

Supplementary motor area regulation training using fMRI neurofeedback for Tourette Syndrome

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Introduction

Tourette Syndrome (TS) is a neurodevelopmental disorder characterized by chronic tics. Although evidence-based treatments are available, a significant proportion of patients do not respond, and new treatment options are needed. Dysfunction in cortico-striato-thalamo-cortical loops has been hypothesized to underlie TS. A component region in these loops of particular interest is the supplementary motor area (SMA). The SMA has been reported to be more active in patients with TS during time periods with more frequent tics¹ and to have elevated activity prior to tics.²⁻⁴ Furthermore, electrical stimulation of this region has been shown to induce involuntary movements or urges to make movement, mirroring the phenomenology of TS symptoms.⁵ Therefore, we reasoned the SMA was a promising candidate region to target with neurofeedback (NF). Our group developed an rt-fMRI NF paradigm training TS patients to control activity in their SMA. In a small, crossover, double-blind clinical trial, we compared the effects of this NF intervention to a sham control intervention.⁶ Clinically meaningful symptom improvements were seen during NF. These symptom improvements were significantly greater than in the sham comparison condition. Furthermore, measures of control over the SMA during the feedback runs were significantly greater during NF than during sham. Our current trial seeks to confirm the efficacy of this intervention in a larger sample and against a different control condition.

Methods

This is a randomized, controlled, double blind clinical trial. Our study aims to recruit 60 participants aged between 10 and 16 who meet the criterion for either TS or chronic tic disorder. Any comorbidities that could impair learning or unwillingness to keep the medication / treatment stable are exclusionary. Each participant undergoes three sessions of neurofeedback, each consisting of six 5-minute runs. Those randomized to the experimental group receive feedback based on their personalized region of interest (ROI) in the SMA which is identified using the localizer task where participants imitate their most troublesome tics. The control participants receive the feedback from a region of BA19 that is minimally connected to their SMA ROI. To encourage engagement, the protocol includes performance based compensation during the neurofeedback runs where the payment depends on how well they control the feedback signal. Primary clinical measure is change in tic severity as assessed by the Yale Global Tic Symptom Severity Scale (YGTSS). A mixed-effects model will be used to ascertain change using baseline, post-NF, 2 week and one month follow up time points. The primary mechanistic measure is change in ability to control SMA, defined as up-regulation versus down-regulation signal contrast during neurofeedback compared to baseline (no-feedback) control task runs. Secondary mechanistic measures include change in functional connectivity between the personalized SMA ROI and the striatal targets identified in prior work, and, association between change in SMA-striatal connectivity and change in tic severity⁷.

Concluding remark

This registered clinical trial is currently ongoing (NCT05558566), with recruitment expected to be completed before the meeting. The results and their clinical implications will be shared at the meeting.

References

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