

Aerobic Exercise Improves Mood, Cognition, and Language Function in Parkinson's Disease: Results of a Controlled Study

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Abstract

Objectives: Parkinson's disease (PD) results in a range of non-motor deficits that can affect mood, cognition, and language, and many of these issues are unresponsive to pharmacological intervention. Aerobic exercise can improve mood and cognition in healthy older adults, although only a few studies have examined exercise effects on these domains in PD. The current study assesses the effects of aerobic exercise on aspects of cognition, mood, and language production in people with PD. **Methods:** This study compares the effects of aerobic exercise to stretch-balance training and a no-contact control group in participants with idiopathic PD. The aerobic and stretch-balance groups trained three times a week for 16 weeks, while controls continued normal activities. Outcome measures included disease severity, mood, cognition (speed of processing, memory, and executive function), and language production (picture descriptions). Cognition and language were assessed in single and dual task conditions. **Results:** Depressive symptoms increased only in the control group ($p < .02$). Executive function improved in the aerobic exercise group only in the single task ($p = .007$) and declined in controls in the dual task. Completeness of picture descriptions improved significantly more in the aerobic group than in the stretch-balance group ($p < .02$). **Conclusions:** Aerobic exercise is a viable intervention for PD that can be protective against increased depressive symptoms, and can improve several non-motor domains, including executive dysfunction and related aspects of language production. (*JINS*, 2016, 22, 878–889)

Keywords: Parkinson's disease, Aerobic exercise, Physical training, Intervention, Executive function, Speech production

INTRODUCTION

Parkinson's disease (PD) is a progressive neurologic disease affecting over a million Americans and over ten million people worldwide (Parkinsons Disease Foundation, 2016). While the cardinal symptoms of PD (tremor, rigidity, bradykinesia, and postural instability) are motoric in nature, individuals with PD also suffer from non-motor symptoms, many of which adversely affect quality of life (Weerkamp et al., 2013), such as changes in cognition and mood (Barone et al., 2009; Martinez-Martin, Rodriguez-Blazquez, Kurtis, & Chaudhuri, 2011).

As many as 80% of individuals with PD develop cognitive impairments (Aarsland, Andersen, Larsen, Lolk, & Kragh-Sorensen, 2003; Cummings, Darkins, Mendez, & Hill, 1988; Pirozzolo, Hansch, Mortimer, Webster, & Kuskowski, 1982), which do not reliably respond to available pharmacological and surgical treatments (Fournet, Moreaud, Roulin, Naegele, & Pellat, 2000; Owen, Iddon, Hodges, & Summers, 1997; Skeel et al., 2001). Although many cognitive domains are impacted by PD, the current study focuses on a few domains that are frequently reported to be impaired: speed of processing, memory, and executive function abilities, such as planning, inhibition, and set shifting (Saint-Cyr, Trepanier, Kumar, Lozano, & Lang, 2000; Taylor, Saint-Cyr, & Lang, 1986).

Furthermore, working memory and executive function abilities predict impairments in language production in PD

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(Bastiaanse & Leenders, 2009; Colman et al., 2009; Troche & Altmann, 2012). Language output in PD is often more sparse and less informative than that of healthy peers (Altmann & Troche, 2011; Bayles, 1990; Murray, 2000). Furthermore, narratives produced by individuals with PD are less fluent (e.g., contain more false starts and word repetitions), less grammatically complex, and shorter than those of controls (Altmann & Troche, 2011; Murray, 2008). Troche and Altmann (2012) demonstrated significant relationships between cognitive abilities and many aspects of language, suggesting that if cognitive abilities improve, some aspects of language may also improve.

Notably, persons with PD who display impairments in cognition frequently also present neuropsychiatric and mood symptoms (Emre, 2003). Depressive symptoms are experienced by as many as 90% of people with PD (Slaughter, Slaughter, Nichols, Holmes, & Martens, 2001), and depression is the single strongest predictor of quality of life in PD, even after accounting for motor function (Jones, Malaty, Price, Okun, & Bowers, 2012). Additionally, apathy without depression is seen in 17–30% of individuals with PD and may contribute to changes in activity level and quality of life (Jones, Butterfield, et al., 2015; Jones, Marsiske, et al., 2015). Consequently, a non-pharmacological intervention for individuals with PD that improves or protects against mood impairments while improving cognition, language, and motor function would be extremely valuable.

The current study tests whether aerobic exercise may be an effective treatment for both cognitive and language impairments as well as mood disorders in people with PD. Many studies have documented that aerobic exercise can improve memory and executive dysfunction, and reduce severity of depression in otherwise healthy older adults (Blumenthal, Babyak, Moore, & et al., 1999; Erickson et al., 2011). Improvements are attributed to exercise-related increases in the release of several neuromodulators responsible for proliferation of synapses and dendritic branching (Cotman & Berchtold, 2002; Dishman et al., 2006). These exercise-induced changes, in turn, have led to: increased volume of white and gray matter (Colcombe et al., 2006), increased hippocampal volumes (Erickson et al., 2011), and improved functional connectivity in both the Default Mode Network and the Frontal Executive Network (Voss et al., 2010). Moreover, the impact of aerobic exercise is similar in impaired elderly populations, such as individuals with mild cognitive impairment (Suzuki et al., 2013), Alzheimer's disease (Coelho et al., 2013), or Huntington's disease (Harrison et al., 2013), suggesting that exercise-related changes in brain function may occur despite brain pathology.

The few exercise intervention studies in PD have also found positive results. Uc and colleagues (2014) reported significant improvements in gait speed, depression, and one measure of executive function, as well as in disease severity in 43 individuals with PD who performed aerobic exercise three times a week for 6 months. Unfortunately, Uc et al. did not have a control group, which is an important consideration when participants have a degenerative disease. Cruise et al.

(2010), using a combined aerobic and strength-training regimen, also reported cognitive improvement following exercise training, but no changes in depression. While Cruise et al. included a no-contact control group, the scores of the two groups were not compared. Other studies in PD assessed combined types of exercise (Tanaka et al., 2009) or strength-training (David et al., 2015), and have found benefits in aspects of executive function. Thus, aerobic exercise has potential as an intervention for cognition and mood PD, although studies with appropriate control groups are needed.

One open question in the exercise literature concerns the resiliency of exercise-induced changes in cognition. Particularly in the PD exercise literature, it is typical for only one of many cognitive tests to improve (e.g., Cruise et al., 2010; Uc et al., 2014). The current study addresses this issue in two ways. First, because no single cognitive measure can adequately assess ability in an entire domain, the current study adopted a statistical approach called parcellation (Little, Rhemtulla, Gibson, & Schoemann, 2013). Parcellation theory recommends using several measures of each construct of interest to triangulate on a participant's true ability in that domain. Second, participants were assessed on cognition and language pre- and post-intervention in both single and dual task conditions. During dual tasks, cognitive resources are shared between the two tasks, so performance typically declines in one or both tasks due to insufficient resources to maintain performance in both tasks at the single task level (Kahneman, 1970).

We hypothesized that any improvements in cognition would be shared between the cognitive and motor tasks during a dual task, but not a single task. Thus, small improvements in cognition would first be detectable in a single task; whereas, cognitive improvements would only manifest in dual tasks if the effect were very robust. However, declines in cognition might manifest first in dual task conditions where cognitive resources were already divided, and it is already difficult to maintain performance in both concurrent tasks. An alternative view would suggest that any improvements or declines in cognition would first manifest in dual task performance, because that is where the demand for cognitive resources is greatest.

As a corollary to these predictions, executive function tasks were expected to be most sensitive to cognitive improvement or decline, because they are highly demanding of cognitive resources. Similarly, language production was predicted to change in concert with cognitive abilities. Additionally, based on previous findings in the literature (e.g., Uc et al., 2014), it was expected that mood and symptoms of disease severity on the Unified Parkinson's Disease Rating Scale (UPDRS; Goetz et al., 2007) would also improve.

METHODS

Participants

Forty individuals diagnosed with idiopathic PD enrolled in the study from the Center for Movement Disorders and

Neurorestoration in Gainesville, Florida. Three participants quit before completing initial assessments, after which participants were randomized into three groups, aerobic exercise, stretch-balance (the contact-equivalent control group), or control (no-contact control group). Four participants did not complete post-intervention testing. Three additional participants completed the intervention and post testing but had incomplete data and were excluded from analysis. Thus, 30 participants were included in the final analyses. Demographic information on participants included in analyses appears in Table 1. Information on participants enrolled in the study but excluded from analysis is in the Supplementary Materials.

Participants were diagnosed with idiopathic PD according to UK Brain Bank criteria, which was confirmed by a movement disorders neurologist. Modified Hoehn and Yahr scale scores ranged between 1 and 3 in the “on” medication state (Hoehn & Yahr, 1967). Participants had a stable response to anti-parkinsonian and/or psychotropic medication. Participants with secondary or atypical Parkinsonism, or severe, unpredictable episodes of motor fluctuation were excluded. Potential participants with a history of falls as shown by a score greater than one in the fall item of the UPDRS Part II were excluded under advisement of the Institutional Review Board to minimize risk to participants. Individuals were excluded from the study if they used medications known to interfere with cognitive function (e.g., anticholinergics), or had symptoms of mild cognitive impairment or dementia as indicated by a score less than 25 on the Mini Mental Status Examination (MMSE; Folstein, Folstein, & McHugh, 1975), a history of psychiatric disturbance (e.g., major depressive disorder or generalized anxiety), or cardiovascular disease.

All participants signed an Informed Consent form approved by the University of Florida Health Sciences Institutional Review Board. Participants were evaluated using the UPDRS while on medication, which was administered by trained personnel and was video-recorded for later scoring by a movement disorders neurologist blinded to treatment condition.

Tasks

General assessments

Disease severity was assessed using the UPDRS. Participants completed the Dementia Rating Scale (DRS; Mattis, 1988) as a measure of general cognition. Mood assessments included the Beck Depression Inventory-II (BDI; Beck, Steer, & Brown, 1996), the Apathy Scale (Marin, Biedrzycki, & Firinciogullari, 1991), and the Beck Anxiety Scale (Beck & Steer, 1993). Sleep was assessed using the Pittsburgh Sleep Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989).

Experimental tasks

Stimuli for cognitive and language tasks were presented by a laptop running MediaLab (Jarvis, 2006b) and DirectRT software (Jarvis, 2006a). Responses for all experimental tasks were oral and recorded *via* a wireless microphone for later scoring by trained research assistants using Audacity software (Bland, Busam, Gunlogson, Mekkes, & Saunders, 2006). Participants received a different list of stimuli at each test session. While the primary outcome measures reported here varied between accuracy and response times (RTs) across tasks, tasks were scored for both wherever possible. Scores on secondary outcome measures are found in the Supplementary Materials.

Cognitive tasks covered three domains: speed of processing, attention/memory, and executive function. Because no single task can adequately assess a particular cognitive construct like speed of processing or executive function, several tasks were used to assess performance in each domain (Little et al., 2013).

Speed of processing tasks

Assessment of speed of processing initially included four tasks: simple attention, 0-back, Stroop Colors, and digit symbol. However, inspection of the data and correlations between variables led to the additional inclusion of the Stroop Color Word task (Lezak, Howieson, Loring, Hannay, & Fischer, 2004) in this composite. The primary outcome

Table 1. Descriptive information for participants when they entered the study

Measure	Exercise Mean (<i>SD</i>)	Balance Mean (<i>SD</i>)	Control Mean (<i>SD</i>)	<i>p</i> -Value
<i>N</i>	11	9	10	
Age	62.8 (8.6)	63.3 (7.3)	67.8 (9.8)	.378
Education (yrs.)	20.0 (4.3)	15.6 (4.1)	17.3 (3.7)	.068
MMSE (max = 30)	29.5 (1.0)	29.4 (.9)	29.2 (1.0)	.820
DRS (max 145)	141.3 (1.7)	141.3 (2.1)	139.9 (4.0)	.437
Schwab & England (max = 100)	90.0 (4.7)	90.0 (5.3)	89.0 (7.4)	.193
UPDRS – total (on medication)	36.6 (12.5)	31.7 (8.7)	32.7 (11.0)	.618
Hoehn & Yahr				
No. at Level 1	1	0	1	
No. at Level 2	8	7	4	
No. at Level 3	2	2	5	

MMSE = Mini Mental Status Examination; DRS = Dementia Rating Scale-2; UPDRS = Unified Parkinson's Disease Rating Scale.

measure for all speed of processing tasks was the RT measured from stimulus onset to voice onset. The Simple Attention task presented a large, blue star centered on the screen at intra-stimulus intervals of 750, 1250, 1750, or 2250 ms. Participants said “Go!” when they saw the star, followed by the next trial. In the 0-back task (Nystrom et al., 2000), participants saw a fixation asterisk followed by a tic-tac-toe figure with two black dots in adjacent or diagonally adjacent squares. Participants said “Yes” if the current figure matched a prespecified target figure (25% of 40 trials), or “No” otherwise.

In the Stroop Colors task (Lezak et al., 2004), participants saw a centered fixation asterisk, and then said the color of font in which four upper-case Xs appeared. In the Stroop Color Words task, following a fixation asterisk, participants saw a color word (e.g., BLUE, RED, GREEN) printed in an incongruent color and said the color of the font in which the word appeared. In an oral version of the Digit Symbol Substitution task (Lezak et al., 2004), participants saw an array of nine digits, each paired with a Korean letter, at the top of the screen, and 750 or 1250 ms later a larger version of one of the Korean letters appeared below it. Participants said the number of the digit associated with the large Korean letter. With the exception of the 0-back task which had 40 trials total, all speed of processing tasks had 20 trials. With the exception of the simple attention task, all tasks featured a one second blank screen between trials.

Attention/ memory tasks

Two verbal and two visual attention-memory tasks were included. Accuracy was the primary outcome measure. In the two verbal tasks, digit span forward and backward (Wechsler, 1997), participants heard increasingly long lists of digits and repeated them in verbatim or reverse order, respectively. Testing continued until the participant erred on both trials of one list length. The score was the proportion of lists (of 14) repeated successfully. The non-verbal tasks comprised 1- and 2-back tasks (Nystrom et al., 2000) using the tic-tac-toe figures described above. As in the 0-back task described above, 1- and 2-back trials began with a fixation asterisk and ended with a 1000 ms blank screen. In the 1-back task, participants said “Yes” when the current figure matched the immediately preceding figure (25% of 40 trials), and “No” otherwise. In the 2-back task, participants said “Yes” if the current figure matched the figure two trials before (25% of 40 trials), and “No” otherwise. The primary outcome measure for these n-back tasks was the proportion correct on “yes” trials. Scores for the secondary outcome measures, RTs for correct trials, are presented in the Supplementary Materials.

Executive function tasks

The three measures were included in the executive function composite. Stroop interference was calculated by subtracting RTs on the Stroop Color-Words task from RTs on the Stroop colors task. Thus, higher magnitude negative scores signified

greater slowing in Stroop Color-Words relative to Stroop Colors. In the visual memory updating task (Fougnie & Marois, 2006), participants saw the words “New Trial,” followed by 1–4 tic-tac-toe figures individually presented for 2000 ms each, and then a horizontal array of the same number of figures. Participants verified whether the figures in the array matched the figures just presented. Stimuli were randomized so participants were unaware how many figures they would have to remember. The outcome measure was the proportion of correct responses in the 16 trials. In the operation span task (Conway et al., 2005), participants were asked to remember a set of six non-rhyming consonants presented for 500 ms. They then verified whether a series of 1–4 one-step arithmetic problems were correct (e.g., $3 + 2 = 5$ “Yes”; $4 - 1 = 5$ “No”), and then recalled the previously presented letters when cued. The outcome measure was the proportion of letters recalled correctly in order across the 20 trials. In the latter two tasks, trials were separated by a 1000 ms blank screen.

Language task

Since people with PD have difficulty with language at the sentence and discourse level (Altmann & Troche, 2011), a sentence generation task previously used with people with PD (Troche & Altmann, 2012) assessed language production. Participants produced a sentence to describe each of 20 black-and-white line drawings from Bock, Loebell, & Morey (1992) and Kempler (2003) depicting a single event involving two or three characters, as shown in Figure 1. Participants were instructed to describe each picture using a grammatical sentence that mentioned each character in the picture without using pronouns. Outcome measures included fluency, grammaticality, and complete information. A fluent response included no “ums” or “uhs,” false starts, or long pauses between words. A grammatical sentence included appropriate articles and auxiliary verbs, correct subject-verb agreement, and no other grammatical errors. Complete information was defined as mentioning all characters pictured plus an appropriate action. Reliability of scoring using Cronbach’s alpha was excellent (fluency .950, grammaticality .936, completeness .905).

Procedure

The 12 experimental tasks described above were administered twice, once in a quiet room and once while riding a stationary bicycle, the dual task condition, before and after the intervention. Participants pedaled at their chosen rates against minimal resistance. At least two experimenters were present during dual task sessions, one explaining and running the cognitive tasks and one running the motion capture system to track cycling speed. Only one experimenter administered the single task testing. Experimenters administering post-intervention assessments were blinded to group membership. To control for learning effects, the order of single and dual task assessment was counterbalanced across participants and was the same pre and post-intervention.

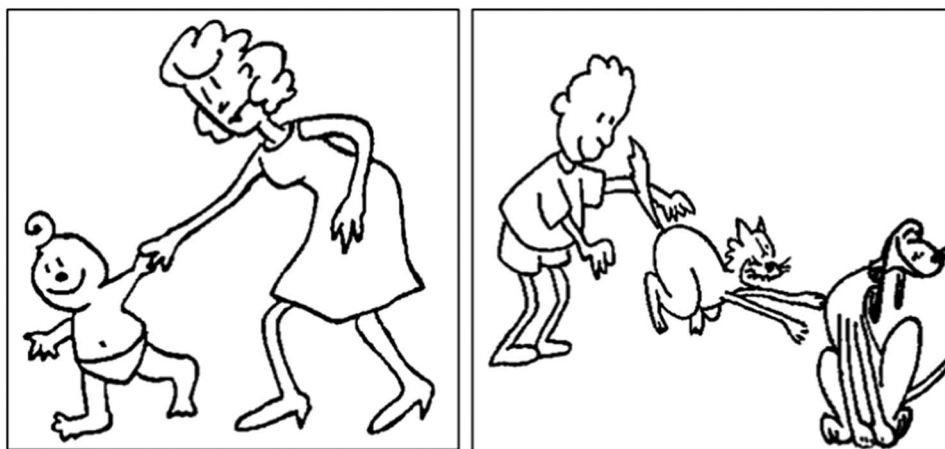


Fig. 1. Sample of stimuli with two or three entities in the picture for the language production task (Kempfer, 2003).

Physical training

After completing all intake testing, participants were randomly assigned to the aerobic exercise, stretch-balance, or no-contact control groups. Participants in the aerobic exercise and stretch-balance groups came to the UF Center for Exercise Science three times a week for 16 weeks for personal training with a cardio-pulmonary resuscitation (CPR) certified, fitness specialist familiar with PD. Following warm-up stretching, exercise duration progressed from an initial 20 min per session to the maximum 45 min by increasing exercise time by 5 min each week. Participants wore a heart rate monitor during all aerobic training. Aerobic exercise, performed on a treadmill, began at low intensity [50% maximal heart rate (HR) reserve] and increased by 5% each week to a maximum of 75% HR. The stretch-balance group did stretching exercises as outlined in the American Parkinson's Disease Foundation publication "Be Active" (American Parkinson Disease Association, 2009), most of which are performed while sitting. Subsequently, they performed balance tasks on a force platform with visual feedback displayed on a large computer monitor. Attendance in both groups was high (>94% of scheduled visits). Participants in the no-contact group continued their regular daily activities and were discouraged from initiating any physical training during the study. Levels of physical activity within the control group were monitored monthly by phone interview and questionnaire (Godin & Shephard, 1997).

Analyses

Scoring

For all experimental cognitive tasks, the dependent variable for each domain was the mean of Z-scores across all tasks in that domain at each time point (e.g., Anderson-Hanley et al., 2012). This was calculated by pooling subjects' scores for all conditions on a task and calculating the Z-scores. In this way, change relative to all conditions could be determined. Z-scores for tasks with RTs as the primary measure were sign reversed, so higher positive scores signified faster responses.

Using Z-scores allowed the inclusion of tasks with different outcome measures (e.g., RTs and accuracy) or very different means (e.g., very fast and very slow RTs) in the same analysis without biasing results. Dependent variables for the language task comprised the proportion of responses meeting each of the three criteria described above. Similarly, raw scores from the UPDRS, general cognition, and mood assessments comprised the dependent variables in those analyses.

Changes in disease severity and mood were assessed with mixed repeated measures analyses of variance in which group (aerobic, balance, control) was a between-subjects variable, and time (pre, post) was a within-subjects, repeated measure. Change within UPDRS domains was assessed with a multivariate analysis of variance (MANOVA) in which subtest scores on mood, activities of daily living, motor, and medication were component variables. The general cognition, mood measures, and sleep were assessed with group \times time analyses of variance (ANOVAs) within each domain. Changes in cognition and language production were analyzed using group \times time \times single/dual task analyses of covariance (ANCOVAs) in which order of single and dual tasks was covaried to control for learning effects. Significant interactions were explored with the appropriate *post hoc* tests, with Bonferroni correction for multiple comparisons. Alpha was set to .05 for all analyses. All statistics were computed using SPSS 22 (IBM, 2013).

RESULTS

Disease Severity and Mood

Scores for UPDRS, general cognition, mood and sleep are found in Table 2. The MANCOVA over UPDRS scores found no significant effects; neither did the analysis of DRS scores. In the analyses of mood and sleep scores, only BDI scores revealed a significant group by time interaction, $F(2,27) = 5.219$, $p = .003$, $\eta^2 .344$. *Post hoc* within-group *t* tests revealed significant increases in BDI scores of the control group at post,

Table 2. Scores on measures of severity and mood measures before and after the intervention

	Aerobic		Balance		Control	
	Pre (SD)	Post (SD)	Pre (SD)	Post (SD)	Pre (SD)	Post (SD)
UPDRS						
Total	36.6 (12.5)	35.4 (11.0)	33.9 (10.1)	37.6 (15.3)	33.8 (11.3)	38.6 (10.1)
Mood	1.7 (1.3)	1.2 (1.3)	2.1 (1.6)	2.9 (3.9)	1.1 (1.5)	1.4 (.9)
ADL	8.8 (3.6)	10.9 (4.4)	10.8 (3.5)	10.9 (4.4)	9.7 (4.0)	11.9 (3.6)
Motor	23.7 (8.7)	22.8 (7.9)	17.5 (6.4)	20.6 (11.5)	20.6 (7.7)	22.7 (7.2)
Therapy	2.4 (1.6)	2.3 (2.1)	3.5 (1.9)	3.3 (2.4)	2.5 (1.7)	2.6 (2.0)
General cognition						
DRS	141.3 (1.7)	140.0 (3.0)	141.3 (2.1)	140.7 (4.3)	139.9 (4.0)	140.0 (4.5)
Mood						
BDI*	5.4 (5.3)	4.7 (5.4)	6.1 (4.2)	5.8 (4.8)	4.2 (3.8)	7.6 (5.3) [‡]
Anxiety	8.0 (6.0)	10.3 (9.1)	12.8 (10.0)	13.0 (11.7)	15.3 (7.6)	14.3 (9.2)
Apathy	8.7 (4.7)	9.4 (6.3)	8.3 (5.1)	10.1 (5.2)	9.3 (6.5)	9.9 (6.2)
Sleep	5.0 (2.6)	4.0 (3.3) [‡]	5.8 (2.5)	6.1 (3.1)	5.6 (2.1)	6.7 (2.8)

*Significant group by time interaction, $p < .05$.

[‡]within group change, $p < .05$.

UPDRS = Unified Parkinson's Disease Rating Scale; ADL = activities of daily living; DRS = Mattis Dementia Rating Scale-2; BDI = Beck Depression Inventory 2; Apathy = Apathy Scale; Anxiety = Beck Anxiety Index; Sleep = Pittsburgh Sleep Quality Index.

$t(9) = 3.161, p = .012$, but no change in BDI scores among aerobic or stretch-balance groups (both $p > .3$).

Cognition

Speed of processing

As shown in Table 3, the ANCOVA analyzing speed of processing revealed a significant main effect of dual task, $F(1,26) = 8.131, p = .008, \eta^2 = .238$, with faster scores in the dual task ($M = +.030, SD = .749$) than the single task ($M = -.038, SD = .700$). Additionally, the group by time interaction was significant, $F(2,26) = 4.113, p = .028, \eta^2 = .240$. RTs of the control group were faster at post

($M = +.187, SD = .545$) than pre ($M = -.242, SD = .938$), $t(9) = 2.631, p = .027$, which was not significant with Bonferroni correction for three comparisons (i.e., $p = .017$). The stretch-balance group showed a similar pattern, with faster response times at post ($M = -.060; SD = .703$) than pre ($M = -.153; SD = .665$), but this was not significant, $t(8) = 2.267, p = .053$. The aerobic group showed little change in RTs on these tasks, $t(10) < 1$.

Attention-memory

The ANCOVA examining performance in attention/working memory accuracy (see Table 4) found no significant effects.

Table 3. Single and dual task scores for speed of processing tasks (RTs), pre and post training in the three groups

Speed of processing tasks	Single or dual task	Aerobic exercise		Stretch-balance		Control	
		Pre (SD)	Post (SD)	Pre (SD)	Post (SD)	Pre (SD)	Post (SD)
Simple Attention	Single	437 (127)	414 (108)	396 (70)	411 (90)	448 (132)	411 (81)
	Dual	438 (120)	423 (116)	407 (60)	423 (64)	448 (132)	391 (66)
0-Back	Single	589 (109)	618 (132)	672 (259)	637 (138)	621 (131)	539 (82)
	Dual	588 (88)	617 (114)	602 (90)	587 (61)	576 (118)	610 (160)
Stroop Colors*	Single	592 (35)	623 (88)	631 (67)	623 (97)	597 (79)	575 (91)
	Dual	613 (96)	613 (104)	666 (133)	613 (97)	695 (172)	621 (90)
Stroop Color Word	Single	870 (155)	851 (112)	923 (179)	911 (261)	1003 (271)	912 (148)
	Dual	871 (183)	845 (172)	945 (253)	906 (244)	959 (147)	878 (134)
Digit Symbol Substitution [‡]	Single	2541 (721)	2508 (731)	2826 (432)	2882 (542)	2728 (708)	2603 (645)
	Dual	2195 (611)	2508 (731)	2600 (449)	2882 (542)	2525 (686)	2196 (293)
Composite Z-scores* [‡]	Single	.083 (.689)	.043 (.736)	-.195 (.758)	-.146 (.790)	-.206 (.915)	.185 (.600)
	Dual	.148 (.832)	.177 (.854)	-.112 (.686)	.027 (.665)	-.277 (1.048)	.188 (.575)

Note. Mean Z-scores are reversed in sign so that higher positive scores indicate improvement, faster responses.

*Significant group by time interaction, $p < .05$.

[‡]Significant dual task benefit, $p < .05$.

Table 4. Single and dual task scores (accuracy) for attention-memory tasks as a percent of possible accurate trails, pre and post training in the three groups

	Single or dual task	Aerobic exercise		Stretch-balance		Control	
		Pre (<i>SD</i>)	Post (<i>SD</i>)	Pre (<i>SD</i>)	Post (<i>SD</i>)	Pre (<i>SD</i>)	Post (<i>SD</i>)
Working memory tasks							
Digit Span Forward	Single	.571 (.172)	.591 (.150)	.603 (.095)	.548 (.107)	.614 (.151)	.636 (.167)
	Dual	.584 (.209)	.591 (.150)	.508 (.121)	.548 (.101)	.621 (.117)	.657 (.161)
Digit Span Backward	Single	.539 (.144)	.533 (.182)	.373 (.100)	.444 (.123)	.421 (.152)	.471 (.185)
	Dual	.520 (.150)	.520 (.163)	.381 (.134)	.389 (.134)	.471 (.179)	.457 (.131)
1-Back Accuracy	Single	.909 (.145)	.973 (.065)	.967 (.071)	.967 (.100)	.903 (.125)	.990 (.032)
	Dual	.964 (.050)	.963 (.069)	.956 (.053)	.944 (.088)	.917 (.111)	.959 (.073)
2-Back Accuracy	Single	.710 (.316)	.770 (.239)	.862 (.155)	.805 (.138)	.876 (.062)	.805 (.138)
	Dual	.741 (.171)	.747 (.238)	.803 (.183)	.856 (.188)	.788 (.149)	.774 (.127)
Composite Z-scores	Single	-.137 (.922)	.145 (.741)	.013 (.486)	-.045 (.507)	-.052 (.532)	.219 (.559)
	Dual	.050 (.716)	.065 (.774)	-.246 (.348)	-.128 (.484)	-.037 (.446)	.101 (.504)

Note. Analyses found no significant effects.

Executive function

The ANCOVA examining executive function performance revealed a nonsignificant trend for higher scores in the dual task ($M = +.077$; $SD = .757$) than in the single task ($M = -.077$; $SD = .671$), $F(1,26) = 3.749$, $p = .064$, $\eta^2 = .128$. Additionally, as shown in Table 5, there was a significant three-way interaction between group, time, and dual task, $F(2,26) = 3.440$, $p = .047$, $\eta^2 = .209$. Paired-sample t tests comparing pre and post scores, separately in single and dual tasks, were completed for each group, leading to six comparisons (required p -level of .008 with Bonferroni correction). Executive function scores of the aerobic group improved significantly in the single task (mean difference = $+.409$; $SD = .403$), $t(10) = 3.358$, $p = .007$, but remained steady in the dual task. In contrast, dual task performance in the control group showed a tendency to decline at post (mean difference = $-.288$; $SD = .403$), $t(9) = 2.260$, $p = .050$, with no significant change ($p = .244$) in the single task. Performance of the stretch-balance group remained stable, both $p > .6$ (Figure 2).

Language

Language task scores are presented in Table 6. The ANCOVA analyzing completeness of information in sentences revealed a significant interaction between group and time, $F(2,26) = 4.440$, $p = .022$, $\eta^2 = .255$. To explore this interaction, a post hoc univariate ANCOVA with difference scores (post-pre) as the dependent variable, controlling for task order, with Bonferroni correction was computed. The aerobic group ($M_{\text{Change}} = +.092$, $SD = .187$) improved significantly more in completeness of information than the stretch-balance group ($M_{\text{Change}} = -.083$; $SD = .140$; $p = .008$), but did not differ from the control group ($M_{\text{Change}} = +.068$; $SD = .132$; $p = 1.00$), nor did the stretch-balance and control groups differ ($p = .103$). The analysis of fluent responses revealed a significant main effect of time, $F(1,26) = 5.412$, $p = .028$, $\eta^2 = .172$. Participants were more fluent during post testing ($M = .700$; $SD = .266$) than during initial testing ($M = .597$; $SD = .288$). Additionally, in the analysis of fluency, the main effect of dual task was significant, $F(1,26) = 5.355$, $p = .028$, $\eta^2 = .161$.

Table 5. Single and dual task scores for executive function tasks, pre and post training in the three groups

	Single or dual task	Aerobic exercise		Stretch-balance		Control	
		Pre (<i>SD</i>)	Post (<i>SD</i>)	Pre (<i>SD</i>)	Post (<i>SD</i>)	Pre (<i>SD</i>)	Post (<i>SD</i>)
Executive function measures							
Stroop Interference (ms)	Single	-278 (152)	-228 (95)	-238 (58)	-217 (77)	-406 (250)	-337 (150)
	Dual	-259 (122)	-232 (113)	-212 (103)	-230 (85)	-263 (146)	-257 (120)
Operation Span* (accuracy)	Single	.605 (.180)	.677 (.159)	.569 (.169)	.595 (.160)	.556 (.070)	.552 (.230)
	Dual	.700 (.169)	.684 (.165)	.664 (.189)	.607 (.206)	.613 (.061)	.533 (.225)
Visual Memory Updating [‡] (accuracy)	Single	.805 (.138)	.879 (.108)	.880 (.132)	.821 (.144)	.747 (.186)	.805 (.162)
	Dual	.817 (.137)	.828 (.130)	.840 (.186)	.877 (.127)	.811 (.140)	.747 (.162)
Composite Z-scores [‡]	Single	-.044 (.760)	.364 (.553)	.029 (.768)	-.048 (.890)	-.528 (.945)	-.266 (.790)
	Dual	.205 (.784)	.253 (.678)	.145 (.799)	.096 (.991)	-.014 (.325)	-.274 (.544)

Note. Analysis revealed a significant effect of dual task ($p = .034$) and a significant group by time by exercise interaction ($p = .033$).

*Significant dual task benefit, $p < .05$.

[‡]Significant group by time by dual task interaction, $p < .05$.

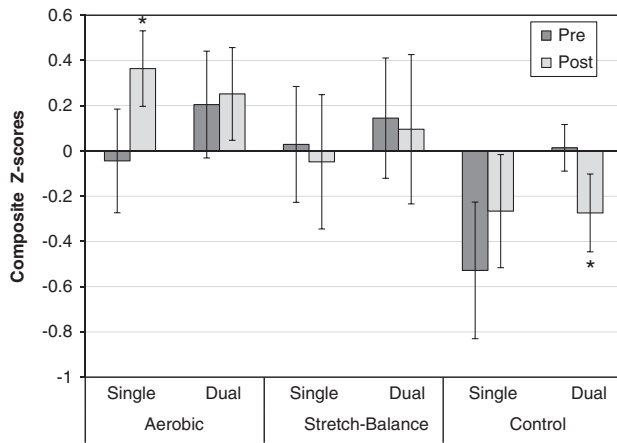


Fig. 2. Composite scores for executive function tasks in the single and dual task conditions before and after the intervention by the three groups. (* signifies $p \leq .05$).

Participants were more fluent in the dual task. The analysis of grammaticality scores found no significant effects.

DISCUSSION

The current study compared the effects of aerobic exercise in PD on disease severity, mood, cognitive and language outcomes relative to effects in both no-contact and contact-equivalent control groups. Furthermore, the study tested performance in both single and dual task conditions. The results demonstrated that the 16-week aerobic exercise intervention elicited significant improvement in executive function in the single task and potentially also improvements in language content in people with PD. In contrast, on timed tasks, control participants responded faster at post, while the aerobic group showed only minimal changes in response times. Finally, participants responded faster in speed of processing tasks, spoke more fluently in the language task, and were marginally more accurate in executive function tasks in dual task rather than in single task conditions.

Our primary finding was that, following training, the aerobic group demonstrated robust improvement in executive function (+.409 SD), but only in the single task condition.

This pattern was evident in all three executive function measures, as shown in Table 5. In contrast, the balance group showed no change, and executive function performance in the control group worsened (-.26 SD), but only in the dual task condition. This pattern of response was predicted in the case of relatively small treatment effects. Specifically, it was argued that cognitive improvements due to exercise would first manifest in the single task, because any improvement in cognitive resources would be diluted by the additional attentional burden of the dual task (Kahneman, 1970).

Similarly, because available cognitive resources are shared between the dual tasks, it was predicted that small declines in cognition might first be noticeable in the dual task. This might explain the drop in executive function performance in the control group while cycling. Notably, there was no change in performance for any group on the DRS, an assessment of general cognition. Thus, in very high functioning, highly educated individuals, such as those in the current study, very demanding tasks in which scores are far from ceiling, such as the executive function tasks used in the current study, may be best for detecting cognitive change due to exercise.

Surprisingly, there was no change in attention-memory performance, even in the two most difficult tasks, digit span backward and 2-back. A potential explanation is that these two tasks relied heavily on immediate, verbatim recall and sustained attention, rather than executive function. Consistent with this argument, in a meta-analysis, digit span tasks dissociated from working memory tasks requiring more manipulation or distraction, such as operation span (Bopp & Verhaeghen, 2005). In the 2-back, only two stimuli were in the focus of attention at a time, minimizing executive function demands.

In contrast, the operation span and visual memory updating tasks required both executive function and working memory. The operation span task required six letters to be recalled after attention had been shifted to a different task, and, thus, was actually a dual task. In the visual memory updating task, incorrect comparison arrays differed from targets only by reversing the order of consecutive figures or off-setting the dots in one figure by one square. Thus, this task was very difficult. Additionally, stimuli were presented randomly, so participants did not know how many figures they would have

Table 6. Single and dual task scores for the sentence production task, pre and post training in the three groups

Language measures	Single or dual task	Aerobic exercise		Stretch-balance		Control	
		Pre (SD)	Post (SD)	Pre (SD)	Post (SD)	Pre (SD)	Post (SD)
Complete responses*	Single	.744 (.180)	.815 (.136)	.848 (.155)	.824 (.160)	.750 (.183)	.840 (.137)
	Dual	.690 (.270)	.833 (.170)	.793 (.212)	.652 (.301)	.757 (.158)	.803 (.163)
Fluent responses [‡]	Single	.534 (.284)	.652 (.253)	.705 (.202)	.760 (.257)	.465 (.301)	.665 (.318)
	Dual	.602 (.260)	.651 (.257)	.731 (.236)	.765 (.178)	.502 (.368)	.663 (.329)
Grammatical responses	Single	.729 (.318)	.718 (.244)	.761 (.239)	.718 (.322)	.755 (.240)	.795 (.148)
	Dual	.719 (.368)	.809 (.223)	.749 (.321)	.727 (.371)	.766 (.183)	.823 (.167)

Note. Analyses found only a significant group by time interaction in the completeness of response and a main effect of time in the analysis of fluent responses.

*Significant group by time interaction, $p < .05$.

[‡]Significant main effect of time, $p < .05$.

to recall, requiring memory representations to be flexible enough that participants could add to them if required, as opposed to the verbatim recall needed in digit span and 2-back. Therefore, digit span backward and 2-back may not have improved, because they were not as dependent on executive function as operation span and visual memory updating.

The findings of the current study are consistent with the three previous studies examining effects of aerobic exercise on cognition in PD. Uc and colleagues (2014) documented significant improvements in depression and resistance to interference on the Eriksen flanker task (Eriksen & Eriksen, 1974), but no significant changes on the Stroop task or other executive function tasks. Uc and colleagues also reported improvement in UPDRS scores, which were not found in the current study. The difference may be attributable to their larger sample size (i.e., 43 participants) or the longer training time (6 vs. 4 months). Unlike the current study, Uc et al. did not include a contact-equivalent control group. Thus, it is unknown how much improvement in that study was due to social stimulation.

In another study, Nocera, Altmann, Sapienza, Okun, and Hass (2010) reported the effects of a 12-week treadmill exercise intervention in one individual with PD, which yielded improvements in verbal fluency and the Stroop task. Finally, it is difficult to compare the current study to the exercise study by Cruise et al. (2010), which reported some improvement in verbal fluency and visual working memory, because it also lacked a contact-equivalent control group and did not directly compare performance of the exercise and no-contact control groups. Therefore, despite several differences, the previous studies and the current one have observed improvements in executive function tasks in individuals with PD following aerobic exercise interventions.

Consistent with Uc et al. (2014), the current study adds to the accumulating evidence that aerobic exercise training can be protective against the increasing incidence of depressive symptoms in people with PD. Mood disorders are common in PD and can be traced to both progressive neurophysiological changes in the limbic system and to the everyday burden of the disease (Cooper, Sagar, Jordan, Harvey, & Sullivan, 1991; Leentjens, 2004). Considering that both the aerobic exercise and stretch-balance groups here showed similarly stable BDI scores, this positive effect may stem from thrice weekly interactions with people outside the home, rather than a particular intervention. Therefore, future research should test whether social interventions involving multiple events per week may be similarly protective against depressive declines for people with PD.

The aerobic group also improved in completeness of responses in the language task significantly more than the stretch-balance group. Unexpectedly, the control group also improved somewhat in completeness, paralleling their non-significant improvements in single task executive function. A possible explanation was that these changes might be related. In fact, changes in completeness of response correlated significantly with changes in single task executive

function, $r(30) = .390, p = .033$. This suggests that executive function plays an important role at the conceptual level of language production. This does not, however, address why the control group improved at all in executive function at post. Their pretest performance was very poor; thus, improvements may simply represent regression to the mean.

An additional, unanticipated effect in the current study was that the control group responded faster in speed of processing tasks at post than they had initially. This pattern is remarkably consistent across single and dual conditions in five tasks. Similar changes in the stretch-balance group were not significant, and the aerobic group showed no change in RTs on these tasks. There are two possible explanations for this. One is that this is also a case of regression to the mean, as overall response times were longer in the control group than in the other two groups at initial testing. A second possibility is that faster speeds on cognitive tasks in PD represent a type of speed-accuracy trade off. Accuracy on two speed of processing tasks (simple attention, Stroop colors) was at ceiling for all groups, and accuracy on two other speed tasks dropped at post in the control group (0-back and Stroop Color Word; see Supplementary Information). Thus, faster responses on speed of processing tasks may not necessarily indicate improved performance, but instead signify a type of cognition festination during which participants respond very quickly before they have fully processed the stimuli. Tracking speed of processing over time in PD may yield new insights into cognitive effects of the disease.

Surprisingly, there were also faster RTs in speed of processing tasks during dual tasks relative to single tasks. Similarly, Altmann et al. (2015) reported faster cycling during these identical tasks in this group at pretest; thus, both motor and cognitive tasks benefitted during the dual task. Altmann et al. attributed increases in cycling speed to a combination of exercise-related arousal and cognitive arousal stemming from the fast pace of the speeded tasks. The current findings support the suggestion in Altmann et al. that the right combination of tasks, an easy motor task with easy, fast-paced cognitive tasks, can improve performance in both.

One limitation of this study was that cognitive testing was only performed while on medication. Future exercise studies in PD should also assess performance off medication. Additionally, due to randomization, groups differed somewhat in age, although not significantly; even so, initially groups were remarkably similar in disease severity, general cognition, and mood level. Indeed, the groups may have been so homogeneous that the findings of the current study may not generalize to more diverse groups of individuals with PD. Another limitation was the small sample size, which limited power to detect small changes.

In summary, the current study adds to the literature on aerobic exercise in PD in several ways. First, the study compared the effects of aerobic exercise on cognition to both contact-equivalent and no-contact control groups, helping to control for effects of both social interaction and passage of time. The results also are consistent with the suggestion that small improvements in cognition following aerobic training

will first be observable in single task settings, but declines in cognition may first be evident in dual task performance. Moreover, results demonstrate that a dual task can selectively improve performance in a variety of tasks. The study also documents that changes in language content may be related to changes in executive function. Most importantly, these findings add to the growing evidence that aerobic exercise can positively impact performance on mood and executive function in people with PD.

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Supplementary material

To view supplementary material for this article, please visit <http://dx.doi.org/10.1017/S135561771600076X>

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