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**Plasticity in the sensorimotor system and innovative sensorimotor training in frailty**

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This dissertation presents two studies, in which the relationship of impairment in sensory and motor systems with frailty was investigated from a conceptual point of view (Study 1) and as a potential target for innovative treatment to reduce frailty (Study 2).

The aim of Study 1 was to identify sensory and motor determinants of frailty as assessed by two common frailty instruments, the frailty phenotype (FP) and the frailty index (FI). Performance measures of sensory and motor function were assessed in 44 pre-frail and frail subjects. Separate multiple logistic regression analyses revealed that frailty as defined by the FP was associated with reduced upper extremity function, while frailty as defined by the FI was independently associated with higher hearing thresholds, reduced lower extremity performance and higher depression scores. This suggests that reduced sensory and motor function contributes to the syndrome of frailty, thereby offering a potential target for treatment, and that different frailty instruments may be differentially sensitive to capture functional impairment in frail populations.

In Study 2, the effectiveness of a 90-day tablet-based sensorimotor training (n=24) targeting the reversal of age-related maladaptive neuroplasticity in the sensorimotor system to counteract frailty was evaluated, compared to a tablet-based relaxation control training (n=24). After 60 days of training, a reduction in frailty as determined by the FP was found for both groups, while the effect tended to be stronger for the sensorimotor training condition. A non-significant reduction in the FI was found irrespective of the group. No training effects were found for sensorimotor brain activity assessed by functional magnetic resonance imaging and corticomotor excitability assessed by transcranial magnetic stimulation. The results suggest that a neuroplasticity-based training may alter frailty, yet the significance of the postulated neuroplastic mechanisms and the specific training characteristics underlying the effect remain to be determined.

Together, the two studies provide evidence that impairment in sensory and motor systems may represent a target mechanism to better understand pathophysiology of frailty and to develop novel, innovative treatment approaches. Longitudinal studies are needed to determine the influence of sensory and motor decline in the development of frailty. The present work may also inspire future large-scale interventional studies to validate the present preliminary, yet promising results and to examine the efficacy and mechanistic principles that approaches targeting the reversal of age-related maladaptive neuroplasticity may have in the treatment of frailty.