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Data sharing statement

All relevant data are within the article. Requests for anonymized data should be sent to M.L. Welter at the Brain Institute, 75013 Paris, France.

Abstract

Background

Exergaming has been proposed to improve gait and balance disorders in Parkinson's disease (PD) patients. We aimed to assess the efficacy of a home-based tailored exergaming training system designed for PD patients with dopa-resistant gait and/or balance disorders in a controlled randomized trial.

Methods

We recruited PD patients with dopa-resistant gait and/or balance disorders. Patients were randomly assigned (1:1 ratio) to received 18 training sessions at home by playing a tailored exergame with full body movements using a motion capture system (Active group) or by playing the same game with the computer's keyboard (Control group). The primary endpoint was the between-group difference in the Stand-to-Walk-Sit-Test (SWST) duration change after training. Secondary outcomes included parkinsonian clinical scales, gait recordings, and safety.

Results

Fifty PD patients were enrolled and randomized. After training, no significant difference in SWST change was found between groups (mean change SWST-duration [SD] -3.71 [18.06] s after Active *versus* -0.71 [3.41] s after Control training, p=0.61). Thirty-two percent of patients in the Active and 8% in the Control group were considered responders to the training program (e.g. SWST duration change ≥ 2 sec, p=0.03). The clinical severity of gait and balance disorders also significantly decreased after Active training, with a between-group difference in favor of the Active training (p=0. 0082). Home-based training induced no serious adverse events.

Conclusions

Home-based training using a tailored exergame can be performed safely by PD patients and could improve gait and balance disorders. Future research is needed to investigate the potential of exergaming.

Key words: Parkinson's disease, gait disorders, falls, exergaming, rehabilitation

Introduction

Gait and balance disorders are common and represent the main motor disabilities in Parkinson's disease (PD).[1,2] With time, these axial motor signs deteriorate, and freezing of gait (FOG) and falls occur.[2,3] These signs become unresponsive to dopaminergic agents or deep-brain-stimulation,[1] imposing a significant burden on patients and families and impaired quality of life, and leading to increased morbidity and mortality rates, and healthcare costs.[3,4]

Physiotherapy is a non-pharmacological treatment including different modalities such as progressive resistance training, treadmill training, cueing and cognitive techniques, aerobic exercise, dance or martial arts.[5,6] Given the progressive worsening of PD, physiotherapy needs to be maintained over prolonged periods of time.[6,7] However, long-term compliance represents a major challenge, due for example to the travel burden and the monotonous and generic training content. Virtual reality and exergaming have emerged as novel rehabilitation methods using enriched immersive and non-immersive environments, with comparable results to traditional physiotherapy if combined with exercise,[8,9] with the potential to make training more engaging and motivating, thus providing long-term engagement.[10] Up to now, four randomized clinical trials have tested such training performed in hospitals or at home with the aim of improving PD motor signs. In one study, hospital-based treadmill training combined with virtual reality compared to treadmill training alone led to a greater reduction in the falls rate, with additional benefits on gait and balance performance.[11,12] Three randomized controlled studies testing home-based commercial or custom-made exergaming training with physical activity training, with on-line supervision by a physiotherapist for two studies (telerehabilitation), showed a good feasibility, with a possible benefit for gait and balance, but no superiority of exergaming

combined training relative to control training.[13–15] Recently, home-based aerobic cycling combined with exergaming and on-line coaching was tested in *de-novo* PD patients.[16] In this study, no significant aggravation of the PD motor symptoms (Off-dopa) was found after 6 months of aerobic cycling exergaming-combined training, while the control patients deteriorated (non-aerobic physical activity). However, no significant effect on gait, balance, or On-dopa motor disability was observed in either group.[16]

These previous trials suggest that combining exergaming with home-based physical activity, enriched with remote coaching, may potentially attenuate PD motor disability. However, the evidence remains insufficient to recommend in-home exergaming with concurrent physical activity to treat gait and balance disorders in advanced stages of PD.[16] Here, we aimed to evaluate the effects of a tailored home-based exergaming ("Toap Run")[17] training combining virtual reality and physical activity, without supervision, to improve gait and balance disorders in PD, in a randomized controlled trial.

Methods

Study design and patients

In this prospective randomized, multicenter, controlled single-blind trial, we recruited PD patients from two hospitals: Brain and Spine Institute (Paris, France) and Radboud University Medical Centre (Nijmegen, The Netherlands). Eligible patients for inclusion were between 18 and 80 years of age, diagnosed with PD according to the UKPD Society Brain Bank, had gait and/or balance disorders unresponsive to levodopa treatment (item 12 of the Movement Disorder Society-Unified Parkinson's Disease Scale (MDS-UPDRS) part II, gait and balance ON-drug ≥1 and/or item 13-FOG ≥1).[18] Additional inclusion criteria included stable dopaminergic medication for at least one month prior to study enrolment, absence of medical conditions that could interfere with the research study, had agreed to participate, provided written informed consent and affiliation to a social security scheme. Exclusion criteria were inability to stand or walk alone (Hoehn and Yahr stage 5), dementia (MMSE < 24),[19] and the presence of impulse control disorders (item 6, MDS-UPDRS part I > 2).[18]

The study was performed in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines and approved by the local ethics committee of both countries and recorded on ClinicalTrials.gov (NCT03560089).

Randomization and masking

Patients were randomly assigned to receive either full-body-controlled exergaming training (Active group), or gaming on a computer keyboard (Control group). Randomization was computer generated and based on random number blocks of four, with 2:2 random ratio, with a location-based stratification factor. Allocation was automatically generated by the RedCap software®. The primary outcome measure, the stand-to-walk-sit test (SWST) time,

was videotaped and scored by an independent investigator unaware of the patients' group allocation.

Procedures

Patients had an assessment at inclusion (baseline), followed by randomization to the Active training or Control group for 6-9 weeks (Figure 2, single-blind period). During this single-blind period, patients played with the videogame 'Toap Run'[17] designed to treat gait and balance disorders for PD patients, 2-3 times/week for a total of 18 sessions. The first two sessions took place at the institute, and the two following at home with a research assistant. Subsequently, patients played independently at home using a web-based platform (Curapy.com). Participants were allowed to reach the investigator by phone if needed.

The Active training group played with full-body movements performed upright in front of a RGB-D Kinect® motion sensor (Version 2, Microsoft, USA). The motion sensor was placed below a television screen, positioned approximately 2 meters in front of the patient. The Control group played seated with a keyboard without any physical efforts. The participants' movements (Active) or keyboard pushes (Control) induced the displacements of a small animal (the avatar) in real time, to gain points by collecting coins and avoiding obstacles (eMethods, Figure 3). For Active training, the required movements consist of large amplitude and rapid movements of all four limbs, pelvis and trunk, with lateral, vertical and forward displacements of the legs, to reinforce foot lifting and postural control. Visual (schematic representation of movements) and auditory (rhythmic music) cues were used to encourage movements. Patients received real-time and on-line feedback while playing, in the form of an auditory or visual stimulus. In addition, their performance was graded at the end of each session.

The programme was divided into three phases of six sessions, with predetermined difficulty levels: easy, medium and difficult (Figure 3). The session duration, number of movements and success rate were automatically recorded, allowing the investigator to follow and individually tailor the game difficulty. Follow-up assessments were done after the 18th session (W6). At the end of this period, patients can continue (Active) or start (Control) active full-body movement training sessions for a period of 3 months (Figure 1, open-label period), and a final follow-up assessment was performed (Post-M3).

Clinical assessments were done at each visit approximately one hour after intake of the usual morning dopaminergic treatment (On-dopa). For participants included at the Brain Institute, gait parameters were also recorded using a force plate (0.9x1.8 m, AMT Inc.LG6–4-1) and a motion capture system (Vicon Nexus, Oxford Metrics, UK, eFigure 1).[17]

Outcomes

The primary outcome measure was the between-group difference in the change in duration of the Stand-Walk-Sit Test (SWST) between baseline and after 18 training sessions (W6). The SWST is a functional mobility assessment where patients are asked to stand up from sitting, walk 5 metres at a comfortable speed, turn around 180 degrees, walk back to the chair, and sit again while turning 180 degrees.[20]

Secondary outcomes consisted of the between-group differences for the changes between baseline and after training (W6), on the following scales: the MDS-UPDRS part I (mental state), part II (activities of daily living-ADL) and part III (motor disability) that comprises the axial score (e.g. sum of the items 9-10-11-12 and 13: 'arising from chair, 'gait', 'FOG, 'postural stability' and 'posture') and part IV (dopaminergic-related complications);[18] the Gait and Balance Scale part B (GABS-B);[21] the Tinetti gait and balance scores;[22] the new

Freezing-of-gait-questionnaire (NFOG-Q);[23] the Activity Specific Balance Scale (ABC);[24] the Montreal Cognitive Assessment (MoCA);[25] the Hospital Anxiety and Depression scale (HADS);[26] and the Parkinson's Disease Questionnaire (PDQ-39).[27] A falls diary was also completed once a week to assess falls frequency. We also assessed the changes in these scales and the SWST duration between baseline and Post-M3.

Adherence endpoints included the between-group differences in the number of sessions, duration, adherence (percentage of sessions performed relative to sessions programmed), and success rate (percentage of movements correctly executed). This was done thanks to the Kinect® system for the Active group and thanks to the computer for the Control group. The acceptability, competence, self-efficacy, usability and difficulty of the exergame training were measured using Likert scales[28] after the first session, weekly, and after the last session.

Additional secondary outcomes for patients at the Brain Institute were the changes in the gait kinetic parameters between baseline and W6, and between baseline and Post-M3 (see supplementary methods). It includes: 1) the anticipatory postural adjustments (APAs), double-stance and single-stance phases duration, 2) the centre of foot pressure (CoP) displacements during the APAs, 3) step length, gait speed and cadence, and 4) gait asymmetry index, defined as the absolute value of gait cycle duration between left and right limbs. Higher displacements, length, speed and cadence, and lower durations and gait asymmetry index indicate better gait and postural control (eFigure 1).[17]

We also assessed the safety, and all adverse events were recorded. Any new symptom was classified as an adverse event and defined as serious if the patient required admission to hospital, if sequelae were present or the clinician considered the event to be serious.

Statistical analysis

Our study was powered to show an effect of active exergame training on SWST duration after 18 sessions. In line with published data regarding the estimated duration and effects of rehabilitation programmes on this test in PD patients,[5,29] we expected a decrease of 2±1 s for the Active group and of 1±1 s for the Control group. Assuming these values, a sample of 50 patients will allow a power of 90% (alpha=5, Mann Whitney Wilcoxon test). To account for premature dropouts, we have planned to include up to 60 patients.

Analyses were done on an intention-to-treat basis in patients who completed the follow-up assessment, regardless of whether they completed the assigned intervention. Missing data for the primary outcome were imputed and the baseline duration of the SWST was used for post-training session for missing post-training values (Post-W6). The primary and secondary outcomes were analysed using non-parametric Mann Whitney Wilcoxon rank tests. We employed Cliff's delta to assess the effect size of the differences between the two groups. It ranges from -1 to 1, with 0 indicating stochastic equality between the two groups. A value around $|0.1|$ is considered a small effect, approximately $|0.3|$ a medium effect, and around or exceeding $|0.5|$ a large effect.[30]

Additional analyses were done to compare 1) the number of patients with a change in the SWST duration of 2 s or more (considered responders) using Fisher's Exact test, and 2) the relationship between baseline characteristics, game parameters and post-training severity of gait and balance disorders to identify potential predictors of good feasibility, adherence, and positive effects, using Pearson correlation tests. Corrected p-values <0.05 were considered significant. All analyses were performed using R statistical software (R Core

team [2021]. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

Results

Cohort analysis

Between 18 July 2018 and 11 June 2021, we screened 176 potential participants, 82 did not fulfil the inclusion criteria and 40 refused to participate. Finally, 54 patients were included. Four patients were screen-failures (failing to meet inclusion criteria) and therefore not randomized (Figure 1). Fifty patients (25 in each center) were randomly assigned to either Active training group (n=25) or Control group (n=25). Due to the COVID-19 pandemic, the assessment of the primary outcome could not be conducted at the hospital for three patients (one from the Active and two from the Control groups) and was instead performed via teleconsultation; and we were unable to replace the two patients (Active group) who left the study prematurely at their own request and were not evaluated after the 18th session. Baseline characteristics of both patients' groups are shown in Table 1. We found no significant differences between groups at baseline (Mann-Whitney test, all p-values > 0.05, Table 1).

Adherence, game parameters and success rate

We progressively increased the game duration, number of movements and movement frequency between the 1st and the 18th session (Figure 3). Both groups adhered and performed well the training sessions, with a mean adherence, duration and number of movements that did not differ between groups (Table 2). The movement frequency and game performance were higher in the Control relative to the Active group (Figure 4, Table 2). Patients also reported high perceived levels of acceptability, competence, self-efficacy and usability, with low difficulty, with no significant difference between groups or over time (eTable 1).

Effects of home-based exergaming on Parkinsonian disability and gait and balance disorders

The changes in the SWST duration between baseline and after 18 training sessions (Post-W6) did not differ significantly between groups (Figure 4, Table 1). Thirty-two percent of patients of the Active group (n=8) and 8% (n=2) of the Control group were considered responders to the exergaming training (e.g. change in the SWST duration ≥ 2 s, p=0.03, Figure 4).

At the end of the randomized training period (W6), axial motor signs severity decreased in the Active group, with no significant change in the Control group resulting in a significant between-group mean difference of 1.24 (Table 1). In addition, a significant decrease in the GABS part B score and increase in the Tinetti gait score were found in the Active group, with no significant change in the Control group, resulting in a non-significant between-group mean difference of 2.03 and 0.58, respectively (Table 1). Due to a significant amount of missing data from the falls diary, we assessed the falls rate using item 4 of the GABS and found no significant change after training (Table 1). For the Control group, we observed a significant decrease in the quality of life (SI-PDQ39) and HADS scores, with a significant between-group mean difference of 4.68 and 1.44, respectively (Table 1). We found no other significant difference between groups (Table 1).

In the Active group, we found a significant negative correlation between the mean success rate during gaming and both the mean post-training SWST duration (r=-0.42, p=0.034) and age (r=-0.48, p=0. 015), with no other significant correlation (not shown).

For gait parameters, at W6 relative to baseline, we found significant decreases in APAs and double-stance durations, and asymmetry index, and increases in CoP displacements, step length, gait speed and cadence in the Active group; and for the Control

group significant increases in step length, gait speed and cadence, with no other significant changes (eTable 2).

During the 3-month open-label period, 15 patients performed Active training with at least 8 sessions of at least 10 minutes and 25 patients performed less than 10 training sessions. We found no significant change in clinical scores at the end of the open label period relative to baseline (not shown). However, we observed non-significant decreases of 4.6 s in the SWST duration and 5.3 points in the MDS-UPDRS part III (On dopa) in PD patients that did Active training during the open label period, and of 0.1 s and 1.4 points in PD patients that did not.

Safety and tolerability of home-based exergaming

Nine adverse events occurred in 8 patients, 4 in the Active and 4 in the Control group (Table 3). Three serious adverse events were reported during the open-label period and found to be unrelated to the intervention and consisted of recurrent falls, or hospitalization for antiparkinsonian medication adjustment. Five non-serious adverse events were reported in 5 patients during randomization and open label periods (Table 3).

Discussion

In this randomized controlled trial of 50 PD patients with medically refractory gait and balance disorders, we observed no significant difference in functional mobility (the SWST duration) between Active full-body movement training and Control gaming. However, Active exergaming training did improve clinical gait and balance disorders scores and postural gait kinetics. The control group showed no changes in motor signs, but improvement in quality of life and anxiety. The exergaming training was well received and tolerated.

The SWST duration was chosen as the primary outcome due to its ease of administration, and the ability to assess video-recorded performances independently. However, it did not significantly change in either group, as recently reported in three recent studies assessing the effects of home-based exergaming training (involving cycling or dancing programs), although improvements in mobility were observed.[13,16,31] Institution-based rehabilitation, with or without exergaming or virtual reality, has shown significant decreases in SWST duration with moderate to large effects ranging from 0.6 to 2.86 s.[5,32,33] This suggests that the intensity of home-based training or the specificity of our exergaming approach may have been insufficient to impact this multifaceted task, which encompasses actions such as rising from a chair, walking, turning, and returning to the starting position. The study duration and targeted patient group may also have contributed to the lack of benefits. Our Active training duration was approximately 100-110 minutes per week whereas recent findings indicate that a minimum of 150 minutes per week of home-based training is necessary to achieve balance improvement in PD.[34] However, the number and frequency of training sessions were comparable to other trials.[11,16,34] Moreover, our patients already exhibited significant impairments in static balance, encountered difficulties in learning,[10] with possible limited application of effective compensation strategies after

training.[35] The higher success rate during training among participants who responded positively and the persistent decrease in the SWST duration and parkinsonian motor disability observed in patients who engaged in longer training during the 3-month period suggest that a better ability to engage in the training is a factor for a more efficient compensation after training.[35] Finally, the SWST duration measurement may have inherent limitations, including high measurement error, and may not be suitable for reliable comparisons at both individual and group levels.[36]

Active training showed positive effects on secondary outcomes, indicating potential improvements in gait and balance disorders, that needs to be interpreted cautiously, however. A similar improvement in gait and balance disorders was also reported after home-based exergaming training with on-line coaching or when performed within institution, sometimes combined with conventional rehabilitation methods.[11,12,14,32,37,38] This indicates that patients in advanced stages of PD can potentially improve their motor function if the training is appropriately tailored to their needs.[39] Our Active training incorporated full body movements, postural tasks, visual and auditive cues, and motivational elements with success rates. Although, we did not analyse the impact of separate training routines on these endpoints, our results indicate that the combination of all these motor, cognitive and emotional components is likely key features to achieving a better effect on gait and balance disorders, that potentially leads to the transfer of acquired skills to other untrained tasks in everyday situations.[5,40] Control gaming also had mild positive effects on gait parameters, along with anxiety and quality of life improvements. These motor and psychological effects of videogame playing may result from a dopamine striatal release, as reported in the limbic striatum of young healthy adults[40,41] and recently in patients with PD.[42]

During the optional open-label training period, adherence was limited with approximately one-third of the patients engaged in active training. This suggests that game-based training alone may be not sufficiently attractive to maintain long-term adherence. Combined training with inertial sensors and smartphone device and/or with daily tele-coaching would probably enhance adherence over time.[16,43] Although our training was individually tailored, the game did not contain automated, performance-based decision making, which has been suggested to improve the efficiency of gait training.[43] These data indicate that training should be personalized and fine-tuned, using highly interactive programs in PD management,[44] and maintained over time, to achieve beneficial results and motor improvement.[6,16,45] Patients faced challenges using the software and conducting the training sessions independently, with older individuals exhibiting lower performance, and a potential fear of falling that could resulted in a voluntary decrease in movement amplitudes to prevent falls. This highlights the importance of user-friendly and interactive systems to enhance patient adherence and motivation over time, particularly for individuals with more severe forms of PD.[33,44]

Limitations

The present study has some limitations. First, two patients of the Active group prematurely dropped out of the study, and they were not replaced due to COVID crisis. This may have resulted in underpowering of the results. However, we performed data imputation and the effect size for the primary outcome was found to be small, suggesting that this may have had a minimal impact on the results. Second, both patient groups received intervention programs, which prevented us from examining the effects of active exergaming training compared to no training or usual care programs. Third, the study design did not allow for a

comprehensive assessment of retention effects as all patients were given the option to engage in Active training after the randomized period.

Conclusions

Home-based full-body movement active training using tailored exergaming shows feasibility and potential improvement in gait and balance disorders in advanced PD patients. While our findings do not definitively conclude on the effectiveness of our exergaming approach, they do contribute valuable insights to the development of rehabilitation programs incorporating exergaming to improve patients' adherence and efficacy. Further research is needed to explore its impact on disease progression in patients with less severe forms of PD, assess the healthcare implications, and gain deeper insights into its effects on brain function.

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Figure and Table captions

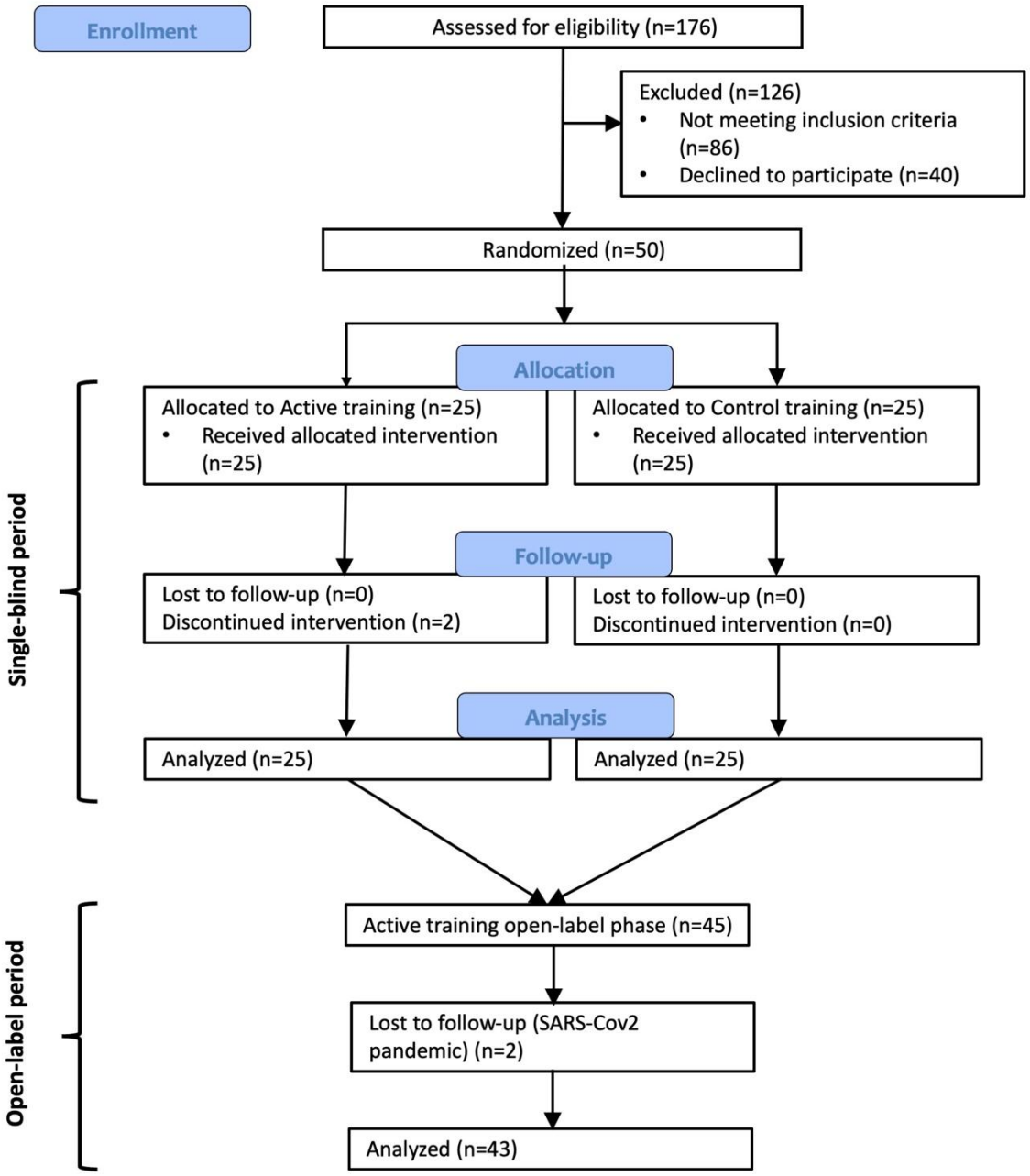

Figure 1. Consort diagram

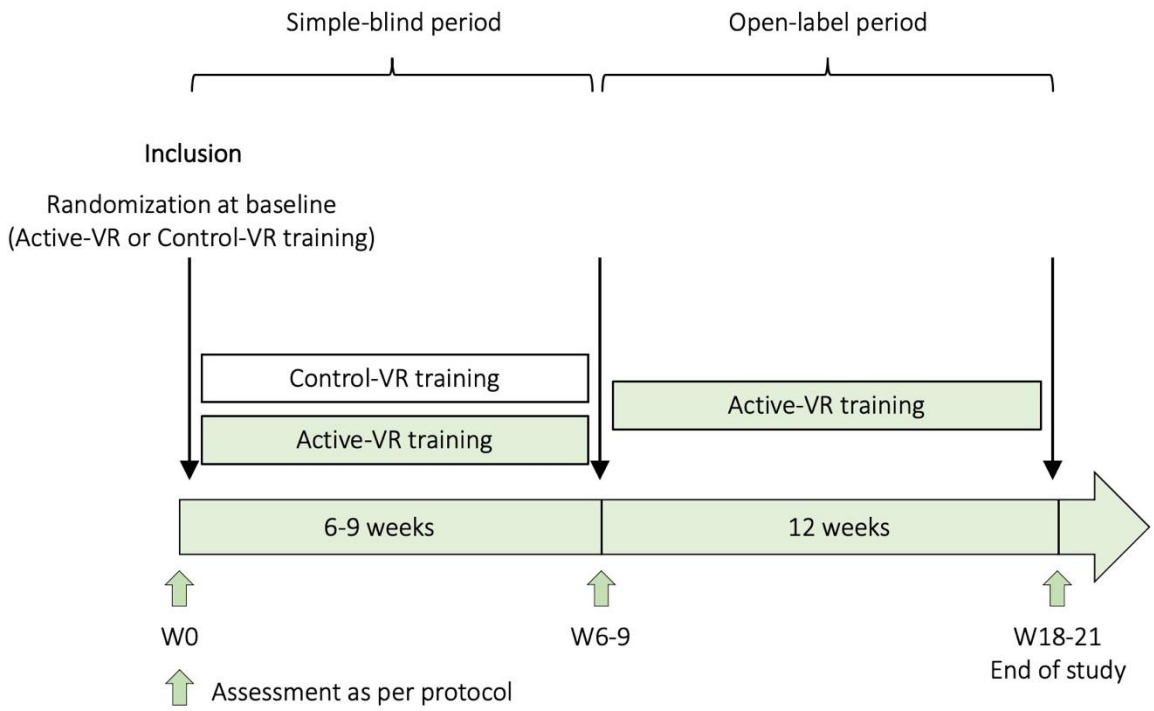

Figure 2. Design of the study

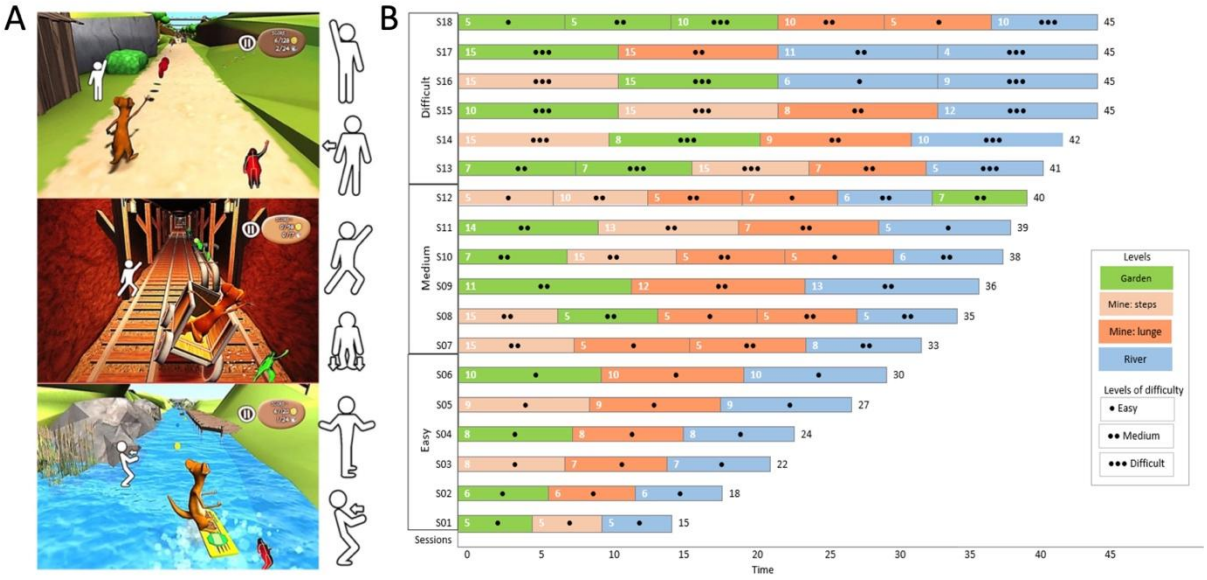

Figure 3. 'Toap Run' exergaming and training program

A) Top to Bottom: 'The Garden', 'The Mine', and The River'. The movements are schematically represented on the right side of the images, from top to bottom: arm extension, lateral shift, trunk lateral displacement with knee flexion, knee flexion/extension, trunk rotation with arm movements, and anteroposterior trunk movement.

B) The diagram represents the changes in the duration = X-axis-Time in minutes (from 15 minutes for the first session S01 to 45 minutes for the last session-S18) and gaming environments = garden in green, mine with steps in light orange, mine with lunge movements in dark-orange and river in blue, for the 2 patient groups. The level of difficulty was also increased with time, from easy (one point) to difficult (three points), for each environment. The duration of training in each environment is shown in white numbers. The level of difficulty was defined according to the frequency of movements to be performed with 3 different rhythms: easy: 20 beats/min, medium: 30 beats/min and difficult: 40 beats/min.

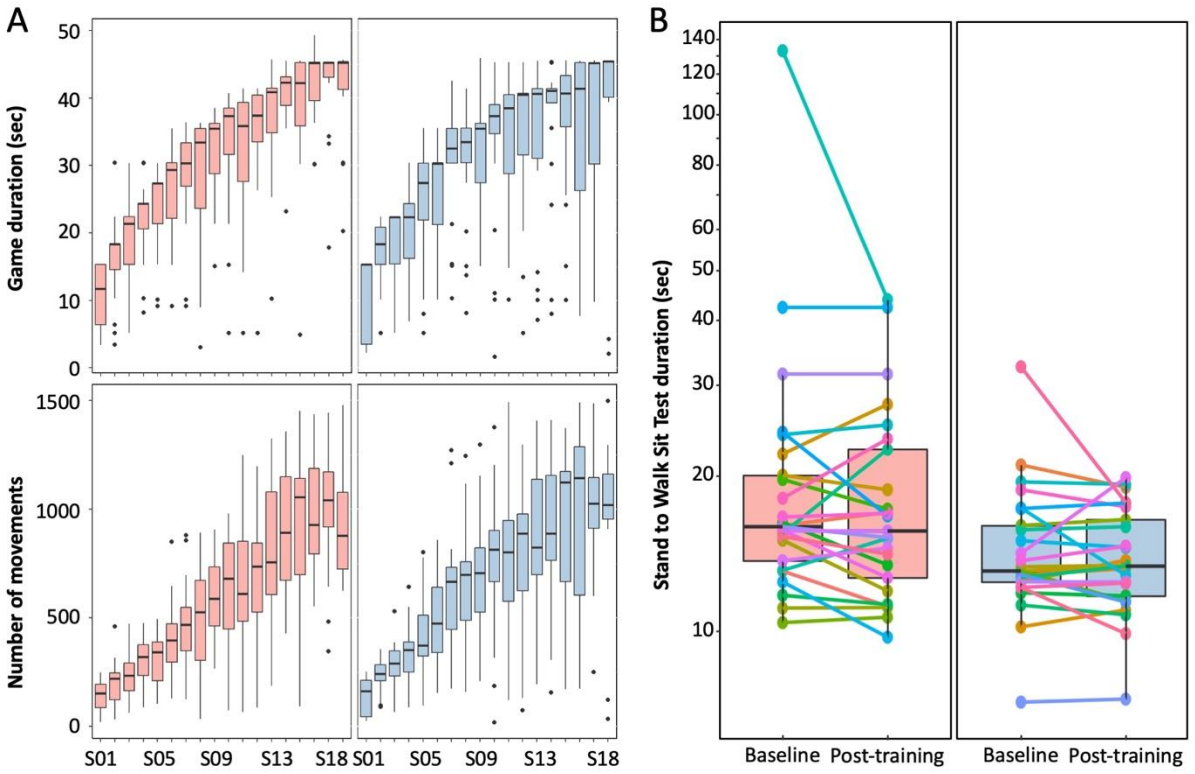

Figure 4. Training programmes and stand-walk-sit test durations before and after Active or Control exergaming training at home

A) Box plots for the duration (upper) and number of movements (bottom) performed during the home-based exergaming training sessions and over time in patients from the Active (pink) and Control (blue) groups, during the 6-week randomized period from the first (S01) to the last training session (S18).

B) Box plots for the Stand-to-walk-sit test (SWST) duration at baseline and after 6 weeks of training (post-training) in patients from the Active (pink) and Control (blue) groups, with a base-10 logarithmic scale. Each dot represents one individual patient.

Table 1. Patient characteristics at baseline and changes in the primary and secondary outcomes after Active or Control training in patients with Parkinson's disease

	Baseline mean (SD)		**6 weeks mean (SD)**		**Within-group change from baseline after 6 weeks Mean ± SD (effect size)**		**Between-group difference in change from baseline**		
	Active group (n=25)	**Control group (n=25)**	**Active group (n=25)£**	**Control group (n=25)**	**Active group (n=25)£**	**Control group (n=25)**	**Mean ± SD**	**Effect size (95%CI)**	**P value**
Age (yrs)	68.6 (6.9)	64.8 (8.2)							
Sex (M/F)	14/11	17/8							
Disease duration (yrs)	11.8 (6.3)	12.0 (5.9)							
LEDD (mg/d)	904 (498)	900 (495)							
Primary outcome									
SWST duration On-dopa (s)	22.5 (24.1)	14.7 (4.8)	18.8 (9.2)	14.0 (3.2)	-3.7 ± 18.1 (0.18)	-0.7 ± 3.4 (0.11)	-3.0 ± 3.83	-0.1 (-0.4_0.3)	0.61
Secondary outcomes									
MDS-UPDRS part I	9.3 (4.2)	9.4 (5.0)	8.5 (3.4)	8.8 (4.9)	-0.9 ± 2.9 (0.20)	-0.5 ± 4.7 (0.01)	-0.35 ± 1.12	-0.2 (-0.5_0.1)	0.41
MDS-UPDRS part II	14.8 (5.4)	15.2 (5.6)	13.4 (4.5)	15.2 (5.0)	-0.9 ± 4.8 (0.21)	-0.0 ± 3.3 (0.06)	-0.83 ± 1.20	-0.2 (-0.5_0.1)	0.49
MDS-UPDRS part III On-dopa	30.2 (14.0)	34.3 (11.2)	26.2 (12.2)	33.7 (11.5)	-3.3 ± 8.6 (0.37)	-1.7 ± 6.9 (0.24)	-1.59 ± 2.26	-0.3 (-0.6_0.1)	0.56
Axial subscore On-dopa	5.6 (3.5)	4.7 (2.5)	3.8 (2.8)	4.7 (2.1)	-1.5 ± 2.0 (0.70)*	-0.2 ± 1.6 (0.04)	-1.24 ± 0.52$	-0.6 (-0.8_-0.3)	0.0082
MDS-UPDRS part IV	4.8 (3.6)	4.7 (2.9)	4.7 (3.7)	4.9 (3.2)	0.0 ± 2.7 (0.03)	0.2 ± 2.3 (0.08)	-0.20 ± 0.73	-0.2 (-0.5_0.1)	0.57
GABS part B On-dopa	18.9 (7.9)	15.6 (8.7)	14.6 (7.3)	15.5 (7.6)	-2.7 ± 4.3 (0.51)*	-0.7 ± 4.3 (0.22)	-2.03 ± 1.24	-0.4 (-0.7_-0.1)	0.22
Falls rate (item 4 GABS part A)	1.4 (1.1)	1.0 (0.9)	1.3 (1.3)	0.6 (0.8)	-0.1 ± 0.7 (0.19)	-0.4 ± 1.0 (0.42)	0.19 ± 0.25	0.0 (-0.3_0.3)	0.39
Tinetti gait score	9.6 (1.7)	10.4 (1.7)	10.5 (1.2)	10.7 (1.3)	0.8 ± 1.6 (0.44)*	0.2 ± 1.3 (0.16)	0.58 ± 0.42	0.1 (-0.2_0.4)	0.23
Tinetti balance score	12.6 (2.0)	13.4 (2.0)	13.2 (1.9)	13.6 (1.4)	0.3 ± 1.0 (0.35)	0.2 ± 1.7 (0.05)	0.14 ± 0.40	0.0 (-0.3_0.3)	0.41
NFOG-Q	10.6 (4.2)	9.6 (3.6)	10.3 (4.6)	8.8 (3.5)	-0.1 ± 3.2 (0.07)	-0.8 ± 3.0 (0.19)	0.71 ± 0.89	0.0 (-0.3_0.3)	0.65

ABC scale	65.6 (19.7)	73.0 (13.6)	63.1 (17.3)	72.3 (14.2)	-2.5 ± 10.1 (0.20)	-0.7 ± 7.9 (0.12)	-1.81 ± 2.63	-0.1 (-0.5_0.2)	0.70
MoCA score	25.8 (2.8)	25.4 (2.8)	26.6 (3.3)	26.4 (2.3)	0.6 ± 2.5 (0.24)	1.3 ± 2.6 (0.50)	-0.71 ± 0.73	-0.3 (-0.6_0.0)	0.47
HADS	9.4 (6.1)	12.3 (5.4)	9.0 (6.4)	10.8 (5.1)	-0.0 ± 3.1 (0.06)	-1.5 ± 2.5 (0.52)*	1.44 ± 0.82$	0.2 (-0.1_0.6)	0.046
PDQ-39 SI	22.8 (8.2)	24.9 (8.4)	25.5 (10.9)	22.1 (9.4)	2.4 ± 4.8 (0.25)	-2.2 ± 6.7 (0.46)*	4.68 ± 1.67$	0.3 (-0.1_0.6)	0.014

*p<0.05 for within-group changes between baseline and after 6 weeks training, $p<0.05 for between-group differences in the change between baseline and after 6 weeks training.

£for the Active group, data were collected from 23 patients for the secondary outcomes due to premature drop-out in 2 patients.

LEDD=levodopa equivalent daily dosage expressed in mg/day.

MDS-UPDRS=Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), part I assesses non-motor aspects of experiences of daily living with scores ranging from 0 to 52, part II reflects motor aspects of experiences of daily living with scores ranging from 0 to 52, part III reflects the parkinsonian motor disability with scores ranging from 0 to 132 and part IV assesses the severity of motor complications with scores ranging from 0 to 24; the axial score is extracted from the UPDRS part III and is the sum of 'arising from chair', 'gait', 'freezing of gait', postural instability', 'posture' items with scores ranging from 0 to 20. The Gait and Balance Scale (GABS) part B reflects the severity of the gait and balance disorders with scores ranging from 0 to 46. The falls rate (item 4 of the GABS part A) ranging from 0 (no falls) to 4 (falls ≥ 1/day). The New-freezing of gait questionnaire (NFOG-Q) with scores ranging from 0 to 24 with higher scores indicating more severe FOG. The Activities Balance Confidence (ABC) scale reflects the feeling of imbalance in various daily life activities, ranging from 0 to 100, and the Tinetti scores for gait and balance reflect gait and balance control with scores ranging from 0 to 12 and 0 to 16, respectively, with higher scores for ABC and Tinetti scores indicating better gait and balance confidence or control. The Montreal Cognitive Assessment score is an education-adjusted scale of cognition with a maximum score of 30. The Hospital Depression and Anxiety scale (HADS) ranges from 0 to 42 with high scores indicating more severe depressive and anxiety signs. The Parkinson's Disease Questionnaire-39 (PDQ-39) is a quality-of-life scale specific to PD with the summary index ranging from 0 to 100 with higher scores indicating worse quality of life.

Table 2. Game adherence, duration and number of movements per session for Active and Control groups during the 6-week randomized period

	Active group					**Control group**				
Session	Adherence (%)	Game duration (min)	Number of movements	Movement frequency (Hz)	Success rate (%)	Adherence (%)	Game duration (min)	Number of movements	Movement frequency (Hz)	Success rate (%)
S01	95.8	10.8 (4.8)	135 (72)	11.8 (2.8)	69.9 (15.7)	100	10.5 (5.8)	138 (83)	12.9 (2.9)	72.0 (20.0)
S02	95.8	16.1 (5.8)	201 (92)	12.5 (2.5)	76.2 (14.0)	100	17.3 (4.4)	239 (74)	14.1 (3.1)	84.9 (13.3)
S03	100	18.6 (6.2)	237 (100)	12.6 (2.9)	75.2 (17.2)	100	18.7 (5.3)	284 (103)	15.6 (3.5)	87.6 (12.8)
S04	95.8	22.3 (5.7)	307 (105)	13.7 (2.5)	81.3 (13.5)	100	21.1 (5.4)	347 (124)	16.5 (4.8)	88.5 (13.7)
S05	100	23.9 (6.0)	311 (115)	12.8 (3.2)	77.5 (19.6)	100	24.3 (8.1)	406 (199)	16.5 (4.7)	89.0 (13.6)
S06	95.8	26.1 (6.2)	392 (153)	14.6 (3.6)	79.6 (16.4)	100	26.5 (7.3)	486 (207)	17.8 (5.1)	88.6 (16.9)
S07	95.8	28.7 (7.1)	460 (187)	15.6 (4.1)	79.3 (17.5)	100	30.7 (7.6)	615 (271)	19.0 (5.5)	88.0 (17.2)
S08	91.6	28.8 (9.9)	501 (245)	15.9 (5.3)	75.0 (21.3)	100	31.0 (8.3)	655 (258)	20.2 (4.6)	87.8 (16.7)
S09	87.5	31.8 (6.3)	594 (185)	18.1 (3.8)	82.4 (10.9)	100	32.2 (8.3)	691 (260)	20.9 (4.0)	90.3 (13.1)
S10	87.5	33.5 (9.0)	630 (238)	17.9 (4.3)	80.1 (13.5)	95.8	33.5 (11.3)	744 (308)	20.9 (6.0)	87.1 (20.6)
S11	87.5	32.5 (10.2)	654 (268)	19.2 (5.3)	82.3 (13.3)	95.8	33.4 (10.1)	755 (333)	20.9 (5.2)	86.7 (19.3)
S12	87.5	35.3 (7.9)	711 (259)	19.4 (4.8)	82.0 (13.6)	87.5	35.0 (10.7)	780 (329)	21.3 (5.5)	89.8 (14.5)
S13	79.1	36.7 (8.6)	809 (314)	21.3 (5.9)	81.4 (12.5)	87.5	34.9 (12.4)	823 (347)	23.4 (5.7)	89.1 (13.3)
S14	70.8	40.4 (5.4)	902 (288)	21.4 (6.1)	80.4 (16.9)	79.1	36.7 (10.6)	883 (336)	23.5 (6.4)	86.5 (18.2)
S15	75.0	39.4 (9.6)	915 (330)	21.6 (7.0)	81.1 (21.7)	79.1	36.8 (10.5)	939 (366)	25.3 (5.9)	88.6 (16.9)
S16	66.6	41.6 (6.3)	980 (268)	23.7 (6.2)	85.0 (12.8)	66.6	35.5 (13.2)	960 (426)	24.9 (5.5)	86.0 (16.1)
S17	66.6	41.8 (7.5)	991 (303)	22.7 (6.2)	81.4 (20.0)	50	37.4 (11.9)	988 (310)	25.1 (4.9)	86.5 (13.8)
S18	62.5	41.0 (7.8)	925 (252)	22.9 (5.4)	86.7 (12.0)	45.8	37.5 (16.2)	945 (437)	21.4 (7.2)	81.2 (25.6)
Mean (sd)	85.6 (12.4)	29.4 (11.5)	554 (345)	17.1 (5.9)	79.4 (16.1)	88.2 (17.6)	28.7 (12.0)	613 (370)	19.5 (6.1)*	86.7 (16.7)*

Data are mean and SD for each session. Adherence is the ratio of the effective duration of the session relative to the programmed duration of the same session. This ranges from 0 (no training) to 100% (complete training duration). *p<0.05 between groups

Table 3. Adverse events

	Active group	**Control group**
Serious adverse events		
Hip fracture	0	1 (P47)
Wrist fracture	1 (P48)	0
Hospitalization for antiparkinsonian treatment adaptation	1 (P52)	0
Non serious adverse events		
Epileptic fit	0	1 (P09)
Ankle tendonitis	0	1 (P23)
Hip osteoarthritis with pain	1 (P27)	0
Fall with hand wound	1 (P39)	0
Ankle sprain	0	1 (P44)

Values are number of adverse events.