

RESEARCH ARTICLE

Maximal strength training in patients with Parkinson's disease: impact on efferent neural drive, force-generating capacity, and functional performance

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Helgerud J, Thomsen SN, Hoff J, Strandbråten A, Leivseth G, Unhjem R, Wang E. Maximal strength training in patients with Parkinson's disease: impact on efferent neural drive, force-generating capacity, and functional performance. *J Appl Physiol* 129: 683–690, 2020. First published August 13, 2020; doi:10.1152/jappphysiol.00208.2020.—Parkinson's disease (PD) is characterized by progressive neurological deterioration, typically accompanied by reductions in skeletal muscle force-generating capacity (FGC) and functional performance. Physical activity has the potential to counteract this debilitating outcome, however, it is elusive if high-intensity strength training included in conventional treatment may improve results. Therefore, we randomly assigned 22 PD patients (74 ± 9 yr) to conventional rehabilitation with or without maximal strength training (MST) performed as leg press and chest press at ~90% of one repetition maximum (1RM), five times per week for 4 wk. FGC, physical performance, and efferent neural drive assessed as evoked potentials (V-wave normalized to M-wave in m. soleus) were measured following training. Results revealed that only MST improved 1RM leg press (101 ± 23 to 118 ± 18 kg) and chest press (36 ± 15 to 41 ± 15 kg), plantar flexion maximal voluntary contraction (235 ± 125 to 293 ± 158 N·m), and rate of force development (373 ± 345 to 495 ± 446 N·m·s⁻¹; all *P* < 0.05; different from controls *P* < 0.05). FGC improvements were accompanied by an increased efferent neural drive to maximally contracting musculature (V-to-M ratio: 0.17 ± 0.12 to 0.24 ± 0.15; *P* < 0.05; different from controls *P* < 0.05), improved physical performance (stair climbing: 21.0 ± 9.2 to 14.4 ± 5.2 s; timed up and go: 7.8 ± 3.3 to 6.2 ± 2.5 s; both *P* < 0.05), and self-perceived improvement in health (3.1 ± 0.5 to 2.6 ± 0.9) and social activities functioning (2.2 ± 1.0 to 1.5 ± 1.1; both *P* < 0.05). No changes were observed in the control group. In conclusion, this study shows that MST improves FGC, neuromuscular function, and functional performance and advocates that high-intensity strength training should be implemented as an adjunct therapy in the treatment of PD patients.

NEW & NOTEWORTHY This randomized, controlled trial documents that supervised high-intensity strength training improves efferent neural drive, maximal muscle strength, rate of force development, and functional performance in patients with Parkinson's disease (PD). In contrast, no differences were observed in these outcome variables in patients receiving conventional treatment consisting of recreational physical activity with low-to-medium intensity. Consequently, this

study advocates that high-intensity strength training should be implemented in the clinical treatment of PD patients.

evoked potentials; functional performance; heavy resistance training; physical function; rate of force development; V-wave

INTRODUCTION

Parkinson's disease (PD) is a progressive degenerative disorder of the nervous system, originating from basal ganglia dysfunction (29). Patients with PD display profound reductions in maximal muscle strength (28, 35) and rate of force development (RFD) (21, 36). In addition, PD patients suffer from functional disability (10), impaired work economy (11), and increased risk of falls and fracture (3).

Maximal force production is dependent on both neural and muscular factors (1), and neural alterations indeed appear to play an important role in the attenuated skeletal muscle force-generating capacity (FGC) in PD. Specifically, PD patients have been shown to exhibit impaired voluntary muscle activation (18), increased antagonist muscle coactivation (36), and variable motor unit discharge rates during submaximal isometric force production (19). The mechanisms underlying these neural impairments remain elusive. Yet, it has been proposed that dysregulated excitatory and inhibitory signaling to the motor cortex leads to abnormal supraspinal efferent neural drive in patients with PD, potentially affecting FGC (13, 47). In contrast, resistance training is documented to enhance efferent neural drive (39), alleviate cardinal motor symptoms (12), and improve FGC (30, 38) in PD patients. However, it remains to be elucidated which strength training intensity and format most effectively may ameliorate the neural remodeling and impaired FGC associated with PD.

Maximal strength training (MST), carried out at ~90% of one repetition maximum (1RM) with maximal intended concentric contraction velocity, is tailored to target the nervous system and shown to be more effective in improving FGC than conventional strength training carried out at ~70–75% of 1RM (23). MST-induced improvements in FGC are shown to be accompanied by enhanced efferent neural drive to maximally

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contracting musculature in both young (17, 40) and old individuals (41) and in other patient groups with neurological disorders (16, 25). Ultimately, improvements in lower extremity FGC following MST are typically shown to result in improved physical function (25, 46).

Recognizing that PD is associated with deleterious remodeling of the nervous system, reduced FGC, and impaired physical function, effective training interventions that can counteract the attenuated physical health are warranted to advance the rehabilitation of PD. Accordingly, the aim of the present study was to investigate if MST could improve the effects of conventional treatment, consisting of physical activity with low-to-moderate intensity. Applying tests of maximal strength, RFD, efferent neural drive (assessed by evoked spinal V-wave recording), and physical function, we hypothesized that MST would improve FGC, efferent neural drive, walking economy, functional performance, and self-perceived functional health more than conventional PD rehabilitation.

METHODS

Patients

A total of 22 PD patients participated in the study. During the study period, all patients continued to use L-3,4-dihydroxyphenylalanine (L-DOPA) medications and kept type and dose constant. Patient characteristics are presented in Table 1. Exclusion criteria were cardiovascular disease, neurological disorders other than PD, and inability to perform the study procedures. The study was approved by the Regional Committee for Medical Research Ethics, and all study procedures were conducted in accordance with the Declaration of Helsinki. All patients signed informed consent before inclusion.

Study Design

The patients were randomly assigned 2:1 to MST or a control group. All patients received conventional rehabilitation treatment, living at the rehabilitation clinic (Hokksund, Norway) for 4 wk. Before and after the intervention, the patients underwent a standardized 2-day testing protocol. On the first test day, plantar flexion isometric maximal voluntary contraction (MVC) was measured along with evoked potentials and RFD. After a rest period of 15 min, dynamic 1RM leg press and chest press were measured. On the second test day, the patients returned for the measurement of walking economy, maximal oxygen consumption ($\dot{V}O_{2\max}$), functional performance, and self-perceived functional health. For each patient, the specific assessment procedures were performed in the same order and

at the same time of the day pre- and postintervention. The subjects were also instructed to keep the timing of their medication intake constant during the test days.

Testing Procedures

Dynamic maximal muscle strength. Leg press 1RM was measured in a seated horizontal leg press apparatus (Gym80 International GmbH, Sygnum Medical, Gelsenkirchen, Germany), using a 90° knee-joint angle in the lower position. Chest press 1RM was measured using a barbell and external loads. For both lifts, the patients completed a standardized warm-up, consisting of two sets of eight repetitions using 50% of estimated 1RM. Both lifts were performed with a marked stop (~0.5 s) between the eccentric and concentric phase of contraction. The loads were gradually increased until failure. A rest period of 3–4 min was given between attempts. The highest lifted load was recorded as 1RM and was attained within three to six attempts.

MVC, RFD, and evoked potentials. All evoked potentials were obtained from m. soleus. Electrical currents were delivered to the tibial nerve by bipolar felt pad electrodes (Lectron 2 conductive gel; Pharmaceutical Innovations Inc., Newark, NJ), 25 mm between tips, 8-mm diameter (Digitimer, Welwyn Garden City, UK), using a constant-current stimulator (DS7AH; Digitimer, Welwyn Garden City, UK). Prior to the reflex recordings, self-adhesive Ag-AgCl electrodes (M-00-S/50; Ambu, Ballerup, Denmark) were positioned according to SENIAM recommendations on the m. soleus (24), to obtain reflex electromyography (EMG). Skin preparation, including shaving, scrubbing, and cleaning of the skin, was conducted before electrode placement, to ensure interelectrode impedance <5 k Ω . Initially, two MVCs were performed to determine maximal isometric plantar flexion strength. The electrodes were positioned in the popliteal fossa, at the stimulus site that best separated the excitement of Ia afferent axons and efferent motor axons, i.e., produced the largest H-reflex response without or with a minimum of direct motor potential response (M-wave). Subsequently, current intensity was increased in increments of 2–5 mA for identification of maximal H-reflex amplitude (H_{\max}) during low force contraction (10% MVC). Thereafter, maximal direct motor potentials (M_{\max}) were obtained, increasing the current intensity by 5–10 mA, until a plateau in M-wave amplitude was observed. Two supramaximal electrical stimuli (150% of the current needed to reach M_{\max}) were then given to ensure a true M_{\max} . Next, eight V-waves were recorded, by delivering a supramaximal electrical stimulus during MVC. The stimulus was delivered after a plateau of force was visually observed, and only the V-wave trials in which the M-wave was $\geq 90\%$ of M_{\max} and the torque was $\geq 90\%$ of MVC were considered for analyses. For analyses of the results, H_{\max} and V_{\max} amplitudes were normalized to M_{\max} and expressed as H-to-M ratio (H/M ratio) and V-to-M ratio (V/M ratio), respectively.

Walking economy, walking work efficiency, and maximal oxygen consumption. Following a 6-min warm-up at low-to-moderate intensity, a 5-min submaximal walking economy test was conducted on a motorized treadmill (Runrace 1200HC, Technogym, Italy). The inclination was held constant at 5%, and the speed was adjusted according to the patient's body mass to obtain a workload of 40 W (27). Heart rate (Polar Accurex Plus; Pola Electro, Kempele, Finland) and pulmonary gas exchange (Cortex Biophysik GmbH, Leipzig, Germany) were measured continuously, and walking economy was defined as the average oxygen uptake during the last minute of the test (46). Walking work efficiency was calculated as [external work accomplished (kcal/min) \times 100]/energy expenditure (kcal/min), where energy expenditure and external work were converted to kilocalories to allow work efficiency to be expressed as percent change (26). At termination of the 5-min work economy test, the patients were also asked to rate perceived exertion on a Borg scale (8), and a blood sample was drawn from the fingertip for analysis of hemolyzed blood lactate concentration (Arkray Inc, Japan).

Table 1. Patient characteristics

	MST Group	Control Group
Male/female	7/8	2/5
Age, yr	72 \pm 8§	62 \pm 11
Height, cm	172 \pm 9	168 \pm 7
Body mass, kg	77.8 \pm 13.7	68.6 \pm 12.3
BMI, kg/m ²	26.8 \pm 3.9	24.4 \pm 4.9
$\dot{V}O_{2\max}$		
L/min	1.83 \pm 0.38	2.20 \pm 0.51
mL·kg ⁻¹ ·min ⁻¹	23.8 \pm 3.6§	32.6 \pm 6.8
L-DOPA, mg/day	693 \pm 473	692 \pm 366
Hoehn and Yahr stage	2.3 \pm 1.0	2.7 \pm 0.7
Years since diagnosis	8.8 \pm 4.9	7.3 \pm 2.5

Data are means \pm SD for patients without (control; $n = 7$) or with maximal strength training (MST; $n = 15$). BMI, body mass index; L-DOPA, L-3,4-dihydroxyphenylalanine; $\dot{V}O_{2\max}$, maximal oxygen consumption. § $P < 0.05$, difference between groups at baseline.

Following the measurement of walking economy, the patients commenced directly to the $\dot{V}O_{2\max}$ test. The speed was set at 5 km/h, and the inclination was increased by 2% every minute, starting from 0%, until voluntary exhaustion, which typically occurred within 6–12 min. Determination of rating of perceived exertion and blood lactate concentration was repeated within 0–1 min of test termination. $\dot{V}O_{2\max}$ was defined as the point of voluntary exhaustion accompanied by at least two of the following criteria: a plateau in oxygen consumption despite increasing workload, blood lactate concentration ≥ 7 mmol/L, and respiratory exchange ratio ≥ 1.05 .

Functional performance. A 6-min walking test (6MWT) was performed indoors. Two cones were positioned 30 m apart, and the patients were instructed to walk forth and back around the cones, aiming to walk the longest possible distance in 6 min. The chair rise performance was assessed by the timed up and go (TUG) test. Patients were instructed to rise from an armchair, walk a distance of 3 m, round a cone, return to the chair, and sit down. The time taken to perform the test was recorded using a handheld stopwatch. Last, the ability to climb stairs was assessed as the time needed to ascend 2 \times 14 stairs of 15 cm each, separated by a flat turning plateau. The use of handrail support was not allowed.

Self-perceived functional health. Self-perceived functional health was assessed using the Norwegian version of the COOP/WONCA questionnaire. COOP/WONCA is developed with the purpose of measuring generic functional health. The Norwegian version has been found to be reliable in healthy and diseased individuals (6). In brief, COOP/WONCA evaluates six components of functional health status: physical fitness, feelings, daily activities, social activities, changes in health, and overall health. Each component is rated on a five-level ordinal scale, with 1 being the best rating and 5 being the worst rating. The reference period is 2 wk.

Maximal Strength Training and Conventional Treatment

MST. The MST group attended five supervised training sessions per week for 4 wk. The training sessions consisted of dynamic leg press and chest press. As for the testing, the leg press was performed in the horizontal leg press apparatus. In accordance with previous training procedure (17, 40), the leg press started with an eccentric phase from a near-180° angle in the knee joint to 90° knee flexion. The concentric phase then followed after a short (~0.5 s) stop and was performed with maximal mobilization of force back to ~180° knee angle, with calf raises at the end of the concentric lifting phase to involve training of plantar flexors. Chest press was performed using a barbell and external loads. Both exercises consisted of four sets of four repetitions at ~90% of 1RM, with an emphasis on slow contraction velocity in the eccentric phase and maximal intended contraction velocity in the concentric phase. Importantly, a marked stop (~0.5 s) was applied between the eccentric and the concentric contraction phases. The sets were separated by 3 min of rest. If the patients were able to complete more than four repetitions in one set, the load was increased by 5.0 kg in the leg press and 2.5 kg in the chest press. The patients were encouraged to maintain their typical daily activities during the period of the intervention.

Conventional treatment. All patients participated in conventional clinic treatment during the 4-wk intervention period. Patients in the control group, receiving only conventional treatment, exercised in the same leg press and chest press apparatus as the MST group, but with low-to-medium intensity (<50% 1RM). Several other body weight-based physical activity exercises (<50% 1RM) were also provided in the conventional clinical treatment: 1-h group sessions were carried out three times per week and consisted of squats, push-ups against a wall, stretching of major muscle groups, balance training (standing with feet together, with feet in semi-tandem position, and on right and left single leg), and walking with long strides. Additionally, patients had the opportunity to do exercise in water, participate in relaxation groups, and do Nordic walking outdoors. Patients also received 30

min of physiotherapy without physical activity three times per week, as well as lectures regarding pathology, drugs, rehabilitation, and information about cognitive strategies for movement.

Statistical Analysis

Statistics were performed using SPSS Statistics 26.0 (IBM, Chicago, IL), and graphical illustrations were made using GraphPad Prism 6.01 (GraphPad Software, San Diego, CA). Normality of data was confirmed by visual assessment of quantile-quantile plots and Shapiro–Wilk tests. Paired-samples *t* tests were used for detecting within-group differences following the study period. For detecting between-group differences, two-way repeated measures ANOVAs were used and followed up by Tukey's post hoc tests when appropriate. Relationships between variables were assessed at baseline and following training with the Pearson test for linear regression, for the MST and control groups collapsed. The level of statistical significance was set at 0.05. Data are presented as means \pm SD in text and tables and as means \pm SE in Fig. 1.

RESULTS

After the randomization procedure at baseline, results revealed that age was significantly lower in the control group compared with the MST group and was associated with a lower $\dot{V}O_{2\max}$ ($r^2 = 0.50$ L/min; $r^2 = 0.66$ mL·kg⁻¹·min⁻¹; $P < 0.01$; Table 1), reduced stair climbing capacity ($r^2 = 0.44$; $P < 0.01$) and 6MWT performance ($r^2 = 0.60$; $P < 0.01$; Table 4), and poorer self-perceived physical fitness ($r^2 = 0.21$; $P < 0.05$; Table 5). No differences were observed between the groups for any other variables. Despite our best effort, we failed to obtain H-reflex measurements at 10% MVC. All 22 patients included in the study completed their training with an attendance of 19 ± 1 of the 20 planned training sessions. No difference in training attendance was apparent between the two groups, and no adverse events occurred during the training or testing procedures. Following the study period, body mass decreased in the MST group ($P < 0.05$), while it increased in the control group (Table 2; $P < 0.05$), and body mass was also apparent as a between-group difference following the training period ($P < 0.01$).

Dynamic Maximal Strength

After 4 wk, the MST group increased 1RM leg press by $20 \pm 16\%$ and 1RM chest press by $25 \pm 27\%$ (both $P < 0.001$). No changes occurred in the control group. A between-group difference was observed following the study period for both 1RM leg press and chest press (both $P < 0.01$; Fig. 1; Table 2).

Maximal Voluntary Contraction, Rate of Force Development, and Evoked Potentials

In the MST group, plantar flexion MVC increased by $25 \pm 27\%$, RFD increased by $32 \pm 37\%$, and V/M ratio increased by $60 \pm 68\%$ (all $P < 0.05$; Fig. 1). No changes were found in the control group. Following training, between-group differences were also observed for these variables (all $P < 0.05$; Fig. 1; Table 2). At pretest, a positive relationship was observed between the V/M ratio and MVC ($r^2 = 0.17$; $P < 0.05$), while changes in the V/M ratio from pre- to posttest were positively associated with changes in leg press 1RM ($r^2 = 0.26$; $P < 0.05$) and chest press 1RM ($r^2 = 0.42$; $P < 0.05$), respectively. No other relationships between the V/M ratio and force-generating capacity were observed at baseline or following the study period.

Table 2. Force-generating capacity and efferent neural drive pre- to posttest

	MST Group		Control Group	
	Pre	Post	Pre	Post
IRM leg press, kg	101 ± 23	118 ± 18 ^{#####}	99 ± 23	99 ± 21
IRM chest press, kg	34 ± 14	40 ± 15 ^{#####}	28 ± 14	27 ± 15
Body mass, kg	77.8 ± 13.7	76.9 ± 13.2 [#]	68.6 ± 12.3	69.7 ± 12.0 [*]
MVC, N·m	235 ± 125	293 ± 158 ^{#####}	262 ± 118	251 ± 112
RFD, N·m·s ⁻¹	373 ± 345	495 ± 446 [#]	437 ± 199	444 ± 219
M _{max} , μV	3,396 ± 1,632	3,564 ± 1,942	3,627 ± 2,823	3,617 ± 2,679
V _{max} , μV	518 ± 329	674 ± 335 [#]	847 ± 603	717 ± 681
V/M ratio	0.17 ± 0.12	0.24 ± 0.15 ^{**#}	0.19 ± 0.17	0.18 ± 0.15

Data are means ± SD for patients without (control; $n = 7$) or with maximal strength training (MST; $n = 15$). IRM, one repetition maximum; M_{max}, maximal M-wave amplitude; MVC, isometric plantar flexion maximal voluntary contraction; RFD, plantar flexion rate of force development; V_{max}, maximal V-wave amplitude; V/M ratio, maximal V-wave amplitude relative to maximal M-wave amplitude. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$, difference within groups between pre- and post-test. # $P < 0.05$; ## $P < 0.01$; ### $P < 0.001$, difference between groups from pre- to posttest.

Maximal Oxygen Consumption, Walking Economy, and Walking Work Efficiency

No changes were found in absolute (L/min) or relative (mL·kg⁻¹·min⁻¹) walking economy or walking work efficiency from pre- to posttest (Table 3). Respiratory exchange ratio, pulmonary ventilation, rating of perceived exertion, and stride frequency measured during the walking economy test were also not altered following the study period (Table 3). However, a within-group reduction in heart rate was observed in the MST group ($P < 0.05$; Table 3). Similarly, no changes were observed in $\dot{V}O_{2max}$, or any of the variables measured during the $\dot{V}O_{2max}$ test, in either group.

Functional Performance

Stair climbing time and TUG decreased with $-27 \pm 19\%$ ($P < 0.01$) and $-17 \pm 19\%$ ($P < 0.05$), respectively, while 6MWT showed a tendency to increase ($12 \pm 21\%$; $P = 0.08$) following MST (Table 4). However, no differences were ob-

served between the groups. At pretest, associations were observed between $\dot{V}O_{2max}$ and TUG ($r^2 = -0.39$; $P < 0.05$), 6MWT ($r^2 = 0.80$; $P < 0.05$), and stair climbing ($r^2 = -0.43$; $P < 0.05$). No correlations were observed between these variables from pre- to posttest. At baseline, a positive correlation was observed between V/M ratio and 6MWT ($r^2 = 0.30$; $P < 0.05$); however, this relationship was not present following the study period.

Self-Perceived Functional Health

Following MST, the training group improved their rating of social activities and change in health ($P < 0.05$). Neither of these within-group differences were apparent between the groups. No changes were found in the control group (Table 5).

DISCUSSION

PD is associated with deleterious remodeling of the nervous system, reductions in skeletal muscle FGC, and impaired

Fig. 1. Changes in skeletal muscle force-generating capacity and efferent neural drive following 4 wk of conventional treatment with (control; $n = 7$ patients) or without maximal strength training (MST; $n = 15$ patients). A: dynamic leg press of 1 repetition maximum (kg). B: dynamic chest press of 1 repetition maximum (kg). C: plantar flexion isometric maximal voluntary contraction (MVC; N·m). D: plantar flexion isometric rate of force development (RFD; N·m·s⁻¹). E: efferent neural drive expressed as V-wave relative to M-wave (V/M ratio) in m. soleus. Data are means ± SE. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$, difference within group from pre- to posttest. # $P < 0.05$; ## $P < 0.01$; ### $P < 0.001$, difference between groups from pre- to posttest.

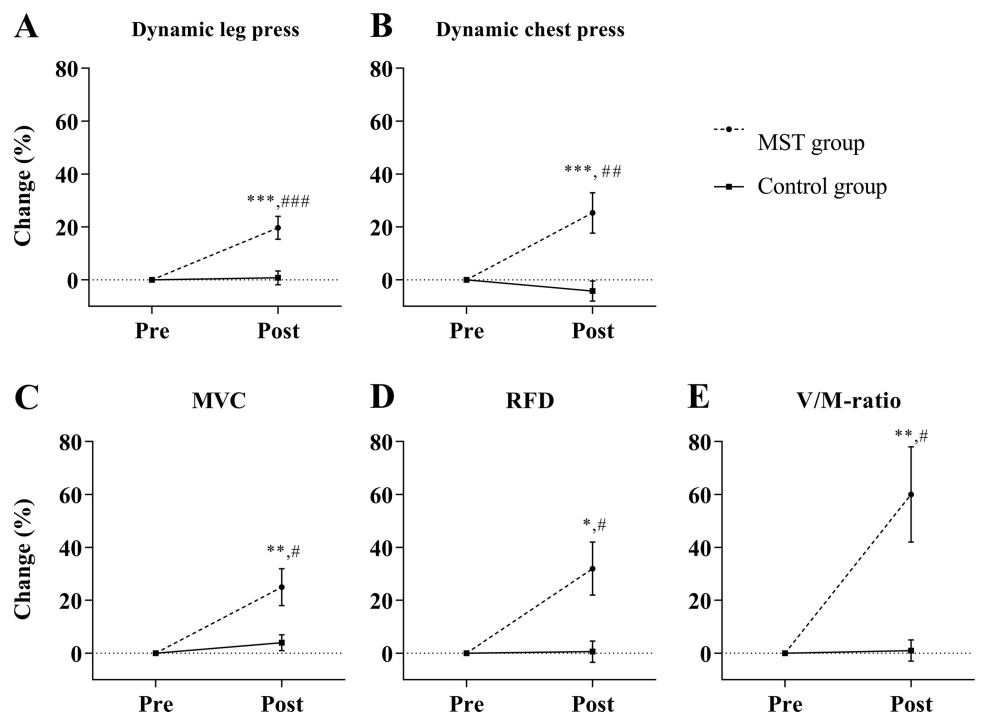


Table 3. Walking work economy and efficiency at pre- and posttest

	MST Group		Control Group	
	Pre	Post	Pre	Post
$\dot{V}O_2$				
L/min	1.15 ± 0.29	1.13 ± 0.24	1.05 ± 0.29	1.06 ± 0.32
mL·kg ⁻¹ ·min ⁻¹	14.8 ± 1.9	14.6 ± 2.1	16.0 ± 3.5	15.0 ± 3.1
Heart rate, beats/min	100 ± 16	90 ± 8*	112 ± 13	109 ± 13
RER	0.80 ± 0.06	0.81 ± 0.02	0.82 ± 0.06	0.82 ± 0.09
$\dot{V}E$, L/min	30.8 ± 11.6	31.7 ± 10.3	29.4 ± 9.2	28.7 ± 9.4
RPE (6–20)	11 ± 3	12 ± 3	12 ± 3	10 ± 4
Stride frequency, strides/min	51 ± 5	51 ± 5	60 ± 16	56 ± 13
Walking work efficiency, %	14.0 ± 3.6	14.0 ± 3.1	15.3 ± 4.4	15.6 ± 5.2

Data are means ± SD for patients without (control; $n = 7$) or with maximal strength training (MST; $n = 15$). RER, respiratory exchange ratio; RPE, rating of perceived exertion; $\dot{V}E$ pulmonary ventilation; $\dot{V}O_2$, oxygen consumption. * $P < 0.05$, difference within groups between pre- and posttest.

physical function. Although resistance training is documented to improve muscle strength in individuals with PD, which strength training intensity and format may yield the most preferable results is unclear, and the underlying neural mechanisms remain largely unknown. Therefore, the present study sought to investigate the impact of MST on FGC and efferent neural drive and to examine the implications for physical function. The major findings were that 1) MST improved upper and lower extremity 1RM, MVC, and RFD; 2) improvements in skeletal muscle FGC were accompanied by enhanced efferent neural drive to contracting musculature; 3) MST resulted in improved physical function in force-demanding daily living activities (stair climbing and TUG) that was accompanied by improvements in self-perceived functional health; and 4) conventional treatment, consisting of physical activity with low-to-medium intensity exercises, did not have any effect on PD patients' FGC, efferent neural drive, or physical function. Taken together, these findings suggest that high-intensity strength training may be included as an integral element in the clinical treatment of PD patients and call into question the effectiveness of traditional rehabilitation.

Force-Generating Capacity

As expected, MST improved FGC. This finding complies with previous literature showing that strength training enhances maximal muscle strength in individuals with PD (22, 33, 38). Notably, despite lower number of total training sessions, the ~20% increase in dynamic leg press is somewhat higher than the 11–18% increase reported by previous studies examining the effects of resistance training in PD patients (22, 33, 38). This may be attributable to the high loading intensity applied in the present study. Indeed, intensity has been identified as a key determinant of neuromuscular adaptations to

Table 4. Functional performance at pre- and posttest

	MST Group		Control Group	
	Pre	Post	Pre	Post
6MWT, m	397 ± 134§	435 ± 131	603 ± 166	611 ± 179
TUG, s	7.8 ± 3.3	6.2 ± 2.5*	6.2 ± 2.6	5.7 ± 2.2
Stair climbing, s	21.0 ± 9.2§	14.4 ± 5.2*	12.6 ± 5.4	11.4 ± 4.6

Data are means ± SD for patients without (control; $n = 7$) or with maximal strength training (MST; $n = 15$). 6MWT, 6-min walking test; TUG, timed up and go. § $P < 0.05$, difference between groups at baseline. * $P < 0.05$, difference within groups between pre- and posttest.

strength training, with higher intensities eliciting larger improvements in FGC as compared with lower intensities (9, 15, 23). In support of this notion, Allen et al. (1) reported no effect of body weight-based resistance training in PD patients. Also, the patients in the current study who received conventional treatment, consisting of low-to-medium intensity strength training (<50% of 1RM), including training in the same leg press and chest press apparatuses as used for MST, did not improve their FGC. Although leg press and chest press apparatuses may vary considerably from the ones used at the rehabilitation clinic in the present study, making a comparison with previous studies somewhat difficult, PD patients' leg press maximal strength in the current study appears to be relatively low, and similar to what has been observed for sedentary, healthy older adults (43). Considering their low initial baseline, and consequently large physiological potential for improvement, it is somewhat surprising that the PD patients receiving traditional rehabilitation in the present study did not exhibit any increase in maximal strength or RFD. This result underpins the fact that a certain intensity threshold may be necessary to induce neuromuscular adaptations even in untrained patients.

MST, PD, and Neural Plasticity

By applying the V-wave technique, the current study demonstrated enhanced efferent neural drive in response to MST in PD patients. It has been suggested that dysregulated excitatory and inhibitory inputs to the motor cortex in patients with PD result in impaired efferent neural drive (13, 47). Interestingly, however, the V/M ratio in the current study was similar to V/M ratios previously reported in healthy, sedentary older adults

Table 5. Self-perceived functional health at pre- and posttest

	MST Group		Control Group	
	Pre	Post	Pre	Post
Physical fitness (1–5)	2.6 ± 1.1§	2.9 ± 1.1	1.4 ± 0.8	1.9 ± 0.7
Feelings (1–5)	2.1 ± 1.2	1.9 ± 1.2	1.7 ± 0.8	2.0 ± 1.4
Daily activities (1–5)	2.6 ± 1.2	2.4 ± 1.3	2.4 ± 1.1	1.6 ± 1.1
Social activities (1–5)	2.2 ± 1.0	1.5 ± 1.1*	2.1 ± 1.3	1.9 ± 1.2
Change in health (1–5)	3.1 ± 0.5	2.6 ± 0.9*	2.9 ± 0.7	2.7 ± 0.8
Overall health (1–5)	3.1 ± 0.9	2.8 ± 0.6	2.6 ± 1.1	2.4 ± 1.1

Data are means ± SD for patients without (control; $n = 7$) or with maximal strength training (MST; $n = 15$). § $P < 0.05$, difference between groups at baseline. * $P < 0.05$, difference within groups between pre- and posttest.

(39–41). This indicates that the attenuated efferent neural in PD patients may as well be a result of an inactive lifestyle as directly caused by the disease. Moreover, the ~60% increase in V/M ratio observed in the present study is comparable to the 30–75% improvements typically observed in both healthy young (2, 40) and healthy old individuals (42) following strength training. Thus the current study indicates that individuals with PD, despite their high age and the presence of neurological impairments, display substantial neural plasticity of the central motor pathway.

After 4 wk of MST, the PD patients exhibited a V/M ratio level that was even higher than what is typically observed in healthy old individuals (43). Notably, this training-induced increase in efferent drive accounted for 26% of the increase in leg press 1RM ($r^2 = 0.26$, $P < 0.05$) and 46% of the increase in chest press 1RM ($r^2 = 0.46$, $P < 0.05$). These results are in accordance with a recent study revealing that PD patients have the potential to improve efferent neural drive in response to strength training (39). Albeit, that study showed that improvements in V/M ratio were only evident if the training was performed while standing on an unstable device. Surprisingly, the Silva-Batista et al. (36) study showed that the direct motor response during rest (M_{\max}) and during MVC (M_{sup}) improved following the unstable strength training in PD. This finding contrasts the current study and previous literature (2, 16, 32, 37, 45), documenting the M_{\max} and M_{sup} to remain unaltered following strength training. Increases in efferent neural drive, as observed in the present study, may be attributed to both enhanced firing frequency and/or motor unit recruitment (2). In support of this notion, David et al. (1) showed that high-intensity strength training improved voluntary muscle activation in PD patients. Collectively, the present data and previous observations (13, 39) demonstrate the effectiveness of strength training performed with high intensity to induce significant neural adaptations in PD patients.

H-reflex assessment was challenging in the present study, and the quality of the obtained data was considered too poor for analyses. It is unclear why it was more difficult to measure the H-reflex in PD patients compared with, for example, older adults with various fitness levels (42, 43) and other neurological diseases like multiple sclerosis (16) in our laboratory. However, it has been indicated that it often may be difficult to selectively recruit Ia afferent fibers without simultaneously recruiting α -motoneurons in PD patients (31), and this can be one explanation for the present challenges. In the Kushnir et al. (27) study, H/M ratios in PD patients were lower than in the healthy controls, and substantially lower compared with what is typically seen in young adults. Albeit, lower H/M ratios have not always been observed in PD patients. In the study by Silva-Batista et al. (36), resting H/M ratios were 0.58–0.85, which is more than twice the values typically observed in healthy old individuals (37, 43) and in fact also higher than many observations in young individuals (2, 20, 45). Surprisingly, the Silva-Batista et al. (36) study also reported an increase in resting H/M ratio with strength training. Again, this finding contrasts previous studies documenting H/M ratio measured at rest to remain unchanged following strength training (2, 14, 20, 34, 37), while, in contrast, increases may be observed after endurance training (45).

MST, PD, and Functional Performance

Increases in force-generating capacity following MST were accompanied by improvements in functional performance, evident as improved stair climbing capacity and TUG performance, and a tendency toward increased 6MWT in the current study. These findings are in accordance with previous observations revealing that the ability to carry out more force-dependent functional tasks, such as tasks with upward displacement of the body mass, is positively associated with muscular strength in the lower extremities in older individuals (44), while the functional impact of increased chest press strength is uncertain. It is also possible that the ability to carry out force-dependent functional tasks relatively easier may have increased the patients' overall physical activity and, in turn, contributed to their decrease in body mass in the present study. Conversely, less force-demanding activities, such as horizontal walking, appear to rely more on endurance factors. Yet, Hill et al. (25) documented that MST-induced improvements in lower extremity FGC were accompanied by improved 6MWT performance, even in the absence of concurrent changes in walking economy and maximal oxygen consumption. The MST-induced improvements in relatively force-demanding tasks were reflected in patients' self-perceived improvement in health and social activities. How PD patients can perform during their everyday life, and experience it, may be considered as the ultimate measure and goal of clinical treatment. In contrast to the MST group, the patients receiving conventional treatment did not improve functional performance in the current study, which is unsurprising considering that FGC also remained unaltered.

High-intensity strength training has been shown to improve work economy in young adults (23), in older adults (46), and in patients (26), likely owing to improved skeletal muscle efficiency (4, 7). By contrast, in the present study, no change in walking economy or walking work efficiency was apparent following MST. The inconsistency between the present data and previous studies may, again, be due to gait abnormalities. In accordance with this notion, PD patients have been shown to exhibit elevated oxygen cost of walking across a range of submaximal walking speeds (11). Indeed, the results in the current study revealed that PD patients had substantially reduced walking work efficiency, with a level similar to, or perhaps even lower than, what previously has been observed in other patients with, for example, chronic obstructive pulmonary disease and coronary artery disease (27). Of notice, the PD patients in the current study exhibited large individual variations in work economy/efficiency. It is conceivable that this could be explained by walking restrictions, such as bradykinesia, freezing of gait, and muscle stiffness, frequently occurring in this patient population (5). This could have masked the typically observed improvements in muscular efficiency and work economy following MST (7, 46). Such walking restrictions may also explain why correlations between lower extremities muscle strength and functional performance, typically observed in healthy individuals, were scarce in the present investigation, despite that both these outcomes were improved following MST. Additionally, day-to-day variability in clinical symptoms may also have contributed to the large individual differences in functional performance.

Clinical Implications

Pharmacological agents, such as levodopa and dopamine agonists, are currently the most widely applied tool in the treatment and control of PD. While these treatments appear to be very effective upon initiation, their application is limited by diminishing effectiveness and an array of slowly arising adverse side effects. In contrast, the present study demonstrates the vast potential for using MST to elicit adaptive changes in skeletal muscle FGC, neural efferent drive, and functional performance in elderly PD patients. MST appears to be safe and feasible for PD patients, with no pain or discomfort reported by the MST group other than the typical muscle soreness associated with introduction to strength training. This is supported by a growing number of MST studies in patient populations without any adverse events (13, 21), indicating that the risk of injuries following MST is small. Importantly, maximal force is exerted only during the concentric phase of the movement, while eccentric actions, which can produce considerably higher forces, are conducted in a slow and controlled manner. Of note, the present regime of conventional PD treatment did not have any measurable effect on neuromuscular, cardiovascular, or functional performance. This is certainly concerning, especially when considering that the patients lived at the rehabilitation clinic, and received a wide range of traditional treatment exercises and physiotherapy, for 4 wk. A likely explanation for this outcome is that the applied exercise intensity in conventional treatment may have been too low to induce cardiovascular changes and improve the skeletal muscle force-generating capacity. An important remaining question is if this result is representative for other rehabilitation clinics. The findings of the present study support previous suggestions of implementation of heavy resistance training in the treatment of PD and extend current recommendations to include high intensity strength training of the lower and upper extremities, the former in particular, considering the close relationship between lower extremity muscle strength and functional performance.

Conclusion

In conclusion, the present study demonstrates that 4 wk of MST may effectively improve skeletal muscle FGC, efferent neural drive, and functional performance in elderly PD patients. In contrast, the present regime of conventional physical treatment did not alter these measures, and questions the effectiveness of traditional rehabilitation exercises. These findings advocate that high-intensity strength training should be implemented as an adjunct therapy in the rehabilitation of PD. Not only may MST improve neuromuscular performance, it may also attenuate functional impairments typically reported in this population.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

J. Helgerud, J. Hoff, G.L., and E.W. conceived and designed research; J. Helgerud, J. Hoff, A.S., G.L., R.J.U., and E.W. performed experiments; S.N.T., A.S., R.J.U., and E.W. analyzed data; S.N.T., R.J.U., and E.W. interpreted results of experiments; S.N.T. and R.J.U. prepared figures; S.N.T. and E.W. drafted manuscript; J. Helgerud, S.N.T., R.J.U., and E.W. edited and revised manuscript; J. Helgerud, S.N.T., J. Hoff, A.S., G.L., R.J.U., and E.W. approved final version of manuscript.

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