related to changes at the periphery (muscle mass), impaired corticospinal activation, consequences of overall diminished activity or a combination of all of the above [26]. The peripheral and central neural adaptations that occur with resistance training may improve these decrements. Indeed, evidence suggests that resistance training can enhance cortical plasticity, improve descending activation from the motor cortex, enhance activation of basal ganglia nuclei, alter functional properties of spinal cord circuitry and cross-transfer training effects from the trained to untrained limb [26]. Despite recommendations for the inclusion of strength training into PD treatment more than 20 years ago [27], very few well-controlled investigations exist on this topic.

The extant literature suggests that resistance training can improve muscle mass, muscle strength and muscular endurance as well as neuromuscular function for patients with PD. Importantly, concomitant with these enhancements were observed reductions in parkinsonian motor disability. For example, Corcos *et al.* [28] observed a 7-point reduction in UPDRS motor scores following 24 months of twice-weekly resistance training. Also of note was that physical training was done at the participants' own gym and not in a strict laboratory setting. Due to disease-related cost and travel limitations, gym- and laboratory-based exercise interventions may not be accessible for all individuals. Importantly, we have shown that home-based exercise intervention focusing on lower-extremity strength can also improve muscle performance that carries over to enhanced balance, as measured by computerized dynamic posturography [29]. As with any exercise modality, it is important to the patient to see that becoming bigger, stronger and faster carries over to enhance functional performance.

Work from our laboratories and others have shown that resistance training in PD can lead to improvements in gait, gait initiation, chair rise, stair stepping and postural control [30, 31]. Gait speed, step length and head posture all improve following training, as well as functional gait outcomes such as walking endurance during the 6-min walk and improved timed performance on timed up-and-go and stair ascent and descent. Resistance training also improves anticipatory postural adjustments during gait initiation leading to larger and faster steps. Similarly, resistance training improves not only the speed of chair rise, but also the biomechanical mechanisms for safe and efficient performance. After resistance training, people with PD also demonstrate an improved ability to maintain balance during quiet and destabilizing balance conditions. Lastly, these improvements in muscular and functional performance lead to improvements in patient-perceived quality of life.

As with many therapeutic interventions, the present state of knowledge is impacted by several limitations that influence our ability to prescribe resistance training to our patients. First, the extant literature is plagued by small sample sizes and a potpourri of outcome measures that, while supporting a broad range effect, also limit our understanding of mechanisms and the ability to target disease-specific manifestations. Furthermore, the true benefits of resistance training are likely masked by evaluation of PD patients in the optimally medicated state. This practice has several ramifications, including masking the effects of training on the disease itself, as well as reducing effect sizes, which influences statistical findings and the conclusions with respect to efficacy. While much of the research has focused on motor benefits in PD, nonmotor features of the disease may also be impacted by resistance training. For example, resistance training in older adults facilitates general cognition. In fact, resistance training has a more beneficial effect on cognition that involves executive control, which, as stated previously, is particularly impacted by PD. The influence of resistance training on affective domains relevant to PD such as depression and apathy are also poorly studied. The long-term effects of progressive resistance exercise are yet to be determined, as well as the interactive effects of resistance training when it is included as part of a comprehensive exercise program including aerobic training and stretching. Furthermore, the optimal prescription of resistance training including the number and types of exercises (machines vs free weights, number of repetitions and sets) is understudied. Lastly, future research should evaluate the benefits of resistance training in the context of the different clinical subtypes of individuals with PD. In spite of these limitations, the literature supports the recommendation of resistance training for patients with PD.

Tai chi

In the healthy older-adult literature, tai chi exercise has gained attention as an attractive intervention because of its potential to reduce falls and improve postural control and walking abilities, while also being safe and at a low cost. Tai chi was first evaluated as a complementary therapy for PD motor symptoms with a case study examining the progress of two 66-year-old males with PD who demonstrated balance improvements after a 3-month fitness program, which involved balance, unsupervised activity at a fitness center and twice-weekly tai chi sessions [2]. A later study, with more focus on tai chi specifically, revealed that an intensive 5-day tai chi program in 17 individuals with mild to moderate PD resulted in improvements in mobility and flexibility, as well as satisfaction and enjoyment with the program [32]. Hackney and Earhart [33] studied 13 individuals with PD who completed 20 1 h lessons of tai chi and compared them with an untreated control group. The findings demonstrated that those who participated in tai chi developed improvements in the Berg balance scale, disease severity, mobility, static balance, endurance and backward walking.

To date, the strongest evidence that tai chi may improve motor impairments related to PD has been provided by a randomized controlled trial that assigned 195 participants to one of the following groups: tai chi, resistance training or stretching (24 weeks, 1 h, twice weekly) [34]. Follow-up analysis revealed that the tai chi group performed consistently better than the resistance training and stretching groups in maximum excursion during a postural stability test. The tai chi group also performed significantly better when compared with the stretching group in measures of gait and strength, scores on functional reach and timed up-and-go tests, and motor scores on the UPDRS. Additionally, the tai chi group improved compared with the resistance training group in stride length and functional reach. Lastly, tai chi lowered the incidence of falls compared with stretching but not resistance training, and the effects were maintained 3 months later. A noteworthy flaw in this study, however, is that the resistance training was very low intensity.

Interestingly, not all PD-related motor outcomes have benefitted from tai chi. For example, Amano *et al.* [35] investigated the effect of tai chi exercise on dynamic postural control during gait initiation and gait performance in people with idiopathic PD. In this multisite investigation, two separate tai chi groups completed 16-weeks of supervised tai chi exercise, while the control groups consisted of either a placebo (i.e. qigong) or nonexercise. The results indicated that tai chi did not significantly improve the UPDRS motor score, selected gait initiation parameters or gait performance. Combined results from both tai chi groups in this study suggested that 16 weeks of class-based tai chi were ineffective in improving gait initiation or gait performance, or reducing parkinsonian disability in people with PD.

Because tai chi is a form of physical activity that demands high cognitive involvement, it may serve as an effective modality for nonmotor symptoms of PD beyond the proven motor outcomes. Interestingly, Lam *et al.* [36] demonstrated that 1 year of tai chi training significantly improved not only balance function but also visual attention in older adults at risk of progressive cognitive decline. They hypothesized that "apart from being a form of physical activity, Tai Chi demands memory training for the complex motor sequences, as well as coordinated pathway between attention, voluntary motor action, postural control, verbal, and visual imagery which provides increased cognitive stimulation." Additionally, tai chi appears to lower feelings of stress and increase vigor in patient populations. Specific to PD, we demonstrated the tai chi three times weekly for 16 weeks significantly improved scores on the 39-Item Parkinson's Disease Questionnaire (PDQ-39) summary index, as well as the emotional well-being subscore when compared with a control group.

A difficult and important element to implementing any life style intervention is to ensure adherence and track attrition. Previous studies examining the use of tai chi in various populations have reported success with participants adhering to the program [33]. In a study by Nocera *et al.* [37], 92% attendance was reported. Equally important to consider is that previous studies have been unable to determine ideal dosage and length of tai chi intervention in PD. Future research is needed to address how tai chi implementation can be maximized for optimal effectiveness in the general PD population.

In summation, tai chi appears to appear to reduce balance impairments in patients with mild to moderate PD, with additional benefits of improved functional capacity and reduced falls. Furthermore, tai chi may have implications for the nonmotor symptoms associated with PD. Importantly, it also appears to be well tolerated by individuals with PD, as few adverse events have been reported, and adherence and self-reported satisfaction are high. It is important to note, however, that not all studies have concluded physical improvement with tai chi exercise in people with PD. Future research is needed to identify the ideal dose response and which motor and nonmotor aspects of PD can be maximized with tai chi.

Massage/acupuncture

Patients with PD also resort to other complementary and alternative medicines in hopes of improving quality of life and motor symptoms. Indeed, previous reports suggest that 40% of patients use some form of alternative therapy, with massage therapy and acupuncture being among the most common [38]. Several studies have shown that routine massage therapy services have led to improvement in performance of ADLs, improved sleep quantity and quality, and lower levels of stress hormones [39]. Unfortunately, mechanism-based research in this area is lacking. Conversely, acupuncture stimulation in PD models suggests that acupuncture may have neuroprotective benefits through the release of various neuroprotective agents such as brain-derived neurotrophic factor, glial cell line-derived neurotrophic factor and cyclophilin A [40]. In an 8-week duration human trial, acupuncture led to a reduction in disease severity and reduced depressive symptoms [41]. However, sham-controlled clinical trials that adhere to the CONSORT (Consolidated Standards of Reporting Trials) and STRICTA (Standards for Reporting Interventions in Clinical Trials of Acupuncture) guidelines are strongly needed to confirm the precise effect of acupuncture on PD [42].

Creative arts therapies

The use of creative arts therapies in the treatment of PD has become popular over the last decade. Complementary therapies including music therapy and dance therapy provide treatment for both the motor and nonmotor complications of PD while tailoring to patient-specific needs and interests. While research remains limited in these areas, support is gaining for the incorporation of creative arts therapies in treatment of PD.

Music therapy

Music therapy is the use of music within a therapeutic relationship to address physical, emotional, cognitive and social needs of individuals. When treating people with PD, music therapists often focus on two main areas; improving movement and voice performance.

To improve movement performance, the music therapist may incorporate the use of various instruments. Music therapists are skilled at adapting instruction and use of the instruments to meet specific therapeutic needs. For example, a person with PD may be learning to play the piano or guitar to improve fine motor and bilateral coordination, or a person with PD may be playing jingle bells fixed to their walker to increase the range of motion for hip flexion. In both examples, one of the most beneficial elements to music therapy is the use of external cues. Abundant evidence demonstrates the benefits of rehabilitative exercise that exploits external cueing [43, 44]. External cuing has improved movement initiation [45, 46], while additional research has shown that people with PD have faster reaction times when externally cued compared with self-initiated movement [47]. Synchronizing movement to rhythm may also enhance movement speed [48]. Yet there remains little explanation regarding the neurophysiological basis for these improvements. Currently, it is suggested that the use of external cues accesses a cerebellar–premotor cortical circuitry, bypassing the basal ganglia–supplementary motor area circuitry typically active during self-initiated movements [39]. Thus, music therapy programs that include external cues in combination with consistent rhythmic auditory stimulation are recommended for people with PD.

Auditory cues, another focus of music therapy, have also been shown to facilitate gait. Research has consistently shown that gait training with regular external rhythmic auditory cues improved gait velocity, stride length, step cadence, timing of EMG patterns and mobility in people with PD. Less is known, however, about the effects of music on gait in PD. Often, the results attributed to the facilitation of gait with auditory cues are extended to include music because of the similarity between the stimuli. However, only one study has examined the effects of music on gait training in people with PD, and this similarly revealed improved gait velocity, stride time and cadence. Interestingly, however, the use of auditory cues during more complex walking tasks such as dual-task walking and obstacle crossing demonstrates similar positive effects on gait, but listening to music while completing these challenging walking tasks may be attention demanding and has negative effects on gait [8, 49]. This evidence provides a conundrum, as there are several anecdotal reports of people with PD using music to walk in various environmental conditions, such as the mall or park, that involve dual tasking. Perhaps the focus of the attentional demand should be an area of consideration. In environments where minimizing external distractions is needed for effective ambulation, focusing on walking with music may be beneficial. Persons with PD may be able to focus more on the walking by synchronizing movement with the music. In contrast, in environments where attention is needed to complete additional tasks while walking, focusing on the additional task may be more beneficial. In these cases, music may indeed be distracting and have a negative effect on performance. Continued research on the appropriate environment in which to use music to facilitate gait is needed and will aid in determining appropriate music therapy strategies for gait disturbances in people with PD.

Group singing has also been used in music therapy for speech impairments in PD. Previous research has revealed mixed reports on the effectiveness of group singing in PD. Improvements in maximum inspiratory and expiratory pressure, voice range, speech intelligibility and vocal intensity have been reported after group singing interventions [50]. However, Shih *et al.* [51] revealed that group singing did not demonstrate improvements in objective measures of voice and speech impairment. A possible explanation for these differences in results may be attributed to the type of instruction being provided. When participating in group singing, specific elements such as learning the words, melody and rhythm could be emphasized over the proper singing technique (i.e. breath support and posture). Thus, the effects of group singing may match the training emphasis: improved working memory for learning a song versus improved voice for proper singing technique. Given that people with PD experience both cognitive and voice deficits, a combination of both may prove to be most beneficial. Yet no study has examined the effects of group singing on cognitive abilities in people with PD. There are additional elements that music may influence (social, quality of life) that have yet to be examined in group singing. Overall, the effects of group singing in people with PD have been underexplored, and there remains a need to better understand the potential benefits of group singing on the voice and on additional related measures. However, the fact that group singing may be able to target multiple treatment aspects such as cognition, socialization and voice performance at one time makes exploring how to most effectively incorporate group singing into the music therapy treatment of persons with PD intriguing.

Music therapists may also directly treat additional areas such as relaxation, cognition, emotional well-being and socialization. Music has been found to activate specific neural pathways associated with emotion and may enhance social relationships. In a study of seated exercises performed to musical cues, 14 participants with PD experienced improvements in the PDQ-39 subscales of emotional well-being, stigma, bodily discomfort, mobility and ADLs [52]. Additionally, music therapy involving rhythmic body movements demonstrably improved scores on the Parkinson's Disease Quality of Life questionnaire [53]. While research supporting the use of music therapy in the treatment of nonmotor symptoms is limited, treating the whole person is very valuable and is recommended in the treatment of people with PD. In fact, it is virtually impossible for a music therapist to treat only one independent objective given the innate emotional and social context associated with music that is nearly impossible to remove. Thus, music therapists tailor the therapeutic experience by using patient-specific music to treat the whole person.

Dance therapy

Effective motor rehabilitation should be safe, be participant friendly, promote high adherence and have demonstrated efficacy in improving disease severity, mobility and quality of life. Traditional exercise programs often suffer from high attrition rates because of high patient task demand and lack of social interaction. Ideally, exercise activities should engage and sustain interest, because 60% of all Americans older than 65 do not achieve the recommended daily amounts of physical activity. Activity levels in individuals with PD are further reduced [54].

However, dance, which is a robust activity that involves mental and physical engagement while coordinating movements to music, when used as a therapeutic tool, may garner adherence through an enjoyable activity. Social and partnered dance could foster community involvement and social support while – crucially – necessitating the practice of dynamic balance and adjustment to environment, both of which are key to rehabilitating balance and axial impairments [55]. Group social dance can enhance motivation to be active and pursue healthy, exercise-related behaviors in older individuals [56, 57]. Older adults who participated in dance also demonstrated improved balance and functional mobility [58]. Greater improvements have been noted in balance and complex gait tasks in older adults who participated in an Argentine tango group than in a walking group [59]. While unconventional as an approach to balance and gait problems for older and/or physically challenged individuals, dance may be appropriate and pleasurable as a therapeutic activity because of its benefits to physical, mental and emotional states.

Recently, a series of studies have investigated the effects of adapted Argentine tango dance (adapted tango) for individuals with PD (Hoehn and Yahr stages 2–4]). Participants experienced significant gains in mobility, balance and quality of life, improvements that were maintained 1 month later [60–62]. After participating in 1 year of tango classes offered in the community, participants with PD also demonstrated decreased disease severity [63]. Recently, a study demonstrated that a 12-week adapted tango program, which was disseminated to several novice instructors and offered in the community, improved spatial cognition as well as disease severity in participants with mild to moderate PD. These improvements were maintained 3 months after cessation of the intervention [64].

Other forms of dance besides tango have been investigated for efficacy for those with PD. A study that investigated the feasibility of Irish set dancing, in comparison with standard physiotherapy, found the dancing safe and feasible. Furthermore, participants tended to improve more in gait, balance and freezing of gait after dancing than after the standard care [65]. Dance may have an immediate effect on mobility in those with PD, as improvements have been found with as little as 2 weeks of tango [66] and contact improvisation training [67]. The UPDRS score, i.e. disease severity, has also been improved in the very short term – after single dance sessions – in before/after contemporary dance class assessments [68]. This same study also reported improved health-related quality of life (HRQoL) for the PD participants as well as for their caregivers.

Other studies examining dance for its therapeutic effects on PD also noted improvements in HRQoL that often accompanied improved motor function. Improvements in HRQoL were found in a participant with PD (Hoehn and Yahr stage 5) who was severely mobility impaired, which demonstrated that even those with end-stage disease could benefit from and enjoy a modified dance class [69]. In a mixed-methods study examining the effects of a ballet class that included participants with PD, the participants reported being highly motivated and valued dance as being important [70]. In a study of modern dance with physically active PD participants, in addition to improvements in balance, social interaction was evident, as participants were observed staying after class to socialize with peers. Modern dance in the guise of the very popular Dance for PD® class format, started by the Mark Morris Dance Company, has also been shown to positively influence HRQoL in those with PD. A study found improvements in social support after 10 weeks, and improvements in activity participation were noted after 12 months of tango dance.

Although several studies have demonstrated the effectiveness of dance for improving both mobility and HRQoL, there is a need for a clinical trial to definitively determine the effectiveness of dance. Importantly, it is also necessary to conduct studies to determine the underlying mechanisms of rehabilitative dance for those with PD. Some possibilities will be introduced in the following paragraphs.

Movement strategies involving strong cognitive involvement and planning are associated with mobility improvements [71]. While learning and practicing dance, one focuses on critical movement aspects (e.g. longer steps or quicker movements), an attentional strategy that may help individuals with PD to achieve nearly normal speed and amplitude [72]. For individuals with PD, having complex movements broken down into simpler elements by the teacher, which would be done in any dance pedagogy, may facilitate motor performance [71]. A dancing partner may enhance balance, as even light touch contact can augment postural control. Improvements achieved via dance may also have resulted because dance addresses PD motor impairments through exploiting external auditory cues, which enhance motor therapy.

Participation, defined as involvement in a life situation, is related to mobility-related HRQoL, and the ability to do functional tasks like rising from a chair. Participation in a year-long program of tango led to participants recovering lost activities, beginning new ones and having the ability to engage in more complex activities [73]. Potentially, individuals with PD have benefitted in HRQoL through dance by the removal of barriers to participation (e.g. availability of dance programs, motor challenges of the steps).

Older adults have benefitted from regular aerobic activity in terms of plasticity-related changes in synaptogenesis, angiogenesis and neurogenesis. There is a strong link between activity, mental engagement and neural pathways. Dancing, whether it be tango, contemporary or folk dance, involves complex, unfamiliar tasks like walking backwards, allowing for problem solving and movement improvisation, possibly targeting mobility issues in individuals with PD through increased mental engagement and strategy development. The creativity involved in a dance form might tap into mechanisms of neural plasticity for novices just beginning classes for therapy. The exposure to novel steps and choreographic patterns could be fodder for expanding neural areas and improving neural pathways. The neuroprotection and neurorestoration that may be derived from consistent, task-specific and frequent exercise could be provided by dance, and may extend into improved mobility and, ultimately, the ability to accomplish ADLs.

Participant-friendly, adapted tango had a low attrition rate (14%), demonstrating patient acceptance and feasibility with a diverse patient population [66]. Several mobility programs are effective (e.g. movement strategies, dance, tandem biking, tai chi) for people with PD. A better mechanistic understanding of beneficial exercise effects could improve the design of targeted motor rehabilitation interventions for particular symptoms (e.g. freezing, bradykinesia and various disease stages of PD). This information would be of great clinical significance to individuals with motor impairment of all etiologies, as well as due to PD. Exercise programs for individuals with PD that are self-guided may not be as helpful as programs that involve a therapist or instructor [74]. Gait and balance are increasingly recognized as especially important for determinants of HRQoL as well as mortality. Tango and other dance forms may improve the axial impairment that greatly affects mobility – and therefore participation – and ultimately HRQoL in those with PD.

Art therapy

Research on the effects of art therapy in people with PD has primarily been limited to case reports, although more recent work has produced larger efficacy trials. The process of creating art, whether it is through brush stroke or molding of clay, allows patients to express their emotions, leading to an apparent reduction in stress and enhanced relaxed meditative states. For example, Elkis-Abuhoff *et al.* [75] observed significant decreases in somatic and emotional symptoms following manipulation of a ball of clay in a large group of patients. Viewing drama and participating in interactive drama projects have also been proposed to improve patients' engagement and a positive sense of self and community. This early evidence suggests that art therapy may also be a complementary treatment modality for patients.

Conclusions

In conclusion, the use of creative arts therapies in the treatment of people with PD shows promise, with initial research showing positive effects. However, there is a substantial lack of research examining the associated brain activity with creative arts therapies. For therapies such as music, dance and art therapy to be validated and incorporated into the treatment of PD, future research in this area is greatly needed. Studies of the human response to music, dance and art remain challenging, however. To elicit controlled responses, much of the creative and personal aspects of music, dance and art are limited. Researchers in this area face an interesting and intriguing quest to determine the neurophysiological basis for mediums such as music, dance and art that can influence the physical, emotional and social well-being at the same time.

Summary

Individuals with PD exhibit cardinal features of the disease that manifest as impaired motor ability, non-motor impairment and ultimately a decreased quality of life. While drug therapy and deep-brain stimulation have proven to provide some positive benefits on clinically observed motor function, there are inherent limitations as well as negative side effects. The current research suggests that exercise therapies may be the most effective strategy for improving function in individuals with PD. Various forms of exercise including multiple aerobic paradigms, strength training programs and perhaps less conventional exercises modules like tai chi, dance and music therapy have all be attributed to improved gait performance, cardiovascular health, functional performance and in some cases multitasking. While this review has focused primarily on examining therapies in isolation, the optimal approach would probably incorporate multiple modes of engagement, each aimed at improving quality of life in areas that meet the needs of the patient. And while the combination of therapies is difficult from a research/statistical standpoint, a few studies have suggested that multicomponent interventions do cast a wider net of positive outcomes. In an effort to evolve our understanding of and clinical application to PD, research should continue to explore novel approaches to exercise interventions based on sound neuroplasticity-based mechanisms so that disease symptoms can be ameliorated and performance and quality of life can be optimized.

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