Department of Sport Science and Sport
Friedrich-Alexander-University Erlangen Nürnberg

Facilitating Motor **S**kill Learning by Aerobic **T**raining in **P**arkinson's **D**isease III

FaST-PD III

Study Protocol

FaST - PD
Facilitating Motor Skill Learning by
Aerobic Training in Parkinson's Disease

02.12.2020

Contact

Principal Investigator:
Dr. phil. Simon Steib
Affiliation: Institute of Sports and Sports Sciences
Heidelberg University
Tel.: +6221 54-4643
E-Mail: simon.steib@issw.uni-heidelberg.de

Sub-investigators:
Florian Ostermair
Affiliation: Department of Sport Science and Sport,
Friedrich-Alexander University Erlangen-Nürnberg
Tel.: +49 9131-8528106
E-Mail: florian.ostermair@fau.de

Philipp Wanner
Affiliation: Department of Sport Science and Sport,
Friedrich-Alexander University Erlangen-Nürnberg
Tel.: +49 9131-8528175
E-Mail: philipp.wanner@fau.de

Collaborators
Klinik für Neurologie, Klinikum Würzburg Mitte, Standort Juliusspital (Prof. Dr. med. Mathias Mäurer)

Funding
Deutsche Stiftung Neurologie (DSN)

Summary

The study is designed to assess the effects of cardiovascular (aerobic) exercise on motor skill learning in Parkinson patients. Specifically, we examine whether learning a novel motor skill over a six-week period is enhanced when skill practice sessions are combined with additional moderate-intense aerobic exercise bouts. In this randomized controlled trial, participants will be allocated to either an intervention group (motor skill practice + aerobic exercise) or control group (motor skill practice + seated rest).

Background

Parkinson's disease (PD) is a progressive neurodegenerative disorder that is characterized by motor control impairments, such as gait disturbances and postural instability. Beneficial effects of exercise are attributed to mechanisms of neuroplasticity, and task-specific motor training (repeated practice of a skill) is consequently considered to be a motor learning process. Importantly, the formation (acquisition) and consolidation of motor memories is impaired in PD compared to healthy individuals of similar age.

Thus, it is crucial to identify strategies to enhance motor learning in people with PD. Recent studies have accumulated evidence to show that acute (single bouts of) and chronic (multiple bouts of)

cardiovascular exercise can facilitate motor skill learning. However, this evidence is mainly derived from studying healthy individuals. In a first study including PD patients, we recently found improved motor memory consolidation, but not skill acquisition, when practice was preceded by a single bout of cardiovascular exercise.

These results suggest that acute exercise may enhance motor memory formation processes, but could potentially interfere with motor skill acquisition when performed prior to practice. Consequently, in a second study including PD patients, we changed the design so that a bout of cardiovascular exercise immediately followed skill practice, and found that exercise facilitated motor memory consolidation as indicated by improved offline learning gains.

Going onward from the previous two studies, the present study will investigate the effects of performing cardiovascular exercise immediately following skill practice over a six-week intervention period on motor memory consolidation. It will be examined how the regular direct coupling of motor learning skill practice and cardiovascular exercise influences the consolidation and automation of the practiced movements.

Aims/Hypothesis

The main question of the study is whether moderate-intense aerobic exercise, performed immediately following motor skill practice over a six-week intervention period, facilitates motor memory consolidation in Parkinson's Disease (PD).

Hypotheses:

1. Learning a novel balance task over a period of six weeks is enhanced when cardiovascular exercise bouts are performed immediately following each skill practice session.
2. We further hypothesize, that improved learning outcome with exercise will result from improved motor memory consolidation (offline gains between practice sessions).

Outcome measures

Motor skill learning

A dynamic balance task will be used to assess participants' motor learning performance (i.e. motor memory formation). The device consists of a 107 x 65 cm wooden platform (stability platform; Lafayette Instrument Europe; Loughborough, United Kingdom), which is mounted on a fulcrum and has a maximum deviation of 15° to either side. Participants are required to stand with both feet on the platform and try to keep the platform as close to the horizontal as possible during a 30 seconds trial. A millisecond timer measures angular displacement from horizontal during each 30 seconds trial. Participants will be secured with a safety harness and instructed to stand in a comfortable position.

Primary outcome measure

Description: Change of time in balance (mean angular displacement ±5° from horizontal within each 30 seconds trial) from pre- to post-assessment.

Secondary outcome measures

- **Motor skill automatization:**
  Description: Change of time in balance (angular displacement ±5° from horizontal) in addition to error score of a backwards-counting-task from pre- to post-assessment

- **Transfer effect:**
  Description: Change of the achieved score on the FAB - Scale from pre- to post-assessment

- **Muscular endurance:**
  Description: Change of time necessary to rise five times from a chair

- **BDNF – Levels:**
  Description: Change of peripheral BDNF - concentration from pre- to post-assessment

- **Cardiorespiratory fitness:**
  Description: Change in maximum oxygen uptake (VO_{2max}) from pre- to post-assessment

- **General motor function:**
  Description: Change in the Parkinson Disease Rating Score (UPDRS) part III (motor part) from pre- to post-assessment

- **Cognitive function:**
  Description: Change in the Montreal Cognitive Assessment (MoCA) Score from pre- to post-assessment.

Memory consolidation (offline learning):
To assess motor skill consolidation (offline learning) primary and secondary outcomes will be calculated as change scores from the final performance (last practice block) of every practice session to the performance of the first practice block of the following practice session, respectively.

Study design

In an experimental trial, participants will be randomly allocated to one of two groups (Figure 1). Each experimental arm includes i) a pre-examination 2 - 14 days before ii) six acquisition sessions where the motor skill will be practiced, followed by a retention test iii) 7 days later (Figure 1). On acquisition days, the experimental group will perform a single bout of aerobic exercise (cycle ergometer) immediately following motor practice, whereas the control group will rest in a seated position.

Conditions:
1. Experimental condition: Participants in the experimental group will practice the ***motor learning task*** followed by a single bout of moderate-intensity ***aerobic exercise*** on a cycle ergometer during acquisition days.

2. Control condition: **Participants in the control group will** practice the ***motor learning task*** followed by a ***seated rest*** period during acquisition day.

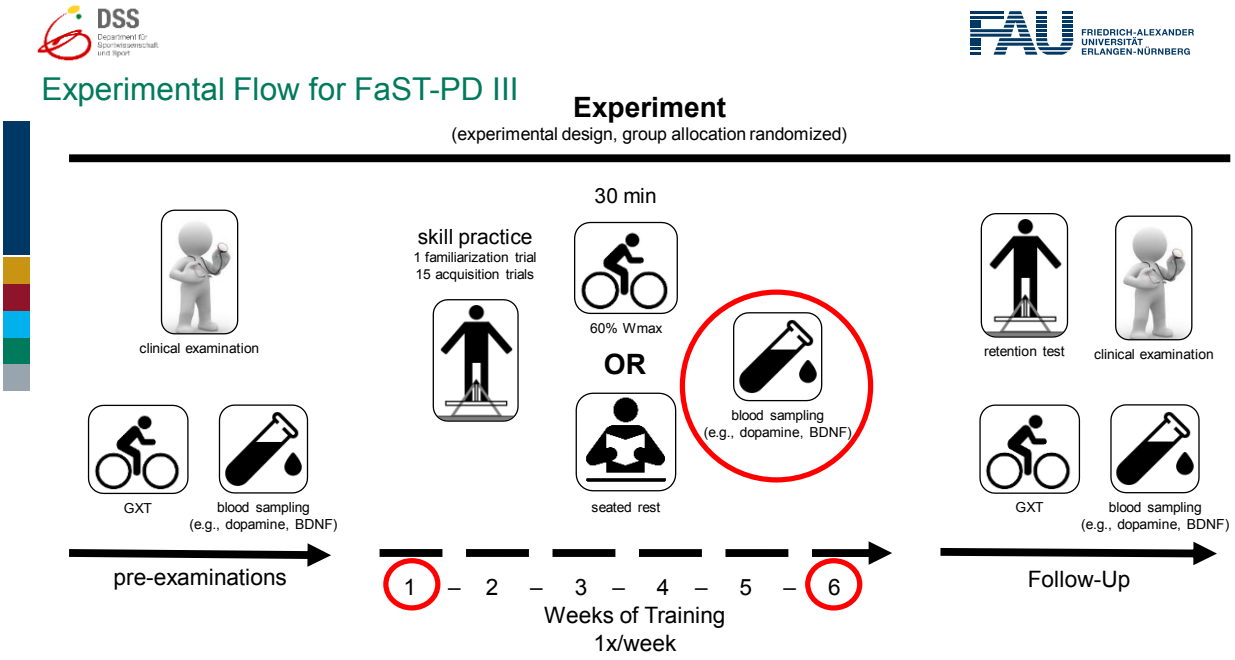

Figure 1 Study Design FaST-PD 3

Aerobic exercise bout:
The acute cardiovascular exercise bout comprises a 5-minutes warm-up (intensity will be progressively increased until target intensity), followed by 25 minutes of pedaling at 60–80 rpm and 60% of maximal power output reached in a graded exercise test during pre-examination.

Rest:
The resting phase includes seated rest on a chair for 30 minutes. Participants will be permitted to watch selected TV shows during the 30 minutes.

Motor skill practice:
Irrespective of group allocation, participants will follow the identical skill practice routine. On acquisition day, participants will perform a familiarization trial followed by 15 practice trials (30 seconds), clustered into 5 blocks of 3 trials, with 60 seconds rest between trials and 120 sec rest between blocks. At a baseline test 7 days prior to and at a retention test 7 days after the intervention period, participants will perform a test consisting of one familiarization trial (to account for potential warm-up effects) and one practice block (3 trials) on the stability platform, respectively.

Study population

Inclusion criteria:
Patients are eligible if they have

- a Hoehn and Yahr score of ≤3;
- a score of ≤1 in the UPDRS item 'postural instability';
- are able to stand and walk independently; and
- are naïve to the motor task.

Exclusion criteria:
Criteria for exclusion are

- higher level of cognitive impairment indicated by a score of <21 in the Montreal Cognitive Assessment (MoCA);
- other clinically relevant neurological, internal or orthopedic conditions besides Parkinsonism that would interfere with the exercise paradigm or motor learning task;
- musculoskeletal conditions or surgery 1 year before the study enrolment;
- smoking>10 cigarettes/day or drinking>6 cups of coffee/day or >50 g of alcohol (equivalent of two glasses of wine) consumption/day (Winter et al., 2007).

Statistical analysis plan

Power calculation:
Considering data from previous experiments (Wanner et al., 2020), an a priori estimation of the required sample size for the primary analysis was performed using the statistics program G*Power (version 3.1.9.4). The estimation was performed for the primary analysis, a 2 (groups) x 6 (training sessions) mixed ANOVA with repeated measures. In order to identify a significant interaction effect of moderate effect size (f=0.25), with a statistical power of 80%, and a significance level of p≤.05, 20 subjects (n=10 per group) need to be included.

Statistical analysis:
The effect of aerobic exercise on motor skill learning will be examined by a 2 (groups) x 6 (sessions) mixed ANOVA with repeated measures, testing for the within-subject factor TIME (mean time in balance of all 15 trials in each of the 6 training sessions, respectively) and between-subject factor GROUP (AEX, REST). A separate 2 (AEX, REST) x 6 (last practice block during each training day, first block during subsequent session) ANOVA will be performed to test skill retention between practice sessions.