JPND research
EU Joint Programme – Neurodegenerative Disease Research

StepuP

Steps against the burden of Parkinson’s Disease

Parkinson’s disease (PD) affects over 10 million people worldwide and is one of the most prevalent neurodegenerative diseases. Despite good effects of medication, unstable gait and falls continue to affect 70% of patients with PD. This leads to loss of confidence, social isolation, fractures, and hospital admissions. Treadmill training has demonstrated substantial and well-proven benefits in improving gait and reducing falls, which can be enhanced by the concurrent use of mechanical or virtual-reality triggered gait adaptations. However, the underlying mechanisms responsible for the effects of treadmill training are poorly understood. It is imperative to disentangle how PD patients benefit from treadmill training to improve and personalize training. To do so, we will determine how the well-proven outcomes from non-pharmacological treadmill training relate to the biomechanical, physiological, and neural changes that underlie intervention success and how these effects transfer to daily life.

Four clinical centers will recruit a total of 168 PD patients. Participants will be randomized 1:1 to intervention or control groups. The intervention groups will receive treadmill training, enhanced at selected sites by mechanical or virtual-reality triggered gait adaptations. All participants will undergo assessments before and immediately after training, and again after 12 weeks to investigate retention. We expect gait speed, step length and step variability to improve by clinically relevant extents. We hypothesize that sensorimotor integration underpinning feedback control of balance during gait explains these effects. This will be probed by analysis of biomechanical data, where we expect enhanced quality of feedback control regulating foot placement in walking. Neurophysiological changes underpinning these behavioral changes will be assessed using a combination of electroencephalography (EEG) and electromyography (EMG). After training, we expect to see improved feedback control of gait stability that is accompanied by decreased EEG beta band power and increased EEG-EMG (brain-muscle) coherence.

Improved gait as assessed in the lab does not always translate to increased daily-life walking. We hypothesize that gait self-efficacy mediates and/or modifies transfer of training effects and will therefore investigate the associations of the above mechanistic probes, gait efficacy and patients’ characteristics with mobility outcomes. Digital mobility outcomes over one week will be assessed remotely using our advanced sensor tools.

We will use machine learning to assess individual improvement, focusing, for example, on understanding why some individuals improve on the lab-based tests and in their daily life, but others do not or only in the lab. This will help us to understand the mechanisms that underlie (individual) translation of treatment outcomes into real-world outcomes and may empower and inform the development of personalized interventions.

In conclusion, the proposed project will provide a mechanistic understanding into how widely used treadmill training changes neural activity in patients with PD, how this translates to improved control of gait, and how this in turn translates to outcomes that are meaningful to patients in their daily life.

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