Deep Brain Stimulation induced changes in monoaminergic neurotransmission and regional cerebral blood flow

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Denmark

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Deep Brain Stimulation induced changes in monoaminergic neurotransmission and regional cerebral blood flow

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Research Abstract
Deep Brain Stimulation (DBS) is a surgical treatment used in medically intractable Parkinson’s disease (PD) and DBS has potential to treat, e.g., depression and addiction. Whereas the therapeutic effect of DBS is well established the mechanism underlying its effect is, however, still unclear. Although research initially focused on DBS effects on the dopaminergic degeneration, attention is now directed also to changes in other brain monoamine systems,

particularly the serotonin (5-HT) system. Given that up to 25% of DBS-treated PD patients experience affective side effects this is very relevant. Positron emission tomography (PET), when used with appropriate radioligands, can non-invasively generate information about changes in 5-HT levels in the entire brain. Studies in non-human primates suggest that two novel PET radioligands, the 5-HT1B receptor radioligand 11C-AZ10419369 and the 5-HT2A receptor agonist 11C-Cimbi36, are sensitive to endogenous 5-HT release in the brain. These radiotracers will be used to investigate the regional changes in 5-HT release in response to the DBS electrode being turned on or off. We here propose, in the pig, first to calibrate the brain PET-signal by measurements of 5-HT levels and microdialysis under various pharmacological challenges. Next, with simultaneous MR-PET we will investigate the effects on 5-HT and brain network with DBS electrode placement in three separate brain regions of relevance for DBS therapy. Finally, we will investigate DBS-operated PD patients to map the changes in 5-HT in response to the DBS electrode being turned on or off and relate that to associated changes in mood. Understanding the effects of DBS on relevant brain targets may contribute to improve medical therapy of, e.g., depression or substance abuse and support the transition of DBS-treatment to patients with such disorders.

Further information available at:

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