A naturalistic trial comparing the efficacy of uni-and bi-lateral theta burst stimulation in treating major depression, a study protocol

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BACKGROUND

• Repetitive transcranial magnetic stimulation (rTMS) is recognized as a major treatment for major depressive disorder (MDD)[1].
• Technological advancements have led to theta burst stimulation (TBS), which reduces treatment time 15 fold, whilst maintaining clinical efficacy[2,3].
• It remains to be determined if TBS is more efficient when applied to one or both prefrontal hemispheres, i.e. unilateral, left dorsolateral prefrontal cortex (DLPFC) and bilateral, left and right DLPFC.
• Very few studies have investigated rTMS maintenance protocols.
• TMS and electroencephalography (TMS-EEG) can be used to track excitability changes following TBS[4,5].

OBJECTIVES

• Compare efficacy of bilateral and unilateral TBS.
• Investigate if baseline capacity for plasticity, assessed with TMS-EEG, is predictive of the clinical response to TBS.
• Compare efficacy of a fixed versus a flexible schedule of maintenance over 6 months.

METHOD

• Participants: 256, male and female, 18+ with primary MDD diagnosis.
• Main inclusion criteria: No symptom improvement after ≥ 1 but ≤ 7 adequate antidepressant trials in current depressive episode.
• Treatment: 5 days per week over 4 to 6 weeks with a Magpro X100 and active/sham 865 cooled-coil.
• Left DLPFC: standard intermittent TBS (iTBS), 80% AMT, 190 sec
• Right DLPFC: standard continuous TBS (cTBS), 80% AMT, 40 sec
• Double-blinded study design:
  • Unilateral = active iTBS followed by sham cTBS
  • Bilateral = active iTBS followed by active cTBS
• Main outcome measures: HRSD-17, MADRS
• Neurorunavation (Brainsight, Rogue Research inc.): Coordinates (x, y, z: +/-38, 44, 26)
• If response or remission is achieved, participants are randomized into either a fixed or flexible 6-month maintenance phase.

DATA ANALYSIS

• EEG data is analyzed using EEGLAB and Matlab (Mathworks Inc)
• Clinical scores and neurophysiological measures will be analyzed using two-way ANOVAs for repeated measures.
• Prediction of response is assessed using correlational analyses and logistic regression models.
• Categorical outcomes (response/remission rates) are examined using Chi-Squared tests.

REFERENCES


RELEVANCE AND IMPACT

• First study comparing unilateral and bilateral TBS in a largescale naturalistic setting.
• Could help elucidate the mechanisms of action of TBS in the DLPFC
• Researching predictors of response could be beneficial in establishing bespoke protocols for individual brain response, increase efficacy rates and save time and money.
• Establish optimal TMS maintenance schedules.