

TITLE: Neurophysiological predictors of response to neurorehabilitation plus rTMS in MS

Short title: Motor threshold predicts gait improvement

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OBJECTIVE

To investigate neurophysiological predictors of response to rehabilitation combining physical therapy and repetitive Transcranial Magnetic Stimulation (rTMS) in pwMS.

BACKGROUND

New treatment approaches are needed for people with Multiple Sclerosis (pwMS)¹. Particularly, further evidence is needed on factors that may modulate the therapeutic efficacy of multidisciplinary neurorehabilitation combined with rTMS, allowing to better identify possible future responders.

METHODS

We analysed the 6-Minutes Walk Test (6MWT) in 43 pwMS who underwent at least three weeks of inpatient intensive multidisciplinary neurorehabilitation combined with 12 sessions of lower limb motor cortex 20 Hz rTMS. All patients completed the 12 planned rTMS sessions. Mean age was 51±10 years, mean disease duration was 15.7±9.7 years, median hospitalization duration was 37 (30-57) days, and median EDSS was 6 (5.5-6.5). The 6MWT was performed before and after treatment; we considered a minimal clinically important difference (MCID) cutoff ≥55 metres to determine clinically significant improvement². We investigated the ability of TMS-evoked visual motor threshold (MT) to predict which patients will improve significantly following treatment. Results are reported as mean±SD or median (1st-3rd quartile).

RESULTS

Following treatment, 6MWT scores improved on average by 38.7±30.0 meters ($p<0.05$), and 15 (35%) patients showed a clinically-significant improvement. There were no significant clinical or demographic differences between patients who improved and those who did not (all $p>0.05$). Mean MT was significantly lower in patients with a clinically-significant improvement (56.4±8.8% vs. 67.5±17.5%, $p=0.009$). A ROC curve analysis showed that mean MT predicts clinically-significant improvement (AUC=0.693, $p=0.039$) using a cutoff intensity of 60% of maximal TMS stimulator output (sensitivity=66.7%, specificity=64.3%).

CONCLUSION

The ability to select pwMS who are more likely to benefit from the combination of rTMS and neurorehabilitation could enable more personalized treatment protocols, thus improving therapeutic efficacy. Future studies should consolidate these preliminary findings and explore strategies to improve outcomes in poor responders, possibly owing to exhausted corticospinal reserve.

References

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