

EEG potentials evoked by deep brain stimulation in patients with treatment-resistant depression

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Introduction: There is growing pre-clinical and clinical evidence supporting deep brain stimulation (DBS) of the superolateral medial forebrain bundle (sIMFB) as a therapeutic option for neuropsychiatric disorders like major depression disorder and obsessive-compulsive disorder [1,2,3]. Typical stimulation occurs in the ventral mesencephalic tegmentum. Despite its benefits, the electrophysiological effects of sIMFB-DBS in the human brain remain to be characterized. Unravelling the *optimal* patient-specific stimulation parameters is a challenging task, and characterizing sIMFB-DBS effects on cortical regions and networks could contribute to the optimization of stimulation patterns in the future. This work presents the protocol to study EEG responses evoked by single sIMFB-DBS pulses and first results on two patients suffering from treatment-resistant depression with bilateral implants in the sIMFB.

Methods and Results: Therapeutic (130 Hz) DBS was discontinued at the beginning of the session. Patients were instructed to fixate their gaze on a cross and remain at rest during 2-min blocks. Several blocks were recorded during which different, patient-dependent, DBS stimulation conditions were applied. DBS was delivered in a 2Hz frequency. DBS-evoked responses were obtained by averaging the pre-processed and cleaned EEG signals (128-channel setup) time-locked to the stimulation artefact (per block, around 240 trials were obtained). Averaging was done separately per DBS condition (Fig.1 corresponds to the results of a single block for one participant). EEG source imaging was used to estimate the sources of specific DBS-evoked components, using patient-specific head models. These are interpreted in the light of patient-specific patterns of structural connectivity, and additionally on the patient-specific clinically relevant responses to DBS.

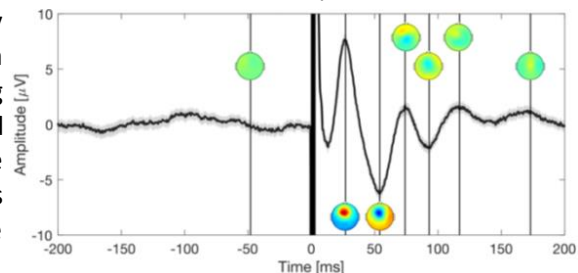


Figure 1. DBS-evoked cortical potential on channel FFC1 ($t = 0$ corresponds to stimulation artefact).

Discussion: We show for the first time that DBS-evoked potentials can be observed as a response to single pulses of stimulation in the sIMFB in patients with depression. Throughout the runtime of this study, with patient recruitment still ongoing, the test-retest reliability of the evoked-responses and their modulation based on different stimulation parameters will continue to be evaluated.

Significance: In the future, such a fast screening of DBS-evoked cortical potentials could become an objective method to measure the DBS target engagement, and thus guide clinicians in finding optimal stimulation parameters within a short period of time.

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References

- [1] Döbrössy, M. D. et al. Neuromodulation in psychiatric disorders: experimental and clinical evidence for reward and motivation network deep brain stimulation: focus on the medial forebrain bundle. *European Journal of Neuroscience* (2021).
- [2] Fenoy, A. J., Quevedo, J. & Soares, J. C. Deep brain stimulation of the 'medial forebrain bundle': a strategy to modulate the reward system and manage treatment-resistant depression. *Mol. Psychiatry* (2021).
- [3] Meyer, D. M. et al. Efficacy of superolateral medial forebrain bundle deep brain stimulation in obsessive-compulsive disorder. *Brain Stimul* **15**, 582–585 (2022).