

SERT AVAILABILITY MODIFIED BY ACCELERATED HF-rTMS IN THE SUBGENUAL ANTERIOR CINGULATE CORTEX: A CANINE [¹¹C]-DASB POSITRON EMISSION TOMOGRAPHY STUDY

Yangfeng Xu^{1,2}, Mitchel Kappen¹, Kathelijne Peremans², Dimitri De Bundel³, Ann Van Eeckhaut³, Nick Van Laeken⁴, Filip De Vos⁴, Andre Dobbeleir², Jimmy H. Saunders² & Chris Baeken^{1,5,6}

¹Department of Head and Skin, Ghent Experimental Psychiatry (GHEP) lab, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium

²Department of Morphology, Imaging, Orthopedics, Rehabilitation and Nutrition, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium

³Department of Pharmaceutical Chemistry, Drug Analysis and Drug Information (FASC), Research Group Experimental Pharmacology (EFAR), Center for Neurosciences (C4N), Vrije Universiteit Brussel (VUB), Brussels, Belgium

⁴Laboratory of Radiopharmacy, Faculty of Pharmaceutical Sciences, Ghent University, Ghent, Belgium

⁵Department of Psychiatry, Universitair Ziekenhuis Brussel (UZ Brussel), Vrije Universiteit Brussel (VUB), Brussels, Belgium

⁶Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, the Netherlands

Background: Repetitive transcranial magnetic stimulation (rTMS) has been proven to be a useful tool for the treatment of several neuropsychiatric disorders by partly exerting the antidepressant effect through the serotonergic system. Accelerated high-frequency rTMS (aHF-rTMS) may have the potential to result in a similar but faster clinical improvement compared to the classical daily rTMS protocols. Given that delayed clinical responses have been reported, the neurobiological effects of accelerated paradigms remain to be elucidated. More, the optimal stimulation parameters need to be refined.

Hypothesis We hypothesized that [¹¹C]-DASB binding alterations occurred in the regions with high SERT density. In line with antidepressant intake, we expected SERT decreases, more pronounced with the 20-sessions as compared to the 5-sessions protocol. No influences on any of the measurements following sham protocol were expected.

Methods: 10 dogs were allocated to the 5-sessions active group, 8 dogs were in the 20-sessions active group, 4 dogs were in the 20-sessions sham group. All dogs underwent four [¹¹C]-DASB PET scans: baseline, 24 hours, 1 month, and 3 months after the last TMS session. A binding index (BI) was calculated for each region of interest (ROI) at each time point with the cerebellum (excluding the vermis) as the reference region.

Results: 5-sessions active protocol did not result in significant SERT BI changes at any time point. For the 20-sessions active protocol, one month after stimulation the SERT BI attenuated in the subgenual Anterior Cingulate Cortex (sgACC). No significant SERT BI changes were found after the 20-sessions sham protocol.

Conclusion: Our results suggest delayed decreased SERT binding by aHF-rTMS in the sgACC, a key region involved in the therapeutic response of antidepressant therapy after 20 sessions and not after 5 sessions of aHF-rTMS. These preliminary findings suggest that an intensified aHF-rTMS protocol may be preferred and that a similar working mechanism compared to pharmacotherapy may be the base of its treatment utility. Further research is needed to explore the exact pathways of the effects on the serotonergic system.

References:

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2. Taylor O, Van Laeken N, Polis I, Dockx R, Vlerick L, Dobbeleir A, et al.: Estimation of the optimal dosing regimen of escitalopram in dogs: A dose occupancy study with [¹¹C] DASB. *PLoS one* 2017; 12:e0179927

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

Dieter Zeeuws^{1,2}, Wietse Wiels^{1,3}, Sebastiaan Engelborghs^{1,3,4} & Chris Baeken^{1,2,5,6}

¹Center for Neurosciences (CAN), Vrije Universiteit Brussel (VUB), Brussels, Belgium

²Department of Psychiatry, Universitair Ziekenhuis Brussel, Brussels, Belgium

³Department of Neurology, Universitair Ziekenhuis Brussel, Brussels, Belgium

⁴Department of Biomedical Sciences, University of Antwerp, Antwerp, Belgium

⁵Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, the Netherlands

⁶Ghent Experimental Psychiatry (GHEP) Lab, Department of Psychiatry and Medical Psychology, Ghent University Hospital, Ghent University, Ghent, Belgium

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*
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