The impact of high intensity physical training on motor and non-motor symptoms in patients with Parkinson’s disease (PIP): A preliminary study

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Abstract

BACKGROUND: Parkinson’s disease (PD) is a neurodegenerative disease caused by loss of dopaminergic nigrostriatal neurons. Several studies have investigated various physical interventions on PD. The effects of a high intensity exercise program with focus on resistance, cardio, equilibrium, and flexibility training have not been evaluated previously.

OBJECTIVE: The aim of this study was to investigate the effects of a complex, high intensity physical training program, with a long duration, on motor and non-motor symptoms in patients with PD.

METHOD: 24 patients with PD Hoehn and Yahr stage 1–3 were non-randomly allocated to an intervention group (n = 12) and a control group (n = 12). The intervention group underwent 32 weeks of high intensity personalized physical training twice a week, with an optional extra training session once a week. The control group received general recommendations regarding physical activity. The primary outcomes were the change in Unified Parkinson’s Disease Rating Scale Subscores (UPDRS) and the Parkinson’s Disease Questionnaire (PDQ-39).

RESULTS: At week 32, the training significantly improved both UPDRS motor subscores (p = 0.045), activities of daily living subscores (ADL) (p = 0.006), mentation subscores (p = 0.004) and complication subscores (p = 0.019).

The effect on the PDQ39 total score was not statistically significant. The intervention group however experienced a substantial improvement of the PDQ39 items emotional well-being (−11.0) and bodily discomfort (−7.14).

CONCLUSION: The results suggest that a personal high intensity exercise program may favorably influence both motor and non-motor symptoms in patients with mild to moderate PD. More studies with both higher methodology in study design and a follow-up examination are recommended.

Keywords: Parkinson’s disease, exercise, resistance training, cardiovascular training, UPDRS, quality of life

1. Introduction

Parkinson’s disease (PD) is a progressive neurodegenerative disease characterized by slowness of sequential movements (bradykinesia), muscular rigidity and rest tremor. In addition to these key motor elements, PD patients experience many non-motor symptoms e.g. depression, cognitive impairments, autonomous dysfunction and sleep disorders. These non-motor symptoms often have a greater impact on patient’s quality of everyday life, than motor symptoms alone, and the pharmacologically treatment options are limited (Müller, Assmus, Herlofson, Larsen & Tysnes, 2013; Santos-García & Fuente-Fernández, 2013).
Accumulation evidence suggests that physical exercise may have a neuroprotective effect on the general population and on patients with a neurodegenerative disease e.g. Parkinson’s disease (Ahlskog, 2011; Smith & Zigmond, 2003; Yoon-Sum, Gauray, Kaber, Weidong, & Omar, 2011; Zigmond, Cameron, Hoffler, & Smeyne, 2012). Furthermore physical exercise may induce brain neuroplasticity and the positive effect of physical exercise on the brain, may be even greater with long duration and high intensity of training (Radák, Kaneko, Tahara, Nakamoto, Pucskó, Savári, Nyakas, & Goto, 2001; Al-Jarrah, Jamous, Zaiyae, & Bweir, 2010; Vuckovic, Quanzheng, Fisher, Nacca, Leahy, Walsh, Mukherjee, Williams, Jakovec, & Petzinger 2010; Wu, Wang, Yu, Jen, Chuang, Wu, Wu, & Kuo, 2011; Devalon, Miller, Squires, Rogers, Bove, & Tyce, 1989; Hirsch & Farley, 2009), which can explain why exercise regimes seem to improve motor and non-motor symptoms in PD patients (Dibble, Hale, Marcus, Droge, Gerber, & LaStayo, 2006; Cruise, Backs, Loftus, Newton, Pegoraro, & Thomas, 2011; Dibdle, Hale, Marcus, Gerber, & LaStayo, 2009; Gobbi, Oliveira-Ferreira, Caetano, Lirani-Silva, Barbieri, Stella, & Gobbi, 2009; Toole, Hirsch, Forkink, Lehman, & Maitland, 2000; Hirsch, Toole, Maitland, & Rider 2003; Scandalis, Bosak, Berliner, Helman, & Wells, 2001; O’Brien, Dodd, & Bilney, 2008; Reuter, Engelhardt, Stecker, & Bass, 1999; Bergen, Toole, Elliot, Wallace, Robinson, & Maitland, 2002).

Although often prescribed to patients with PD, consensus for the optimal physical exercise program has not been established. In the USA, Canada, the UK and the Netherlands, national guidelines, which give recommendations on physical activity for patients with PD (Cianci, 2006; Parkinson Society Canada, 2003; National Institute for Health and Clinical Excellence, 2006; Keus, Hendriks, Bloom, Breders-Cohen, de Goede, van Haaren, Jaspers, Kamsma, Westra, Wolff, & Munneke, 2004), exist. These list training principles made for the general population, and do not include specific physical interventions for PD patients. The Dutch guidelines do not include a specified training program, but focuses instead on the evidence for physiotherapy as a treatment for PD patients and general guidelines for practice of physiotherapy. The other national guidelines include specific physical interventions based on low-level strength, cardiovascular, flexibility and balance training. Unfortunately, the training principles listed in these guidelines are based on studies not rated higher than evidence level B, with many studies ranking lower.

Falvo, Schilling and Earhart (2008) reviewed the effects of exercise, including resistance training, on patients with PD. They mentioned the possibility of transferring the guidelines for resistance training for healthy individuals to patients with PD. Similarly Ahlskog (2011) recommends vigorous cardiovascular training on a regular basis for patients with PD. An evidence-based analysis by Keus, Bloom, Hendriks, Breders-Cohen and Munneke (2007) suggest four specific treatment recommendations: cuing strategies to improve gait, cognitive movement strategies to improve transfers, exercises to improve balance and training of joint mobility and muscle power to improve physical capacity. Furthermore the analysis propose that future studies should include a follow-up period for at least 6 months to determine the long duration treatment effect.

Exactly a long duration of physical exercise combined with personalized training has been shown to be essential in order to maintain a sufficient progression and high intensity in an exercise program (Ahlskog, 2011; Kostopoulos, Chouvarda, Kontiakos, Kokonori, van Gilis, & Maglaveras, 2011). When analyzing data regarding PD and physical training in general, it becomes evident that many studies are based on simple and short duration training protocols. Commonly the duration of the physical exercise programs is less than 6 months and often consists of various types of physical training e.g. boxing, Tai Chi, dancing and Nintendo Wii (Combs, Diedel, Staples, Conn, Davis, Lewis, & Schaneman, 2011; Amano, Noceira, Vallabhapurolu, Juncos, Gregor, Waiddell, Wolf, & Hass 2011; Houston & McGill, 2013; Heiberger, Maurer, Amitage, Mendez-Baluena, Schulte-Mönting, Hepp-Reymond, & Kristeva, 2011; Pompeu, Mendez, Silva, Lobry, Oliveira, Zomigrani, & Pienomonte, 2012). Other exercise programs are mainly based on group training or simple exercises with low intensity (Hirsch et al., 2009; Gobbi et al., 2009; Toole et al., 2000; Hirsch et al., 2003; Keus et al., 2007; Combs, Diedel, Chrzastowski, Didrick, Mccoin, & Mox, 2013; Smania, Corato, Tinnari, Stanzani, Fiaschi, Girardi, & Gandolfini, 2010; Fisher, Wu, Salem, Song, Lin, Yip, Cen, Gordon, Jakowec, & Petzinger, 2008; Poliaeff, Gulpin, Kellett, Dick, Hayes, & Wearden 2013).

Personalized training ensures that each patient achieves optimal intensity by taking into account the individual physical and mental level of the patient. It also allows for verbal and tactile cuing, and the performance of complex exercises. We hypothesized that such a training program will maximise the effect on motor and non-motor symptoms in PD patients.
2. Method

2.1. Study design and setting

We designed a pilot-study involving 24 patients with idiopathic PD to study the long-term effects of high intensity physical training on motor and non-motor symptoms. Patients were allocated to an intervention group (n = 12) and a control group (n = 12) in a non-random manner. Neither the patients, nor the instructors and the neurologists performing the intervention and UPDRS, respectively, were blinded. Participants in the intervention group were selected based on their proximity to the training center. The intervention period took place from October 2010 to June 2011.

2.2. Participants

24 patients with idiopathic PD corresponding to stage I-III on the Hoehn and Yahr scale were non-randomly allocated to an intervention group (n = 12) and a control group (n = 12). Participants were recruited from the Movement Disorder Clinic at Odense University Hospital, Funen, Denmark, and were selected by two senior neurologists specialized in movement disorders. Patients who responded first and fulfilled the inclusion criteria were rolled in the study. The intervention group and control group were approximately matched on gender, age and Hoehn and Yahr stage.

2.3. Primary and secondary outcome measures

The primary outcomes were the change in UPDRS total score and subscores and the Single Index of the PDQ-39 total score. The outcomes were measured both for the intervention group and the control group at baseline and at endpoint.

As secondary outcome, we used the Parkinson’s Disease Questionnaire (PDQ 8) and numerous nonspecific PD tests: timed-up-and-go (TUG), ten-meter-walk (TMW), senior fitness test (SFT), WHO-FIVE Well-being index (WHO-5), the HAM-D6 questionnaire (HAM-D6), major depression inventory (MDI) and the repetition max test (RM test – strength test). SFT was measured only in the intervention group, every fifth week.

Senior neurologists specialized in movement disorders performed the UPDRS testing on both groups.

2.4. Exercise regime

The intervention consisted of a 32-week high intensity physical training program based on resistance, cardiovascular, balance and flexibility training. The exercise regime was specifically aligned towards the physical and mental deficits that characterize patients with PD, and had an explicit focus on individualized physical performance. Two personal trainers supervised the training.

The resistance training consisted of 4–6 basic free weight exercises, designed to influence the major muscle groups in the body. The intensity of the resistance training started at a 15 repetition maximum (RM), ending at a 6 RM in the final period of the study. The flexibility training was incorporated into the resistance exercises. The cardiovascular training consisted of individually selected cardio machines starting at 5-minutes exercise with intensity based on Karvonen formula of 50–60%, ending at 20-minutes exercise with an intensity of 85%, by the end of the study period. The balance training consisted of free weight, gym ball and balance board exercises. The participants trained twice a week with an optional third training session.

The exercise program and physical tests were conducted in a private training center.

2.5. Ethical considerations

The Regional Ethics Committee of Southern Denmark, and The Danish Data Protection System approved the study protocol.

2.6. Statistical analysis

In the analysis we investigated the effects of physical training, using our primary and secondary outcomes, on both the control and intervention groups. The statistical analysis was made using IBM SPSS statistics 19. Student t test was used for comparison. The homogeneity of control and interventional group at baseline were analyzed by the chi-square test. A p value of less than 0.05 was considered statistically significant. In figures and tables * is indicative of p<0.05, **p<0.01 and ***p<0.001.

3. Results

3.1. Baseline characteristics

Baseline characteristics of participants are shown in Table 1.
All 24 patients were treated pharmacologically with various orally active antiparkinsonian drugs (especially levodopa in combination with benserazide or carbidopa and dopamine agonists). The medication remained unchanged during the study. At baseline the control group scored better on the UPDRS (total score 16.9) and PDQ39 (total score 13.9) than the intervention group UPDRS (total score 29.3) and PDQ39 (total score 16.2), indicating less PD symptoms in the control group. This could be due to a lower Hoehn and Yahr stage in the control group, a point not accounted for in this study.

### 3.2. Follow-through on exercise regime

As shown in Fig. 1 there were four drop-outs in the intervention group. The drop-outs were not related to the intervention, but due to musculoskeletal disorders (two patients) and personal reasons (two patients).

### 3.3. Primary outcome measurements

Primary outcomes for the intervention group and control group are listed in Tables 2 and 3 respectively. Overall, the UPDRS total score improved significantly in the intervention group, while there was no significant change in the control group.

Concerning the PDQ-39, there were no significant changes as seen for the Single Index (SI) neither in the intervention group nor in the control group.
Table 4: Results secondary outcomes intervention group

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>End-point</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDQ-8</td>
<td>22.06</td>
<td>21.91</td>
<td>0.981</td>
</tr>
<tr>
<td>MDI</td>
<td>10.58</td>
<td>7.00</td>
<td>0.141</td>
</tr>
<tr>
<td>WHO-5</td>
<td>37.00</td>
<td>66.00</td>
<td>0.318</td>
</tr>
<tr>
<td>HAM-D 6</td>
<td>3.43</td>
<td>2.53</td>
<td>0.600</td>
</tr>
<tr>
<td>TUG</td>
<td>7.14</td>
<td>5.14</td>
<td>0.001</td>
</tr>
<tr>
<td>TMW</td>
<td>6.62</td>
<td>5.17</td>
<td>0.001</td>
</tr>
<tr>
<td>Senior Fitness Test (SFT)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4 top-and-go</td>
<td>6.47</td>
<td>4.64</td>
<td>0.001</td>
</tr>
<tr>
<td>Sit-to-stand</td>
<td>11.38</td>
<td>18.38</td>
<td>0.001</td>
</tr>
<tr>
<td>2 min. Knee flexion</td>
<td>84.00</td>
<td>127.13</td>
<td>0.004</td>
</tr>
<tr>
<td>Upper Body Flexibility</td>
<td>-5.66</td>
<td>-1.50</td>
<td>0.142</td>
</tr>
</tbody>
</table>

Paired Samples T Test (Baseline-Endpoint), Intervention group \((n = 8)\).

Table 5: Results secondary outcomes control group

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>End-point</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDQ-8</td>
<td>11.57</td>
<td>16.26</td>
<td>0.204</td>
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<tr>
<td>MDI</td>
<td>6.78</td>
<td>3.56</td>
<td>0.208</td>
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<tr>
<td>WHO-5</td>
<td>75.20</td>
<td>76.40</td>
<td>0.024</td>
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<tr>
<td>HAM-D 6</td>
<td>1.38</td>
<td>0.75</td>
<td>0.180</td>
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<tr>
<td>TUG</td>
<td>8.11</td>
<td>8.08</td>
<td>0.346</td>
</tr>
<tr>
<td>TMW</td>
<td>7.23</td>
<td>6.86</td>
<td>0.314</td>
</tr>
<tr>
<td>Senior Fitness Test (SFT)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>-1.50</td>
<td>0.142</td>
</tr>
<tr>
<td>Lower Body Flexibility</td>
<td>9.68</td>
<td>14.42</td>
<td>0.033</td>
</tr>
</tbody>
</table>

Paired Samples T Test (Baseline – Endpoint), Control Group \((n = 10)\).

The control group \((p = 0.848)\). The intervention group showed a non-statistically significant improvement \((p = 0.141)\) regarding the item emotional well-being. The numerical improvement in this item is substantial, starting at baseline with the score 32.43 ending at 21.43.

3.4. Secondary outcome measures

Secondary outcomes for the intervention group and control group are listed in Tables 4 and 5 respectively. TUG and TMW improved significantly in the intervention group \((p = 0.001\) and \(p = 0.001\), respectively), but not in the control group \((p = 0.95\) and \(p = 0.31\), respectively).

The intervention group experienced statistically significant improvements in the SFT \((p = 0.05)\) in all but one parameter, upper body flexibility \((p = 0.14)\). The control group did not perform the SFT so no comparison between groups was possible.

4. Discussion

This preliminary study demonstrates that high intensity personalized physical exercise has a beneficial effect on motor and non-motor symptoms in PD patients as measured by the UPDRS. No statistical difference could be found when using the PDQ39.

The statistically significant beneficial effect on the UPDRS mentation subscores is noteworthy, as non-motor symptoms have a negative impact on health status in PD (Hinnell, Hurt, Landau, Brown, & Samuel, 2012).

This study supports the results of previous studies testing the effect of physical exercise in PD (Dibble et al., 2006, 2009; Cruise et al., 2011; Gobbi et al., 2009; Toole et al., 2000; Hirsch et al., 2003; Scandalis et al., 2001; O’Brien et al., 2008; Reuter et al., 1999; Bergen et al., 2002; Cianci, 2006, Combs et al., 2011, 2013; Amano et al., 2013; Houston et al., 2013; Heiberger et al., 2011; Pompeu et al., 2012; Smania et al., 2010; Fischer et al., 2008). The results indicate that physical exercise has a positive effect on the symptoms seen in PD, regardless the type of training, method and duration. A potential problem is that patients with PD probably do not perform physical exercise with sufficient intensity, thereby not gaining the full potential physical training offers (Heggelund, Finland, Helgerud, & Hoff, 2013). The reason might be that the patients are not trained individually, and that the often short duration of training makes it impossible to gain a physical state necessary for high intensity physical exercise.

Personalized training with a long duration, take into account the fact that patients with Parkinson’s disease have fluctuating cognitive deficits and energy levels, while at the same time enables exercise with high quality and intensity. This is obviously a different physical intervention than used in other studies (Dibble et al., 2006; Hirsch et al., 2003; Scandalis et al., 2001; O’Brien et al., 2008, Keus et al., 2007; Combs et al., 2011, 2013; Amano et al., 2013; Houston et al., 2013; Pompeu et al., 2012; Smania et al., 2010; Fischer et al., 2008).

In our opinion the duration of the physical exercise program is crucial due to PD patients cognitive problems, especially difficulties memorizing and recalling complex multitask exercises. During this study, we experienced that the intervention group, following 8 months of personal training still required extensive guidance during exercise performance. This confirms the need of personal supervised training one to one. The personal training furthermore enabled guidance and cueing, which increased the cognitive focus and the intensity of the exercises. We witnessed that the intervention group improved in task solving during the full training period, new specific exercises were...
memorized at a faster pace during the exercise period than at baseline.

Personal training one to one makes it possible to evaluate the daily needs and functional levels of the PD-patient, which is very important due to the fluctuating of the their motor and non-motor symptoms. Ridgel, Vitek and Alberts (2009) confirm the importance of individualized gradation of exercise intensity. This study also differentiates from other studies regarding duration of training period. With 32 weeks of individualized personal training, high intensity in the training program is ensured while minimizing the risk of sustaining injury.

The specific guidelines made for patients with PD (Cianci, 2006; Parkinson Society Canada, 2003; National Institute of Clinical Excellence, 2006; Keus, 2004) are based on training methods, which do not in general take into account the progression in exercise intensity needed to profit from long-term improvement of muscle strength, -endurance, -flexibility and balance. This means that the exercise intensity, is not matching the fitness level of the patient as the training proceeds, thereby diminishing the positive gains of physical exercise, and ultimately also diminishing the positive effects of physical exercise on the various symptoms in PD. The Dutch guidelines advocate that the patients should not perform multiple tasks during physical training. We experienced that our patients responded positively when facing multitask assignments, and thus enhanced their benefits of physical training.

Our study has several limitations. As in many previous studies within this area, the size of the study population is small. This might bias the outcome. We calculated the numbers of participants, required to reach a level of power of 90% and a significance level of 5%, to be 64 persons. Due to lack of resources it was not possible include 64 persons.

A limitation of this study is the lack of randomization and blinding process. Participants should have been randomized to either intervention or control group. At endpoint testing we discovered that several of the control group participants had started exercising beyond normal recommendations for persons with PD, which is probably the reason for their improvement in TMW and TUG. The study might have made the control group aware of the beneficial effects of physical exercise. This might have had positive effects on the results seen in the control group regarding improvements in TUG and TMW results.

Despite these limitations, to our knowledge, no earlier studies have implemented high intensity, long duration, individual personalized training into their intervention programs. Our results indicate that high intensity, long duration, individual personalized training has positive effect on motor and non-motor symptoms seen in PD patients. Unfortunately there was no follow up in the study to evaluate the long-term effects. We emphasize that further studies are needed in this area.

Acknowledgments

We would like to thank Fitness DK for providing training locations.

Declaration of interest

There are no declarations.

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References


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