

Diffuse axonal injury influences the effect of brain stimulation on cognitive function after Traumatic Brain Injury

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Non-invasive brain stimulation has been widely investigated as a potential treatment for brain injury. However, the behavioural effects of brain stimulation are very variable, for reasons that are poorly understood. This is a particular challenge for traumatic brain injury, where patterns of damage and their clinical effects are heterogenous. Here we test the hypothesis that the response to transcranial direct current stimulation following traumatic brain injury is dependent on white matter damage within the stimulated network.

We used a novel simultaneous stimulation-MRI protocol applying anodal, cathodal and sham stimulation to 24 healthy and 35 moderate/severe traumatic brain injury patients. Stimulation was applied to the right inferior frontal gyrus/anterior insula node of the Salience Network, which was targeted because our previous work had shown its importance to executive function. Stimulation was applied during performance of the Stop Signal Task, which assesses response inhibition, a key component of executive function. Structural MRI was used to assess the extent of brain injury, including diffusion MRI assessment of diffuse axonal injury. Functional MRI, which was simultaneously acquired to delivery of stimulation, assessed the effects of stimulation on cognitive network function. Anodal stimulation improved response inhibition in control participants, an effect that was not observed in the patient group. The extent of diffuse axonal injury within the Salience Network strongly influenced the behavioural response to stimulation. Increasing damage to the tract connecting the stimulated right inferior frontal gyrus/anterior insula to the rest of the SN was associated with reduced beneficial effects of stimulation. In addition, anodal stimulation normalised Default Mode Network activation in patients with poor response inhibition, suggesting that stimulation modulates communication between the networks involved in supporting cognitive control. These results demonstrate an important principle: that white matter structure of the connections within a stimulated brain network influences the behavioural response to stimulation. This suggests that a personalised approach to non-invasive brain stimulation is likely to be necessary, with structural integrity of the targeted brain networks an important criteria for patient selection and an individualised approach to the selection of stimulation parameters.