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24.06.2024

Promotionsverfahren von **Frau M.Sc. Carolin Balloff**
Auslage der Dissertation und Gutachten sowie Termin der mündlichen Prüfung
Anlage: Einseitige Zusammenfassung der Dissertation

Sehr geehrte Damen und Herren,

in dem oben genannten Promotionsverfahren wird die Annahme der Dissertation

**Quadripulse-stimulation-induced plasticity in patients with multiple sclerosis and its functional
relevance**

von den Berichterstattenden Prof. Dr. A. Buchner und Prof. Dr. I.-K. Penner beantragt. Sie kann zusammen mit
den Gutachten in der Zeit

vom 28.06.2024 bis 09.07.2024

eingesehen werden. Bitte wenden Sie sich zur Einsicht an das Promotionsbüro (promotionmnf@hhu.de).

Einsprüche gegen diese Dissertation können nur zwei Tage nach der vorgenannten Frist
geltend gemacht werden. Erfolgt kein Einspruch, so gilt die Dissertation als angenommen
(§ 7 Ziffer (5) PO).

Sofern die Dissertation angenommen wird, findet die mündliche Prüfung am

12.07.2024 um 11:00 Uhr

im **Raum 23.02.U1.24** statt. Als Prüferinnen bzw. Prüfer sind vorgesehen:
Prof. Dr. S. Becker, Prof. Dr. J. Musch und Prof. Dr. med. P. Albrecht.

Die Öffentlichkeit ist bei der Befragung zugelassen.

Mit freundlichen Grüßen
im Auftrag

Daniela Schleiffer

Abstract

Despite advancements in understanding the pathophysiology of multiple sclerosis (MS), predicting individual clinical trajectories remains elusive. Compensatory mechanisms of neuroplasticity are gaining recognition as potentially significant contributors to shaping clinical outcomes and may hold prognostic value for disease progression. Synaptic plasticity, an early-phase neuroplasticity mechanism, can be non-invasively investigated at the motor cortex using repetitive transcranial magnetic stimulation (rTMS). In patients with MS, the quadripulse-stimulation (QPS) protocol in particular shows promise for effective induction of synaptic plasticity.

This thesis investigated QPS-induced plasticity in patients with MS both in cross-sectional and longitudinal contexts. Four empirical studies were conducted to compare plasticity across MS subtypes and healthy controls (HCs), assess its correlation with cognitive and motor function, study alterations in plasticity during acute relapses, and analyze its association with disease progression over time. The primary aim was to investigate QPS-induced plasticity as a potential biomarker for predicting disease progression.

The first study revealed a positive correlation between cognitive performance and QPS-induced plasticity in patients with relapsing-remitting MS (RRMS), with plasticity serving as a distinguishing factor between patients with and without cognitive impairment. RRMS patients did not exhibit diminished plasticity compared to HCs. In the second study, QPS-induced plasticity did not significantly differ between patients with MS during acute relapses, stable patients with MS, and HCs. Exploratory findings suggested higher plasticity in relapsing patients with motor disability. Similarly, the third study found no significant differences in QPS-induced plasticity among patients with different MS subtypes and HCs. Additionally, correlations with motor and cognitive functions were evident only in MS patients with intact corticospinal tract integrity. Longitudinal analysis in the fourth study revealed that patients experiencing clinically relevant decline in manual dexterity or visuospatial short-term learning and memory after a median follow-up of two years exhibited lower levels of baseline synaptic plasticity. However, overall functional outcomes remained relatively stable over time, with a similar number of patients experiencing improvement and decline.

In summary, this thesis indicates preserved QPS-induced plasticity across all MS subtypes and disease activity levels. Furthermore, it highlights the need to consider clinical characteristics in synaptic plasticity research in patients with MS and proposes a potential link between the degree of QPS-induced plasticity and functional decline. However, the role of QPS-induced plasticity as an independent biomarker for predicting disease progression at the individual level currently remains uncertain due to various methodological challenges.