Central assessment of motor dysfunction using transcranial magnetic stimulation

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Conventional paired-pulse transcranial magnetic stimulation (TMS) techniques of assessing cortical excitability have tended to be limited by fluctuations in the motor evoked potential (MEP) amplitude.

Over recent years, a new technique of threshold tracking TMS has been developed for the assessment of cortical excitability in a clinical setting. Initial studies in healthy controls, tracking the MEP response from *abductor pollicis brevis*, established that short-interval intracortical inhibition (SICI) occurred up to an interstimulus interval (ISI) of 7-10 ms, with two distinct peaks evident, at ISIs of ≤2 and 3 ms, followed by intracortical facilitation to an ISI of 30 ms. Long-interval intracortical inhibition (LICI) occurred at ISIs of 50-300 ms, peaking at 150 ms.

Having confirmed the effectiveness of the threshold tracking TMS technique as a reliable and valid measure of cortical excitability, simultaneous assessment of upper and lower motor neuronal function with threshold tracking techniques have recently been undertaken to investigate the site of onset and patterns of disease progression in a number of neurodegenerative diseases, particularly motor neurone disease (MND), Parkinsons disease and dementia.

In the case of MND, with the evolution into a new therapeutic era, there remains a clear need to develop a diagnostic and treatment-responsive biomarker. Threshold tracking TMS studies undertaken in sporadic and familial MND patients have consistently demonstrated the presence of cortical hyperexcitability. The development of cortical hyperexcitability precedes manifestation of the disease in pre-symptomatic carriers of genetic mutations linked to MND. Threshold tracking TMS has also effectively differentiated clinical phenotypes from a range of mimic syndromes and has been used to demonstrate an effect of riluzole therapy in MND patients.