DEEP BRAIN STIMULATION TARGETING THE CAUDAL ZONA INCERTA AS A TREATMENT FOR PARKINSONIAN AND ESSENTIAL TREMOR

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Akadémisk avhandling

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**Abstract**

**Background:** Deep brain stimulation (DBS) is used as a treatment for Parkinson's disease (PD) and Essential tremor (ET) when medications are insufficient. In the early 2000s, the posterior subthalamic area (PSA) was introduced as an alternative to other more established DBS-targets, and PSA-DBS showed good results on PD and ET. However, these were non-blinded, non-randomised, and mostly with short follow-up period. Different structures in the PSA, such as caudal zona incerta (cZi), have been targeted but an optimal target has not been established. Furthermore, there has been an increased interest in asleep DBS surgery but with a paucity of results of asleep surgery for ET as the DBS-target traditionally used for ET is not visible on magnetic resonance imaging.

**Aims:** To evaluate DBS targeting the cZi for PD in a blinded, randomised manner. To spatially map the effects of DBS within the PSA. To evaluate the long-term effects of cZi-DBS on PD tremor and ET. To analyse the outcome of awake and asleep cZi-DBS surgery for ET.

**Method:** The thesis is based on five studies. Bilateral cZi-DBS was compared to Best Medical Treatment for PD in a randomised blinded trial. The long-term effects of unilateral cZi-DBS on PD tremor were evaluated retrospectively. Prospectively collected data on cZi-DBS for ET were used to evaluate long-term effects and compare awake and asleep surgery. The effects of cZi-DBS were spatially mapped within the PSA using electric field simulations and contact location in relation to the STN.

**Results:** Bilateral cZi-DBS improved motor symptoms and quality of life in patients with PD in both blinded and unblinded evaluations with a pronounced effect on tremor and a modest on bradykinesia. The effects of unilateral cZi-DBS on PD tremor remained undiminished at a mean of five years after surgery. cZi-DBS significantly improved ET 10 years after surgery with a slight deterioration over time. Asleep surgery had similar effects and side effects as awake surgery for patients with ET. Electric field simulations did not reveal an optimal target but together with contact location analyses consistently found that the stimulation was concentrated in the PSA, overlapping the cZi and the cerebellothalamic tract. In addition, the stimulation volume and locations were unchanged over time.

**Conclusion:** DBS targeting the cZi reliably achieved a pronounced effect on PD tremor and ET up to at least five and ten years after surgery respectively. In addition, cZi-DBS had a modest effect on bradykinesia. Finally, targeting the cZi enabled asleep surgery with seemingly similar efficacy as awake surgery.

**Keywords**

Deep brain stimulation, parkinson’s disease, essential tremor, zona incerta, posterior subthalamic area, movement disorder, tremor