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Cognitive effects of Deep Brain Stimulation

Focus on caudal Zona Incerta for Essential Tremor and Parkinson´s Disease, and on Bed Nucleus of Stria Terminalis for Obsessive Compulsive Disorder

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Hörsal D, Nio trappor, Norrlands Universitetssjukhus, fredagen den 3 mars, kl. 09:00.

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Abstract
The aim of this thesis was to evaluate the cognitive effects of DBS in a new target, the caudal Zona incerta (cZi), which has shown promising results in patients with both Parkinson's Disease (PD) and Essential Tremor (ET). Given that this is a novel target, the effects on cognition were lacking in the literature. In the same manner, the cognitive effects in patients with Obsessive-Compulsive Disorder (OCD) receiving DBS in the Bed Nucleus of Stria Terminalis (BNST) lacked long-term follow-up.

The main findings from the studies included in this thesis, suggest that DBS in the cZi in patients with PD and ET, and in the BNST in patients with OCD, does not generate any major cognitive effects and can be considered safe from a cognitive perspective. However, subtle effects involving aspects of executive function may be present following cZi DBS in patients with PD. cZi DBS in patients with ET generated fewer cognitive effects, including a decrease in semantic verbal fluency 12 months after DBS in the cZi. fMRI results evaluating the effects of cZi DBS on brain activity during a working memory task, did not show any significant changes when DBS was ON or OFF. This study also revealed a significant Task-x-DBS interaction, with faster response times during DBS ON relative to DBS OFF for the more cognitively demanding "manipulation" task. In OCD patients with BNST DBS, improved results on the Color-Word Inhibition/switching subtest were found, indicating a possible improvement in cognitive flexibility. However, there was a decrease of performance in visuo-spatial learning at 12 months after surgery.

The studies in patients with PD and ET were the first to report comprehensive neuropsychological data regarding cZi DBS. The fMRI study was the first in patients with ET treated with cZi DBS, focusing on cognitive effects during a working memory task in on/off DBS conditions. The OCD study was the first to report long-term data on cognitive effects after BNST DBS. By showing that DBS in these targets does not produce any major cognitive side effects, valuable knowledge in terms of safety has been added. This will hopefully contribute to increased treatment options in DBS.

Keywords
Deep brain stimulation. Neuropsychology. Cognition. Parkinson's disease. Essential tremor. Obsessive-compulsive disorder. Caudal zona incerta. Bed nucleus of stria terminalis. Functional MRI.

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