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DOCTOR IN INTERDISCIPLINARY STUDIES: PSYCHOLOGY AND PHYSIOTHERAPY

## of Mr. Mahyar Firouzi

Which will take place on 04/10/2024, 15:30 (Brussels Time) Promotiezaal D.2.01 – VUB Main Campus Brussels Pleinlaan 2 – 1050 Brussel

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# NEURAL UNDERPINNINGS OF IMPLICIT MOTOR SEQUENCE LEARNING: EFFECTS OF NON-INVASIVE BRAIN STIMULATION IN HEALTHY ADULTS AND PARKINSON'S DISEASE

## JURY

**INTERNAL:** 

Prof. dr. Eva Dierckx (Chair) Vrije Universiteit Brussel

- Prof. dr. David Beckwée Vrije Universiteit Brussel
- dr. Elien Heleven Vrije Universiteit Brussel

#### EXTERNAL:

Prof. dr. Christophe Lafosse RevArte Revalidatieziekenhuis

Prof. dr. Koen Cuypers Katholieke Universiteit Leuven Universiteit Hasselt

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### PROMOTORS

Prof. dr. Natacha Deroost Vrije Universiteit Brussel

Prof. dr. Kris Baetens Vrije Universiteit Brussel

Prof. dr. Eva Swinnen Vrije Universiteit Brussel



# SUMMARY

Nearly all our daily motor activities, from getting out of bed to driving, walking and typing, involve executing movements in a specific order. Our ability to incidentally learn such sequential motor actions is termed "implicit motor sequence learning" and is thought to be mediated by two interconnected sets of brain circuits: the basal ganglia network and the cerebellar network. However, their exact contributions across different stages of learning remain unclear.

This dissertation aimed to explore the neural underpinnings of implicit motor sequence learning, using transcranial direct-current stimulation (tDCS), a non-invasive brain stimulation technique. To this end, the effects of tDCS were assessed across the acquisition, short-term and long-term consolidation phases of learning, in healthy adults, and in individuals with Parkinson's disease, where this skill is impaired. In Parkinson's disease, basal ganglia dysfunction leads to alterations in cerebellar brain activity as well, making it a prime neural model to study the contributions of these networks to implicit motor sequence learning. Given the importance of this skill in our daily motor activities, its impairment not only affects the daily lives of people with Parkinson's disease, but also impedes their successful motor rehabilitation. Therefore, an additional goal of this dissertation was to determine the potential of tDCS to enhance implicit motor sequence learning in Parkinson's disease.

This dissertation showed a beneficial effect of tDCS applied to the primary motor cortex and cerebellum on the acquisition of sequential knowledge in healthy young adults. It also revealed for the first time that tDCS can enhance sequential knowledge acquisition in individuals with Parkinson's disease. Based on the overall result pattern, and in particular, comparing acquisition and consolidation stages, we propose the expectancy hypothesis: tDCS enhances the implicit acquisition of motor sequences by increasing susceptibility to sequence disruptions in early learning, leading to heightened awareness of potential disruptions, which ultimately induces more flexible responding during consolidation. With regard to stimulation site, the positive effects of primary motor cortex stimulation seem to stem from co-stimulation of the primary motor and the motor association cortex, rather than focal stimulation of the primary motor cortex alone. This suggests that the motor association cortex's importance during early implicit motor sequence learning might have been previously underestimated. Cerebellar tDCS similarly enhanced sequential knowledge acquisition, supporting the sequence detection hypothesis, which posits that the cerebellum serves a sequence-specific role within the motor learning network. This challenges previous claims and the traditional view that the cerebellum exclusively supports non-sequence-specific motor adaptation processes.

Finally, our clinical studies showed that, in particular, patients with Parkinson's disease *and* mild cognitive impairments benefitted from the positive effects of tDCS. These results show that it is important to take the cognitive status of patients into account when considering neurostimulation.

Overall, our findings provide valuable insights into the neural underpinnings of implicit motor sequence learning, and identify several important implications for both research and clinical practice in this domain.



# CURRICULUM VITAE

Mahyar Firouzi obtained his Master's degree as a physiotherapist specialized in neurological rehabilitation from the Vrije Universiteit Brussel (VUB) in 2019. Fascinated by the brain and its disorders, he started his interdisciplinary PhD in psychology and physiotherapy in 2020, at his alma mater.

Since then, his research has focused on the intersection between motor and cognitive functioning, and how deficits in these domains might be tackled using technology. In 2021, he was granted a personal fundamental research fellowship by the Research Foundation Flanders (Fonds Wetenschappelijk Onderzoek, FWO), which enabled him to conduct his PhD research on the neural underpinnings of implicit motor sequence learning.

Beyond this fundamental research objective, an additional goal of his PhD project from a clinical perspective was to investigate whether non-invasive brain stimulation techniques can effectively enhance implicit motor sequence learning in individuals with Parkinson's disease, in whom this skill is impaired.

Another research interest of his concerns the use of exoskeletons, both for the rehabilitation of individuals with neurological disorders (e.g., stroke) and in the context of healthy ageing.