Abstract

Depression is a disabling illness for individual sufferers and has a large societal economic burden. Treatment is often inadequate with only 1/3 of patients achieving remission with pharmacotherapy. Repetitive transcranial magnetic stimulation (rTMS) is a treatment alternative for pharmacotherapy non-responders, although remission is also difficult to achieve with rTMS. The antidepressant effect of rTMS was believed to result from plasticity of the left dorsolateral prefrontal cortex, the commonly used target site. However, recent research from my lab has shown that the subgenual anterior cingulate cortex (sgACC), downstream from the dorsolateral prefrontal cortex and inaccessible to direct stimulation, is functionally modulated by rTMS. This result is consistent with the antidepressant effect of targeting the sgACC with deep brain stimulation. Additionally, TMS modulates the level of gamma-aminobutyric acid (GABA) in the medial prefrontal cortex, an effect that correlates with treatment response. I will discuss the implications of these findings for understanding the antidepressant mechanisms of TMS and for developing predictive biomarkers and biomarkers of treatment response.