Impact of deep brain stimulation in the caudal zona incerta on voice tremor and speech in persons with essential tremor

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av filosofie/medicine doktorsexamen framläggs till offentligt försvar i Sal A, psykiatriska kliniken, målpunkt F, plan o, Norrlands universitetssjukhus, Fredagen den 31 januari, kl. 09:00.
Avhandlingen kommer att förvaras på engelska.

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Abstract

Objectives: Deep brain stimulation (DBS) is a symptomatic treatment for people with essential tremor (ET) who have unsatisfactory tremor relief with pharmaceutical treatment alone. A common symptom of ET is voice tremor, but only about 50% of patients with voice tremor get a satisfactory result with DBS. Moreover, stimulation-induced adverse effects on speech are often reported, especially with bilateral stimulation. In recent years, the caudal zona incerta (cZi) has been highlighted as a particularly efficient DBS-target for tremor; however, less is known about the effects of cZi-DBS on voice and speech. The aims of this thesis were to (i) describe how voice tremor and speech production are affected by habitual cZi-DBS optimized to treat the motor symptoms of ET, (ii) investigate how voice tremor and speech production are affected by unilateral cZi-stimulation at increasing amplitudes, with a particular focus on high-amplitude stimulation, and (iii) explore the extent to which patient characteristics and DBS related factors, such as electrode location and stimulation settings, influence the outcome.

Methods: This thesis comprises two different study protocols. Study I was a retrospective study of 19 patients with ET and voice tremor, and DBS effects on voice tremor were evaluated from clinical assessments made at baseline and 1, 3, and 5 years after surgery, respectively. Studies II-V included 37 persons with ET, and DBS effects on voice tremor and speech production were evaluated off- and on habitual stimulation, as well as in an experimental protocol with unilateral stimulation at increasing amplitudes (up to a maximum of 4.5V). Voice tremor (study II, III) was assessed by two listeners using the Visual Sort and Rate (VISOR) method. Speech intelligibility (study IV) was estimated from orthographic transcriptions of nonsense sentences made by two speech-language pathology students. Speech function, including articulation and voice quality (study V) were analysed in 14 participants and assessed by two speech-language pathologists using VISOR. Voice and speech outcomes following the experimental stimulation condition were evaluated in relation to the location of the active electrode contacts.

Results: Habitual cZi-DBS reduced voice tremor at all examinations and did not affect speech production on the group-level. By contrast, during unilateral high-amplitude stimulation, more negative effects on speech were noted, and the proportion of individuals with affected speech more than doubled at maximal amplitude stimulation compared with habitual cZi-DBS (40% compared to 17%). While most of these adverse effects were mild in general, a few participants exhibited more severe impairments of high-amplitude stimulation, especially on speech intelligibility and articulation. There were also cases in which high-amplitude stimulation worsened voice tremor or even induced the symptom. As for the contribution of electrode location, a deeper and more posterior stimulation origin were found to yield the most efficient voice tremor reduction, more medially located electrodes were associated with affected articulation, whereas deteriorated speech intelligibility was related to stimulation originating from a more superior location.

Conclusions: cZi-DBS is relatively safe in the sense that adverse effects on speech production are rarely seen during stimulation with the clinical settings. Furthermore, voice tremor can be expected to improve, both short- and long-term, although not always to such an extent that the symptom is alleviated completely. However, by increasing the stimulation amplitude beyond the clinical setting, one increases the risk of inducing unwanted speech-related effects and worsen voice tremor. Thus, it appears as though the challenge in the postoperative management of the DBS treatment lies in maintaining the therapeutic effect while still keeping the stimulation amplitude at a low level. The combined results of this thesis indicate that the best outcome for voice and speech might be achieved by stimulating the posterior-inferior-lateral part of the cZi.

Keywords

caudal zona incerta, deep brain stimulation, essential tremor, speech function, speech intelligibility, speech production, voice tremor

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