 DOI: 10.3217/978-3-99161-050-2-169

DBS-evoked ECoG responses in depression: first characterization and possible implications for closed-loop applications

J. Pereira[1,2,3]*, M. Dold[2,1], B. Sajonz[1], M. Tangermann[2], V.A. Coenen[1,3,4]

[1]*Department of Stereotactic and Functional Neurosurgery, University Medical Center of Freiburg University, Germany;* [2]*Data-Driven NeuroTechnology Lab, Donders Institute for Brain, Cognition and Behaviour, Radboud University, The Netherlands;* [3]*BrainLinks-BrainTools, University of Freiburg, Germany;* [4]*Center for Deep Brain Stimulation, University of Freiburg, Germany*

*Neurozentrum, Breisacher Str. 64 – 79106 Freiburg, Germany. E-mail: joana.pereira@uniklinik-freiburg.de

Introduction: Deep brain stimulation (DBS) of the superolateral medial forebrain bundle (slMFB) has shown promising results in the treatment of patients with otherwise treatment-resistant major depression disorder (MDD) and patients with obsessive-compulsive disorder [1]. Inspired by DBS research in Parkinson's disease, for which DBS-evoked cortical responses are seen as candidate biomarkers for closed-loop DBS, we investigate for the first time the cortical responses of slMFB-DBS using ECoG.

Material, Methods and Results: During the implantation of two therapeutic bilateral slMFB-DBS leads, four patients with MDD additionally received a unilateral and epidural 4-channel ECoG strip placed towards the prefrontal cortex to ideally cover BA8. The ECoG strip was removed after four days. During the measurements on the ward, our aim was to screen several 2Hz-DBS parameters (stimulation channels, pulse width, and amplitude) over a series of 90-120 seconds runs during which the patients remained at rest. Due to two medical complications unrelated to our protocol, the measurements in two patients (P01 and P03) did not result in a comprehensive screening of DBS parameters. For the parameters screened, no clear evoked responses were observed. For P02, a comprehensive screening was possible, but no clear evoked response was visible. Interestingly, we found a fast and early (~2-10 ms) oculomotor response, measured via electrooculography, time-locked to the DBS pulses, despite the patient not reporting any side-effects at the screened DBS parameters. For P04, a very comprehensive screening was possible (Day 1: 11 runs, Day 2: 16 runs, Day 3: 25 runs). Consistent slMFB-DBS-evoked responses, distinct wr.t. timing (peak around 25 – 30 ms) and morphology from the oculomotor responses, were observed along a range of DBS parameters. These were modulated by the stimulation parameters, and stronger for the ECoG channels covering pre-frontal sites. Fig. 1 exemplifies the responses for P04 on ECoG01 when stimulating the left slMFB.

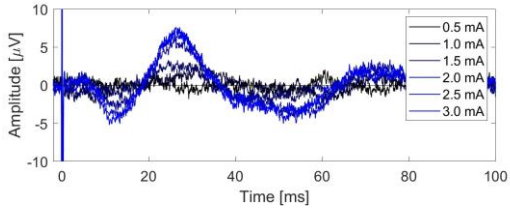

Figure 1: *slMFB-DBS evoked responses at ECoG01 for P04, day 3, for different amplitudes. Stimulation channel: 1, return channels 2-3-4, pulse width: 60 μs, frequency: 2 Hz (t = 0 shows stimulation artefact).*

Conclusion: Our first results indicate that it is possible to measure DBS-evoked responses to slMFB-DBS, although only one patient out of four displayed a clear response, replicable over 3 days of measurements. Our measurements also highlight the particular issue of side-effects related with slMFB-DBS (co-activation of oculomotor nerve fibers) which can affect the outcome of the electrophysiology analysis, particularly if these side-effects are too subtle to be noticed by the patient. In the future, DBS-evoked responses could help guiding clinicians in the selection of optimal slMFB-DBS parameters and eventually be a candidate biomarker for a closed-loop DBS setting in MDD.

Acknowledgments: Work funded by the DFG Walter Benjamin Programme (510112977). Measurements were performed with Dareplane [2], a software platform supported by the Dutch Brain Foundation.

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] Dold, Matthias, et al. "Dareplane: A modular open-source software platform for BCI research with application in closed-loop deep brain stimulation." *arXiv preprint arXiv:2408.01242* (2024).

 Published by Verlag der Technischen Universität Graz