



Towards a Prescription for Exercise for Persons Living with Parkinson's Disease

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Exercise is increasingly recognized as an effective treatment for persons with Parkinson's disease (PD) that can complement conventional medical management. It has the potential to improve general health (e.g. cardiovascular fitness) and thereby lower comorbidities and disability. Exercise may also have symptomatic effects on the manifestations of PD itself. The number of publications supporting a symptomatic effect on functional outcomes such as gait or global motor scores are increasing fast. There is even some experimental evidence, mainly from animal work, that exercise might have a disease-modifying potential. Also, large epidemiological studies in healthy people indicate that those who exercise have a lower risk of developing PD. However, only few studies have convincingly shown a clinically significant and long lasting impact of exercise on PD symptoms, while evidence on disease-modification in persons with PD is still lacking. Although many clinicians are convinced of the positive effects of exercise and frequently recommend persons with PD to incorporate exercise routines in their daily life, the absence of convincing evidence on the clinical benefits often keeps affected individuals from following this advice.¹ Clinical trial data demonstrating the benefit(s) of exercise are therefore urgently needed. One major challenge in providing high-quality evidence on the effects of exercise, however, lies in the nature of the intervention. Not only does it require a behavioral change (and therefore consistent motivation), exercise as an intervention is also extremely difficult to blind and to dose. That is, in contrast to a readily administered drug, for which an identically appearing placebo pill can be provided, exercise is hard to compare to a control group without the psychological confound of the control participants clearly being aware they are not receiving the actual intervention that is potentially beneficial to them. In a recently published aerobic exercise study (the Park-in-Shape study) a unique design was used that resembles a double-blind approach.² Participants were unaware of the content of the two study arms beforehand and were only informed about the content of their own assigned group. Participants were only informed on the general goal of the study (evaluating the effect of physical activity on PD symptoms), but were unaware of the main objective (evaluating the effect of aerobic exercise on PD symptoms). Together with another recent high-quality aerobic exercise trial (the SPARX study) that was performed in persons with de novo PD who were unmedicated,³ these two studies jointly provide high-quality evidence of an attenuating effect of aerobic exercise on PD motor symptoms when assessed without medication. Although the minimal effective exercise dose is still unclear, these studies show that a moderate to vigorous intensity is required to reach the observed effect, whereas a lower intensity was unable to show an effect after 6 months of exercise. This further underlines the dose-effect relationship that is also observed for other interventions.⁴



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Several challenges still remain to be solved in future studies. First, whether aerobic exercise can induce a clinically relevant effect on motor symptoms while participants are tested on medication, on non-motor symptoms and ultimately on quality of life should be examined in future large trials with longer follow-up. Second, the sustainability of the observed effects needs to be addressed. Third, adherence and safety of aerobic exercise in persons with PD should be explored further in implementation studies. The Park-in-Shape study showed that home-based aerobic exercise is feasible for persons with PD, however, some form of sustained supervision is probably necessary for motivation and safety. Versatile gaming techniques and innovative technology to provide both remote supervision and remote assessment can be instrumental in this matter. Finally, the pressing question whether disease-modification can be achieved by high-intensity aerobic exercise still needs further research. It is encouraging to see that the aerobic exercise group in these two recent trials stabilized their motor symptoms, whereas the control group progressed. These effects are by themselves not incompatible with a possible disease modification, but certainly also do not prove disease modification, as symptomatic effects could well have contributed to the group differences immediately after the intervention. Other trial designs are needed to examine this further, including e.g. wash-out periods (to see if group differences persist after cessation of exercise) or a delayed start design, which has been advocated as one possible way to test the disease-modifying potential of drugs like rasagiline or levodopa.⁵⁻⁸

Until these questions are answered and a personalized prescription for exercise can be provided, the current evidence should be used to increase the intrinsic motivation among persons with PD to perform regular exercise.

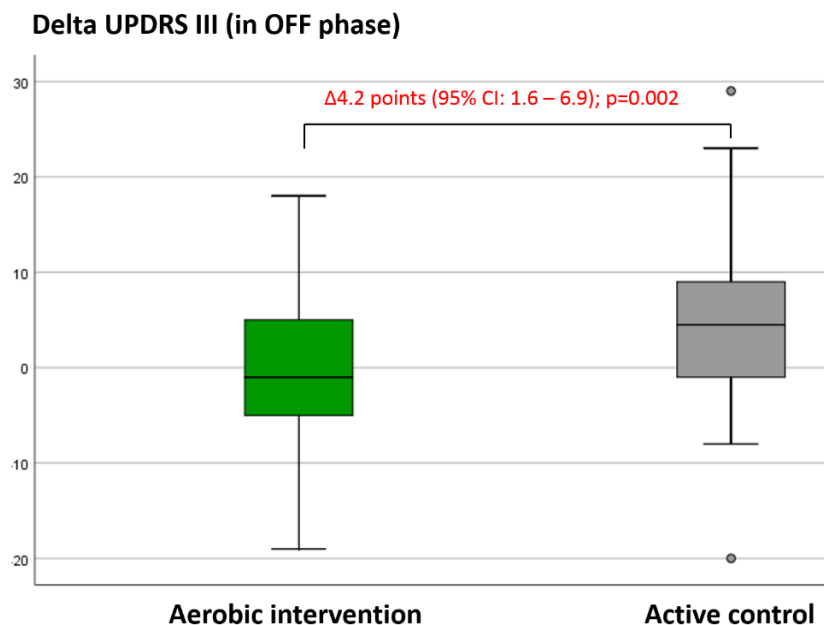
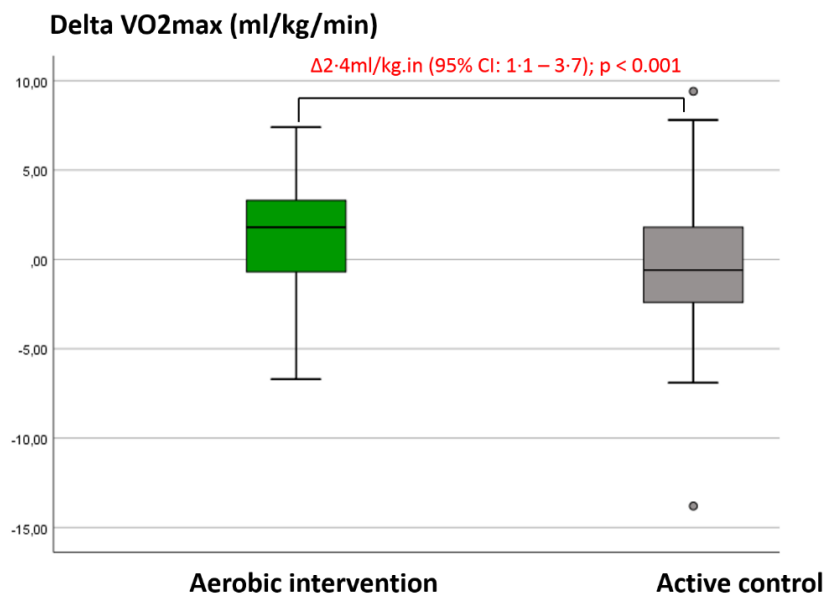


Figure 1. Difference scores between baseline and follow-up after 6 months of either aerobic intervention or active control (stretching, relaxation exercises) in the Park-in-Shape study.

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