

ACCELERATED dTMS IN THE ELDERLY DEPRESSED: PRELIMINARY INSIGHTS ON SAFETY, TOLERABILITY AND APPLICABILITY

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Background: Following encouraging results of our (Dardenne et al. 2018) pilot study with Accelerated High Frequency repetitive Transcranial Magnetic Stimulation (TMS) using a figure of eight coil in the elderly depressed, we started a more adapted randomized control trial (ClinicalTrials.gov) for this specific population with use of the H1 helmet coil for accelerated deep TMS (adTMS).

Methods: At time point T0 subjects are randomized (1:1) to either 20 sessions of real adTMS or sham. The sessions are spread over four succeeding days (5 sessions daily) with a stimulation intensity of 120% of the subject's resting MT, at a frequency of 18 Hz. Each dTMS repetition includes 2-sec. pulse trains separated by 20-sec inter-train intervals. Patients receive 55 trains, for a total of 1980 pulses per session. This makes 9900 pulses/day, and in total 39600 pulses per treatment. After each adTMS (real or sham) day, patients score a Visual Analogue Scale (VAS) about feeling any inconvenience. If such is the case, they can report any possible side-effect as well. Participants are also assessed for treatment-related adverse events (AE) by questionnaire on each time point.

Results: None of the first participants included (3 female, 1 male) dropped-out. For adTMS the VAS for discomfort values were never elevated above 50 mm, and AE questionnaires reported only (n=2) transient headache (rated as 'almost not' and 'sometimes').

Conclusion: Our preliminary observations indicate that adTMS was well tolerated and was safe to be used in elderly depressed patients.

References:

1. *ClinicalTrials.gov Identifier: NCT04783103*
2. Dardenne A, Baeken C, Crunelle C, Bervoets C, Matthys F and Herremans S: Accelerated HF-rTMS in the Elderly Depressed : a Feasibility Study. *Brain Stimulation* 2018; 11:247-248

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TRANSLATING TMS-EEG METHODS INTO CLINICAL NEUROPSYCHIATRY: ILLUSTRATIVE CASE STUDIES

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Neuropsychiatric complaints are complex and varied, and often overlap across diagnostic entities. The underlying neurophysiologic signature of specific neuropsychiatric complaints can provide insights into the proximal substrate of a given patient's disability and suggest specific therapeutic targets and strategies. TMS-EEG provides a powerful approach to identify the neurophysiologic substrate of specific neuropsychiatric complaints and thus guide personalized therapeutics. I will show data from various clinical patients in whom TMS-EEG was used to identify bioelectrical features of their presenting and disabling complaints, and thus guide non-invasive brain stimulation treatment strategies. Single and paired pulse TMS, targeting DLPFC and M1 bilaterally, was used with concurrent EEG to map potential abnormalities in cortical excitability and inhibition balance, as well as TMS evoked response propagation patterns. These observations were used to inform and tailor noninvasive brain stimulation interventions for each patient. We report the clinical outcome of this approach and propose future directions to improve its clinical utility.

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PLACEBO AND (UN)SPECIFIC EFFECTS OF TMS

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Placebo effect is an inescapable element of nearly all treatment interventions used in health care. Nonetheless, some health conditions as well as some treatment interventions are more susceptible to its effects. In that sense, it has been repeatedly argued that a large portion of responses to various interventions used for the treatment of depressive disorder can be attributed to placebo effects. However, these portions vary significantly as expectations, formed around more or less subtle cues about care setting, change. Transcranial magnetic stimulation (hereinafter TMS) has some unique and rather distinct features when compared with other usual treatment interventions (as psychoactive medication, that is, antidepressants). The placebogenic effect TMS has been widely discussed, both in research and clinical context, however still without any kind of firm conclusions.

Here we present a series of cases in which response to TMS was unusual and unexpected. We use these outlier cases to map out and disentangle possible specific and unspecific effects that total treatment setting in general and TMS in particular yielded. Further on, practical issues and challenges related to controlling the placebo effects in care settings are discussed.

As placebo is inevitable, and we might add critical, part of treatment interventions within the realm of mental health, in care settings it should be carefully harvested, so that it serves our patients and us for better and not for the worse.

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