

Forced, Not Voluntary, Exercise Improves Motor Function in Parkinson's Disease Patients

Angela L. Ridgel, PhD, Jerrold L. Vitek, MD, PhD, and Jay L. Alberts, PhD

Background. Animal studies indicate forced exercise (FE) improves overall motor function in Parkinsonian rodents. Global improvements in motor function following voluntary exercise (VE) are not widely reported in human Parkinson's disease (PD) patients. **Objective.** The aim of this study was to compare the effects of VE and FE on PD symptoms, motor function, and bimanual dexterity. **Methods.** Ten patients with mild to moderate PD were randomly assigned to complete 8 weeks of FE or VE. With the assistance of a trainer, patients in the FE group pedaled at a rate 30% greater than their preferred voluntary rate, whereas patients in the VE group pedaled at their preferred rate. Aerobic intensity for both groups was identical, 60% to 80% of their individualized training heart rate. **Results.** Aerobic fitness improved for both groups. Following FE, Unified Parkinson's Disease Rating Scale (UPDRS) motor scores improved 35%, whereas patients completing VE did not exhibit any improvement. The control and coordination of grasping forces during the performance of a functional bimanual dexterity task improved significantly for patients in the FE group, whereas no changes in motor performance were observed following VE. Improvements in clinical measures of rigidity and bradykinesia and biomechanical measures of bimanual dexterity were maintained 4 weeks after FE cessation. **Conclusions.** Aerobic fitness can be improved in PD patients following both VE and FE interventions. However, only FE results in significant improvements in motor function and bimanual dexterity. Biomechanical data indicate that FE leads to a shift in motor control strategy, from feedback to a greater reliance on feedforward processes, which suggests FE may be altering central motor control processes.

Key Words: *Parkinson's disease; Exercise; Manual dexterity; Motor control; Grasping forces; Movement disorder*

Forced exercise (FE), an intervention in which the animal is forced to maintain a running speed greater than its preferred pace, improves motor function and is neuroprotective in Parkinsonian-treated animals.^{1,2} Data indicate that the rate of FE may be an important factor in global motor improvements.² Dramatic effects of exercise have not been reported in human PD exercise trials. Variation in exercise rate may underlie differences in animal and human results. Unlike the effective FE paradigms used in animal studies, interventions for PD patients involve exercise that is under voluntary control and self-paced.^{3,4}

Neurophysiological,⁵ functional magnetic resonance imaging (fMRI),⁶ and positron emission tomography (PET)⁷ data indicate that PD results in an overall decrease in the level of neural activation of cortical motor areas, which likely contributes to the general poverty of movement in PD patients and limits their ability to consistently exercise at a high frequency or rate. To compensate for diminished voluntary neural activity, exercise rate may need to be augmented externally if PD patients are to fully realize the benefits of exercise described in the animal literature. Motor cortex function and excitability can be modulated by augmenting proprioceptive sensory signals in healthy human subjects.^{8,9} Peripheral nerve stimulation

increases excitability in the motor cortex, as measured by transcranial magnetic stimulation (TMS), and has been useful as a neurorehabilitation method in individuals with stroke. Takahashi and colleagues examined the effectiveness of a hand-wrist robot in improving motor function and brain reorganization in individuals with chronic stroke.¹⁰ They showed that active robotic assistance resulted in significantly greater gains in motor function than in individuals who received passive robotic assistance. The authors suggest that the active assist mode results in greater proprioceptive sensory signals to the brain and that this afferent feedback is responsible for improvements in motor function and increased motor cortical activation.¹⁰

Based on these findings, we hypothesize that to maximize the benefits of physical exercise on motor function in Parkinson's patients, a forced or augmented rate of exercise may be necessary. To test this hypothesis, a lower extremity FE intervention was developed for PD patients using a stationary tandem bicycle. Patients' pedaling rate was increased to approximately 30% more than their preferred rate. If FE leads to changes in central motor processing, improved motor function in the nonexercised effectors (upper extremity) was expected for the FE, but not the voluntary exercise (VE) group.

From the Department of Biomedical Engineering, Cleveland Clinic, Cleveland, OH (ALR); the Center for Neurological Restoration, Cleveland Clinic, Cleveland, OH (JLV, JLA); the Center for Functional Electrical Stimulation, Louis Stokes Veterans Administration, Cleveland, OH (JLA); and the Department of Neuroscience, Cleveland Clinic, Cleveland, OH (JLV). Address correspondence to Jay L. Alberts, PhD, Cleveland Clinic, Department of Biomedical Engineering/ND-20, 9500 Euclid Ave, Cleveland, OH 44195. E-mail: albertj@ccf.org.

Table 1
Group Demographics^a

	Forced (n = 5)	Voluntary (n = 5)	<i>P</i> ^b
Age (y)	58 ± 2.1	64 ± 7.1	.08
Duration of PD (y)	7.9 ± 7.0	4.4 ± 4.0	.36
UPDRS motor III score			
Baseline	48.4 ± 12.7	49.0 ± 15.4	.95
Cadence (rpm)	85.8 ± 0.8	59.8 ± 13.6	.002
Absolute power (watts)	47 ± 16	67 ± 24	.17
Heart rate (bpm)	116.8 ± 4.8	121.2 ± 20.5	.65
Total work (kJ)	129.2 ± 26.2	149.6 ± 59.3	.50
Estimated $\dot{V}O_2$ max (mL/kg/min)			
Baseline	26.1 ± 6.1	22.5 ± 2.0	.29

Abbreviations: bpm, beats per minute; EOT, end of training; EOT+4, 4 weeks after EOT; kJ, kilojoules; PD, Parkinson's disease; rpm, revolutions per minute; UPDRS, Unified Parkinson's Disease Rating Scale.

^aValues are mean ± standard deviation. The groups did not significantly differ from each other at baseline.

^b*P* values from unpaired Student's *t* test statistics.

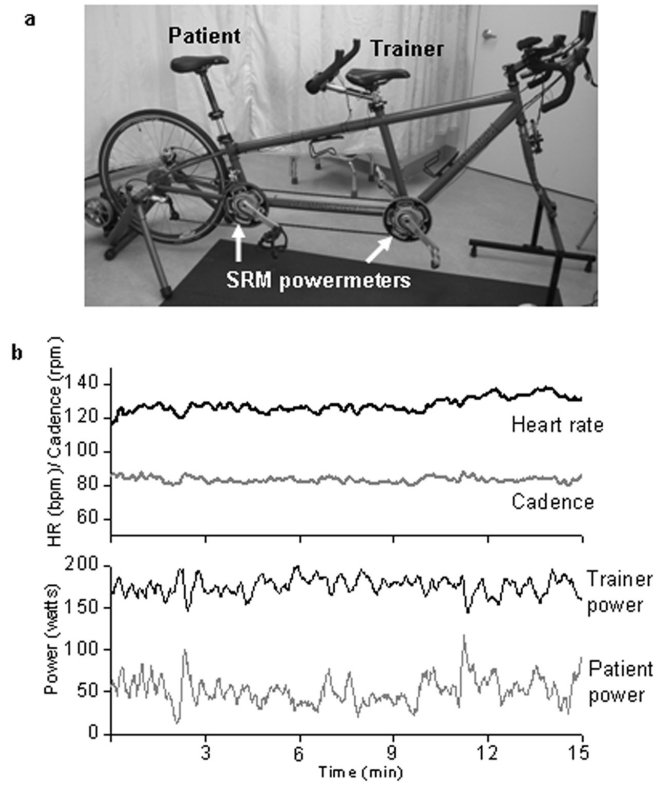
Methods

Ten patients with idiopathic PD (8 men and 2 women; age 61.2 ± 6.0 years, Table 1) were randomly assigned to complete an 8-week FE or VE exercise intervention. Following the 8-week intervention, patients were instructed to resume their pre-enrollment activity levels; follow-up patient interviews indicated compliance with this request. Patients in the FE group exercised with a trainer on a stationary tandem bicycle (Figure 1a), whereas the VE group exercised on a stationary single bicycle (Schoberer Rad Meßtechnik [SRM]). The work performed by the patient and the trainer on the tandem bicycle was measured independently with 2 commercially available power meters (SRM PowerMeter; Jülich, Germany).

Protocol

All patients completed three 1-hour exercise sessions per week for 8 weeks. Each session consisted of a 10-minute warm-up, a 40-minute exercise set, and a 10-minute cool-down. The subjects were given 2- to 5-minute breaks, if needed, every 10 minutes during the 40-minute main exercise set in the initial 2 weeks of the study and were encouraged to exercise for 20 minutes at a time with a single break in later sessions. Power, heart rate, and cadence values were sampled and collected at 60 Hz.

To control for any changes owing to fitness, both groups exercised at similar aerobic intensities (eg, 60%-80% of their individualized target heart rate [T_{HR}]). The T_{HR} was calculated using the Karnoven formula, where maximum heart rate was defined as 220 minus the patient's age.¹¹ Patients in the VE group were instructed to pedal at their preferred voluntary rate and to maintain their heart rate within T_{HR} . Patients in the FE group were instructed to maintain their HR within their T_{HR} as well. Patients in both groups were also encouraged to increase

Figure 1
A Stationary Tandem Bicycle Was Used to Deliver the Forced-Exercise Treatment

Note: a, A tandem bicycle was mounted on a mechanical trainer with the front fork secured. SRM cranks were installed at both the trainer (front) and patient (rear) positions. b, During this FE session the human trainer produced 175 ± 11 watts of power and the patient produced 54 ± 17 watts. Cadence and heart rate for the patient participants were 83.2 ± 1.7 rpm and 128.8 ± 5.3 bpm, respectively.

their heart rate range every 2 weeks by 5% (eg, 60%, 65%, 70%, 75% T_{HR}). The FE group, assisted by an able-bodied trainer, maintained a pedaling rate between 80 and 90 revolutions per minute (rpm), or 30% more than their VE rate. The trainer modulated the resistance to ensure patients were actively engaging in pedalings, which allowed the patients to maintain T_{HR} . Representative training data (pedaling rate, HR, and trainer and patient power) during a 15-minute exercise block of FE are shown in Figure 1b. For both groups, an exercise supervisor provided encouragement throughout each exercise session and ensured that patients maintained their heart rate within T_{HR} . Medications for PD remained constant throughout the study. The levodopa equivalent daily dose (LEDD) was calculated for each patient, as described previously.¹² All subjects provided informed consent, following Cleveland Clinic IRB policy, prior to randomization.

Baseline Fitness Evaluation

The YMCA submaximal cycle ergometer test was used to estimate maximal oxygen uptake ($\dot{V}O_{2max}$) prior to and after

the intervention. Heart rate–workload values were obtained at 4 points and extrapolated to predict workload at the estimated maximum heart rate. Vo_2max was then calculated from the predicted maximum workload using the formulas of Storer and colleagues.¹³ Prior to starting the test, patients cycled at a self-selected cadence and resistance for 3 minutes. This time served as a warm-up and a measure of voluntary cadence. For the test, patients pedaled the ergometer for 9 minutes (three 3-minute stages). The resistance was increased by 25 watts at each stage according to YMCA guidelines.^{14,15} For the analysis, average heart rate during the final 30 seconds of the second and third minutes was plotted against workload for each stage to gain an estimate of Vo_2max . A cool-down period of 5 minutes was performed after the test. Patients were allowed to stop the test at any time if they experienced discomfort; no patient stopped the exercise test.

Motor Function Evaluation

The Unified Parkinson's Disease Rating Scale (UPDRS) Part III motor exam and manual dexterity assessments were completed while patients were “off” anti-Parkinsonian medication for 12 hours. Blinded UPDRS ratings were completed by an experienced movement disorders neurologist. Assessments were performed on 3 occasions: pretreatment (baseline), end of treatment (EOT), and EOT plus 4 weeks (EOT+4). Manual dexterity was quantified using a paradigm described previously in our studies with PD.^{16,17} The technician completing data collection was not blinded to group assignment. However, to avoid bias, the technician read an identical script to each subject explaining task requirements prior to all data collection sessions. This paradigm replicates functional manual dexterity tasks performed on a daily basis: the 2 limbs working together to separate 2 objects (similar to opening a container).

Ten trials were performed at 8 N resistance at each of the 3 evaluation time points. Interlimb coordination, as determined by the time interval between onset of grip force in manipulating and stabilizing hands and rate of grip-force production, were used to quantify bimanual dexterity.¹⁶ Furthermore, the center of pressure (CoP) was computed from the moment caused by the pinch force about the true origin of the transducer and the pinch force itself. The x-coordinate of the CoP was defined as the ratio of the moment in y-direction to the pinch force (ie, force in z-direction), and the y-coordinate was defined as the ratio of the moment in x-direction to the pinch force. Additionally, principal component analysis was performed to quantify the CoP data.¹⁸ An ellipse that encompasses 95% of the CoP was constructed to calculate the area of the ellipse. The area of the ellipse defines the spread or the variation in the CoP data and serves as a measure of consistency of digit placement.¹⁷

Statistical Analysis

A 2×3 (group-by-time) repeated-measures analysis of variance (ANOVA) was used to compare the group versus time

(baseline, EOT, EOT+4) interaction between the variables. Post hoc multiple comparison tests were performed using the Bonferroni method, which adjusts the significance level for multiple comparisons. Student's *t* tests were used to compare exercise-based variables (eg, cadence, heart rate, Vo_2max , work, power) and patient demographics between the FE and VE groups. All analyses were performed with SPSS 14.0 (SPSS, Inc, Chicago, IL, 2005).

Results

Age, duration of PD, baseline fitness (estimated Vo_2max) and initial UPDRS III score while “off” anti-Parkinsonian medication were comparable between groups (Table 1). To assess workload, the total work produced during cycling was calculated; total work = power (as measured by the SRM PowerMeters) \times exercise time. The total work for the FE group was then calculated for the trainer and patient individually. Patients in the FE group contributed 25% of the total work performed during pedaling, and the trainer produced the remaining 75%. The total work (Kj) produced by the patients and T_{HR} during the exercise intervention did not differ between the groups. Average cadence during FE was significantly greater (30%) than in the VE group (Table 1, $t_8 = 4.264$, $P = .002$). Aerobic capacity improved by 17% and 11% for the VE and FE groups, respectively; this difference between groups was not statistically significant.

A significant group-by-time interaction was present for UPDRS scores ($F_{2,6} = 15.062$, $P = .005$) (Table 2, Figure 2). For the FE group, UPDRS scores improved by 35% from baseline to EOT ($P = .002$), whereas no improvements were observed for the VE group ($P > .17$). Four weeks after exercise cessation, the UPDRS was 11% less than baseline for the FE group. The improvement at the EOT+4 evaluation for the FE group approached significance ($P = .09$), and improved UPDRS at this point was present in 4 of the 5 patients in this group. In the VE group, UPDRS scores from baseline and EOT+4 were similar. Furthermore, improvements in each UPDRS motor subscale varied from patient to patient, but across the FE group, rigidity improved by 41%, tremor improved by 38%, and bradykinesia improved by 28% after 8 weeks of forced exercise (Table 3).

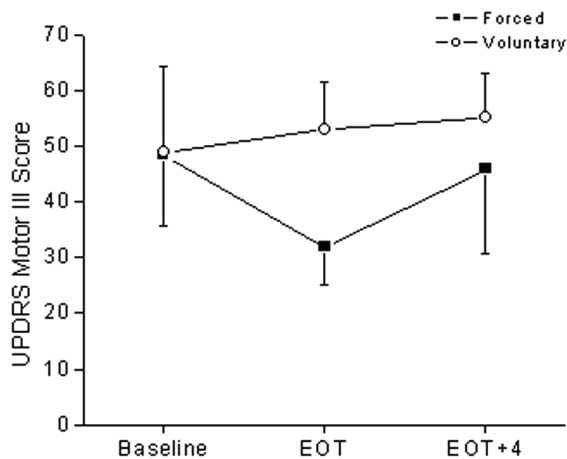
Prior to exercise, coupling of grasping forces was irregular and inconsistent in both groups (Figure 3a), which is consistent with our previous studies with PD patients.^{16,17,19} However following forced exercise, grip-load profile plots were more consistent and increased in a more linear fashion for both limbs. No changes in coupling of grasping forces were noted in the VE group. Interlimb coordination, as assessed by grip time delay, improved significantly for the FE group but did not change for the VE group (Figure 3b; $F_{2,46} = 4.634$, $P = .015$). Neither group exhibited significant improvements in rate of force production for the stabilizing limb. A group-by-time interaction was present for the rate of grip force for the manipulating limb ($F_{2,36} = 6.195$, $P = .005$); the FE group increased

Table 2
Demographic and Total UPDRS Motor III Scores for Individual Subjects at Each Evaluation Point^a

Patient	Group	Age	Disease Duration (y)	H & Y	Medication (LEDD in mg)	UPDRS Baseline	UPDRS EOT	UPDRS EOT+4
1	FE	58	5	I-II	200	45	28	53
2	FE	60	10	II-II	275	58	35	49
3	FE	60	11	II-III	420	65	42	66
4	FE	57	5	I-II	225	38	29	28
5	FE	55	3	I	100	36	25	34
6	VE	65	10	III	–	73	63	–
7	VE	55	0.5	I	120	30	44	50
8	VE	61	5	I-II	360	48	52	67
9	VE	74	6	I-II	–	49	59	56
10	VE	67	0.5	I-II	470	45	45	49

Abbreviations: EOT, end of treatment; EOT+4, end of treatment plus 4 weeks; FE, forced exercise; LEDD, levodopa equivalent daily dose; VE, voluntary exercise; UPDRS, Unified Parkinson's Disease Rating Scale.

Figure 2
Mean Change in UPDRS III Motor Scores Decreased Significantly After 8 weeks of Forced Exercise but Returned Toward Baseline After the Exercise Training Was Completed



Note: Unified Parkinson's Disease Rating Scale (UPDRS) score were unchanged in the voluntary exercise group. Error bars = standard deviations. EOT indicates end of treatment; EOT+4, end of treatment plus 4 weeks.

the rate significantly ($P = .006$), whereas a slight decrease was observed for the VE group ($P = .405$; Figure 3c). Following exercise cessation, improvements in the rate of force production were maintained for the FE group, whereas the VE group did not change from baseline. These improvements in the coupling of grasping forces, interlimb coordination, and rate of force production indicate that manual dexterity was improved for patients in the FE group compared to those patients performing VE.

The CoP data for each trial for all patients at each evaluation point for stabilizing and manipulating limbs are provided in Figure 4. A significant group-by-time interaction was present for area of CoP for the manipulating ($F_{2,36} = 7.85, P < .001$)

and stabilizing ($F_{2,36} = 6.41, P < .001$) limbs. At baseline, patients in both groups, on average, were highly variable in digit placement for both limbs. The average area of the ellipse for the manipulating and stabilizing hand was 4.1 cm^2 and 3.1 cm^2 for the FE group, respectively, whereas the VE group had areas of 3.8 cm^2 and 3.1 cm^2 for the manipulating and stabilizing hands, respectively. In general, the VE group did not exhibit any improvement in consistency of digit placement: at EOT, 2.9 cm^2 and 2.8 cm^2 for the manipulating and stabilizing limb, respectively, and at EOT+4, 2.9 cm^2 and 2.5 cm^2 . Forced exercise resulted in a significant improvement in the consistency of digit placement for both limbs. At EOT, the area of the ellipse decreased to 1.1 mm^2 and 1.0 mm^2 for the manipulating and stabilizing limbs, respectively ($P < .01$ for both). These improvements were maintained at the EOT+4 week evaluation, as area was 1.74 cm^2 and 0.89 cm^2 ($P < .01$ for both).

Discussion

This preliminary study demonstrates that 8 weeks of VE or FE improves aerobic fitness of PD patients. However, only FE produces global improvements in motor function, as evidenced by improvements in clinical ratings and biomechanical measures of upper extremity dexterity. Although not statistically significant, levels of rigidity were the same or better for all patients in the FE group after exercise cessation compared to baseline rigidity. Similarly, bradykinesia was improved in 3 of the 5 patients at the EOT+4 follow-up compared to baseline levels. These clinical data suggest that the effects of FE are not transitory but may be maintained, albeit to a lesser degree than the immediate effects. A limitation of the UPDRS is its rather limited range and its subjective scoring. Based on objective biomechanical measures, gains in upper extremity function following FE were maintained at 4 weeks after cessation of FE.

Previous studies indicate that PD patients produce irregular grip-load profiles, are limited in the rate of digit and overall force production,²⁰ and are variable in the placement of their digits during the performance of dexterous actions.¹⁷ These

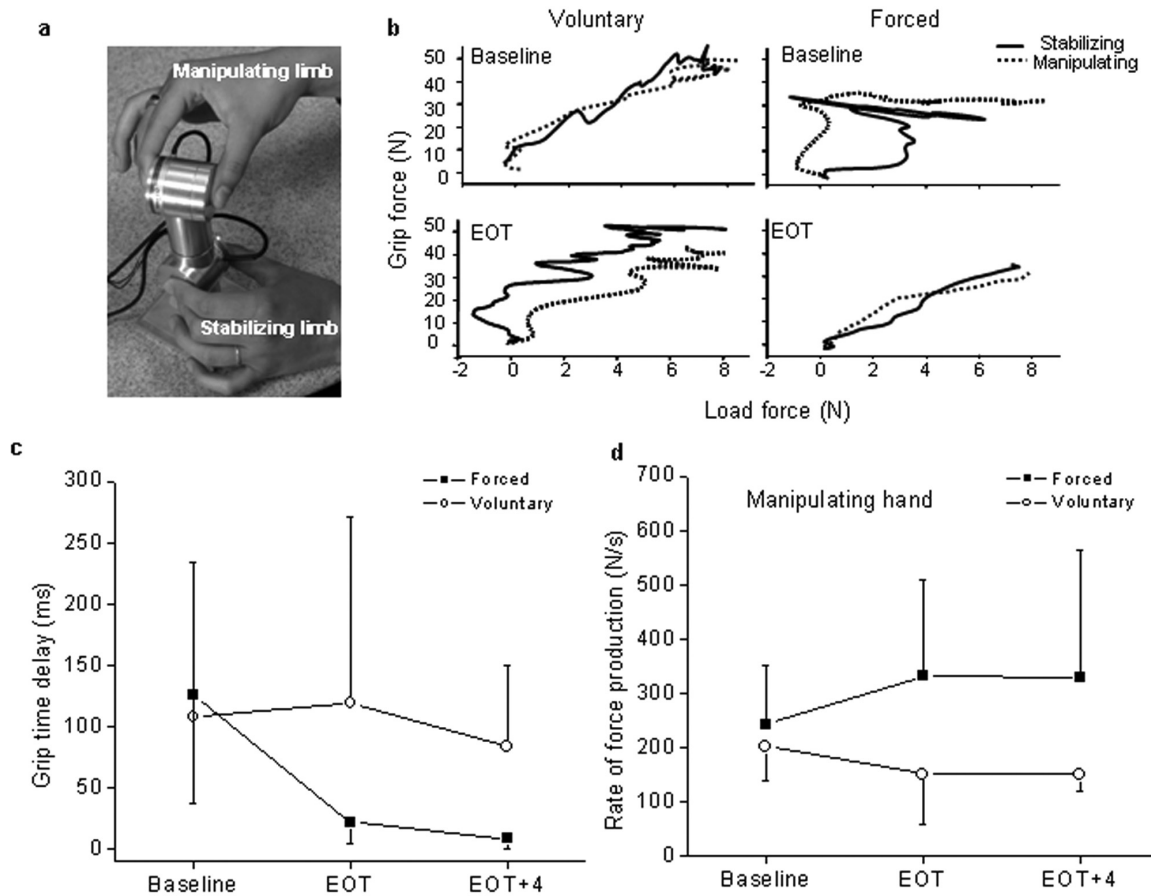
Table 3
Subscale Analysis of UPDRS Motor III Scores for Individual Subjects at Each Evaluation Point^a

Patient	Group	Rigidity	Tremor	Bradykinesia	Gait	Postural Stability
		Base/EOT/EOT+4	Base/EOT/EOT+4	Base/EOT/EOT+4	Base/EOT/EOT+4	Base/EOT/EOT+4
1	FE	12/7/12	8/5/10	19/10/21	1/1/2	1/1/2
2	FE	13/6/9	7/4/8	24/18/23	3/2/2	2/1/1
3	FE	17/6/12	9/5/14	25/21/25	3/1/3	3/2/3
4	FE	9/7/9	6/3/1	16/13/15	1/2/1	0/1/1
5	FE	8/6/7	7/6/10	16/11/15	1/1/1	1/0/1
6	VE	14/14/-	18/15/-	28/22/-	4/3/-	2/3/-
7	VE	6/10/10	5/7/12	13/22/22	1/1/1	1/1/2
8	VE	12/16/18	10/6/10	20/22/30	1/2/2	1/1/1
9	VE	8/12/11	9/10/10	22/24/24	3/3/2	2/2/2
10	VE	9/8/12	11/13/15	17/14/15	2/2/2	1/2/2

Abbreviations: base, baseline; EOT, end of treatment; EOT+4, end of treatment plus 4 weeks; FE, forced exercise; VE, voluntary exercise; UPDRS, Unified Parkinson’s Disease Rating Scale.

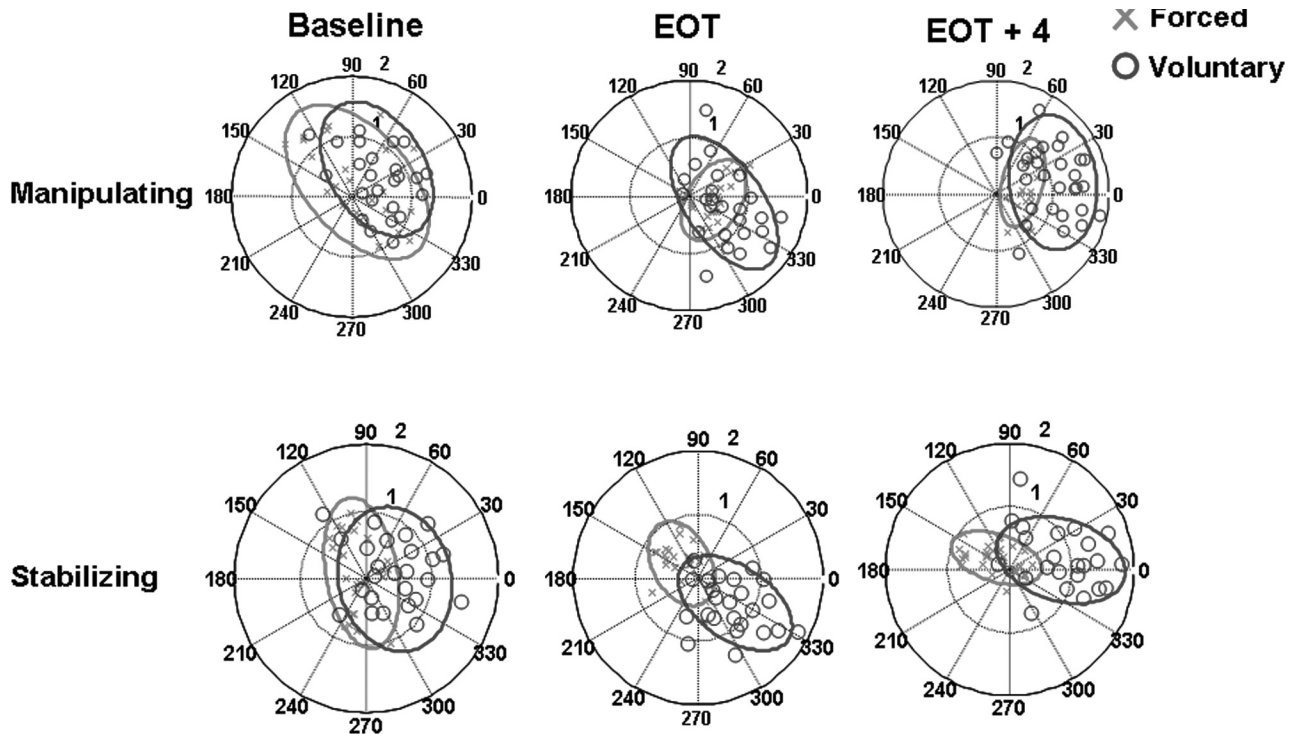
^aRigidity motor score taken from item 22, tremor taken from items 20 and 21, bradykinesia taken from items 23-26 and 31, gait taken from item 29, and postural stability taken from item 30.

Figure 3
Biomechanical Measures of Bimanual Dexterity Improved Significantly Following Forced-Exercise and These Improvements in Function Were Sustained Following Exercise Cessation (EOT + 4)



Note: (a) Illustration of bimanual dexterity task. (b) Representative grip-load coordination plots for the stabilizing and manipulating limbs. Grip-load relationships in PD are typically uncoupled and irregular. After 8 weeks of exercise, grip-load relationships appear more coupled in the FE group but were unchanged after VE. (c) Mean changes in grip time delay were significantly reduced in the FE group from baseline to EOT and EOT+4. No changes in grip time delay were noted in the VE group. (d) Mean changes in rate of force production in the manipulating hand were significantly increased after 8 weeks of FE but were slightly reduced after VE. Error bars = standard deviations. EOT indicates end of treatment; EOT+4, end of treatment plus 4 weeks; FE, forced exercise; VE, voluntary exercise.

Figure 4
Center of Pressure for all Dexterity Trials for Patients in the Forced (x) and Voluntary (o) Groups at Baseline, End of Treatment (EOT), and End of Treatment Plus 4 Weeks (EOT+4)



Note: Ellipses define the area of spread that encompasses 95% of the data.

impairments in force control suggest PD patients use a method of feedback control to a greater extent than age-matched controls,¹⁹ likely as a method to compensate for increased variability in force production.²¹ Following FE, PD patients' biomechanical data, improved coupling of grasping forces, and more simultaneous production of grasping forces between the limbs suggest a transition from feedback to a greater reliance on a feedforward or predictive mode of controlling grasping forces. The CoP measure, a measure of both end point control and consistency of digit placement, provides additional evidence that FE may be altering motor control processes subserving upper extremity function in PD patients. This transition from primarily a feedback to feedforward control for an upper extremity action, following a lower extremity exercise intervention, suggests that FE may alter or improve central motor control processes. The exact mechanism(s) responsible for the change in central function following FE is unknown.

Our data are consistent with exercise studies in animal models that suggest that an important factor contributing to the positive effects of exercise on PD motor function is exercise rate (eg, higher rate results in improved motor function and greater dopamine sparing).² Forced exercise may be altering cortical excitability in PD patients via an increase in the quantity (faster pedaling) and consistency (low variability) of afferent information compared to voluntary exercise. Models of basal

ganglia function and PD indicate decreased cortical excitability and motor cortical output.^{22,23} Diminished motor cortical output is thought to underlie bradykinetic movements^{24,25} and impaired sensory integration^{26,27} in PD patients.

Previous studies have also shown that PD patients experience a degradation in the quantity, consistency, and processing of afferent information.²⁸⁻³⁰ Patients with PD, owing to diminished motor cortical activation, produce slow and irregular movements and may be limited in their ability to exercise at the relatively high rates that appear necessary to improve motor function. Therefore, FE can be used to augment the patient's voluntary exercise rate through mechanical assistance. It is important to note that FE augments, but does not replace, the active efforts of the PD patient. Data from studies in healthy adults provide the rationale for augmentation of active effort rather than passively moving the limbs of the patient throughout the range of motion at a higher than voluntary rate. Active training of the upper³¹ or lower³² extremities results in increased motor cortical activation, whereas passive training does not. Furthermore, active robotic assistance resulted in significantly greater gains in motor function and led to an increase in sensorimotor cortex activation compared to patients with stroke who received passive robotic assistance.¹⁰ The authors suggest that an active-assist robotic device increases the proprioceptive sensory signals to the brain and

that this increase in afferent feedback may underlie increased cortical activation, which improves motor function.¹⁰ Previous studies support this argument, as the quantity and consistency of afferent information is greater during consistent and rapid movements,^{33,34} such as those produced during robotic assistance or in our case, forced exercise.

The FE intervention used in this preliminary, proof-of-concept study may be augmenting the PD patient's voluntary levels of neural output by increasing the consistency and quantity of afferent input to the central nervous system by reducing or normalizing the altered patterns of neuronal activity in the basal ganglia thalamo-cortical circuit. Forced exercise, at a high rate of pedaling, may lead to peripheral changes in the musculature as well. Farina and colleagues have shown that higher rates of pedaling lead to greater recruitment of fast-twitch motor units.³⁵ However, this finding would not explain the motor improvements that we noted in the upper extremity.

Lastly, based on the results from animal studies, it is possible that FE may facilitate the release of neurotrophic factors such as GDNF or BDNF that are believed to underlie improved motor function.³⁶ A logical next step in this line of investigation is to directly assess levels of neurotrophic factors in patients completing a FE and VE intervention. Regardless of the mechanism, FE resulted in a 35% improvement in clinical ratings, which is similar to that reported with surgical interventions such as deep brain stimulation or ablative procedures such as pallidotomy.^{16,37}

Several studies have examined the therapeutic value of exercise in Parkinson's disease, including tai chi/martial arts, gait/balance training, strength training, and aerobic exercise,^{3,38-42} but few have reported improvements in posttreatment UPDRS motor scores. Baatile and colleagues reported a 30% decrease in UPDRS motor scores after 8 weeks of pole striding, but only 6 subjects were studied and individual patient improvement ranged from 0% to 100%.³⁸ Qigong exercise resulted in decreased UPDRS motor scores, but the mean change from baseline was 5 points⁴² compared to a 16-point decrease in our study after forced exercise. Furthermore, Reuter and colleagues⁴¹ reported a 43% improvement in the UPDRS motor score after 14 weeks of variable exercises in the gym and in the water.

It is possible that a longer treatment of forced exercise (greater than 8 weeks) would result in further improvements in UPDRS motor score approaching that documented by Reuter. Treadmill and gait training show some promise in PD motor performance.^{40,43,44} Herman and colleagues showed that non-weight-supported treadmill training for 6 weeks resulted in a 24% improvement in the UPDRS, and gait speed increased by 13%. These improvements were maintained 4 weeks after the treatment. They hypothesized that the treadmill provides an external cue for the defective rhythm of the basal ganglia and that training promoted motor learning in these patients.⁴³ A fundamental limitation of treadmill studies is that motor learning or practice may be responsible for the improvement in gait

parameters. The lower extremity exercise training paradigms and biomechanical evaluations of gait were relatively similar within a given study. The similarity between the intervention and testing procedure limits the ability to determine if exercise actually improves PD motor function via enhanced motor control and processing (ie, changes in CNS function).

To determine if exercise alters central motor processes in PD, motor assessments must be unique from the training protocol to minimize any improvements as a result of practice. If exercise does lead to changes in motor control processes, then improvements in the motor performance of the non-exercised effectors would be expected (ie, improved upper limb function following lower extremity exercise).

An advantage of a forced cyclical intervention is that a greater range of exercise rates may be used. Body weight-supported treadmill training (BWSTT) allows for PD patients to exercise at a rate greater than what the patient could achieve without support.⁴⁵ However, owing to safety concerns, the exercise rate under BWSTT paradigms may be limited. The BWSTT interventions also require a large facility to accommodate the treadmill and safety equipment as well as a therapist to oversee training, which limit their possibility for clinical or home adoption.⁴³

Implications and Limitations

Our current data indicate that when PD patients engage in an exercise intervention in which their voluntary efforts are augmented to achieve a rate of exercise that is significantly greater than their voluntary exercise rates, significant improvements in PD motor symptoms occur, compared to patients completing VE. Although VE does lead to improvements in aerobic fitness, a more intensive intervention with respect to exercise rate appears necessary if global improvements in motor function are to occur. A recent report from the Winstein laboratory provides support for the use of a challenging (ie, high contextual interference) or more intense rehabilitation environment to enhance motor learning in PD patients.⁴⁶ They contend that PD patients are not sufficiently challenged in most rehabilitation settings because of cognitive or motor deficits⁴⁶; a similar statement could also be made for most physical interventions designed for PD patients. However, the current data indicate that PD patients can exhibit significant gains in motor function following a relatively intense (with regard to rate of exercise) intervention.

From a clinical perspective, our results suggest that exercise intervention programs for PD patients can be relatively intensive from an aerobic perspective and that patients may need to be pushed beyond their voluntary limits to exercise at rates sufficient to induce global improvements in motor function. The enhanced control and coordination of upper extremity motor activities, following a lower extremity FE intervention, provides preliminary evidence that FE does alter central motor control processes. One implication of improved central motor processing is that FE is enhancing neuroplasticity or altering

brain biochemistry, both of which could alter the course of PD.

We acknowledge that the use of an actual tandem cycle is not feasible from a clinical perspective for a number of reasons (eg, accessibility, requirement to have a relatively fit exercise partner, practicality). Therefore, the next step in this line of investigation is to determine the clinical efficacy of FE in a larger group of PD patients using a paradigm readily and rapidly adapted to clinical and home use. A follow-up study in which a motor-driven stationary cycle is used for VE and FE is currently underway. Future studies will also be directed at identifying the duration of the motor benefits, the effects of FE on biomechanical measures of lower extremity function and postural stability, the optimal rate and dose of FE, and mechanism(s) underlying the benefits of FE compared to VE.

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