Clinicaltrials.gov ID 43421

Title: Rapid Non-Invasive Brain Stimulation for OCD (oTMS)

Update 4/22/21

Published Results: Accelerated neuromodulation therapy for Obsessive-Compulsive Disorder. Williams NR, Sudheimer KD, Cole EJ, Varias AD, Goldstein-Piekarski AN, Stetz P, Lombardi A, Filippou-Frye M, van Roessel P, Anderson K, McCarthy EA, Wright B, Sandhu T, Menon S, Jo B, Koran L, Williams LM, Rodriguez CI. Brain Stimul. 2021 Mar-Apr;14(2):435-437. PubMed 33631349.

Study Protocol (see published results – citation above for further details)

Between 7/2018 and 7/2019, eligible participants were recruited from the community by advertisements and referrals. Eligibility included being age 18 to 80, meeting OCD DSM-5 criteria, with at least moderate symptoms (Yale-Brown Obsessive-Compulsive Scale [Y-BOCS] score ≥ 18), and having failed ≥ one prior adequate trial (using APA Guidelines' dose and duration definitions) of first-line OCD treatment (SRI or CBT). The Stanford Institutional Review Board approved the study, and all participants provided written informed consent. Participants who were already taking an SRI remained on a stable dose for ≥ 12 weeks before study entry. Exclusion criteria were: severe depression (Hamilton Depression Rating Scale [HDRS-17] > 20); age of OCD onset > 30 years; comorbid medical or psychiatric conditions making participation unsafe; or taking medications that increase cortical excitability, inhibit brain excitability, or create hazard with TMS. Subjects planning to commence CBT within 8 weeks before enrollment were also excluded. Independent raters administered the Y-BOCS (primary outcome measure) weekly for 4 weeks. Response was defined *a priori* as a ≥ 35% reduction in Y-BOCS score. The primary outcome was change in Y-BOCS score at Day 14.

Before beginning the accelerated cTBSmod protocol, each participant completed a neuroimaging session that included a resting sequence for determining a personalized frontal pole TMS target and task-based fMRI elicited by the Go/No-Go task (Supplementary Material). All scans were acquired using a 3-tesla GE Discovery MR750 scanner with a NOVA Medical 32-channel head coil and a 3x accelerated multi-band (simultaneous multi-slice) imaging sequence with a repetition time of 2 seconds.

The resting state fMRI sequence was acquired to generate each participant's personalized right frontal pole TMS target (Supplementary Material). The right frontal pole subunit showing greatest connectivity across all the ventral striatum subunits was selected as the stimulation target in each participant (target generation methods and commentaries are provided elsewhere).[5, 10]

Participants received 5 consecutive days of accelerated cTBSmod to the right frontal pole. Each cTBSmod session was comprised of 1800 pulses, delivered in a continuous train of 600 bursts. Each burst contained 3 pulses at 30 Hz, repeated at 6 Hz.[1] Ten sessions were applied per day (18,000 pulses/day, hourly) (90,000 total pulses) using a Magventure Magpro X100. Stimulation was delivered at 90% resting motor threshold (depth corrected). Localite Neuronavigation System was used to position the TMS coil over the individualized stimulation target.

Statistical Analysis Plan

Mann-Whitney nonparametric test with Y-BOCS change score as outcome was conducted to determine the group difference (responders vs nonresponders) in magnitude of change in left and right DLPFC activity, elicited during inhibitory control, from before to after treatment with the cTBSmod protocol. The Wilcoxon signed rank test (i.e., paired test) was used to determine within individual differences between left and right side of the DLPFC in cognitive control activation evoked by the No-Go condition of the Go/No-Go task. One participant was removed from the neuroimaging analysis due to excess motion.