Objective analysis of postural instability and stability in patients with Parkinson's disease following intensive agility therapy

THESIS OF DOCTORAL (Ph.D) DISSERTATION

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Introduction

Physical performance reaches its peak in young adulthood, then decreases continuously. With the extent of biological changes, the loss of performance is directly proportional to the individual. The loss of muscle fibers is accompanied by a decrease in speed, strength, and endurance. In addition to the deterioration of conditioning capabilities, there are also changes in coordination capabilities. By reducing the body's water content, the connective tissues lose their elasticity, resulting in a deterioration in flexibility and a narrower range of joint movement. The speed of pacing is slowing down, the neuromuscular relationship deteriorates, the time span of the spinal reflexes increases, the reaction time increases, and coordination decreases.

Most of the functional loss that occurs naturally in the aging organism is associated with changes in the neuromuscular (nerve) and bone system. Age-related neural modifications include muscle atrophy (sarcopenia), weakness, poor physcial fitness, mobility limitation, impaired postural control, increase in reflex latency, slowing of reaction time, impaired neuromuscualar coordination, respiratory dysfunction, arthritis, and osteoporosis.

The described changes, the weaker and shortened muscles, reduced flexibility, posture deterioration, reduced stamina, balance problems, slower reaction are all areas that can be positively influenced by the proper tasks.

Regular movement has proven to contribute to the preservation of health, as activity helps it to take care of ourselves. In order to maintain body balance and overcome gravity, our short muscles need to be stretched, weakened muscles need to be strengthened to prevent muscle imbalance. These special systems can only be developed with motion and proper stimulation.

Aim of the study, arising questions

Parkinson’s disease (PD) is associated with a decline in postural control, walking ability, an increased risk for falling, and a deteriorating quality of life. While pharmacological treatments are still the mainstream to treat motor symptoms, physical exercise can also favorably affect PD patients’ postural control and mobility. Recommendations urge the use of high intensity exercise stimulus to produce rapid and lasting improvements in PD symptoms. However, the results are inconsistent. Even at the same disease stage, treadmill exercise improved gait speed and cardiovascular fitness independent of exercise intensity. In addition, high compared with low frequency exercise can unfavorably affect functional outcomes. Yet there is also evidence for short-term, high-intensity ‘shock therapy’ improving meaningfully early-stage PD patients’ symptoms. (Bloem BR. 2015)

How long such exercise effects last after the exercise stimulus is withdrawn is also unclear because, despite recommendations to measure the effects at least for 24 months, in 16 studies the average follow-up time was 5.5 months. (Klamroth 2016) The only study with a 24-month-long maintenance program reported favorable effects on selected motor symptoms but also numerically almost identical elbow flexion torque at baseline (50.8 Nm) and at 24

months (50.2 Nm) when measured in the state of ‘on medication’. Yet a second booster dose of multidisciplinary intensive rehabilitation exercise at Year 1 after an initial bout at baseline even without a maintenance program, improved, at Year 2, UPDRS III scores (+3.4 points), 6-minute walking distance (41.4 m), and timed up and go performance (1.1 s).
Whether exercise can reduce patients’ drug dose is unclear. In one case, L-dopa equivalent increased moderately by 38.4% in the intensive exercise group compared with 327.4% in the no-exercise controls at the end of the 2-year follow-up period, suggesting that intense exercise without a maintenance program could moderate drug dose. Despite the 2-year low-intensity exercise maintenance program, L-dopa equivalent, however, still increased by 29%. (Corcos DM. 2013) It is thus unclear if a high-intensity and long-term exercise maintenance program could reduce the increase normally seen in PD patients’ medication or perhaps even reduce the absolute drug dose.
Conventional therapy in Parkinson's disease (PD) has a positive effect on patient mobility and maintenance instability. Motor responses of PD patients to exercise stimuli may vary widely. (Frazzitta 2013) The effect or progression of the disease on the movement affects the patient's ability to work and develop. International studies really encourage the development of high intensity posture and instability systems supported by multi-sensory gaming technology. (van der Kolk NM. 2013)
Programs can provide visual and acoustic feedback on the range of motion, performance, and increase motion intensity. (Ribas CG. és mtsai 2017)
The rehabilitation of PD patients is assisted by a number of therapies. At present, the use of virtual spaces associated with gaming technology is the most advanced, but significant results have been achieved in the field of mobility and coordination with hydrotherapy, Thai Chi and dance. (Vergara Diaz 2018)

Test objectives and questions

In the study of the Neurological Department of Somogy County Moricz Kaposi Teaching Hospital, we conducted diagnostic tests in patients with Parkinson's disease, specifically targeting maintenance instability, coordination, agility, quality of life and severity of motor and non-motor symptoms of the disease. The aim of our research whether the symptoms of PD patients and the results of our tests could be improved by an intensive therapy and in a two-year level program.

Considering the previously discovered and described literary results, we have set the following objectives.
1. Is it possible to measure objective deviation in patients with Parkinson's disease, which is characterized by disturbance of balance.
2. A 3-week-long intensive movement change the balance of Parkinson's patients.
3. A 3-week-long intensive exercise change the motor performance, mood, and quality of life of Parkinson's patients.
4. If there is any change in motility, motor and non-motor performance, mood and quality of life and the amount of medication used.

5. How do patients with Parkinson's disease change their balance and exercise performance parameters with the treatment they use.

We designed the following tests to answer our goals:

1. Comparison of instability (posturographic) results of Parkinson's patients
2-3. After 3 weeks of intensive movement, we measured posturographic, motor performance, mood, and quality of life parameters, matching results with patients' pre-treatment performance, and data from patients with Parkinson's who were just drogs therapy.
4-5. Treated patients were followed for 2 years. Three groups of patients were trained: in the first group, after 3 weeks of treatment, continuous maintenance was used for the next 2 years. there was no further maintenance treatment in the second group after 3 weeks of treatment. There was no initial or maintenance treatment in the third group. Comparing the results of these three groups, we planned to evaluate the duration of the intensive treatment efficacy.

Hypotheses

I.

- It is assumed that an intensive therapy will have a positive effect on the severity of motor and non-motor symptoms in the treated group, while no change in the control group is observed.
- Intensive therapy significantly improves the quality of life of the patients being treated, the results of the control group do not change significantly.
- Depressive Disease (BDI) results may be moderately improved as a result of group therapy, while results in the Control Group remain unchanged.
- The results of the Mobility Test (TUG) will show a sig- nificant improvement in the intensive care group, and the results in the control group will not change.
- Maintenance instability parameters of treated patients will show significant change compared to control group results.

II.

- We assume that the results of the UPDRS.M-EDL test do not show a significant deterioration in the control group, continuous deterioration of the active control group can be observed, or there is a continuous deterioration in the passive control group during the 2-year follow-up.
- The results of the quality assurance tests do not change the results of the scoring group, the results of the active and passive control group will show significant deterioration.
- We do not expect a significant difference in the depressive test in the groups, but there is a significant change in the active and passive group.
- In the TUG test results, the passive and active group will show a steady deterioration, while the results of the scoring group will not show a significant change in the negative direction.

- Posturography results will bring minimal change in the groups, with active and passive control status deterioration.
- The L-Dopa equivalent dose value in the maintenance group does not show a significant increase, with a significant difference in the active and passive group relative to the baseline values.

Material and methods

Three weeks of intensive treatment

Based on referrals from area neurologists and by calling patients listed in the hospital's database, we identified 72 eligible participants who met the UK Brain Bank criteria for PD. Eight patients were excluded (n = 3 did not meet inclusion criteria, n = 5 declined to participate). A physical therapist not involved in the trial performed the randomization of the remaining 64 patients to a high-intensity and high-frequency agility intervention group and to a no physical intervention control group. By assigning the 5^{th} or 6th patient to the intervention group, we biased the assignment toward the intervention group in anticipation of dropouts. The final sample size in the analysis was n = 55, with 35 and 20 patients in the intervention and control group, respectively, as 9 patients after randomization to the control group declined to be tested at baseline, withdrew, and were excluded.

The preliminary screening included a full neurological exam by a neurologist specialized in movement disorders. PD severity was assessed by the validated Hungarian version of MDS-UPDRS and by the Hoehn and Yahr scale. Based on recommendations, levodopa equivalents were computed for each drug and then summed to determine the total levodopa equivalent dose, following an established protocol. The neurologist and the exercise therapist performed a gait and posture exam focusing on the quality of postural stability, turns, rigidity, inter-joint coordination, trunk posture, and equilibrium while subjects walked forward, backwards, and sideways. The entry exam concluded with a quantitative posturography and then a neuropsychologist evaluated patients' cognitive function. Exclusion criteria included cognitive impairment (Mini Mental State Examination score < 24), depression (Beck Depression Inventory score > 40), severe cardiac disease (including congestive heart failure, ischemic disease, presence of pacemaker, orthostatic hypotension), uncontrolled diabetes, history of stroke, traumatic brain injury, seizure disorder, or current participation in a self-directed or formal group exercise program. In each patient, a diagnostic MRI was used to identify lesions and not PD-related neurodegeneration and if present, exclude such patients. To minimize motor fluctuation and variability of motor symptoms, all patients remained 'on' medication during the study. None of the patients had previously or were currently receiving deep brain stimulation therapy. The testing order was standardized among patients and testing sessions. Pretests and posttests were performed within 3 weeks of the intervention. Before baseline assessment, participants were familiarized with the tests and gaming by watching and performing elements of the Xbox kinect program.

Postural stability has been enhanced by agility, dynamic and static balance, coordination, external and internal perturbations, dual task response, and the ability to quickly and

continuously move body positions, postures, and tasks. As exercise improves the quality of life and mood of healthy older adults and PD patients, we also had a positive effect on these non-motor outcomes. The aim of the randomized clinical trial was to develop and manipulate the clinical symptoms, mobility and balance of non-demented PD patients in combination with intensity and high frequency agility training, combined with the use of sensomotor and visual motors, game technology.

I. Intervention

All potential participants have given their written consent to participate in the study, approved by the SMKMOK Institutional Research Ethics Committee (IKEB).
The intervention (15 sessions over 3 weeks, n = 35, 17 males) targeted PD patients' postural instability and mobility deficits. We designed a high-intensity and high-frequency sensorimotor and visuomotor agility training program conceptualized but seldom implemented previously. Patients exercised in small groups. Sessions were offered at multiple time slots during the day in the hospital's physical therapy gym. Patients exercise without shoes on soft gym mats and under the supervision and verbal encouragement of up to three physical therapists who implemented strict safety guidelines. Each session lasted 60 minutes and consisted of: 1) 10 minutes of warm-up, 2) 20 minutes of sensorimotor and visuomotor agility training, 3) 20 minutes of sensorimotor agility training using one of three X-box virtual reality exergame modules (Microsoft Xbox 360 Core System with Kinect, Microsoft Corp.), and 4) 10 minutes of cool down.
The warm-up focused on spinal mobilization and stabilization and patients exercised on large inflated fitness balls and performed two-handed coordination end-weighted stick exercises. The sensorimotor and visuomotor agility training consisted of blocks of: 1) gait training, 2) coordination training, 3) posture training with and without an augmented sensory input, 4) balance exercises with and without a peer, assistive devices, height stimuli, surface modifications, and directional changes, 5) body scheme exercises, and 6) posture-corrective exercises.

Vizualmotor agility

We used the X-box virtual reality exergame for our observations. During the use of the equipment, it gives a visual assessment on the monitor of the degree of similarity between the virtual stimuli presented by the user. The video exergame virtual reality creation program is able to instruct you to change the intensity of your exercise by acoustic and visual feedback. On the monitor, during and at the end of the exercise, the evaluation appears in the form of scoring, both visually and acoustically. In addition, it can set new goals for the user, provide feedback on performance, and determine later difficulty levels.

Sensomotor agility training

Structure of training:
1) district development
2) coordination training
3) exercise schema development with and without exercise-enhanced sensory devices
4) equilibrium exercises with and without tools
5) use of elevation stimuli, surface changes and direction changes
6) posture correction exercises
7) bodybuilding exercises

During the training, the difficulties and speed of the tasks were adjusted to the improving performance of the patients. So the increasingly difficult tasks were done faster.
One-person, motorized, motor-cognitive dual tasks make the texture of instability, center of gravity, obstacles and moving objects more difficult with competitors or avatars in programs, and continuously increase the intensity of the load. Tracking the intensity based on the points evaluated by the machine (the higher the point the higher the load), the time-bound performance of the tasks (the faster you performed the better the intensity of the patients).
Controlling (subsequently passive) control without physical intervention from PD patients (n = 20, 12 males) continued their usual activities, did not receive therapy, and took the prescribed medication.

Two-year follow-up

This is a three-group, randomized clinical trial involving PD patients who met the UK Brain Bank criteria and were of stages 2-3 on the Hoehn and Yahr scale (Consort diagram, Supplement 1). Patients (n=55, 29M) were randomly assigned to an: Exercise+Maintenance (E+M, n=19, 11M); Exercise only group (E, n = 16, 6M), and to a no exercise and no maintenance control group (C, n=20, 12 M). At the time of the start of the study and for the two-year period preceding it, none of the patients were enrolled in rehabilitation. The initial high-intensity and high-frequency agility E program lasted three weeks. The M program lasted two years. **All patients were assessed eight times: before and after the 3-week exercise program and then at 3, 6, 9, 12, 18, and 24 months.** Wait-listed patients in C had the opportunity to enroll in the exercise program after the end of the trial.
Based on international studies, it is expected that the 2-year maintenance program will stabilize the equivalent levels of the initial L-dopa, which may result in a relative decrease in the drug dose.

II. Intervention

The Exercise program comprised a high-intensity agility intervention, detailed previously. Briefly, PDt+M and PDt completed 15, 1-h-long, sessions over 3 weeks and targeted deficits in postural control and mobility. Three therapists delivered the program by having patients exercise in small groups at individual times in the hospital's physical therapy

gym. They were then randomized to two in a randomized trial. In the PDt + M group, patients continued high-intensity treatments 3 times a week for 2 years. The PDt group, after the intensive therapy, was acting as an active control group because it did not continue the therapy we prescribed, but they were involved in the 2-year follow-up.

Maintenance program

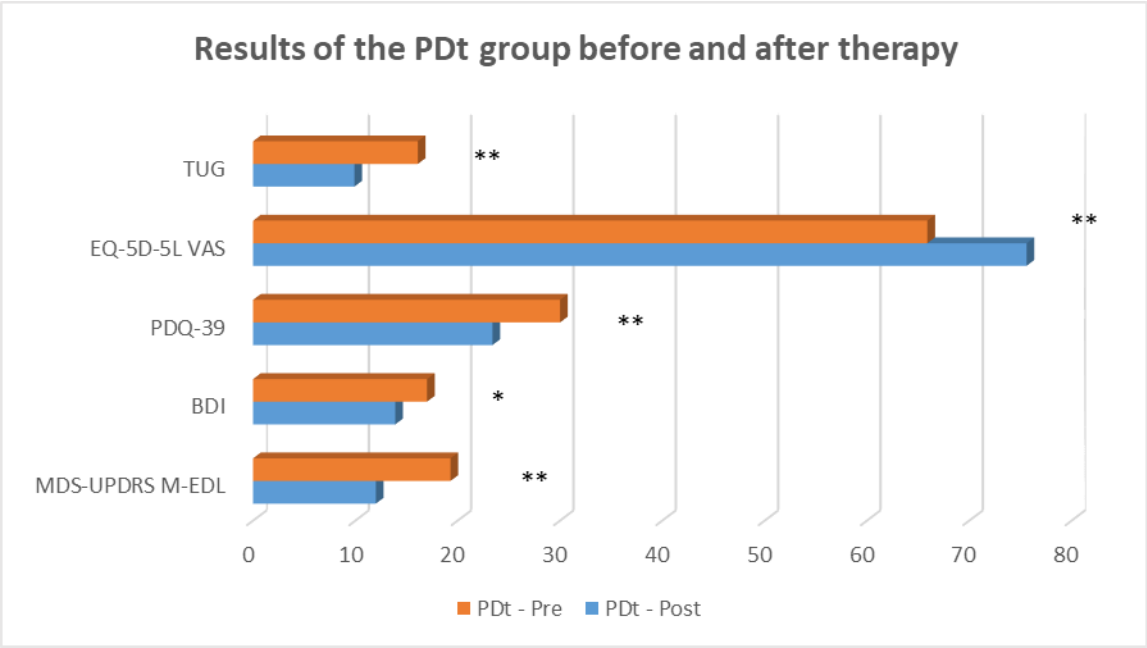
After the 3-week-long, daily, high-intensity Exercise intervention, PDt+M continued the Maintenance program three times per week for two years in the hospital's physical therapy gym using the same exercises used in the 3-week-long initial exercise program. The three therapists supervised each session attended by small groups of 3-5 patients who exercised at the same time of the day for 1 h. The aim of the maintenance program was to determine if patients can endure a high-intensity rehabilitation program for an extended time period and if such a program can slow disease progression. E did not perform the maintenance phase and C received no Exercise therapy and no Maintenance either.

Results

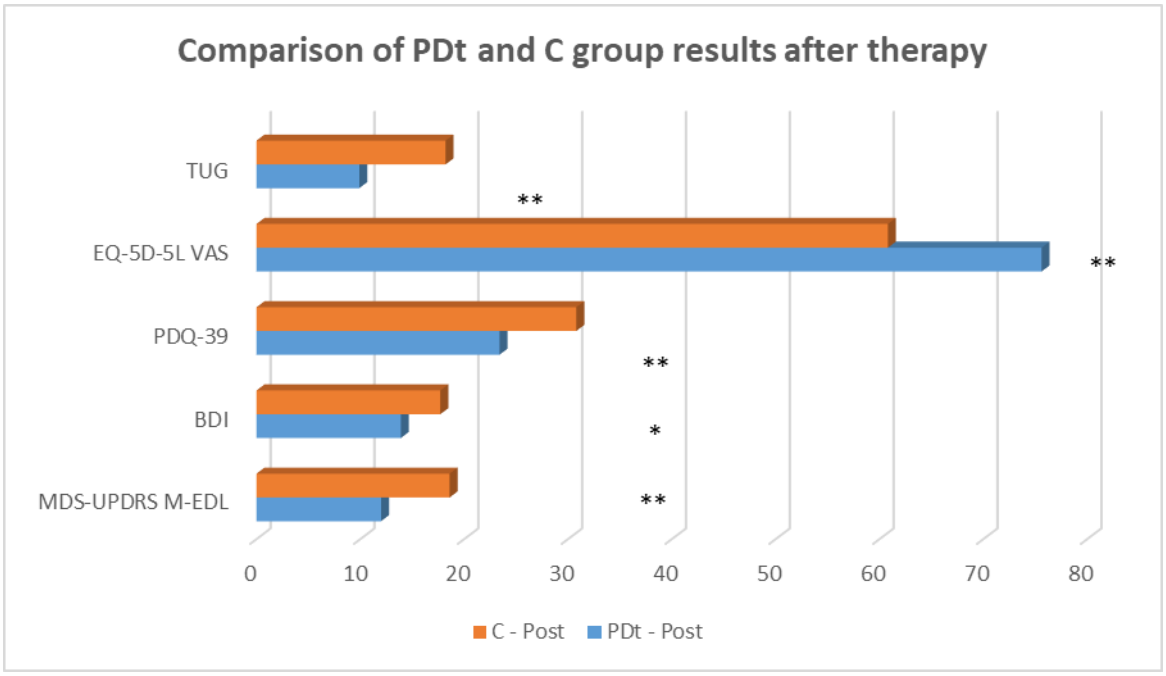
I. Three-week intensive therapy

The investigated PDt group participated in intensive three-week movement therapy for three weeks as described above. The groups examined in the dissertation can be considered homogeneous as the results of the patients' demographic survey, their clinical status (Hohn Yahr scale 2-3), their equivalent dose of L-Dopa (PDt: 843.4 ± 308.8, PDc: 884.8 ± 332, 0, day / mg) and their mobility (PDt: 16.1, PDc: 18.6, sec) showed no significant difference. Just like their postural control and quality of life compared to their baseline values.

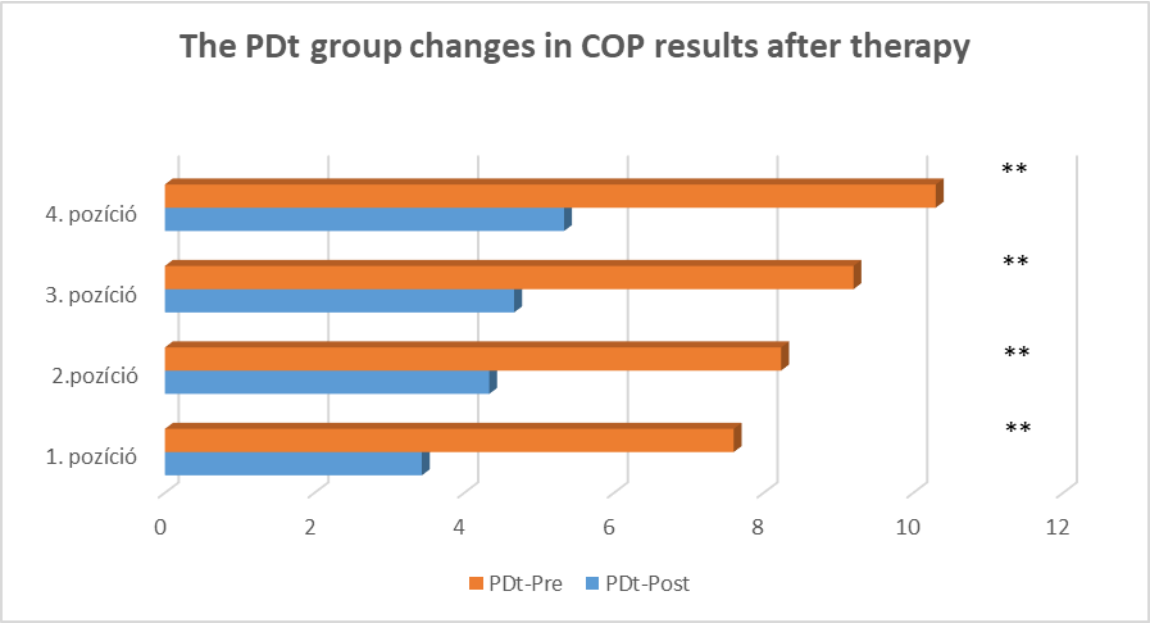
In the PDt group, the motor power showed a mean reduction of 7.3 points after the therapy, an improvement of 38% on the MDS-UPDRS M-EDL scale. The magnitude of the change exceeded the rate of improvement considered clinically significant in international literature. (MCID threshold, point 3.1). Parkinson's disease was on the PDQ-39 scale, while the change improvement was 6.6 points. The rate of improvement here also exceeded the level of international clinical significance. (MCID threshold of 4.7 points). Significant improvements were detected in the TUG test for functional motion and motor performance. Patients needed an average of 39% less time to take the prescribed distance. Using the Beck Depression Index, depression points showed an average reduction of 18% in the patients treated, and 15% in the EQ5D VAS scale, 15% in the Schwab and England ADL scales. All changes showed statistically significant results ($p < 0.001$). Patients did not report any newly developed physical or locomotor complaints during the treatment period, no one was injured during the treatments, and no other unwanted events occurred during the interventions (fall, nausea, fever, etc.). No significant improvement was observed after week 7 (total $p > 0.05$,). The condition of the patients was the same. The members of the control group did not report any locomotor injuries, nausea and unwanted events. Their status did not change according to the tests.



a. figure. Comparison of Parkinson's Training Group's Own Results Before and After Therapy: *Comparison of Parkinson's Training Results compared to Self-Treatment after 3 weeks of intensive therapy. The PDt group showed significant improvements in the tested tests PDt - pre: First Parkinson's Training Group, PDt - post: Parkinson Training Group After Therapy*



b. figure. Comparison of results after Parkinson's training group and control group: *Comparison of results of Parkinson's training group and control group after intensive therapy. The Parkinson's Training Group performed better on the benchmarking tests than the control group. PDt - post: Parkinson training group after therapy, C-post: Parkinson's control group after three weeks*



c. figure. Parkinson's training group maintenance instability changes after therapy: *Comparison of Parkinson's training balance results after three weeks of intensive therapy. Patients showed significant improvements in all postures. PDt - pre: First test of Parkinson's training group, PDt - post: Parkinson training group after therapy. Position 1: Girder position open eye, position 2: Girder position closed eye, position 3 closed position open eye, position 4 closed position closed eye*

MDS-UPDRS M-EDL, Movement Disorders Society-Unified Parkinson's Disease Rating Scale - Motor Experiences of Daily Living
PDQ-39, Parkinson's Disease Questionnaire (minél alacsonyabb a pontszám annál jobb a beteg állapota)
BDI, Beck depression inventory (0 to 20, lower value less depression)
EQ-5D, EuroQol five dimensions questionnaire, VAS: visual analog scale
TUG, timed up and go tests (lower value denotes better mobility)
COP. center of pressure
*, baseline difference between groups, $p<0.05$, ** Group by Time interaction, $p<0.001$
Statistical results were performed with SPSS version 22. The variables: Shapiro-Wilk test, variance analysis interaction: Tukey post-hoc test, p-value correction: Holm method corrected. The correlation was compared with the Pearson test.

II. Two years of follow-up treatment and follow-up

In addition to the two-year follow-up, we maintained a steady treatment for some patients in the PDt group. The treatment group was randomized. The PDt + M group performed agility therapy 3 times a week. After 3 weeks of intensive therapy, the PDt group did not undergo sustained rehabilitation movements. The three groups had similar demographics, clinical status, L-Dopa equivalence, mobility, and postural control at baseline. The largest baseline-difference, 3.5 s, was between PDt and C in TUG and between PDt+M and C in the Mobility item of EQ-5D ($p<0.05$). During the 3-week high-frequency segment and also during the 2-year-long maintenance program, attendance and compliance were 100%. The agility program improved MDS-UPDRS M-EDL by 30.4% (±10.23) or 6.3 points (±3.06) in E+M and by 42.8 % (±9.43) or 7.8 (±1.57) points in E (all $p<0.05$). These changes

were similar but greater than the changes in C that did not change (Group by Time interaction, $F_{12,258}=32.7$, $p=0.001$,.

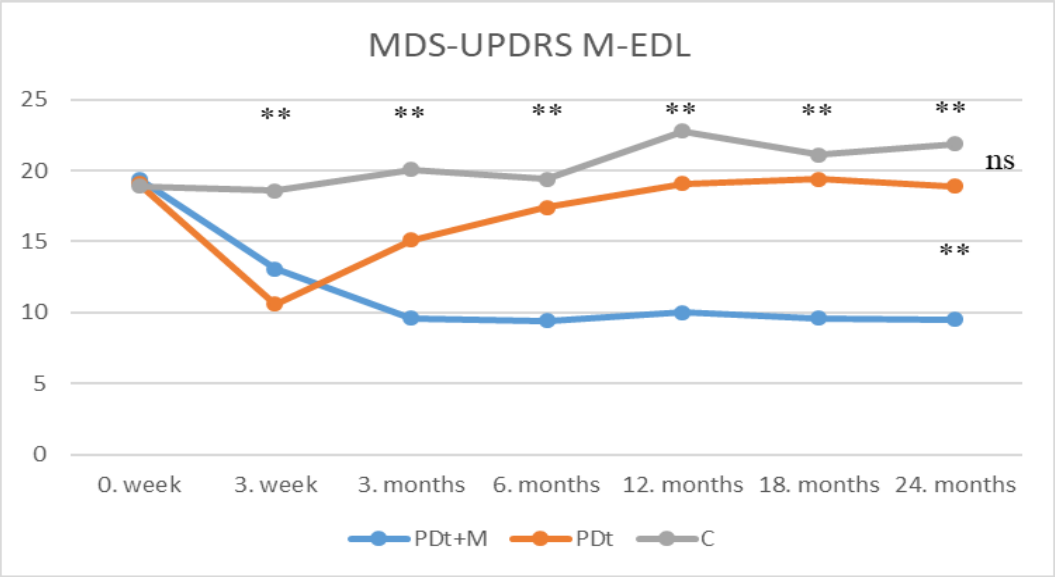
PDt+M sustained the exercise-induced benefits. In PDt, the exercise-induced improvements were still present at 3 months but the scores then worsened and at year 2 were at the level of baseline. C exhibited a gradual worsening over the two years. At year 2, there was a 12.4 points difference in favor of PDt+M vs. C ($p<0.05$). This difference is four times greater than the 3.1 points clinically meaningful threshold (14). The PDt vs. C had 3.0 higher score and 24 months (n.s.).

Over two years, the MDS-UPDRS M-EDL score had decreased by 6 points in C, about twice the level of clinically meaningful change. The agility program improved the PDQ summed scores by 12.8 points (±5.29) or 26.0% (±7.36) in PDt+M and by 13.8 points (±3.91) or 28.9% (9.31) in E, more than the 1.2 (±3.55) or 6.8% (±16.85) worsening in C. PDt+M kept the exercise-induced improvements in PDQ for two years at a steady level. In PDt, the exercise effects were still present at 12 month, as the summed PDQ scores were 7.3 (±4.89) points or 14.6% (±8.97) better than at baseline. At 24 months, PDt+M vs. PDt and PDt+M vs. C had 15.3 and 24.4 better PDQ score (both $p<0.05$) and PDt still had a 9.1 better score than C ($p<0.05$). Over the two years, the PDQ score had decreased by 20 points in C.

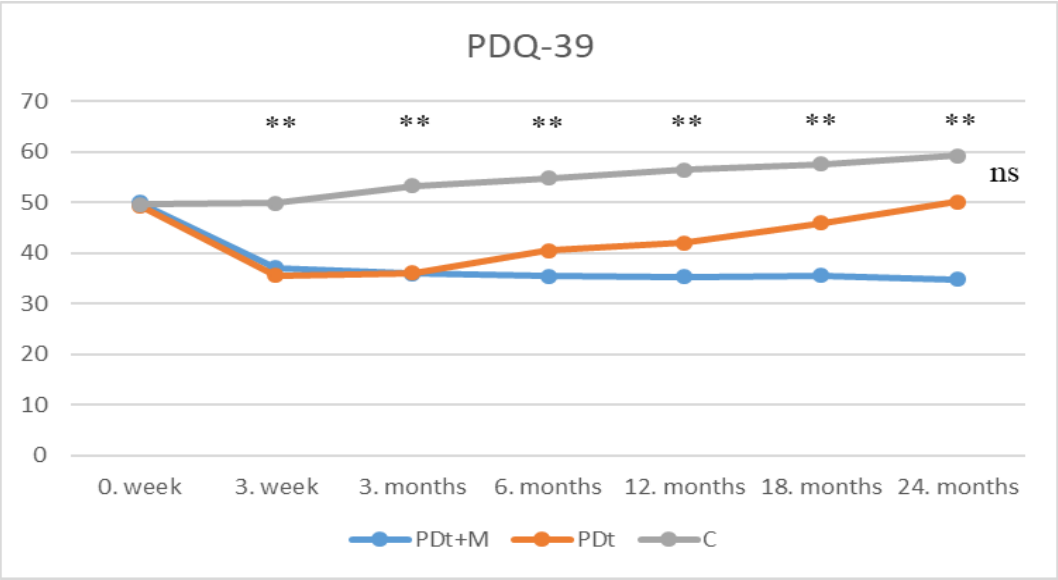
The exercise intervention uniformly improved the Beck Depression Index ($F_{12,258}=12.5$, $p=0.001$), the Schwab and England ADL inventory ($F_{12,258}=8.9$, $p=0.001$), the EQol VAS scores ($F_{12,258}=10.3$, $p=0.001$), and the EQoL summed scores ($F_{12,258}=21.5$, $p=0.001$) in E+M (range of improvements: 13% to 21%) and in E (14% to 20%, all $p<0.05$). In E, these effects lasted for three months. At 24 months, PDt+M still showed the exercise-induced gains and E returned to baseline. Compared with PDt+M at 24 months, the scores in C were all worse in the Beck Depression Index by 6.8 points, Schwab and England ADL inventory by 13.8 points, the EQol VAS scores by16.4 mm, and in the EQoL summed scores by 5.7 points (all $p<0.05$). TUG improved by 6.3 s (±2.75) or 36.9% (±11.74) in PDt+M and by 6.0 s (±2.96) or 39.7% (±10.30) in E (all $p<0.05$) compared with the 0.6 s (±0.76) or 3.0% (±4.13) change in C (n.s.). These effects lasted for 18 months in PDt. At 24 months, there was a difference of 3.6 s between PDt+M vs. PDt (n.s.) and 6.8 s between PDt+M vs. C ($p<0.05$) in TUG in favor of PDt+M. Unlike other variables, TUG remained unchanged over two years in C (n.s.). Even though there was a difference of 3.2 mm in COP path between the easiest and most difficult standing condition, the exercise effects and the patterns during the follow-up were similar between the four conditions of posturography. Exercise decreased COP path in the four conditions similarly in PDt+M and PDt (range: 2.0 to 6.9 mm). PDt+M sustained the exercise-induced improvements as a result of the maintenance program in the four posturography measures. In PDt, the exercise effects lasted until month 12 in the four posturography measures. At 24 months, PDt+M vs. PDt had shorter COP path in the four measures (range of differences: 4.7 to 2.5 mm, all four differences $p<0.05$) and PDt+M vs. C had even larger range of differences in COP path (range: 4.2 to 6.7 mm, all four differences $p<0.05$).

MDS-UPDRS M-EDL at baseline correlated with the change in MDS-UPDRS M-EDL at 3 weeks $r=-0.803$ and this correlation essentially remained unchanged by 24 months ($r=-0.683$, $n=18$, $p< 0.05$).

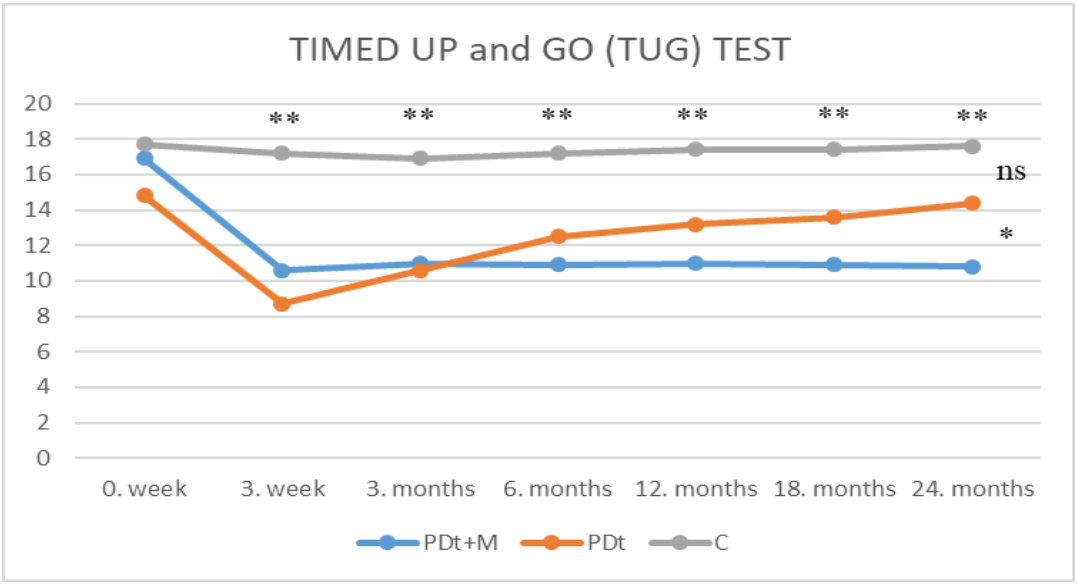
Because the primary outcome reached a plateau at month 3 during follow up in E+M (n=18), we determined the relationship between changes in the primary outcome, MDS-UPDRS M-EDL, for the period from baseline to 3 month and the changes over the same period in PDQ (r=0.422), Beck depression score (r=0.198), EQ VAS (r=-0.181), TUG (r=0.126), and the four postural measures (range of r = 0.092 to 0.297). None of these correlations were significant (p>0.05) as was the relationship between changes in MDS-UPDRS M-EDL and number of PD years (r=0.271). In contrast, even if a program is very intense and personalized, the effects of the exercise are short-lived and last for up to 3 months. In Group C, MDS-UPDRS M-EDL and PDQ scores increased, but TUG values were not.



d. figure. MDS-UPDRS M-EDL over two-year maintenance period: *Comparison of motor test severity test results between the three patient groups. The PDt + M and PDt groups showed significant improvement after three weeks of intense therapy, PDt + M improved and maintained status improvement over two years as a result of leveling therapy. The PDt group, following withdrawal of treatment, showed a steady state shift from month 3 onwards. Group C did not change significantly during the observation period. The results of Group C and the results of the PDt + M group show a very significant result, but the results of the PDt group showed significant results at the end of the two-year observation compared to the C group. MDS-UPDRS M-EDL: Movement Disorders Society-Unified Parkinson's Disease Rating Scale - Motor Experiences of Daily Living*



e. figure. Changes in PDQ-39 test results over a two-year follow-up period: *Results of the PDQ-39 test showed a significant improvement in PDt + M and PDt after three weeks of intensive therapy. Significant differences were observed between the treated groups and the C group. The results of the PDt + M group did not change during the two-year follow-up. The PDt group deterioration was measurable from the 6th month and at the end of the two-year follow-up cycle we measured a significant difference compared to the PDt + M group. The results for Group C have not changed. PDQ-39, Parkinson's Disease Questionnaire (the lower the score the better the patient's condition)*



f. figure. Changes in exercise performance over the two-year follow-up period: *After studying the movement performance, the three-week intensive therapy groups (PDt + M, PDt) showed a significant improvement over themselves and the C group. PDt + M retained its results and showed no progression. The PDt group showed steady performance from month 3 onwards. By the end of the study period, the PD + M group had the best results and showed significantly better results compared to the PDt group, and showed a significantly significant result compared to the C group.*

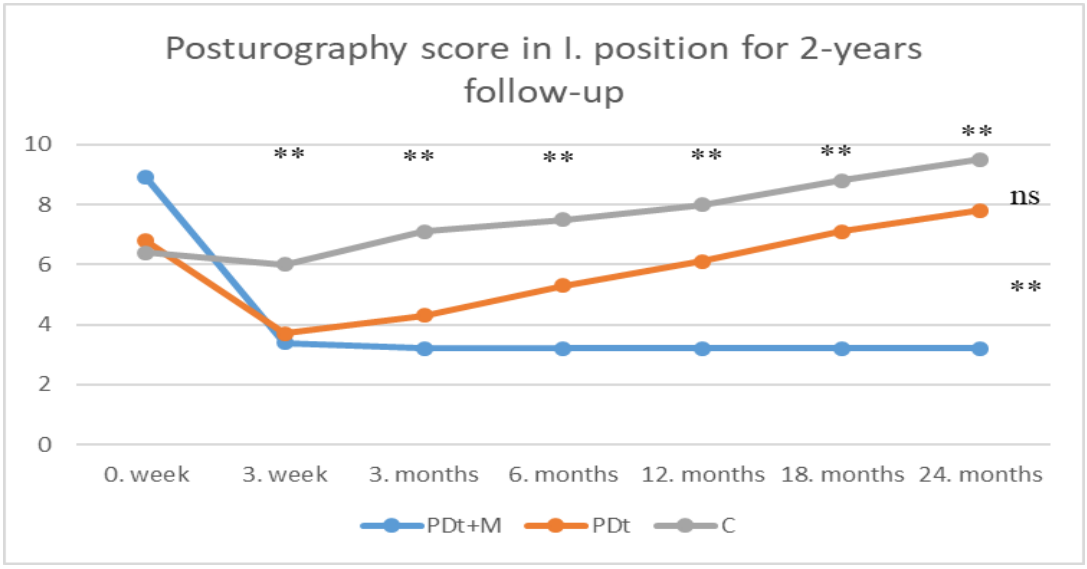
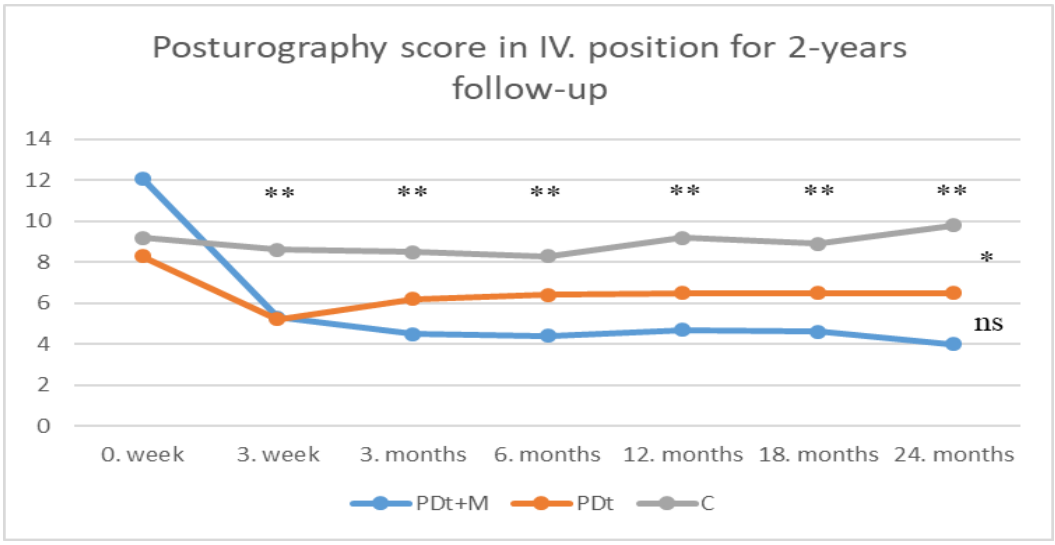


Figure g. Results of the posturography study at position I during the two-year follow-up: *The PDt + M and PDt groups showed significant improvement in self-efficacy compared to the C group after three weeks of intensive therapy. The improvement was maintained by the PDt + M group throughout the 24 months and produced a significant difference over the C group. The PDt group showed steady state regulation, the end of which was to reach the baseline value compared to group C, and their difference was not significant. PDt + M was significantly better in the 24-month tests than in the PDt group, compared to the PDt group..*



h. figure. Results of posturography examination IV. in the two-year follow-up: *In the fourth position of the maintenance instability, the groups performing intensive therapy showed significant improvement compared to themselves and to the C group. (PDt + M, PDt) By the end of the two-year follow-up cycle, the PDt group deteriorated, but no differences were found in the PD + M group. The results of group C are significant compared to the PDt group, with a significant result compared to the PDt + M group.*
PDt + M: Parkinson's Leveling Training Group, PDt: Parkinson's Training Group Without Maintenance, C: Control Group.

*, baseline difference between groups, $p<0.05$, ** Group by Time interaction, $p<0.001$, ns: no significant
Statistical results were performed with SPSS version 22. The variables: Shapiro-Wilk test, variance analysis interaction: Tukey post-hoc test, p-value correction: Holm method corrected. The correlation was compared with the Pearson test.

Key findings of the study

- The results confirm that high intensity agility therapy has a beneficial effect on the quality of life of PD patients, improves their mobility, improves postural control and motor and non-motor function.
- The agility program continuously improved MDS-UPDRS M-EDL, which was the primary result: 34 out of 35 patients improved their results by 7.3 points (38%, ES = 1.2)
- The results suggest that clinically significant increases in HRQoL and a 15% increase in EQ5D VAS were due to an improvement in motor symptoms, which was observed with moderate (ES: 0.69) but a significant 10-point increase in Schwab-England ADL. scale. Test data support the emerging view that high-intensity movements are effective enough to temporarily improve the daily routine of PD patients.
- Significant reductions in TUG (6.2 sec, 39%, ES: -2.54) reflect better transfer, dynamic balance (walking speed) and indirectly neuromuscular functions such as agility and muscle strength.
- Beck depression scores showed a decrease of 3.1, which did not significantly reduce the mood of our PD patients.
- Decreased COP pathways are relevant for PD patients, our agility program has consistently reduced the length of the COP pathway in 12 measured positions ($p < 0.05$)
- The results of the intensive care but PDt and C groups significantly deteriorated over the 3-12 months compared to the results after three weeks of intensive therapy.
- The 2-year review maintenance program maintained positive changes, but did not further improve the improvement after three weeks.
- The benefit of the 3-weeks agility program lasted for 3-12 months with motor and non-motor symptoms. In the non-interventional control group, patient outcomes continued to deteriorate over the two years. Therapy with and without maintenance programs did not reduce the dose of the drug.
- Agility can improve motor and non-motor symptoms and maintain these improvements. MDS-UPDRS M-EDL scores in our patients are 12.4 points lower (better) than control group C. The 24-month MDS-UPDRS M-EDL score was 17.9 points after the resistance training scoring program, thus showing a much higher (worse) value in the patients in the observed C group.
- Prolonged and high intensity exercise involving sensomotor and visuomotor stimuli may slow the progression of the disease in PD patients.

List of scientific publications

(Cumulated impact factors: 16,984; As first author: 14,494)

T. Hortobágyi, A.Uematsu, L. Sanders, R. Kliegl, **J. Tollár**, R. Moraes, U. Granacher
Beam Walking to Assess Dynamic Balance in Health and Disease: A Protocol for the "BEAM" Multicenter Observational Study, Gerontology. 2018 Oct 18:1-8. doi: 10.1159/000493360. **(IF: 3,532)**

J. Tollár, F. Nagy, T. Hortobágyi
Vastly different exercise programs similarly improve parkinsonian symptoms: A randomized clinical trial, Gerontology. 2018 Oct 18:1-8. doi:10.1159/000493360. PMID: 30336478 **(IF: 3,532)**

J. Tollár, F. Nagy, N. Kovács, T. Hortobágyi
Two-Year Agility Maintenance T raining Slows the Progression of Par kinsonian Symptoms Med Sci Sports Exerc. 2018 Oct 9. doi:10.1249/MSS.0000000000001793. PMID: 30303934 **(IF:4,141)**

J. Tollár, F. Nagy, N. Kovács, T. Hortobágyi
A High-Intensity Multi-Component Agility Intervention Improves Parkinson's Patients' Clinical and Motor Symptoms. Arch Phys Med Rehabil. 2018 Jun 7. pii: S0003-9993(18)30353-8. doi: 10.1016/j.apmr.2018.05.007. **(IF: 3,289)**

M. Váczi, **J. Tollár**, B. Meszler, I. Juhász, I. Karsai
Short-term high intensity plyometric training program improves strength, power and agility in male soccer players , JOURNAL OF HUMAN KINETICS 36:(1) pp. 17-26. (2013)
Link(ek): DOI, PubMed, WoS, Scopus **(IF:1,51)**

M.Vaczi, E. Tekus, M. Kaj, T. Koszegi, M. Ambrus, **J. Tollar**, T. Atlasz, K. Szabadfi, I. Karsai
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M. Váczi, É. Tékus, M. Kaj, T. Kőszegi, M. Ambrus, **J. Tollár**, T. Atlasz, I. Karsai, K. Szabadfi
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MAGYAR SPORTTUDOMÁNYI SZEMLE 13:(2) p. 73. (2012)
IX. Országos Sporttudományi Kongresszus. Szeged, Magyarország: 2012.05.24 -2012.05.26.
Link(s): Teljes dokumentum, Matarka

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