# Approaches to Optimise Neuroplasticity Induction in the Human Motor Cortex

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## ABSTRACT

The human brain can change its connectivity with experience, and such neuroplasticity is critical for learning, memory, and recovery from brain injury. A number of non-invasive brain stimulation techniques can induce neuroplastic changes in the brain. In order to maximise the therapeutic potential of these techniques, we need to understand the factors influencing their effectiveness. This thesis investigates approaches to optimising neuroplasticity induction in the human motor cortex, focussing on a widely-used repetitive Transcranial Magnetic Stimulation (rTMS) paradigm, Theta Burst Stimulation (TBS).

Subject responses to neuroplasticity induction methods are characterised by high inter- and intra-individual variability. One factor which may contribute to this variability is the excitability state of the targeted cortex at the time stimuli are applied. In Chapter Two, I investigate whether power in several electroencephalography (EEG) frequency bands can be used as a state-marker to predict responses to experimental (TBS) and behavioural (visuomotor training) plasticity induction. The results suggest pre-stimulation EEG power is not useful for predicting responses to plasticity induction. However, an interesting finding is a large increase in alpha (8-12 Hz) power following visuomotor training, which positively correlates with changes in cortical excitability. Although speculative, this may be related to disengagement of the somatosensory system important for motor memory consolidation.

Inhibition in the cortex exerts a powerful modulatory influence over plasticity induction. Therefore, in Chapters Three and Four I examine approaches that might be useful for

optimising (reducing) the level of inhibition in the motor cortex during plasticity induction. Although Chapter Two provides no evidence that pre-stimulation EEG can predict responses to plasticity induction, the timing of stimuli relative to *ongoing* oscillatory activity may be more important. In Chapter Three, I question whether timing of stimuli to different phases of an intrinsic brain rhythm might allow plasticity-inducing stimuli to be applied during natural oscillations in inhibitory tone within the cortex. Alpha, a prominent rhythm in the resting human brain, has been proposed to reflect bouts of cortical inhibition. In this chapter I undertook the technical challenge to develop a method to trigger TMS on different phases of alpha. Whilst Short Interval Intracortical Inhibition (SICI) is unchanged by alpha phase, Motor Evoked Potential (MEP) amplitude is 30% greater on the downgoing phase compared to the upgoing phase. The results may suggest some other inhibitory network is down-regulated during this phase of the alpha rhythm, and provide an opportunity for enhancing neuroplasticity induction by applying stimuli during optimal temporal windows.

In Chapter 4, I investigate whether it is possible to selectively down-regulate activity in inhibitory cortical networks using a modified TBS technique. Many rTMS paradigms affect both inhibitory and excitatory pathways. As intracortical inhibitory pathways have a lower threshold for activation than excitatory pathways, I aimed to target cortical inhibitory circuitry by reducing the intensity of TBS. The results demonstrate it is indeed possible to reduce SICI without concurrent effects on the MEP.

In summary, this thesis provides approaches that may be useful for targeting or creating a more favourable cortical environment for neuroplasticity induction.

## DECLARATION

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Suzanne McAllister and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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McAllister, S. M., Rothwell, J. C. and Ridding, M. C. (2009) Selective modulation of intracortical inhibition by low-intensity Theta Burst Stimulation. *Clin Neurophysiol*, **120**(4), 820-826.

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## LIST OF FIGURES