Lifestyle Factors that May Influence TMS−Induced Neuronal Plasticity

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Abstract

Background & Aim: Repetitive Transcranial Magnetic Stimulation (rTMS) is an FDA−approved treatment for major depressive disorder that is theorized to work by strengthening neuronal connections of key networks through a process known as long term potentiation (LTP). We tested this hypothesis in a double−blind crossover study with 10 healthy subjects by administering an rTMS 'plasticity protocol'. This protocol is designed to enhance excitability in the presence of pharmacologic activation of NMDA receptors with 100 mg d−cycloserine. NMDA receptors are well−known to be necessary and sufficient for LTP.

Methods: We assessed changes in excitability with single−pulse TMS 'probes' over the motor cortex, and tested the downstream effects on the associated hand muscles using electromyography (EMG). To better understand how real−world factors might influence neuronal plasticity, we also collected participant characteristics that could affect plasticity including caffeine use, alcohol use, and musical/athletic experience.

Results: We found that when subjects had NMDA activation they had greater potentiation in response to our plasticity protocol, consistent with an LTP−like mechanism for rTMS. We also found that while caffeine is an excitatory agent, chronic use of the substance resulted in a significantly blunted plasticity response with the effects of d−cycloserine. Chronic alcohol demonstrated a trend towards the opposite effect. Musicians and athletes (M/As) have previously been shown to have increased cortical volume specific to the brain regions involved with repeated use compared to non−M/As. Among our tested subjects, we found that experienced M/As (who have practiced for over 14.5 years and for 5 hours per week) had a substantially more robust response to our plasticity protocol in the presence of d−cycloserine.

Conclusion: Taken together, these results suggest an LTP−like mechanism for rTMS. Further, they suggest that lifestyle factors such as exogenous substance use as well as repetitive practice, or lack thereof, may alter our ability to undergo neuronal plasticity.

Clinical Implications: Our results hold implications for anyone engaged in learning processes that may facilitate long term potentiation−like pathway activation in key networks, including recovery from neurological/mental disorders. Substance use may produce lasting changes to neuronal populations and understanding these changes on the human level is critical for informed decisions on lifestyle guidelines and treatment protocols.