

Motor Cortex Inhibition: A Marker of Motor Function in Neurofibromatosis Type 1

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Introduction: Neurofibromatosis type 1 is a neuro-cutaneous disorder commonly associated with motor and cognitive defects. These deficits greatly impact children's quality of life. With little to no specific treatments for these deficits, more reliable and objective measures are needed to assess future treatment efficacy besides the traditional subjective measurements. Transcranial magnetic stimulation (TMS) motor physiology data may provide a window into cortical motor function that can be used to assess future treatment efficacy.

Hypothesis: Impaired motor function in NF1 is linked to deficient motor cortex inhibition.

Methods: Youth ages 8 to 16 were recruited from an NF1 specialty clinic (n=22). Standard safety precautions and exclusions for TMS were applied. Motor function was evaluated with the Physical and Neurological Examination for Soft Signs (PANESS) test. Motor cortex thresholds, inhibition and facilitation were measured with single and paired pulse TMS. Single pulse TMS measures included Resting Motor Threshold (RMT) and Active Motor Threshold (AMT). Paired pulse TMS measures included short interval cortical inhibition (SICI) and intracortical facilitation (ICF). Spearman Rank Correlations were used to assess associations between developmental motor skills and neurophysiological measures, PANESS motor data, TMS physiology data, and age.

Results: Twenty-two youth (82% male, 100% white, non-Hispanic, mean age= 12) were recruited. Mean PANESS score was 47 (SD= 15.8), which falls in the highly impaired range. Worse motor function (higher PANESS scores) correlated with less motor cortex inhibition (SICI) ($r=.58$, $p<0.01$). Reduced SICI also correlated with poorer sub-scores ($p<0.05$), particularly slower timed tasks ($r=.702$, $p<0.001$). Similarly, slower timed tasks correlated with excessive ICF and higher RMT. Motor function failed to demonstrate expected improvement with increasing age ($p=0.88$).

Conclusion: Motor physiology assessed with TMS reflects motor function in kids with NF1. TMS SICI holds promise as a biomarker useful for clinical trials.

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