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Exercise and Parkinson's: benefits for cognition and quality of life

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Objectives – The benefits of physical exercise for psychological aspects of quality of life (QoL) are well established in normally ageing adults, yet potential benefits for people with Parkinson's disease (PD) have received limited attention. This study evaluated the benefits of exercise for cognitive functioning, mood and disease-specific QoL for people with PD. *Methods* – Twenty-eight individuals with PD were allocated to an exercise intervention program (EIP, $n = 15$) or control group ($n = 13$). The EIP group undertook a programme of progressive anabolic and aerobic exercise twice weekly for 12 weeks. The control group maintained their usual lifestyle. *Results* – Exercise was shown to have selective benefits for cognitive functioning by improving frontal lobe based executive function. No significant effects were demonstrated for mood or disease-specific QoL. *Conclusions* – These results are consistent with previous research demonstrating selective benefits of exercise for executive function among normal ageing adults and PD.

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Introduction

Parkinson's disease (PD) is classically defined as a disorder of movement. However, a spectrum of cognitive, affective and psychiatric symptoms are now recognized among people with PD (1). Psychosocial well-being is now thought to have more of an impact on the quality of life (QoL) of people with PD than physical functioning (2); with depression identified as the most important predictor of QoL (3). Cognitive impairment has also been identified as an important predictor of QoL among people with PD (4). Subtle cognitive impairment is characteristic of early PD and severe cognitive impairment and dementia frequently occur with longer disease durations (1).The most frequently observed neuropsychological deficit in PD is impaired executive function (EF) (5), which is defined as the ability to plan, organize and regulate goal directed behaviour (6).

Current pharmaceutical treatments primarily treat the physical manifestations of PD and have inconsistent effects on cognitive function (7). Depressed mood is a common co-morbid condition among people with PD (5, 8); and anti-depressant medications used to treat depression in PD have been reported to exacerbate the motor symptoms in some instances (8).

One intervention that improves both cognitive functioning and psychological well-being is exercise. There is evidence of the benefits of regular exercise for neurologically normal older adults (9). Exercise reduces mood disturbances such as depression among both young and older adults (10). Improvements in cognitive functioning as a result of exercise have also been widely demonstrated, with selective benefits for executive functioning (EF) (11, 12). Improvements in EF have been associated with increased cardiovascular fitness, with combined cardiovascular and strength training demonstrating the greatest benefits for EF (11). However, the selective benefits of exercise on EF among degenerative conditions such as PD has received limited attention, with only one study to date demonstrating significant benefits of exercise on EF among people with PD (13). Daily activities requiring active problem solving, efficient organization strategies, working memory and regulation of behaviour rely on efficient EF. Improving the cognitive deficits associated with EF may therefore

have an important impact on QoL. Given the predominance of EF deficits among people with PD and the selective benefits of exercise on EF, exercise may be particularly beneficial for improving the cognitive functioning of people with PD.

Although there is convincing evidence that exercise improves the cognitive and mood domains of QoL in normally ageing adults (9–12), the potential benefits of exercise on these domains for people with PD has received limited attention. Given the importance of non-motor symptoms (e.g. cognition and mood) for predicting QoL outcomes in PD (3, 4) and the difficulty associated with treating these symptoms with pharmaceutical approaches, behavioural interventions are needed to manage the non-motor symptoms of PD. The current study investigated the benefits of an exercise-centre based exercise programme for improving the non-motor symptoms of PD, in particular deficits of EF and mood. The impact of exercise on disease-specific aspects of QoL was also investigated.

Methods

Participants

Participants were recruited from the Perth metropolitan area via the Parkinson's Association of Western Australia (PWA). All participants were diagnosed with idiopathic PD following clinical evaluation by a neurologist or geriatrician and were under specialist care for PD at the time of the study. All had Hohen Yahr scores of between I and III, indicating mild to moderate PD. Those on medications for PD had been so for at least 6 months prior to the study. Participants were excluded: if they were in the advanced stages of the disease (e.g. severe disability/wheelchair bound: Hohen and Yahr IV–V); if they had significant cognitive impairment (i.e. Mini Mental State Examination: MMSE (14) score of < 24); if they had any musculo-skeletal or neurological condition (other than PD) or cardiovascular disorder that could inhibit them from exercising; or if they had participated in regular (e.g. 2–3 times per week) resistance training in the previous 12 months.

Participants obtained GP approval before being accepted into the study. Thirty-five participants were selected to complete baseline assessments and were allocated to either to an immediate exercise intervention program (exercise; EIP) or delayed exercise group (control) based on a convenient sample method. The flow of participants from telephone screening to inclusion in the primary analysis is depicted in Fig. 1. The EIP was conducted at the Vario Health Institute, Exercise Clinic at Edith Cowan University (ECU), Western Australia and was approved by the ECU Human Research Ethics Committee and the PWA Research Committee. All participants provided written informed consent to participate in the research.

Study design

All participants underwent baseline neuropsychological and mood assessments before allocation to a 12-week intervention period of either an EIP or a delayed exercise (control) group (Fig. 1). Participants in the control group were asked to maintain their usual activities for the 12-week intervention period. On cessation of the 12-week period, participants who remained in the study completed post-assessments. Baseline and follow-up assessments were conducted during the 'ON' phase of participants' medication schedules (i.e. 1–2 h after taking dopaminergic medication) to ensure a good response to medication. Participants in the control group were offered the same 12-week EIP following the post-assessment period.

The EIP involved a combination of strength and cardiovascular training as recommended in the joint statement on physical activity for public health from the American College of Sports Medicine and the American Heart Association (15, 16). The EIP involved twice weekly exercise sessions of approximately 60 min duration. Each session began with a 5 min warm up comprising of low-level aerobic activity such as walking, stationary cycling and stretching. Six resistance exercises targeting the major upper and lower body muscle groups were performed. To ensure the progressive nature of the training programme, participants were encouraged to work past the specific Repetition Maximum (RM) prescribed. The workload was increased by a 5–10% increment for the next set or training session if participants were able to perform past the specified RM. The aerobic component comprised 25–30 min of stationary cycling, rowing or treadmill activity at 60–85% of heart rate maximum. Participants were asked to maintain customary physical activity and dietary patterns over the intervention period.

Neuropsychological assessments

Global cognitive functioning was assessed using the MMSE (15) and WAIS verbal IQ was estimated using the Australian National Adult Reading Test [AUSNART (17)]. In order to investigate selective benefits of exercise on frontal

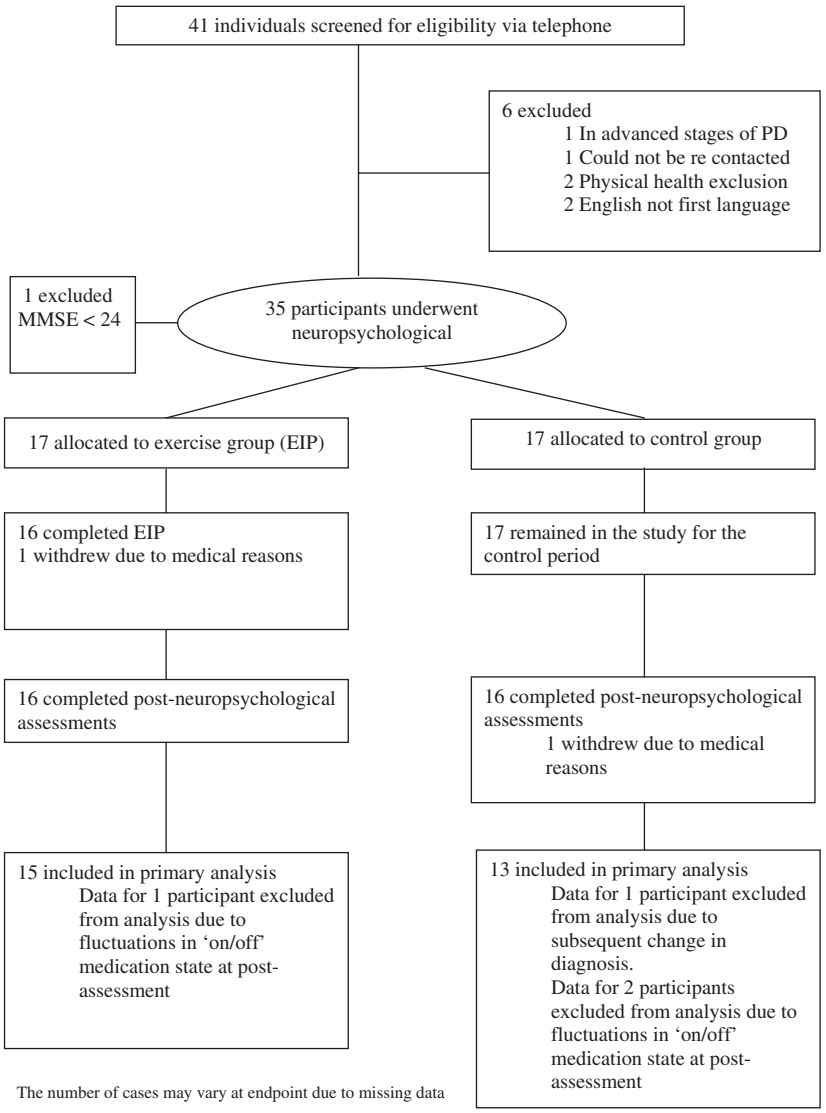

Figure 1. Flow of participants from screening to final inclusion in primary analysis.

lobe based EF, neuropsychological assessments were selected based on differential sensitivity to frontal, fronto-temporal and temporal lobe function (see Table 1). The authors recognize, however, that no one test fully loads onto a particular neuroanatomical region and that there is a certain degree of overlap between tests. The tasks included a test of verbal fluency for words starting with the letters F, A and S for one minute each (18) and a test of semantic fluency for animals in a 1 min period (19). Selected computerized tests were administered using the Cambridge Neuropsychological Test Automated Battery (CANTABelipse^{TM}) software (20) and included the Pattern and Spatial Recognition Memory (PRM and SRM respectively); Spatial Working Memory (SWM);

Table 1 Neuroanatomical correlates of each neuropsychological assessment

	Brain region		
	Frontal	Fronto-temporal	Temporal
Neuropsychological assessment	Verbal fluency (F, A, S) Spatial working memory (SWM) Stocking of Cambridge (SOC)	Spatial recognition memory (SRM)	Pattern recognition memory (PRM) Semantic fluency for animals

and Stockings of Cambridge (SOC; a measure of working memory and spatial planning) subtests.

Assessment of mood and disease-specific QoL

Level of depressed mood was measured using the 15 item Geriatric Depression Scale (GDS) (21). The GDS focuses on the psychological and social aspects of depression avoiding somatic symptom overlap with medical disorders and ageing (22) and has demonstrated validity as a screening tool for depression in both normal ageing (23) and PD (22).

The Parkinson's Disease Questionnaire (PDQ-39) (24) assesses disease-specific QoL in eight domains: mobility, activities of daily living, emotional well-being, stigma, social support, cognitive impairment, communication and bodily discomfort. Scores for these eight domains can be validly summed to produce a single index (SI) or measure of total QoL (24). The SI has the advantage of reducing the number of statistical comparisons and is useful for evaluating the overall effect of a treatment on QoL (24). For these reasons, the SI was used to evaluate the benefits of exercise on QoL.

Statistical analysis

Mean substitution was used to impute missing values when calculating total scores for the GDS and PDQ39 SI. Total scores involving more than one missing value were excluded from further analyses. Means, SD and % change pre to post were calculated for both groups for each outcome measure. Given the small samples used in this study, conventional inferential statistics using *P*-values were, arguably, not the most appropriate approach to making an inference about the true effect of the intervention on our outcome measures. Accordingly, inferences about the true value of the change scores were calculated as recommended by Hopkins (25). First, paired samples *t*-tests were calculated for pre–post comparisons within each group. The resulting *P*-values and mean % change scores were then used to calculate 90% CI (for percentage change) and clinical inferences. Clinical inferences are presented as % chance that the true value of the % change scores was beneficial, trivial or harmful (25). These chance scores are reported with verbal descriptors: 0 (most unlikely), 0.5 (very unlikely), 5 (unlikely), 25 (possibly), 75 (likely), 95 (very likely), and 99.5 (most likely) (25).

For all neuropsychological measures, a 10% change was deemed clinically meaningful. This threshold was determined based on consideration of previous clinical trials for improving cognitive functioning (26). For the GDS, a 20% change was deemed clinically meaningful based on previous research into the benefits of exercise for reducing depressive symptoms in Alzheimer's disease (27). No research to date has shown a benefit of exercise on depressive symptoms in PD (28). A 50% change for the PDQ39-SI was deemed clinically meaningful based on research demonstrating the benefits of exercise on QoL for PD (29).

Results

Description of the sample

The EIP and control group involved approximately equal numbers of males and females with similar mean ages. Both groups had been diagnosed with PD for similar mean durations and there was no significant difference between the groups for either WAIS Verbal IQ or MMSE scores (see Table 2).

Neuropsychological assessments

Qualitative outcomes for clinically beneficial effects of exercise are outlined in Table 3. Exercise was shown to be of 'likely benefit' for improving performance on verbal fluency and for reducing spatial working memory (SWM) errors. Exercise was shown to be of 'possible benefit' for category or semantic fluency for animals (CFA). Both EIP and non-exercise (control) conditions were described as 'possibly' beneficial for the stocking of Cambridge (SOC) task and no clinically beneficial effects were demonstrated for the EIP or control group for the pattern or spatial recognition tasks (PRM and SRM respectively). Exercise was not considered to have any negative impacts on any outcome measure.

Mood and disease-specific QoL assessments

Both EIP and no-exercise (control group) were shown to have similar 'possibly beneficial' effects for reducing depression. Both EIP and control

Table 2 Participant demographic features

	EIP	Control
Sex (M:F)	9:6	9:4
Mean age (years)	59.47 ± 11.54	60.6 ± 7.34
Disease duration (years)	5.87 ± 3.18	5.46 ± 3.63
WAIS Verbal IQ*	109.41 ± 7.69	111.39 ± 5.91
MMSE*	28.13 ± 1.84	27.62 ± 1.32

*There were no significant differences between groups on Verbal IQ or MMSE score.

Table 3 Qualitative outcomes for EIP and control group

						Qualitative Outcome[1] Percentage chance that the change is clinically meaningful (verbal descriptor)		
Measure	Group	Pre Mean	Post Mean	% Change Mean	90% Confidence Limit of % Change	Substantially beneficial	Negligible or trivial	Substantially harmful
SWM	EIP	33.8 ± 24.06	25.40 ± 21.58	−19.55 ± 43.46	−35.7–−3.4	84.3% likely	15.4% unlikely	0.3% most unlikely
	Control	43.54 ± 17.54	42.38 ± 13.39	45.6 ± 193.01	−283.4–374.6	38.4% likely	4.1% unlikely	57.5% possibly
PRM	EIP	21.00 ± 2.42	21.40 ± 1.76	2.62 ± 9.77	−2.8–8.0	1.5% very unlikely	98.5% very likely	0.1% most unlikely
	Control	20.54 ± 3.23	20.46 ± 3.02	.90 ± 16.0	−15.1–16.9	16.6% unlikely	70.9% possibly	12.5% unlikely
SRM	EIP	15.80 ± 2.11	16.53 ± 1.77	5.27 ± 8.71	0.9–9.6	3.9% very unlikely	9.6% very unlikely	0% most unlikely
	Control	15.85 ± 1.86	15.85 ± 1.28	1.05 ± 12.45	[2]	50% possibly	0% most unlikely	50% possibly
SOC	EIP	7.67 ± 2.22	8.13 ± 2.20	9.12 ± 24.77	−7.3–25.5	46.3% possibly	50.7% possibly	3.0% very unlikely
	Control	7.62 ± 1.56	7.77 ± 1.83	8.23 ± 41.61	−61.5–78.0	48.2% possibly	19.3% unlikely	32.5% possibly
FAS	EIP	40.27 ± 8.54	46.40 ± 10.20	15.78 ± 14.81	9.1–22.5	92.4% likely	7.6% unlikely	0% most unlikely
	Control	43.15 ± 17.04	42.46 ± 15.73	.02 ± 12.66	−0.1–0.1	0% most unlikely	100% most likely	0% most unlikely
CFA	EIP	17.93 ± 5.08	20.00 ± 4.56	21.09 ± 46.74	−11.5–53.7	72.1% possibly	22.2% unlikely	5.8% unlikely
	Control	19.85 ± 3.95	20.62 ± 5.55	3.48 ± 11.06	−2.7–9.6	4.2% very unlikely	95.7% very unlikely	0.1% most unlikely
GDS	EIP	2.07 ± 1.73	1.71 ± 1.68	−27.38 ± 48.31	−61.0–6.3	64.8% possibly	33.9% possibly	1.4% very unlikely
	Control	3.89 ± 3.33	2.89 ± 3.41	−25 ± 56.19	−49.5–−0.5	64.3% possibly	35.2% possibly	0.5% most unlikely
PDQ39 SI	EIP	16.42 ± 7.68	17.87 ± 7.38	17.17 ± 39.02	−11.0–45.3	0.1% most unlikely	99.9% most likely	0%most unlikely
	Control	27.94 ± 18.03	24.71 ± 18.13	−7.08 ± 40.59	−16.7–2.5	0% most unlikely	100% most likely	0% most unlikely

SWM: spatial working memory between errors; higher scores indicate worse performance and a negative change score reflects improvement over time; SRM: spatial recognition memory; PRM: pattern recognition memory; SOC: stockings of Cambridge; FAS: verbal fluency for letters F, A and S; CFA: category fluency for animals; GDS: geriatric depression scale; PDQ39-SI: Parkinson's Disease Questionnaire, summary index.

[1]Qualitiative outcomes reflect the chance that the change in each outcome measure, for each of the EIP and control groups, is likely to be beneficial, trivial or harmful to participants. For the purposes of this calculation, a 10% change in SWM, SRM, PRM, SOC, FAS and CFA scores, a 20% change in GDS scores and a 50% change in PDQ39 SI scores, was deemed to be clinically meaningful.

[2]CI could not be calculated for SRM control group as there was no mean difference between pre and post scores.

conditions were not shown to improve QoL, as indicated by the PDQ39-SI.

Discussion

This study examined the benefits of exercise for improving the quality of life (QoL) of people with PD in the domains of cognitive functioning, mood and disease-specific QoL. Exercise was shown to exert a selective benefit for frontal lobe based executive function (EF) (i.e. spatial working memory and verbal fluency, both semantic and category) compared to tasks mediated by the fronto-temporal (spatial recognition memory) and temporal lobe (pattern recognition memory). However, exercise did not show benefit for mood or disease-specific QoL.

The current results provide support for previous research demonstrating selective benefits of exercise on frontal lobe based EF in normally ageing adults (11, 12). In particular, this research is consistent with evidence that a combined strength and aerobic training intervention leads to greater benefits for EF than aerobic exercise alone (11). Beyond the results presented here, only one other study has confirmed the benefits of exercise on EF among people with PD (13). Only one measure of EF (the Wisconsin Card Sorting Task) was examined in this research and psychological variables such as depression and anxiety were treated as confounding variables rather than as independent variables that may benefit from exercise. Exercise was, however, shown to have selective benefits on areas of EF related to mental flexibility and inhibition.

The two frontally mediated tasks (spatial working memory and verbal fluency) which demonstrated exercise-specific benefits in this study both place a substantial load on working memory and require effective and organized search and thinking strategies (6). In contrast, while still sensitive to frontal lobe function, we did not observe any differences between the groups for the Stockings of Cambridge (SOC) task which requires both working memory and spatial planning ability. The SOC task employed in this research required participants to reorganize one display of coloured balls to match another existing display in a minimum number of moves. In contrast, other variants of the task require one mentally to work out how many moves the solution requires in order for the displays to be matched. As such, it could be argued that the SOC task employed in this research is more heavily reliant on spatial planning ability than spatial working memory. Hence, in light of these results it seems reasonable to suggest that

exercise has a selective benefit on frontal lobe based tasks that are more highly associated with working memory and organization of search and thinking strategies. This interpretation is further supported by the possibly beneficial effects of exercise on semantic or category fluency. Although there is a strong association between verbal and semantic fluency tasks with the frontal and temporal cortices respectively (30), both tasks have been associated with some level of activation in frontal cortical regions (31). Both tasks place demands on frontal lobe based EF as they rely on working memory processes and require organized verbal retrieval strategies and self-monitoring of responses (31). Hence, although semantic fluency tasks are more heavily associated with the temporal lobe (30) the nature of the task requirements for working memory and organized search strategies implies some involvement of the frontal lobe which may account for the benefits demonstrated for semantic fluency and not for the pattern and spatial recognition tasks.

Mood and disease-specific QoL were not improved by exercise, in keeping with a recent study conducted with individuals with multiple sclerosis (32). These null effects may be explained by a floor effect in the data. Seventy-one percent of the sample ($n = 17$) were classified within the normal range for depression (GDS 0–4) and only two participants reported baseline PDQ39 SI scores greater than 50 out of 100 (higher scores indicating poorer QoL). Given that the majority of participants were in the normal range for depression and did not report poor disease-specific QoL at baseline, it is reasonable to suggest that exercise would not improve these areas beyond the normal range. One limitation of this research therefore relates to sampling bias. Participants for this research were recruited from PD support groups and likely involved people who are quite active at support seeking and disease management. The research itself involved a substantial commitment on behalf of the participants and it is likely that more self-motivated and independent people took part. This limitation could be addressed firstly with a larger sample size and secondly, by recruiting participants from a clinic setting. Similarly, specifically screening participants for depression as an inclusion criterion would allow for a more in depth assessment of the benefits of exercise on mood.

Another limitation of the research regards the treatment of the control group. The improvements demonstrated by the EIP group could potentially result from the benefits of social interaction rather than exercise *per se*. However, following this rationale, social interaction would have been expected to have a greater impact on mood and disease-specific QoL than cognitive function. Also, it is our experience of over 20 years of exercise intervention research that 'sham' conditions are more of a contaminant than the potentially confounding effects of social interaction. When participants are randomized to a 'sham' control group we have found that they will form social networks and then alter their behaviours. Often participants initiate exercise programmes which totally invalidates them as experimental controls.

Conclusion

This study has demonstrated exercise-specific benefits for EF in a group of people affected by PD. Improvements in frontal lobe based EF may have important implications for people with PD, not only because EF deficits are frequently observed in PD, but because effective EF is important for activities of daily living. Future research should aim to examine the relationship between EF and QoL fully to assess the benefits of exercise. Although exercise was not shown to benefit mood or disease-specific QoL, this effect can be accounted for by sample characteristics. Nonetheless, this research provides an important foundation for future research in the area of exercise and PD and provides a platform for research aimed at the management of the non-motor symptoms of PD.

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Conflict of interest

None declared.

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