INTRODUCTION
Deep brain stimulation (DBS) is currently being investigated as a potential therapy for treatment-resistant depression. To date, a promising target for DBS as therapy is the subcallosal cingulate gyrus or medial prefrontal cortex (mPFC), with approximately 60% of patients being characterized as responders. Despite the encouraging findings, the long-term stimulation (LTS) effects on anxiety-like behaviour have not been extensively investigated. In the present study, we report on the effects of acute and long-term bilateral mPFC DBS tested across different paradigms of anxiety-like behaviours. We hypothesized that LTS would exert its therapeutic effects by altering the dysfunctional neural activity leading to normal functional brain circuits.

METHODS
In acute stimulation, rats with mPFC electrodes were stimulated at 50, 100, 200, or 400 μA, 100 μs of pulse width, and either 100 Hz (high frequency stimulation; HFS) or 10 Hz (low frequency stimulation; LFS). Rats were then tested in the Elevated-Plus Maze (EPM) (I), and the Social Interaction setup (II).

RESULTS & DISCUSSION
The most effective stimulation parameter in the bilateral mPFC DBS of acute experiments was used for LTS experiments. LTS was conducted by daily 1h stimulation for 14 days. Rats were then tested without DBS (E, F) in the EPM and the Light-Dark Box (III), and with 1h DBS (G, H) in the Home-cage Emergence Test and Open-Field Test (IV).

CONCLUSION
- The effects of mPFC DBS in the anxiety tasks were dependent on current intensity and stimulation frequency.
- Acute HFS at 200 μA produced anxiolytic effect and increased number of social interaction behaviour.
- LTS with 1h DBS prior to testing induced a clear anxiolytic-like response, while LTS without DBS showed no significant difference, indicating that constant stimulation is necessary to maintain an anxiolytic condition.

Project Title: Interaction of Epigenetic Regulation and Antidepressant Effects by Medial Prefrontal Cortex Stimulation
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