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Effects of 12 weeks of aerobic or strength training in addition to standard care in Parkinson's disease: a controlled study.

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ABSTRACT

BACKGROUND: Physical exercises in addition to standard care (SC) in patients with Parkinson's disease (PD) are now common practice in many care units. However, exercises can cover a wide range of interventions, and the specific effects of different interventions still deserve to be further investigated.

AIM: To compare the effects of 12 weeks of two different types of physical exercises with SC in patients suffering from PD.

DESIGN: Pseudo-randomized controlled trial.

SETTING: University laboratory for outcomes, University Hospital Centre for interventions.

POPULATION: Fifty-two outpatients suffering from mild to moderate PD at baseline.

METHODS: Participants were allocated to 3 groups: the strength training (ST) group performed individualized upper and lower limbs strength training, the aerobic training (AE) group performed tailored gradual aerobic cycling, and the third group received SC. The effects of the interventions on body function were assessed by measuring isokinetic concentric peak torque for knee extension and flexion, peak oxygen consumption (VO_2peak) and peak work load (PWL) during an incremental maximal cycling test. Changes in mobility were evaluated from spatial-temporal gait features measured by mean of an accelerometer system and the six-minute walk distance (6mwd) test. We used questionnaires to estimate health-related quality of life and habitual physical activity.

RESULTS: No significant changes in any outcome measures occurred in the SC group. More than 80% of the participants adequately completed the AE and the ST interventions. The ST group significantly improved all peak torque measures ($p \leq 0.01$), except knee extension in the least affected side ($p=0.13$). This group also improved the PWL ($p=0.009$) and 6mwd ($p=0.03$). The AE group improved the VO_2peak ($p=0.02$) and PWL ($p<0.001$).

CONCLUSION: Physical fitness in patients with PD rapidly improved in compliance with training specificities, but better fitness hardly translated into better mobility and health-related quality of life.

CLINICAL REHABILITATION IMPACT: Physiotherapists can efficiently propose physical conditioning to patients with mild to moderate PD, but these interventions are insufficient to improve gait and participation. Notwithstanding, ST is an efficient intervention for improving walking capacity.

Key words: Parkinson's disease, rehabilitation, aerobic exercise, strength training

TEXT

Introduction

People with Parkinson's disease (PD) suffer from reduced movement efficacy caused by motor symptoms like bradykinesia, rigidity, tremor, stooped posture, impaired automatic control of movement and postural adaptation. Along with movement disorders, aging and non-motor symptoms like depression, fatigue and apathy may precipitate patients in sedentary behaviour.[1-3] The resulting physical deconditioning and social isolation may worsen functional consequences of the disease. For these reasons, prevention of inactivity is an important objective for physiotherapists across all stages of the disease.[4]

The meta-analysis of Tomlinson et al. showed that physiotherapy can improve the condition of patients suffering from PD.[5] But they also concluded that physiotherapy covers a wild range of interventions with different levels of metabolic solicitation and attentional demand (e.g. cued gait training, dance, yoga, Nordic walk, stretching, weight lifting, treadmill walking, etc.). Yet, the specific improvements brought by each type of exercise remain to be highlighted by further studies comparing the effects of different types of exercises.[6-8] Besides, a *one size fit all* approach may not be the most appropriate model of rehabilitation and the identification of factors associated with good response to the interventions would help with individualising exercise prescription.

Based on this background, the aim of this study was to investigate the short-term effects of structured and gradual group physical exercises focused on two different aspects of physical fitness: muscle strength or cardiorespiratory endurance. A large spectrum of outcomes that encompassed the three domains of function according to the International Classification of Function, Disability and Health (i.e. body function, activity and participation) was selected in order to thoroughly depict the effects of the interventions on

different aspects of the disease.[9] Body function was assessed through measures of muscle strength and cardiorespiratory fitness; the activity domain was mainly appraised by walking capacity and spatial-temporal gait analysis; the participation domain was assessed by questionnaires about health-related quality of life and physical activity habits. We hypothesised that these structured group exercise programs would improve physical performances and participation of the patients, whereas effects on walk and mobility were uncertain because these skills were not specifically trained during the interventions. As secondary analysis, we also studied correlations with magnitude of improvement for outcomes with significant changes in order to observe the characteristics associated with a better response to the trainings.

Materials and Methods

Recruitment and inclusion criteria

We contacted 120 eligible patients from the Movement Disorders clinic (department of Neurology, University Hospital Centre, Liège, Belgium) by phone call. The diagnosis of idiopathic PD was confirmed by a Movement Disorders specialist in agreement with the PD Society Brain Bank criteria.[10] Exclusion criteria were scores IV or V on the Hoehn & Yahr scale,[11] a score below 24 at the Mini Mental Scale Exam,[12] history of neurologic disease other than PD, inability to walk independently, or *ON*-state freezing. Patients were excluded if suffering from significant rheumatologic diseases, cardiac or respiratory conditions documented or fortuitously discovered during testing, that might interfere with exercises. All participants were requested to obtain a medical certificate from their physician stating "no contra-indications to vigorous physical exercise and testing". We did not exclude patients already engaged in sports, physiotherapy or physical exercise programs, but we asked all

participants to keep their habitual amount, type and frequency of physical activities during the study period. This protocol was approved by the research ethic board of the University of Liège and all patients gave their written informed consent prior to their participation, according to the declaration of Helsinki 1975.

Study design

We conducted a prospective, single-centre, pseudo-randomised controlled trial between February 2011 and May 2014. Fifty-two participants were enrolled in a 12-week study that compared the evolution in a standard care control group (SC) and two experimental groups that underwent either aerobic (AE) or muscle strength training (ST) in small group (five to six patients). Because of difficulties with recruitment, full randomisation to the different groups was impossible. The patients living in an area further than 30 km from the hospital were allocated to the SC group. At the beginning of each bloc of experimental session, the remaining patients were randomly assigned to one of the intervention group after stratifying for age and gender. Group assignment was not blinded to the experimenters, who were also involved in data collection.

Interventions

Participants in the AE and ST groups trained twice to thrice a week for 12 weeks, with at least one day rest between sessions. The sessions had identical frequency and duration (60-90 min) and were performed at the same time of the day. All session were conducted under the direct supervision of a physiotherapist and two master students in physiotherapy. At the beginning of each session, the patients in the ST group received personalised oral and

written instructions for machines adjustment, number of repetitions to perform and loads to lift, while patients in the AE group received oral and written instructions for speed, resistance and timing of cycling. The supervisors checked participant's compliance with these instructions and guided them through the proper use of the material. Specific trainings were preceded by five to 10 min of warming up (i.e. dynamic movements of upper and lower limbs with very light solicitation of the cardiorespiratory system and minimal solicitation of balance) and ended with short stretching. At the end of the sessions, patients rated physical exhaustion by mean of the Borg scale. [13] The evolution of perceived exertion over time during the two exercise interventions is presented in Appendix 1. In both groups, the first session emphasised familiarisation with the equipment, safety and good practice in order to avoid injuries and maximise the efficacy of the trainings.

Aerobic training group. Trainings were conducted on the same stationary bikes and the intensity of the training was individualised according to the peak work load (PWL) reached during the incremental cardiorespiratory effort pre-training. During the first week, AE training consisted in 30 min of cycling at 50% of the PWL. From the second to the fourth week of training, patients performed 30 to 45 min of cycling between 50 and 55% of individual PWL with small duration and workload increment weekly adjusted according to a standardized progression. From the fifth week to the last one, the AE group performed one session a week of interval training and at least one session a week of continuous training. Interval training sessions consisted in fractions of 30 s to three min of high intensity cycling at 70% to 80% of PWL, interspersed with active recuperation fractions around 50% of PWL during 30 s to 90 s. Interval training sessions had total durations between 16 and 24 min and were preceded by warming-up and cool-down periods of 10 min of cycling at 40-50% of

PWL. Intervals intensity and duration evolved gradually according to a standardized protocol. The continuous training consisted in 40 to 45 min of cycling between 50% and 60% of PWL and gradually evolved according to a standardised protocol. Blood pressure was measured before, during, and five min after exercise completion, and heart rate was continuously monitored during the session. These parameters serve as monitoring in order to detect abnormal response to effort (e.g. effort hypotension), but they were not systematically recorded, nor presented in the present paper. A supervisor constantly checked that the patients reached the target workload and the appropriate timing of exercise or restrained them in case of abnormal monitoring.

Muscle strength training. The ST program consisted in exercises performed on machines (i.e. leg extension, leg curl, latissimus pull down, calf and leg press) or using weights (i.e. overhead pull-up and arm flexion). Loads were quantified in fractions of the measured one repetition maximum (1RM). The 1RM was the heaviest weight lifted on the complete range of motion and it was measured within five trials separated by at least 1.5 min of rest after a standardised warming-up on the machine. From the first to the fifth week of training, patients performed 10 to 15 repetitions at 50% to 60% of the 1RM. And from the sixth to the twelfth week of training, patients performed five to eight repetitions at 80% to 90% of the 1RM. Each exercise counted two to three sets left on the judgment of the patient according to exhaustion. Patients were instructed to lift the load as fast as possible for the concentric phase, and then to drop it back slowly during the eccentric phase of the movement. The program was completed with qualitative trunk exercises (i.e. abdominals and core strengthening) performed according to a standardised progression in order to prevent the subjects from back pain and injuries.

Standard care group. Patients of the SC group were asked to follow their standard care program and not to modify their level of exercises and physical activity during three months.

Efficacy measures

Pre- and post-training evaluations were performed using a standardized protocol, during the clinical *ON* state of the patients, at the same time of the day.

Muscle strength. We evaluated concentric strength of knee extensor and flexor muscles using an isokinetic dynamometer (Cybex HUMAC Norm, CSMI medical solutions Stoughton, Massachusetts). Patients seated on the dynamometer with the knee joint centre matching the dynamometer rotation centre and the range of motion was fixed between 0° and 90° of flexion. A short standardized practice at $120°.s^{-1}$ was performed. Then, the patients performed three sub-maximal repetitions at $60°.s^{-1}$ as familiarization. Finally, three maximal voluntary movements of knee extension and flexion at the speed of $60°.s^{-1}$ were performed and the best peak torque value of the three repetitions was recorded. Auditory cues were provided in order to reach the appropriate movement speed during familiarization and test. Data were scaled for body weight and presented for the most affected side, for the least affected side, and after summing both.

Cardiorespiratory fitness. Aerobic performances of the patients were recorded during an incremental exercise test on a cycle ergometer until exhaustion. Respiratory gas exchanges

were collected and analysed by a metabolic monitor *Vmax Spectra V29 System* (SensorMedics, Yorba Linda, CA). Subjects were also monitored by a 10-lead electrocardiogram (SensorMedics, Yorba Linda, CA). The test used a ramp protocol with a slope of 10 or 20 $W.min^{-1}$ according to age and physical activity level (i.e. patients older than 70 years and those performing less than 30 min of exercise a week had a slope of 10 $W.min^{-1}$ whilst younger active patients followed a 20 $W.min^{-1}$ ramp). The same ramp was used for pre- and post-training tests for each patient. During the incremental test, patients had to keep a stable cycling rate between 60 and 70 rotations per minute and were encouraged to go on cycling despite the increasing workload. Auditory cues were provided in order to help patients maintaining an appropriate cycling rate, except when inconvenient. The test was stopped when patients were unable to sustain the cycling speed despite encouragements. No major events sped up the ending of the test in the present study. Primary outcomes were PWL and peak oxygen consumption (VO_2peak) averaged during the last 30 s of the test. Respiratory exchange ratio and heart rate reserve were secondary outcomes. The criteria of maximal metabolic exhaustion were: (a) average heart rate of the last 30 s of the test ≥ predicted maximal heart rate –10%; (b) respiratory exchange ratio at completion of the test >1.1; (c) ceiling of oxygen consumption during the last 30 s of the test. Tests fulfilling at least two of these criteria were regarded as maximal.[14]

*Gait analysis***.** The standardised protocol and the thorough method of data extraction are detailed in a previous study of our group.[15] The main spatial-temporal parameters (i.e. speed, stride length and cadence) of gait were recorded at self-selected speed. Speed ($m.s^{-1}$) was inferred from the time needed to cover 30 m with acceleration and deceleration phases excluded, in a straight and clear hallway without marks on the floor. Cadence (Hz) was

automatically extracted from the cranial-caudal acceleration signal recorded with a trunk accelerometer. It was computed by mean of a fast Fourier Transform applied to the signal. Mean stride length was automatically computed from speed divided by cadence.

The timed up and go test. The Timed Up and Go test (TUG) was used to assessed walk and transfers ability of the patients.[16] Patients seated in an armchair (seat height: 0.5 m, depth: 0.5 m) placed at the start of a three meter-long path and they were instructed to complete the test as fast as possible. The time between the *go* and the moment the patient touch the back of the seat with his back was recorded by mean of a stopwatch. We recorded the best time of two successive trials.

The six-minute walk distance. Walking capacity was assessed by the six-minute walk distance (6mwd) test.[17] Patients walked back and forth along a 30-meter long path in a straight and wide hallway. Instructions and encouragements respected the recommendations of the American thoracic society,[18] except that patients were instructed to make about-turns as narrow as possible.

Habitual physical activity level. Physical activity, exercises and sport habits were assessed by the physical activity status scale (PASS) developed by Jackson et al.[19] The total score ranges between zero and seven, with a score of zero indicating no exercise or physical activity at all and a score of seven indicating at least three hours of intense physical exercise per week.

Health-related quality of life. The Parkinson's disease questionnaire- 39 items (PDQ-39) assessed quality of life in 39 questions according to eight specific dimensions: mobility (10 items), activity of daily living (six items), emotional well-being (six items), stigma (four items), social support (three items), cognition (four items), communication (three items), body discomfort (three items).[20] The scores of each dimension and the total score range from zero (no incidence of PD) to 100 (highest impact on quality of life).

Statistical analyses

Results are presented as mean ± standard deviation for normally distributed data and as median and interquartile range for data that do not reach a Gaussian distribution after logarithmic transformation. Comparisons of clinical and demographic characteristics at baseline were performed using a one-way parametric ANOVA for data following a Gaussian distribution, and using a non-parametric ANOVA of Kruskal-Wallis for skewed continuous data. Categorical variables are presented as proportions and were analysed by mean of Chi-squared tests. The effects of the trainings were statistically tested by mean of a two-level ANOVA for repeated measures after checking the distribution of the residues. P-values were reported for the effect of "group" (AE versus ST versus SC), the effect of "time" (pre-training versus post-training) and their interaction. When a significant main effect of the ANOVA was present, post-hoc multiple comparisons were performed with Student t-tests for paired sample corrected by the Bonferoni's method. Effect size (ES) was appraised by mean of the *d* of Cohen and its 95% confidence interval ($IC_{95\%}$) for data with a Gaussian distribution, but this method was not appropriate for skewed data.[21] For variables showing significant post-hoc effects after interventions, we computed simple correlations between pre and post-training changes (i.e. raw difference between the two tests) versus clinical

characteristics, number of sessions completed or baseline features, in order to identify the potential predictors of response to the interventions. Correlation analyses were conducted by mean of the correlation coefficient of Pearson (r_p) or the correlation coefficient of Spearman (r_s) when appropriate. For all statistical analyses, the level of significance was set at $p < 0.05$. Statistical analyses were conducted by mean of the Statistica 12 (Dell Software, France) and the Excel spreadsheets.

Results

Participants and tolerability

Of the ±120 patients contacted, 52 accepted to participate and met inclusion criteria between February 2012 and May 2014. Fifteen of them were allocated to the SC. Twenty patients were allocated to the AE group and 17 patients were allocated to the ST group. Nine patients in the SC group were already engaged in individual physiotherapy or planned exercises while six patients in the AE group and eight patients in the ST group were already engaged in regular exercises or physiotherapy at the beginning of the study.

Forty-six patients in the three groups (88%) completed the study. Sixteen (80%) patients from the AE group adequately completed the program; one patient left AE program because of a lack of time, a second one because of a surgical intervention not related to the rehabilitation, a third one because of a severe bronchitis and one other because of lack of interest. Fifteen patients (88%) from the ST group completed the program. One patient left because of excessive tiredness attributed to the training and a second one because of

exacerbation of back pain linked to a spinal stenosis. The patients flow throughout the study is presented in Figure 1.

Safety and adverse events

Adverse events probably linked to the trainings and the subsequent adaptations of the programs are listed in Appendix 2. Five and seven adverse events were reported in relationship with AE and ST, respectively.

Attendance and Adherence

The completers in the AE group attended a mean 31.3 ± 5.5 total sessions per patient. The completers in the ST group attended a mean 31 ± 5.5 sessions per patient. The mean adherence rate in the AE group was a 30.1 ±5.1 sessions per patient completed at the prescribed intensity. The mean adherence rate in the ST group was 27.8 ± 4.9 sessions completed at the prescribed intensity.

Clinical and demographic data

Baseline characteristics of the completers are presented in Table 1. Groups did not differ significantly in terms of demographic or biometric ~~or clinical~~ features at baseline. Disease duration, Hoehn &Yahr stage, activities of daily living and motor examination scores from the Unified Parkinson's Disease Rating Scale (UPDRS),[22] side of symptoms at disease onset were also reported at baseline, and did not significantly differ between groups. The number of patients regularly engaged in physical exercise or physiotherapy was not significantly

different between groups. The levels of dopaminergic medication pre- and post-trainings were computed using the levodopa equivalent daily dose (LEDD).[23] It was not different between groups at baseline and it did not significantly change over the study period (group effect: $p = 0.748$; time effect: $p = 0.22$; interaction: $p = 0.821$). The post-training LEDD in the three groups were: AE: 390 [375-695]; ST: 594 [157-949]; SC: 441 [210-750] mg.

Effects of the training

Muscle strength. The effects of the interventions on muscle strength are presented in Table 2. Peak torque values of all strength measures showed significant interactions ($p < 0.03$), except for the knee flexors in the most affected side ($p = 0.054$). Peak torque values for knee extensor and flexor muscles in the most affected side and the bilateral sums for knee extensor and flexor muscles showed significant time effect ($p \leq 0.007$). Post-hoc analyses showed significant peak torque improvements after ST for the extensor muscles in the most affected side ($p=0.008$), for bilateral sum of the extensors ($p = 0.006$), and for all peak torque measures of the flexor muscles ($p \leq 0.01$). Peak torque changes for knee extension in the most affected side, for bilateral extension measures, and for all measures of flexion reached moderate ESs in the ST group. Peak torque improvement for the knee extensors in the most affected side also reached a moderate ES in the AE group. No significant correlations with the strength improvements were seen.

Cardiorespiratory fitness. Results of the maximal incremental test are presented in Table 3. The maximal incremental effort test showed significant interactions for VO_2peak and PWL. In the AE group, 56% of the patients reached the criteria of maximal metabolic solicitation

during pre-training tests and 62% of them reached the same criteria during post-training tests. Post-hoc analyses revealed that the AE group significantly improved VO_2peak and PWL ($p = 0.02$ and $p < 0.0001$, respectively), and these results were accompanied by ESs around 0.5. In the ST group, 29% of the patients reached the criteria of maximal test during the pre-training evaluations and 43% of them reached these criteria during the post-training evaluations. Post-hoc analyses showed that the ST group significantly improved PWL after training ($p = 0.009$). In the SC group, respectively 40% and 67% of the patients reached a maximal test during pre- and post-training tests and no significant post-hoc changes were seen. Correlation analyses revealed that changes in PWL were positively associated with the Hoehn &Yahr stage and the motor score on the part III of the UPDRS in the merged intervention groups ($r_s = 0.47$; $p = 0.009$ and $r_s = 0.44$; $p = 0.001$, respectively). Changes of PWL in merged intervention groups were also correlated with pre-training LEDD ($r_s = 0.4$; $p = 0.02$) and with being a man ($r_s = 0.41$; $p=0.02$). Finally, PWL changes in merged intervention groups were positively correlated with 6mwd improvement ($r_s = 0.5$; $p = 0.005$). No correlations with improvement of VO_2peak were found in the AE group.

Mobility. Effects of the training are presented in Table 4. No significant changes in the spatial-temporal characteristics of gait were seen in any group, although there was a significant "time" effect for cadence ($p = 0.02$). The log-transformed TUG duration also showed a significant "time" effect ($p = 0.016$), without significant post-hoc effect. The 6mwd showed significant "time" effect and interaction ($p = 0.008$ and $p = 0.029$, respectively). A significant longer distance was covered by the ST group during post-training evaluations ($p = 0.03$) and it was accompanied by a medium ES ($d = 0.5$). No association was found between the 6mwd changes and clinical characteristics of the patients

in the ST group. But the 6mwd change was positively correlated with PWL improvement in the merged intervention groups ($r_s = 0.5$; $p = 0.005$).

Health-related quality of life and habitual physical activity level. Results are presented in Table 5. There were significant "time" effect and interaction for the habitual physical activity level measured by the PASS (respectively, $p = 0.004$ and $p = 0.02$). There were also a significant interaction for the *stigma* sub-scale ($p < 0.05$) and a significant "time" effect for *affective well-being* sub-scale ($p = 0.03$) of the PDQ-39. No post-hoc analysis reached level of significance, but the PASS change in the AE group showed a trend after post-hoc analysis ($p = 0.06$), and the changes on the PASS reached a medium ES in this group ($d = 0.54$).

Discussion

To our knowledge, this controlled study is the first one to observe the effects of two different physical conditioning interventions tailored on measured peak performances and under group supervision in patients with PD. The main results showed a satisfying adherence rate and improved fitness in compliance with training goals. Notwithstanding, mobility and health-related quality of life did not respond to the interventions, except improved 6mwd after ST.

Comparable effects on strength and aerobic performances after appropriate training were previously reported in patients with PD compared with healthy subjects.[24, 25] Yet, improved performances after AE or ST are not certain, even in healthy populations.[26, 27] In a study about physical reconditioning in healthy older subjects, AE and ST increased

VO2peak and knee extension strength by 8%,[26] which is of the same order than the results in the present study. Although, training of healthy older people had a great heterogeneity of response, with 13% of participants showing no VO_2peak changes after AE and 30% of them showing no strength improvement after ST.[26] The rate of responders was slightly lower in the present study: 25% of patients with PD in the AE group did not improve VO_2peak, while 43% of the patients in the ST group did not improve one of the peak torque measures. Indeed, improving physical fitness in subjects suffering from motor impairments doesn't come naturally since poor movement efficacy may prevent them from reaching adequate metabolic solicitation during exercises. Besides, non-motor symptoms may also interfere with exercises (e.g. sympathetic denervation decreases cardiac response to effort). In the present study, some adaptations were provided during training and testing in order to be as close as possible to the recommendations in healthy population (e.g. cueing strategies for reaching appropriate cycling speed, complete range of motion during the concentric phase of weight lifting, or training intensity inferred from PWL rather than predicted maximal heart rate).[14] In healthy older subjects as in the present study, neither adherence rate nor baseline performances were associated with strength or aerobic capacity improvements.[26] Nevertheless, PWL was positively correlated with the clinical Hoehn & Yahr stage and the score on the motor subscale of the UPDRS in the merged trained groups. This suggests that reconditioning may be particularly efficient for patients with moderate PD.

In the literature, patients with PD showed overall good trainability of aerobic capacity, despite high variability in methodology and metabolic solicitation across studies.[28-31] In contrast, response to ST in patients with PD seems more variable and may differ according to muscle groups, training and testing methodologies.[32] In the present study, strength significantly improved after ST, except peak torque of the knee extensors in the least affected side. ST performed both legs together whilst isokinetic peak torque was

measured unilaterally during testing may explain insufficient overload to the extensor muscles in the stronger side.[33] For this reason, it may be preferable to train each limb individually in the context of this asymmetric disease, although it is rarely performed in practice likely because of time-savings or technical configuration of the equipment.

Shulman et al. compared AE and ST interventions during the same period and with comparable sample characteristics as the present trial.[30] Differently, they used treadmill instead of bike for AE, and ST was limited to the lower limbs. Similarly to the present study, self-selected speed did not improve after interventions, but fast walking speed improved after treadmill AE, and both types of training increased 6mwd. Better mobility after AE in the study of Shulman et al. could be linked to treadmill that trains cardiorespiratory fitness and constitutes an intensive walking exercise at the same time.[34] Inconstant effects of ST, AE and exercises in general have been reported on gait in PD.[31, 35-37] In the present study, better fitness after physical conditioning exercises did not translate into better mobility, except better walking capacity in the ST group. Interventions combining physical conditioning and task-oriented exercises could overcome benefits from each therapy applied separately and deserve to be further studied. For example, two studies showed that ST under balance challenging conditions or aerobic treadmill training combined with cueing strategies had better impact on transfers or mobility than the same exercises performed under usual conditions.[38, 39] Improvement may also have been limited by the slightly altered gait of the patients in the present study.[40] Yet, gait improvements have already been observed after exercise in PD patients with comparable or better baseline performances.[41, 42] Even if participants seem to keep improvement possibilities, a refined gait analysis could be more appropriate for tracking gait improvement in such mildly affected patients. Likewise, studies that recorded advanced outcomes (e.g. energetic cost, joints kinematics, postural adaptation) showed significant effects on gait with rehabilitation, [7, 43, 44] whilst studies that recorded

basic spatial-temporal outcomes often failed to identify gait changes.[45, 46] The 6mwd investigates a more functional aspect of mobility and depends on the efficacy of several systems (i.e. cardiorespiratory, musculoskeletal, peripheral and central nervous systems). For these reasons, this test may be more appropriate for patients with well-preserved gait. In the present study, ST significantly improved 6mwd, and these results are consistent with a previous transversal study that identified quadriceps strength as a main contributor to 6mwd in mild and moderate PD.[47] Besides, better ability to perform strenuous effort (i.e. increased PWL) was correlated with better 6mwd in both groups of trained patients, and this correlation emphasises the importance of high-intensity physical performances on walking capacity in PD.

Unfortunately, better walking capacity after ST did not translate into better perceived mobility assessed by the PDQ-39. And more generally, no evident effects on health-related quality of life were observed. Nevertheless, it seems wise to highlight some encouraging trends: the significant interaction found for *stigma* sub-scale of the PDQ-39 with improvement around 30% in both trained groups whilst the SC group worsened; the significant time effect for *emotional well-being* sub-scale with a moderate ES in the ST group; the non-significant improvement of 32% in *social support* in the AE group. Even if these results were balanced, they may be promising insights into improved coping with psycho-social aspects of PD with group exercises.

The small sample size, lack of full randomisation and blinding of the assessors were limitations in this study. Indeed, the low participation rate prevented from reaching high methodologic quality. Other weaknesses were the short period of rehabilitation and follow-up. In healthy athletes, detraining has a worse impact on cardiorespiratory fitness than muscle strength.[48] In the context of PD, detraining may also be influenced by other factors

like disease progression, age, along with physical activity level. Promisingly, the significant time effect and interaction on the PASS score showed that structured exercises may encourage patients being active after completion of the intervention. Although post-hoc analyses did not reach significance, it may be one of the most promising result since lasting adherence to active behaviour could have remarkable positive impact on cerebral plasticity, neuroprotection and motor function in patients with PD.[34, 49] One-year follow-up of quality of life and physical activity in a subset of participants is presented in Appendix 3. However, material and recruitment issues prevented to report the evolution of all outcomes in the whole sample of participants. The PASS and the total PDQ-39 score showed significant time effects suggesting lasting impact of these group interventions on the behaviour of patients suffering from PD.

Conclusion

This study showed that group sessions of high intensity physical conditioning in patients suffering from mild to moderate PD is feasible and that it improves fitness in compliance with training specificities. However, short-term benefits on mobility and health-related quality of life are limited in both training interventions. Notwithstanding, ST could be recommended in order to improve walking capacity of the patients with mild to moderate PD, and structured physical training may influence further exercise participation.

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TITLES OF TABLES

Table 1. Demographics of the three groups of subjects

	AE group n=16	ST group n=15	SC group n=15	ANOVA p-values
Age (years)	65 ± 8	67 ± 10	63.3 ± 6	0.436
Gender (males %)	73	56	67	0.601
Height (m)	1.67 ± 0.11	1.68 ± 0.11	1.71 ± 0.11	0.746
Weight (kg)	71 ± 16	71 ± 13	81 ± 16	0.153
BMI ($kg.m^{-2}$)	26 ± 3.3	25 ± 2.5	27.3 ± 4.1	0.212
Disease duration (years)	5 [2.5-8]	7 [2-9]	5 [3-7]	0.857
H&Y scale (range: I-III)				
Median score	1.5 [1-2.5]	2 [1-2.5]	1.5 [1-2]	0.466
Counts of patients (%)	I: 44% I.5: 19% II: 12% II.5: 25%	I: 40% II: 27% II.5: 20% III: 13%	I: 47% I.5: 13% II: 33% II.5: 7%	0.313
UPDRS II	10 [7.5-17.5]	10 [3-14]	10 [5-11]	0.361
UPDRS III	16.9 ± 6.8	20 ± 7.8	16.3 ± 9.2	0.32
Side of symptoms at onset (% right)	47	44	32	0.601
MMSE (total=30)	28 [27-29]	28 [26-30]	28 [27-29]	0.859
LEDD pre-training (mg)	402 [307-632]	594 [157-855]	381 [157-750]	0.753
Physiotherapy or	60	37.5	53.3	0.431

structured exercise participation (patients %)

AE: aerobic training group; BMI= body mass index; H&Y scale= Hoehn and Yahr scale of disease severity; LEDD= Levodopa equivalent-day dose; MMSE= mini-mental state exam; SC: standard care group; ST strength training group; UPDRS: unified Parkinson's disease rating scale.

Data are presented as mean ± standard deviation and compared using a 1-way ANOVA if they follow a Gaussian distribution. Skewed data were presented as median [interquartile range] and compared using an ANOVA of Kruskal-Wallis. Binary and ordinal variables are presented as percent and compared using Chi-squared tests.

Table 2. Effects of the interventions on muscle strength

	PRE-TRAINING	POST-TRAINING	EFFECT SIZE d Cohen [$IC_{95\%}$]	ANOVA p-values of the main effects
Peak torque for knee extension -most affected side ($Nm.kg^{-1}$)				
AE (n=16)	1.52 ± 0.401 +13%	1.72 ± 0.34	0.52 [-0.18-1.23]	Group: 0.815 Time: 0.0003 Interaction: 0.029
ST (n=15)	1.488*± 0.528 +17%	1.736*± 0.453	0.5 [-0.04-1.44]	
SC (n=15)	1.535 ± 0.415 +0%	1.537 ± 0.37	0.01 [-0.71-0.72]	
Peak torque for knee extension -least affected side ($Nm.kg^{-1}$)				
AE (n=16)	1.743 ± 0.416 +6%	1.854 ± 0.395	0.28 [-0.44-0.99]	Group: 0.619 Time: 0.232 Interaction: 0.007
ST (n=15)	1.537 ± 0.602 *+15%*	1.769 ± 0.581	0.37 [-0.33-1.11]	
SC (n=14)[a]	1.74 ± 0.513 -10%	1.576 ± 0.346	-0.37 [-1.1-0.35]	
Peak torque for bilateral knee extension –sum ($Nm.kg^{-1}$)				
AE (n=16)	3.27 ± 0.759 +9%	3.572 ± 0.714	0.41 [-0.31-1.13]	Group: 0.778 Time: 0.007 Interaction: 0.003
ST (n=15)	3.025*± 1.108 +16%	3.505* ± 0.999	0.45 [-0.27-1.17]	
SC (n=14[a])	3.29 ± 0.892 -5%	3.126 ± 0.688	-0.21 [-0.95-0.53]	

Peak torque for knee flexion -most affected side ($Nm.kg^{-1}$)				
AE (n=16)	0.706 ± 0.207 +12%	0.789 ± 0.174	0.43 [-0.27-1.13]	Group: 0.904 Time: 0.003 Interaction: 0.054
ST (n=15)	0.636*± 0.25 +23%	0.789*± 0.277	0.56 [-0.17-1.29]	
SC (n=15)	0.728 ± 0.225 -1%	0.728 ± 0.211	-0 [-0.72-0.71]	
Peak torque for knee flexion -least affected side ($Nm.kg^{-1}$)				
AE (n=16)	0.785 ± 0.225 +4%	0.816 ± 0.234	0.14 [-0.58-0.85]	Group: 0.757 Time: 0.083 Interaction: 0.001
ST (n=15)	0.66*± 0.285 +24%	0.819*± 0.293	0.52 [-0.21-1.25]	
SC (n=14[a])	0.832 ± 0.219 -8%	0.767 ± 0.198	-0.31 [-1.06-0.43]	
Peak torque for bilateral knee flexion -sum ($Nm.kg^{-1}$)				
AE (n=16)	1.482 ± 0.424 +8%	1.609 ± 0.399	0.31 [-0.41-1.03]	Group: 0.85 Time: 0.006 Interaction: 0.002
ST (n=15)	1.305*± 0.515 +23%	1.611*± 0.557	0.56 [-0.17-1.29]	
SC (n=14[a])	1.564 ± 0.463 -5%	1.487 ± 0.403	-0.18 [-0.93-0.56]	

AE: aerobic training group; SC: standard care group; ST strength training group.

Data are presented as mean ± standard deviation and the percentage of change between pre- and post-training evaluations. The main effects of the two-level ANOVA for repeated measures are reported. The effect sizes are reported by mean of the d of Cohen and its $IC_{95\%}$.

*Show a significant change between pre- and post-training tests after post-hoc analyses ($p < 0.05$).

[a]One patient of the SC group did not perform the test for the least affected side because he had a total knee arthroplasty which was a contraindication to maximal isokinetic test.

Table 3. Effects of the interventions on outcomes of the maximal incremental test

	PRE-TRAINING	POST-TRAINING	EFFECT SIZE d Cohen [$IC_{95\%}$]	ANOVA p-values of the main effects
Vo2 peak ($ml.kg^{-1}.min^{-1}$)				
AE (n=16)	23.4*± 5.2 +12%	26.2*± 6.5	0.47 [-0.2-1.17]	Group: 0.336 Time: 0.079 Interaction: 0.015
ST (n=14)[a]	20.9 ± 8.5 +2%	21.4 ± 8.5	0.06 [-0.68-0.80]	
SC (n=15)	23.5 ± 6 -3%	22.8 ± 6.7	-0.11 [-0.83-0.6]	
PWL ($w.kg^{-1}$)				
AE (n=16)	1.68*± 0.45 +18%	1.98*± 0.61	0.55 [-0.16-1.25]	Group : 0.494 Time: < 0.0001 Interaction: 0.0006
ST (n=14)[a]	1.45*± 0.74 +16%	1.68*± 0.78	0.3 [-0.44-1.05]	
SC (n=15)	1.72 ± 0.57 -2%	1.68 ± 0.52	-0.06 [-0.78-0.65]	
Respiratory exchange ratio				
AE (n=16)	1.1 ± 0.07 +0%	1.11 ± 0.06	0.14 [-0.55-0.83]	Group: 0.253 Time: 0.02 Interaction: 0.128
ST (n=14)[a]	1.06 ± 0.07 +6%	1.12 ± 0.12	0.12 [-0.62-0.86]	
SC (n=15)	1.06 ± 0.06 +0%	1.07 ± 0.08	0.12 [-0.6-0.84]	

Heart reserve (bpm)				
AE (n=16)	58 ± 18 +0%	58 ± 19	-0 [-0.7-0.69]	Group: 0.505 Time: 0.485
ST(n=14)[a]	54 ± 21 -0%	53 ± 23	-0.11 [-0.85-0.63]	Interaction: 0.78
SC (n=15)	51 ± 18 -0%	49 ± 22	-0.16 [-0.88-0.55]	

AE: aerobic training group; SC: standard care group; ST strength training group.

Data are presented as mean ± standard deviation and the percentage of change between pre- and post-training evaluations. The main effects of the two-level ANOVA for repeated measures are reported. The effect sizes are reported by mean of the d of Cohen and its $IC_{95\%}$.

*Show a significant change between pre- and post- training tests after post-hoc analyses ($p < 0.05$).

[a]*One patient of the MS group was not allowed by her physician to perform the maximal aerobic test.*

Table 4. Effects of the interventions on mobility

	PRE-TRAINING	POST-TRAINING	EFFECT SIZE d Cohen [$IC_{95\%}$]	ANOVA p-values of the main effects
Speed ($m.s^{-1}$)				
AE (n=16)	1.26 ± 0.24 +5%	1.32 ± 0.19	0.27 [-0.43-0.96]	Group: 0.188, Time: 0.092 Interaction: 0.363
ST (n=15)	1.16 ± 0.2 +5%	1.22 ± 0.1	0.41 [-0.31-1.13]	
SC (n=15)	1.28 ± 0.13 -0%	1.27 ± 0.14	-0.05 [-0.77-0.66]	
Stride length (m)				
AE (n=16)	1.34 ± 0.18 +1%	1.36 ± 0.15	0.07 [-0.62-0.76]	Group: 0.08 Time: 0.582 Interaction: 0.632
ST (n=15)	1.24 ± 0.19 +2%	1.27 ± 0.14	0.16 [-0.56-0.87]	
SC (n=15)	1.38 ± 0.13 -0%	1.37 ± 0.13	-0.01 [-.81-0.62]	
Cadence (Hz)				
AE (n=16)	0.93 ± 0.11 +4%	0.97 ± 0.08	0.34 [-0.35-1.04]	Group: 0.689 Time: 0.02 Interaction: 0.348
ST (n=15)	0.93 ± 0.08 +4%	0.97 ± 0.07	0.52 [-0.21-1.24]	
SC (n=15)	0.93 ± 0.07 -0%	0.93 ± 0.05	0.06 [-0.66-0.78]	

Tug, log-transformed (s)				
AE (n=16)	1.8 ± 0.3 -6%	1.7 ± 0.2	-0.33 [-1.02-0.37]	Group: 0.751 Time: 0.016
ST (n=15)	1.9 ± 0.4 -5%	1.8 ± 0.3	-0.28 [-1-0.44]	Interaction: 0.437
SC (n=15)	1.8 ± 0,2 -0%	1.8 ± 0,2	-0.12 [-0.83-0.6]	
6mwd (m)				
AE (n=16)	553 ± 67 +6%	584 ± 91	0.38 [-0.31-1.08]	Group: 0.11 Time: 0.008
ST (n=15)	486*± 88 +10%	535*± 104	0.5 [-0.23-1.22]	Interaction: 0.029
SC (n=15)	541 ± 65 -2%	532 ± 70	-0.13 [-0.85-0.58]	

AE: aerobic training group; SC: standard care group; ST strength training group; Tug: timed and go test; 6mwd: six- minute walk distance.

Data are presented as mean ± standard deviation and the percentage of change between pre- and post-training evaluations. The main effects of the two-level ANOVA for repeated measures are reported. The effect sizes are reported by mean of the d of Cohen and its $IC_{95\%}$.

*Show a significant change between pre- and post-training tests after post-hoc analyses ($p<0.05$).

Table 5. Effects of the training on physical activity level and health-related quality of life

	PRE-TRAINING	POST-TRAINING	EFFECT SIZE d Cohen [$IC_{95\%}$]	ANOVA p-values of the main effects
PASS (highest=7)				
AE (n=16)	2.6 ± 1.2 +23%	3.2 ± 0.8	0.54 [-0.17-1.25]	Group: 0.205 Time: 0.004 Interaction: 0.022
ST (n=15)	2.1 ± 1.8 +29%	2.7 ± 1.7	0.34 [-0.38-1.06]	
SC (n=15)	3.4 ± 1 -3%	3.3 ± 1.5	-0.10 [-0.82-0.61]	
PDQ-39, mobility (%)				
AE (n=16)	10 [0-22,5] +12%	11.25 [3.75-30]	N/A	Group: 0.59 Time: 0.821 Interaction: 0.704
ST (n=15)	15 [7.5-20] +0%	15 [7.5-22.5]	N/A	
SC (n=15)	10 [0-22.5] -8%	7.5 [0-20]	N/A	
PDQ-39, activities of daily living (%)				
AE (n=16)	30 ± 18 -6%	29 ± 19	-0.1 [0.79-0.59]	Group: 0.614 Time: 0.278 Interaction: 0.99
ST (n=15)	26 ± 21 -10%	24 ± 17	-0.13 [-0.85-0.58]	

SC (n=15)	25 ± 17 -9%	23 ± 15	-0.14 [-0.86-0.57]	
PDQ-39, emotional well-being (%)				
AE (n=16)	33 ± 16 -13%	29 ± 19	-0.24 [-0.94-0.45]	Group: 0.067 Time: 0.034
ST (n=15)	22 ± 16 -37%	14 ± 11	-0.59 [-1.32-0.14]	Interaction: 0.495
SC (n=15)	21 ± 22 -9%	19 ± 21	-0.09 [-0.81-0.62]	
PDQ-39, stigma (%)				
AE (n=16)	28 ± 23 -30%	19 ±19	-0,41 [-1.11-0.29]	Group: 0.546 Time: 0.11
ST (n=15)	23 ±18 -26%	17 ±14	-0.38 [-1.11-0.37]	Interaction: < 0.05
SC (n=15)	11 ±12 +27%	14 ±15	0.27 [-0.48-1.01]	
PDQ-39 social support (%)				
AE (n=16)	25 [0-33] -32%	17 [0-29]	N/A	Group: 0.012 Time: 0.923
ST (n=15)	0 [0-17] -0%	0 [0-0]	N/A	Interaction: 0.488
SC (n=15)	0 [0-17] +0%	0 [0-25]	N/A	

PDQ-39, cognition (%)				
AE (n=16)	35 ± 24 -3%	34 ± 26	-0.03 [-0.72-0.66]	Group: 0.393 Time: 0.155 Interaction: 0.666
ST (n=15)	30 ± 22 -20%	24 ± 20	-0.3 [-1.02-0.4]	
SC (n=15)	27 ± 18 -7%	25 ± 18	-0.17 [-0.88-0.55]	
PD-39, communication (%)				
AE (n=16)	33 [12-42] -12%	29 [16-37]	N/A	Group: 0.25 Time: 0.366 Interaction: 0.38
ST (n=15)	42 [16-50] -40%	25 [0-58]	N/A	
SC (n=15)	25 [0-33] +0%	25 [8-33]	N/A	
PDQ-39, body comfort (%)				
AE (n=16)	46 ± 23 +0%	46 ± 26	0 [-0.69-0.69]	Group: 0.262 Time: 0.089 Interaction: 0.323
ST (n=15)	42 ± 20 -21%	33 ± 15	-0.52 [-1.24-0.21]	
SC (n=15)	37 ± 19 -11%	33 ± 21	-0.19 [-0.91-0.52]	
PDQ-39, total (%)				

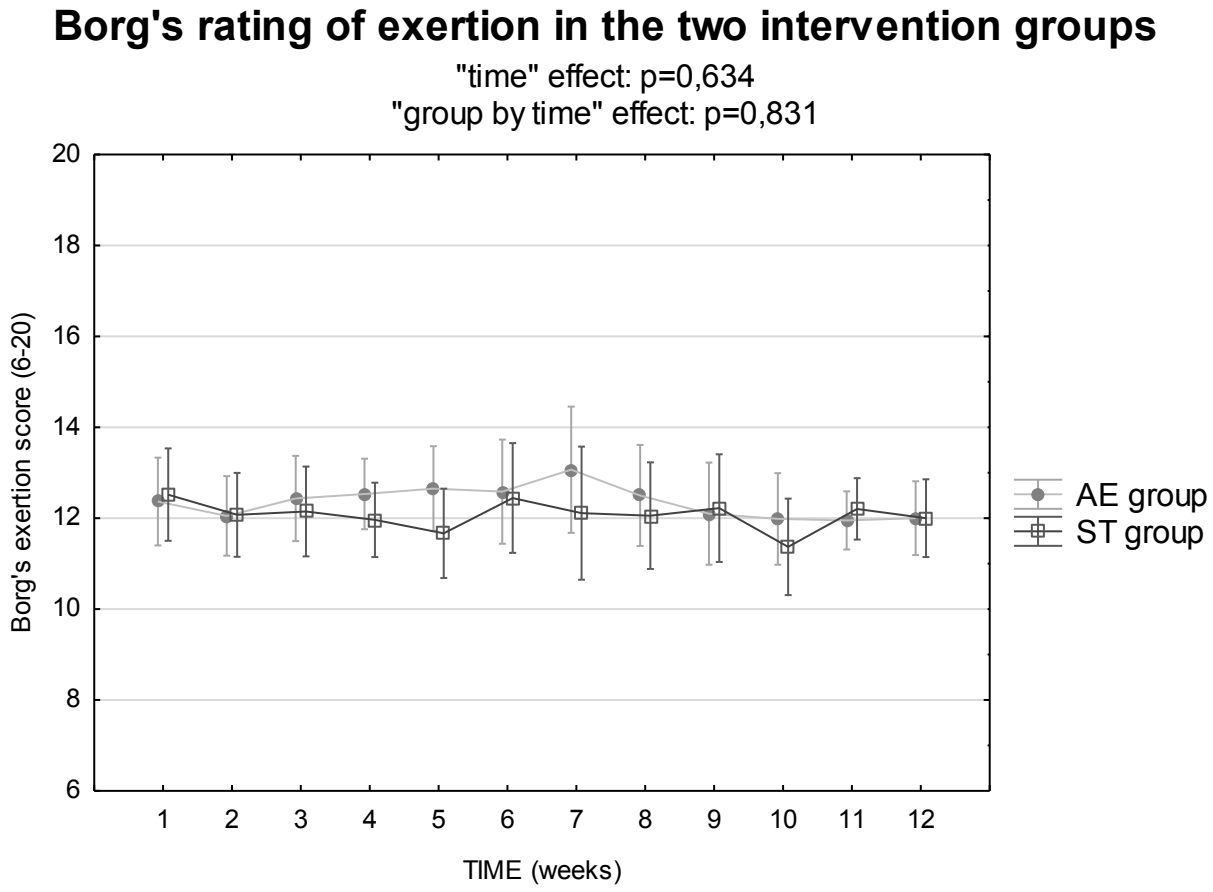
AE (n=16)	28 ± 12 4%	27 ± 15	-0.1 [-0.8-0.59]	Group: 0.168 Time: 0.073
ST (n=15)	24 ± 12 -21%	19 ± 7	-0.42 [-1.15-0.3]	Interaction: 0.433
SC (n=15)	20 ± 13 -5%	19 ± 13	-0.06 [-0.78-0.65]	

AE: aerobic training group; N/A: non-appropriated; PASS: Physical Activity Status Scale; PDQ-39: Parkinson's disease questionnaire; SC: standard care group, ST strength training group.

Data are presented as mean ± standard deviation for normally distributed data or presented as Median [Interquartile range] for skewed data, and as percentage of change between pre- and post-training evaluations. The main effects of the two-level ANOVA for repeated measures are reported. The effect sizes are reported by mean of the d of Cohen and its $IC_{95\%}$, except for data with non-Gaussian distribution.

Appendix 1. Follow-up of physical exertion during the AE and ST programs.

The score of perceived exertion was measured by mean of the Borg scale after all sessions and then weekly averaged. The mean exertion score across all sessions was compared between the 2 intervention groups by mean of a Student's t-test and it was not significantly different between the 2 groups (AE group: 12.3 ±1.2; ST group: 12 ± 0.7, p=0.475). A score of 12 correspond to a rating between "fairly light" and "somewhat hard". This light perceived exhaustion was obtained through progressive and individualized programs with standardized resting periods and workloads.



This graph shows the time course of the weekly exertion scores in the two exercise groups. No significant time effect was detected by mean of an ANOVA for repeated

measures, and the evolution was not significantly different between the two groups ($p>0.6$). In the AE group, we observed peak exhaustion during the seventh week followed by a gentle decrease of perceived exhaustion to values similar to baseline. This coincides with the continuous training reaching 60% of PWL, the highest workload, for the first time. In the ST group, a peak was reached during the sixth week of training when loads were increased at 80% of the 1RM. These complementary results show consistency between perceived exertion and workload progression.

Appendix 2: adverse events related to the physical activity rehabilitation programs and their impact on the adherence to the training program for the patient.

Events	group	consequences
Light knee sprain at the end of the last session	AE	Referral to individual PT session, and delay of the post-training assessment.
Reappearance of knee pain linked to a *Baker* cyst	AE	One week off and delay of the following sessions.
Headache	AE	Shortening of 2 sessions. The patient did not reach the goals of these sessions.
Tiredness	AE	Do not reach the training goals for eight sessions.
effort persisting hypotension	AE	Three sessions shortened and rest. The patient did not reach the goals of these sessions.
Excessive tiredness	ST	One week rest and delay of the six last sessions.
Patella pain syndrome (2 participants)	ST	Suppression of the leg extension exercise for six consecutive sessions and then lowered loads for the next three weeks.
	ST	Lowered load for leg extension for three consecutive weeks.
Back pain	ST	Delay of one session and lowered loads from the 7^{th} week to the end of the training.
Reappearance of pain linked to an previous elbow	ST	Avoid upper limb strengthening for the three last weeks of training.

fracture		
Exacerbation of pain from a previous wrist sprain	ST	Lowering of the upper limb loads for six sessions.

AE: aerobic training group; ST: strength training group.

Appendix 3. One-year follow-up of health-related quality of life and physical activity level after completion of the exercise programs.

One year after rehabilitation completion, participants were invited to reply to a mailing survey and to complete the PASS questionnaire and the PDQ-39. Unfortunately, several participants did not reply or sent incomplete responses. Data were compared by mean of ANOVAs for repeated measures. Results showed a significant *time* effect for the PASS. The scores in AE and ST groups seemed to maintain at a higher level after rehabilitation and follow-up, but intragroup changes after post-hoc analyses remained not significant. Significant *interaction* for the affective well-being sub-scale and significant *time* effect for the total score on the PDQ-39 were observed. Although post-hoc analyses did not show significant effects, the scores for these items seem to remain quite stable in the AE and SC groups after follow-up, but tend to return to baseline measures (worse) in the ST group. These results have to be cautiously interpreted because of missing data.

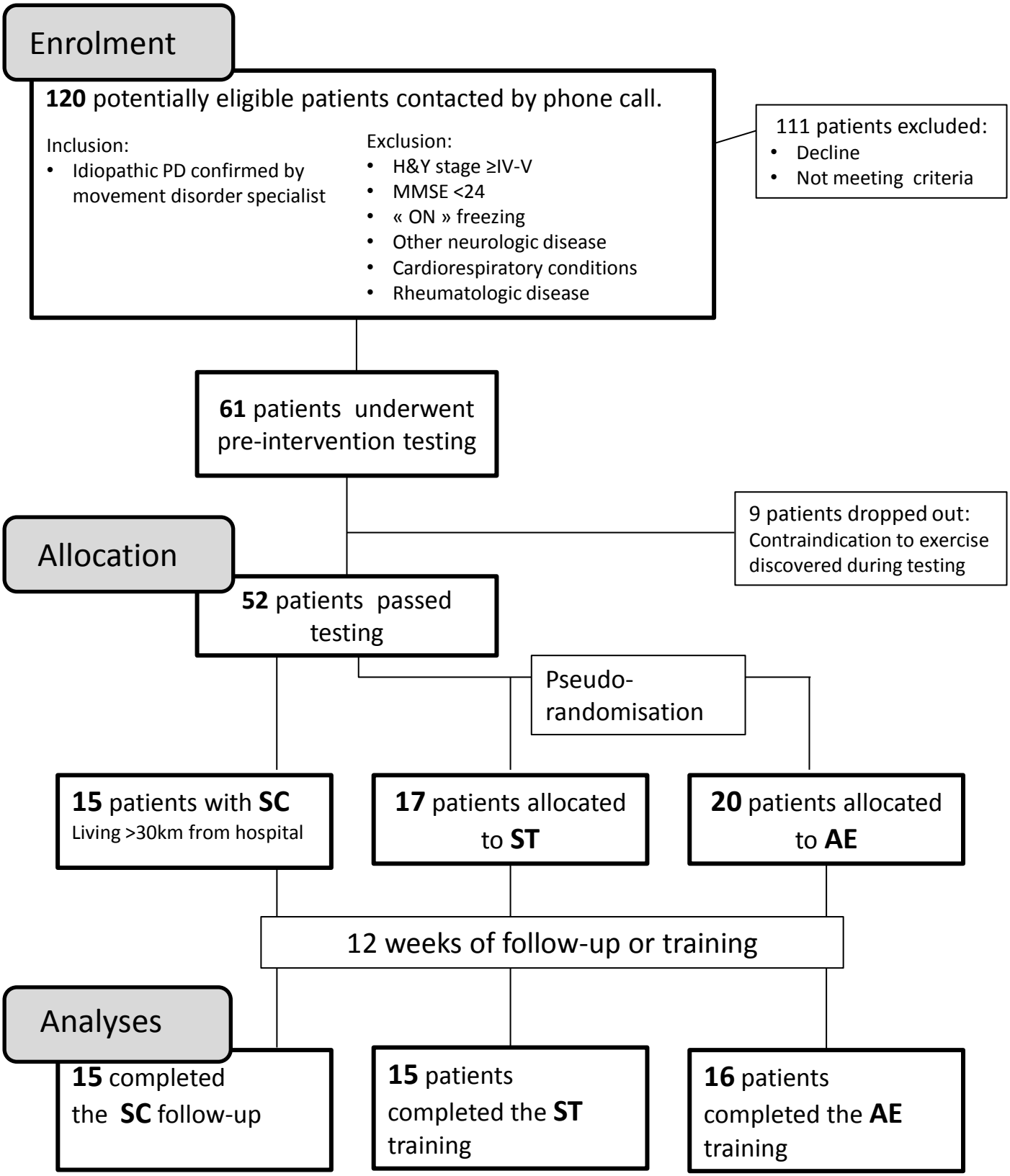
	PRE-TRAINING	POST-TRAINING	One year FOLLOW-UP	ANOVA p-values of the main effects
PASS (highest=7)				
AE (n=12)	2.5 ± 1.2	3.1 ± 0.9	3.5 ± 1.17	Group: 0.09
ST (n=9)	1.8 ± 1.3	2.3 ± 1.7	3.1 ± 2.4	Time: 0.031
SC (n=12)	3.5 ± 0.9	3.6 ± 0.99	3.4 ± 1.8	Interaction: 0.297
PDQ-39, mobility (%)				
AE (n=12)	10 [9-20]	10 [2-21]	13.7 [9-30]	Group: 0.143
ST (n=9)	17 [12-25]	17.5 [10-22]	30 [15-35]	Time: 0.1017
SC (n=12)	11 [0-16]	11 [0-19]	14 [4-35]	Interaction: 0.805
PDQ-39, activities of daily living (%)				
AE (n=12)	30 ± 18	26 ± 20	28 ± 24	Group: 0.705
ST (n=9)	30 ± 23	25 ± 20	35 ± 20	Time: 0.28
SC (n=12)	22 ± 18	24 ± 14	26 ± 13	Interaction: 0.678
PDQ-39, affective well-being (%)				
AE (n=12)	38 ± 15	31 ± 21	27 ± 19	Group: 0.317
ST (n=9)	24 ±10	12 ± 9	24 ± 17	Time: 0.006
SC (n=12)	25 ± 23	22 ± 23	25 ± 25	Interaction: 0.024
PDQ-39, stigma (%)				
AE (n=12)	27 ± 22	21 ± 21	23 ± 20	Group: 0.572
ST (n=9)	24 ± 16	17 ± 15	22 ± 16	Time: 0.5
SC (n=12)	15 ±20	18 ±23	16 ± 19	Interaction: 0.608

PDQ-39 social support (%)				
AE (n=12)	17 [0-33]	24 [0-42]	12.5 [0-21]	Group: 0.236
ST (n=9)	0 [0-8]	0 [0-0]	0 [0-17]	Time: 0.705
SC (n=12)	0 [0-21]	4 [0-21]	15 [0-33]	Interaction: 0.108
PDQ-39, cognition (%)				
AE (n=12)	34 ± 20	29 ± 27	31 ± 23	Group: 0.879
ST (n=9)	31 ± 20	26 ± 14	35 ± 18	Time: 0.134
SC (n=12)	29 ± 18	25 ± 19	29 ± 14	Interaction: 0.798
PD-39, communication (%)				
AE (n=12)	33 [21-42]	29 [16-37]	21 [17-42]	Group: 0.334
ST (n=9)	33 [17-50]	31 [0-58]	50 [8-58]	Time: 0.415
SC (n=12)	29 [4-33]	21 [4-37]	21 [0-37]	Interaction: 0.616
PDQ-39, body comfort (%)				
AE (n=12)	45 ± 22	42 ± 22	43 ± 19	Group: 0.565
ST (n=9)	47 ± 23	38 ± 15	46 ± 20	Time: 0.161
SC (n=12)	33 ± 24	33 ± 17	42 ± 29	Interaction: 0.536
PDQ-39, total (%)				
AE (n=12)	28 ± 11	25 ± 15	25 ± 13	Group: 0.56
ST (n=9)	26 ± 12	20 ± 7	30 ± 11	Time: 0.029
SC (n=12)	21 ± 13	20 ± 14	22 ± 12	Interaction: 0.119

AE: aerobic training group; N/A: non-appropriated; PASS: Physical Activity Status Scale; PDQ-39: Parkinson's disease questionnaire; SC: standard care group, ST strength training group.

Data are presented as Mean ± Standard deviation for normally distributed data or presented as Median [Interquartile range] for skewed data. The main effects of the two-level ANOVA for repeated measures are reported. No significant post-hoc results were observed.

Figure 1. Flow chart of the patients through the study



AE: aerobic training group, PD: Parkinson's disease, H&Y: Hoehn and Yahr, MMSE: mini-mental scale exam, SC: standard care group, ST: strength training group.