Deep brain stimulation in the caudal zona incerta in patients with essential tremor: effects on cognition 1 year after surgery

Johanna Philipson, MS,¹ Patric Blomstedt, MD, PhD,¹ Marwan Hariz, MD, PhD,^{1,2} and Marjan Jahanshahi, PhD^{2,3}

¹Department of Pharmacology and Clinical Neuroscience, Umeå University, Umeå, Sweden; ²Unit of Functional Neurosurgery, UCL Institute of Neurology, London, United Kingdom; and ³The Clinical Hospital of Chengdu Brain Science Institute, MOE Key Lab for Neuroinformation, University of Electronic Science and Technology of China, Chengdu, China

OBJECTIVE The ventral intermediate nucleus (VIM) of the thalamus is currently the established target in the use of deep brain stimulation (DBS) to treat essential tremor (ET). In recent years, the caudal zona incerta (cZi), a brain target commonly used during the lesional era, has been revived as the primary target in a number of DBS studies that show evidence of the efficacy of cZi targeting in DBS treatment for controlling the symptoms of ET. The authors sought to obtain comprehensive neuropsychological data and thoroughly investigate the cognitive effects of cZi targeting in patients with ET treated with DBS.

METHODS Twenty-six consecutive patients with ET who received DBS with cZi as the target at our department from December 2012 to February 2017 were included in this study. All patients were assessed using a comprehensive neuropsychological test battery covering the major cognitive domains both preoperatively and 12 months postoperatively.

RESULTS The results show no major adverse effects on patient performance on the tests of cognitive function other than a slight decline of semantic verbal fluency.

CONCLUSIONS This study indicates that the cZi is a safe target from a cognitive perspective in the treatment of ET with DBS.

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KEYWORDS zona incerta; essential tremor; deep brain stimulation; cognition; functional neurosurgery

STEREOTACTIC functional neurosurgery with lesional procedures was introduced in 1947.⁴¹ Although attempts at stimulation of the brain occurred earlier,^{7,21} the marking of a new starting point for deep brain stimulation (DBS) came with a report published in 1987,⁶ and since then DBS has revolutionized the treatment of movement disorders, in particular Parkinson's disease and essential tremor (ET).¹¹

In DBS, different brain structures are targeted depending on the symptoms of the patient. The ventral intermediate nucleus (VIM) of the thalamus is the established target for ET treatment.^{5,28,30,43} In recent years, several studies have, with promising results, revived the caudal zona incerta (cZi), a brain target often used during the lesional

era, for use with DBS treatment of ET.^{1,15,24,34,42} This target is situated below the VIM, between the red nucleus and the posteromedial border of the subthalamic nucleus (STN).^{8,13} There is increasing evidence of the efficacy of DBS with cZi as the primary target for controlling the symptoms of ET.^{7,18,36}

Cognitive deficits in patients with ET have received increasing attention during the last 2 decades.²⁶ There are now several reported studies showing executive difficulties and attention deficits in patients with ET.^{19,23,32,45} The severity of cognitive dysfunction is not necessarily correlated with ET disease severity. However, the same authors demonstrated an association between cortical volume loss and cognitive dysfunction in ET. Bilateral structural

ABBREVIATIONS BVMt-R = Brief Visuospatial Memory Test-Revised; CWIT = Color Word Interference Test; cZi = caudal zona incerta; DBS = deep brain stimulation; ET = essential tremor; ETRS = Essential Tremor Rating Scale; MCI = mild cognitive impairment; NART-SWE = Swedish version of the National Adult Reading Test; PASAT = Paced Auditory Serial Addition Test; STN = subthalamic nucleus; TMT = Trail Making Test; VIM = ventral intermediate nucleus; VL = ventrolateral nucleus; WAIS-IV = Wechsler Adult Intelligence Scale-IV.

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changes were noted in the cerebellum as well as in various cerebral regions. Gray matter volume loss was found in the medial frontal gyrus, anterior cingulate cortex, insula, and postcentral gyrus, all of which are important in high-level cognitive functions.⁴

There is also increasing interest regarding social cognition and theory of mind in relation to ET. In one study,⁴⁰ cognitive and affective theory of mind in ET patients were investigated. The results showed deficits in cognitive aspects of social cognition, i.e., when patients were asked to deduce and attribute mental states to others. The authors interpreted the results as a consequence of a neurodegenerative process involving a dysfunctional dorsolateral prefrontal cortex-cerebellum circuit. In contrast, the authors of another study found that facial emotion recognition was inversely correlated with tremor severity in ET patients and concluded that their observations needed further investigation to determine whether the deficits were caused by cortical dysfunction or were secondary to abnormal processing in cerebello-cortical loops.²

The cognitive effects of DBS treatment in ET have been investigated using a variety of neuropsychological tests in a number of studies (see Table 1 for a summary). For thalamic (VIM) DBS treatment in patients with ET, some studies have shown a slight cognitive improvement in certain cognitive domains and also postoperative cognitive decline in verbal fluency.^{14,16,33,44} In one reported case the authors also found declines in verbal fluency and verbal recall in a patient treated with bilateral VIM stimulation. However, these declines were only found with stimulation turned off.³³ Some reported studies have found no cognitive change related to DBS in the thalamic area,^{22,27} while others have shown that low-frequency stimulation of the ventrolateral nucleus (VL) has less impact on phonemic and semantic fluency than high-frequency stimulation.³⁵ In all of the studies we have reviewed, the authors concluded that thalamic stimulation for ET is safe and does not affect higher cognitive processes.

To our knowledge, the cognitive effects of cZi as the target for DBS in ET have not previously been thoroughly reported. There has been a previous report of transient decrease of verbal fluency in patients with ET after cZi DBS,¹⁸ but no other cognitive measurements were included in that study. Here, we report comprehensive neuropsychological data on patients with ET with DBS in the cZi.

Methods

Study Design

All 26 patients (14 male, 25 right-handed) with ET who received DBS with cZi as target at our department from December 2012 to February 2017 were included in this study. Their mean ($\pm$ SD) age was 65.8 ± 6.66 years, with 12 ± 2.95 years of education. The average duration of ET was 30.6 ± 20.1 years. Patients with other preexisting conditions were excluded as well as patients who had already had DBS surgery in other targets and had additional electrodes implanted in the cZi during the inclusion period. Both unilateral ($n = 18$ left cZi, 2 right cZi) and bilateral ($n = 6$) procedures were included. In total, 26 patients consecutively treated with DBS at our center were included.

All patients were assessed at baseline and 12 months postoperatively according to the Essential Tremor Rating Scale (ETRS). This rating scale is a compound rating scale with separate sections for impairment, disability, and activities of daily living (ADL).¹⁷

In our sample, 3 patients fulfilled criteria for mild cognitive impairment (MCI). One patient received bilateral DBS and the other 2 patients received a unilateral DBS treatment procedure. We chose to use the MCI consensus criteria established by the Movement Disorder Society Task Force Guidelines.³¹ MCI was therefore considered to be present when impairments (test results a minimum of 1 SD below normal performance of nonimpaired individuals) were found on at least 2 tests within a single cognitive domain, with other domains unimpaired, or on at least 1 test in 2 or more cognitive domains.

Surgical Procedure

Stereotactic implantation of the DBS electrodes 3389 (Medtronic) was performed using the Leksell frame model G (Elekta Instruments). To identify and target the cZi (slightly posteromedial to the tail of the STN, at the axial level of the maximal diameter of the red nuclei), stereotactic T2-weighted 1.5-T MRI sequences were used (Fig. 1). Typically, the center of the deepest contact was targeted 4 mm below the anterior commissure–posterior commissure line and 12 mm lateral and 7.5 mm posterior to the midcommissural point. The same surgeon (P.B.) performed all surgical procedures.

Neuropsychological Evaluation

All patients were assessed by the same senior neuropsychologist (J.P.) preoperatively and 12 months postoperatively. The major cognitive domains were assessed by using the following tests.

Global Cognitive Function

Ravens colored matrices is a nonverbal measure of intelligence and global mental ability and nonverbal reasoning with a maximum score of 36. Results are presented in percentiles standardized based on age group.³⁷

A Swedish version of the National Adult Reading Test (NART-SWE) is designed to estimate premorbid IQ with the use of irregularly spelled and pronounced words. The patient is asked to read the words aloud and from the number of correct pronunciations an estimate of premorbidity was obtained. The results are presented as index scores, with a mean score of 100 ± 15 .³⁸

Memory

The Claeson-Dahls test is a test of verbal learning and memory (retention) administered in Swedish. Ten words are read out loud to the patient, and after a 15-second pause, the patient recalls as many as possible. This portion of the test is completed after a maximum of 10 repetitions, or when the patient has succeeded in recalling all 10 words correctly 2 consecutive times. After 30 minutes the patient is asked to again recall as many words as possible. In addition to delayed recall, a delayed recognition task is also administered. Four alternate versions are available for

TABLE 1. Summary of previous studies examining the effects of DBS of the VIM or the VL of the thalamus or the cZi on cognitive function in essential tremor

Authors & Year	Target	Sample Size, n	Time of Assessment	Neuropsychological Tests	Main Findings
Tröster et al., 1999	VIM	40	Baseline, 3 mos postop	MDRS; Brief Test of Attention; Stroop Neuropsychological Screening Test; Wisconsin Card Sorting Test; Cognitive Estimation Test; semantic (category) fluency; lexical (letter) fluency; Boston Naming Test; Grooved Pegboard Test; Benton Facial Recognition; Hooper Visual Organization Test; WMS-R; figural memory: CVLT	Significant improvements in MDRS (construction) ($p = 0.001$), visual span backward ($p = 0.01$), Hooper Visual Organization Test ($p = 0.01$), Grooved Pegboard Test ($p = 0.001$), CVLT (delayed word recognition) ($p = 0.05$), WMS-R (delayed prose recall) ($p = 0.01$)
Lucas et al., 2000	VIM	1	3 mos postop on/off	WMS-R: digit span & visual memory span; Controlled Oral Word Association Test; CWIT; TMT; Judgment of Line Orientation; Hopkins Verbal Learning Test-Revised; mood states profile; State-Trait Anxiety Inventory	Stimulation on vs off improved performance on measures of verbal fluency & verbal recall; verbal learning & delayed recognition hits not affected by stimulation; no statistical analysis
Fields et al., 2003	VIM	40	Baseline, 3 & 12 mos postop	MDRS; Brief Test of Attention; Stroop Neuropsychological Screening Test; Wisconsin Card Sorting Test; Cognitive Estimation Test; semantic (category) fluency; lexical (letter) fluency; Boston Naming Test; Grooved Pegboard Test; Benton Facial Recognition; Hooper Visual Organization Test; WMS-R; figural memory: CVLT	MDRS: 5 subtest scores combined changed significantly over time ($p < 0.001$); Hooper Visual Organization Test score improved significantly from baseline to 12 mos ($p < 0.01$); improvements (all $p < 0.01$) from baseline to 12 mos in CVLT immediate, short-delay, & long-delay recall & recognition hits, & in delayed recall of prose passages (WMS-R, logical memory); CVLT immediate recall ($p = 0.01$) also improved btwn 3 & 12 mos
Fytogoridis et al., 2013	cZi	17	Baseline, 3 days, & 12 mos postop; 10 pts w/ DBS on/off 12 mos postop	Verbal fluency: 4 1-min subtests, mention as many words as possible 1) beginning w/ A; 2) 5-letter words beginning w/ M; 3) professions names beginning w/ B; 4) 5-letter animal names beginning w/ S	Statistically significant tendency toward reduced verbal fluency ($p = 0.036$) after cZi DBS measured immediately postop; after 1 yr reduction diminished at group level & no longer statistically significant ($p = 0.268$)
Heber et al., 2013	VL	9	Baseline, 1- & 6-yr FU DBS on/off	"Leistungsprüfsystem"; Regensburg Wortflüssigkeits Test: vocabulary & reasoning; CWIT; WMS digit span forward; WAIS-R digit span backward; Corsi Block Tapping Test; German version of Rey Auditory Verbal Learning Test; TAP: alertness	Neither stereotactic surgery nor electrical stimulation affected higher cognitive processes such as verbal fluency, memory, & executive & intellectual functions at 1- or 6-yr FU. At both FU times, pt reaction time significantly slower w/ DBS off vs baseline & DBS on ($p = 0.04$) at 1 & 6 yrs ($p = 0.03$)
Pedrosa et al., 2014	VL	17 included, 14 fulfilled study protocol	No baseline; high (120–150 Hz) or low frequency (10 Hz), or DBS off	Forward & backward digit span; CWIT; phonemic & semantic verbal fluency	Phonemic & semantic fluency better during low- than high-frequency stimulation ($p = 0.012$ & $p = 0.045$). Digit span & Stroop tests unaffected
Ehlen et al., 2017	VIM	13 pts, 15 healthy controls	No baseline; on/off testing compared w/ matched control group	PANDA; Regensburg Wortflüssigkeits Test (verbal fluency measure)	Pts produced fewer words than healthy controls ($p = 0.008$); DBS on vs off aggravated this deficit by prolonging intervals btwn words w/in clusters, whereas switches remained unaffected; stimulation effect correlated w/ more anterior electrode positions

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Authors & Year	Target	Sample Size, n	Time of Assessment	Neuropsychological Tests	Main Findings
Klein et al., 2017	VIM	26 pts <70 (n = 12) or ≥70 yrs old (n = 14)	Baseline, 3–18 mos FU	MDRS; FAB	Cognitive parameters (MDRS score) significantly lower in elderly (p = 0.02) vs younger pts preop, no significant differ- ences post-DBS; FAB-measured cognitive frontal function showed no significant differences btwn 2 groups preop & post-DBS

CVLT = California Verbal Learning Test; FAB = frontal assessment battery; FU = follow-up; MDRS = Mattis Dementia Rating Scale; PANDA = Parkinson Neuropsychometric Dementia Assessment; pt = patient; TAP = Test for Attentional Performance; WMS-R = Wechsler Memory Scale-Revised.

FIG. 1. The target point in the cZi (red X), medial to the tail of the STN. Rn = red nucleus. Figure is available in color online only.

retest conditions. Results are calculated based on the number of words recalled and the number of times the list of words needs to be repeated. A low score indicates a faster learning curve.¹⁰

The Brief Visuospatial Memory Test–Revised (BVMTR) is a test for assessment of visual memory and comprises 6 alternate, equivalent forms (forms 1 through 6). Each form consists of 6 geometrical figures and 12 recognition items. The figures are presented for a 10-second period, after which the participant is asked to draw as many geometrical figures as possible, preferably matching the stimulus card with regard to placement and accuracy. The figures are presented 3 times to assess for short-term spatial memory and learning. After 30 minutes, delayed recall is tested, followed by a delayed recognition task during which the patient is presented with 12 figures, of which 6 are the original figures presented previously. Scores are given for accuracy and placement of the figures. Scores range from 0 to 12 in each of the 3 trials, and thus the maximum scores are 36 in the learning task and 12 in the recognition task. Higher scores indicate better visual memory.³

The Wechsler Adult Intelligence Scale–IV (WAIS-IV) digit span forward and digit span backward are tests of short-term verbal memory and verbal working memory. Digit sequences are presented to the patient starting with a length of 2 digits. Testing stops when the patient incorrectly reports both trials at 1 sequence length, or when all sequences are reported correctly (9 digits forward, 8 backward). Scores range from 0 to 18 forward and 0 to 16 backward, with higher scores indicating better performance. Raw scores are converted to age-corrected scaled scores, ranging from 1 to 19, with higher scores indicating better performance.⁴⁷

Executive Function

The Delis-Kaplan Executive Function System (D-KEFS) is a set of 9 standardized subtests for assessing higher-level cognitive functions, referred to as executive functions.¹²

The Trail Making Test (TMT), a D-KEFS subtest, is used to assess visual attention, behavioral regulation, task switching, and processing speed. The test consists of 5 individual subtests: 1) visual scanning, in which the participant marks all circles with the number “3” presented among both letters and other numbers; 2) number sequencing, in which the participant connects all numbers in successive order, ignoring any letters on the sheet; 3) letter sequencing, in which the participant connects letters in alphabetical order, ignoring any numbers on the sheet; 4) number-letter switching, in which the participant connects circles by switching between digits and letters (1-A-2-B-... etc.) in an alternating sequence; and 5) motor speed, in which as a measure of general motor speed the participant traces a dashed line connecting empty circles as fast as possible. Executive functions believed to be important for successful completion of this test are behavioral regulation, cognitive flexibility, and inhibition of perseverative responding. Scores are based on the time needed to complete the individual subtests. Results are transformed to scaled scores, ranging from 1 to 19, and a higher score indicates better performance.

Verbal Fluency

The verbal functioning test consisted of the following 3 tasks: phonemic fluency, semantic fluency, and switching category fluency. For each subtest, participants are given 1 minute to produce as many unique words as possible within a semantic category or starting with a given letter. The participant's score in each task is the number of unique correct words, excluding intrusion and repetition errors. In the switching category task the participant is asked to shift between semantic categories. Two alternative versions of the test are available. Raw scores are transformed into scaled scores ranging from 1 to 19, and a higher score indicates better performance.

The Stroop Color Word Interference Test (CWIT) includes the following 4 subtests: 1) color naming: naming the colors of colored rectangles; 2) word reading: reading the color words “red,” “green,” or “blue” printed in black ink; 3) color/word interference/inhibition: naming the color of color words printed in incongruent ink, for example, the word “red” printed in blue ink. These subtests assess the participant's ability to inhibit the more habitual response of reading the words to engage in the alternative response of naming the color of ink in which they are printed. 4) Inhibition switching: the same conditions as subtest 3, except when there is a box around the word, the participant has to read the word. Thus, subtest 4 requires both the inhibition of habitual responses and a switching response strategy across trials. The total time to complete each of the subtests and the number of self-corrected and uncorrected errors are recorded. Scores are transformed into scaled scores ranging from 1 to 19. A higher score indicates a better result.

Attention

The dichotic listening task is a test for studying brain asymmetry in auditory processing. Different sounds are sent to the participant's right and left ear at the same time. Three conditions are used to assess different kinds of cog-

nitive processes: 1) a nonforced condition normally used to determine speech lateralization, 2) a forced-right condition focusing on attention processes, and 3) a forced-left condition evaluating an executive cognitive control process. The results from the 2 forced-attention conditions are calculated as correct score percentages of the 30 dichotic stimuli presented separately to the right and left ear. The raw score is transformed to a t score ranging from < 20 to > 80. Interpretations of the t scores are made with respect to the condition being tested and indicate, for instance, the patient's ability to shift auditory attention.²⁵

The Paced Auditory Serial Addition Test (PASAT) assesses attention, working memory, and speed of auditory information processing, as well as calculation ability. To ensure standardization in the rate of stimulus presentation, the test is administered using a prerecorded audio tape. Every 3 seconds, single digits are presented and the patient is asked to add each new digit to the one presented directly prior to it and verbally report the sum. The correct answers given constitute the raw score, which is then transformed to percentiles and z scores. Higher scores indicate better performance.

Statistical Analysis

Statistical analyses of neuropsychological data were performed on normative scores corrected for age, sex, and/or education. These results are presented in Table 2. Since the data were not normally distributed, the Wilcoxon signed-rank test for paired samples was used to compare pre- and postoperative scores. A p value < 0.05 was considered statistically significant.

Results

The total ETRS score at baseline was 46.32 ± 14.08 . At 12 months follow-up, the total ETRS score on stimulation was 17.0 ± 9.48 ($p = 0.0001$) and off stimulation was 53.26 ± 15.57 ($p = 0.11$), indicating significant improvement of ET after surgery with stimulation on.

Measures of global cognition were only used preoperatively to ensure eligibility for the procedure. During the course of enrollment, we changed from using Ravens matrices to the NART-SWE due to the lack of updated normative data. The results of both tests show mean results within the normal range (Ravens matrices 56.75 ± 29.93 , NART-SWE 105.43 ± 9.99).

The pre- and postoperative patient results on the cognitive measures are shown in Table 2. The only cognitive test that showed a significant decline at the 12-month follow-up relative to the preoperative assessment was semantic verbal fluency ($p = 0.027$). None of the other measures of cognitive function showed any significant change from pre- to postoperative assessment. We found no differences in change in the cognitive measures from pre- to postoperative assessment when we compared the 6 patients with bilateral DBS with the 19 patients with unilateral DBS.

Discussion

ETRS scores show a marked improvement 12 months after cZi DBS, with a symptom reduction of almost 63%

TABLE 2. Scores on tests of cognitive function before (at baseline) and 12 months after surgery

Test	Baseline Score	12-Mo Score	p Value at Baseline vs 12 Mos
Memory			
Claeson-Dahls test (t score)			
Verbal learning	46.60 ± 9.99	44.72 ± 11.46	0.193
Retention	43.52 ± 11.90	47.52 ± 12.60	0.117
BVM-T-R (t score)			
Recall	49.68 ± 13.70	48.92 ± 9.22	0.987
Learning	49.36 ± 8.08	51.69 ± 9.16	0.344
Delayed recall	48.56 ± 15.11	49.92 ± 10.33	0.566
WAIS-IV digit span forward (scaled score)	9.69 ± 2.80	10.04 ± 3.13	0.710
Executive function			
TMT, shifting (scaled score)	10.52 ± 2.24	10.85 ± 2.66	0.135
TMT, shifting total errors (scaled score)	10.68 ± 1.25	10.38 ± 2.12	0.851
Verbal fluency			
Phonemic fluency (scaled score)	10.08 ± 3.63	9.27 ± 4.20	0.061
Semantic fluency (scaled score)	11.77 ± 4.09	10.46 ± 4.18	0.027*
Switching category fluency (scaled score)	10.27 ± 3.00	9.76 ± 3.09	0.210
Correct switches (scaled score)	10.62 ± 2.45	10.24 ± 2.65	0.385
CWIT (scaled score)			
Inhibition	9.73 ± 3.31	9.96 ± 3.01	0.675
Shifting	9.23 ± 3.33	9.64 ± 3.34	0.399
Inhibition errors	10.73 ± 2.39	10.88 ± 2.25	0.425
Shifting errors	9.50 ± 3.85	10.68 ± 3.17	0.059
Attention/working memory			
PASAT (z score)	-0.53 ± 0.78	-0.46 ± 0.93	0.553
Dichotic listening (t score)			
Nonforced RE	53.57 ± 10.61	50.75 ± 10.74	0.247
Nonforced LE	43.50 ± 6.71	42.75 ± 10.57	0.442
Forced right RE	51.64 ± 9.63	48.55 ± 11.01	0.152
Forced right LE	48.79 ± 7.51	46.18 ± 10.02	0.953
Forced left RE	58.07 ± 9.78	58.33 ± 7.99	0.919
Forced left LE	43.93 ± 6.96	42.08 ± 7.56	0.959
WAIS-IV digit span backward (scaled score)	9.46 ± 2.85	9.65 ± 3.60	0.569

LE = left ear; RE = right ear.

Values are presented as mean ± SD unless otherwise indicated.

* Statistically significant ($p < 0.05$).

compared to symptoms present at the presurgical baseline, results indicating an effective alleviation of motor symptoms. In this sample, we found no significant changes of main cognitive domains assessed (memory, executive function, attention) 12 months after cZi DBS compared to the presurgical baseline. When the group with MCI at baseline ($n = 3$) was evaluated postoperatively, the results were similar to those found in the non-MCI group.

The only significant adverse finding in the study patients was a decrease in semantic fluency postoperatively. Decline in verbal fluency has previously been reported following STN DBS and globus pallidus internus DBS in patients with Parkinson's disease, which has been described in a rather comprehensive meta review.⁴⁶ Decline in verbal fluency has also been reported after VIM DBS in ET, as

mentioned previously.^{14,16,33,44} So far there is no consensus as to what causes this deterioration. In line with the results from these earlier studies, we too noted a slight decrease in phonemic fluency, but this did not reach significance in our sample. Since we did not conduct repeated testing with stimulation on versus off, we cannot determine whether the decline in verbal fluency was caused by the surgical procedure or by the DBS. A previous study¹⁸ found that the detected effects on verbal fluency did not increase with stimulation of the cZi. Thus, rather than being a result of stimulation of the cZi itself, the changes observed on verbal fluency could have been the consequence of a secondary influence on other structures. Any eventual effect of the surgery (i.e., insertion of DBS lead, edema) should dissipate within 2–3 weeks after the surgery and would not

be present at the 12-month follow-up. All surgeries in the present study involved only 1 pass of the DBS electrode and were conducted without the use of microelectrode recording. However, this study cannot settle the issue of whether the surgical procedure or the stimulation caused the decline in verbal fluency in our sample.

Even though similar side effects have been reported in both VIM and STN DBS, we posit that cZi should be considered an important and perhaps, at times, superior target in the treatment of tremor in ET. Several VIM DBS studies have been found to have the active contacts situated below the VIM in the zona incerta, including the cZi. STN stimulation also seems to be most effective in the area between the upper STN (sensorimotor part) and the subthalamic area. Structures of importance in this area are STN projections, fields of Forel, and the zona incerta. It has also been pointed out that DBS in the cZi is more efficient than in the VIM, since the same amount of tremor reduction can be attained with lower energy consumption, hence prolonging battery life.^{9,20,39}

Our sample is relatively small. This may of course affect our results, especially when comparing the bilateral and unilateral cases, as well as the impact of MCI at baseline. We must therefore be careful when drawing conclusions from these small groups.

The experience we have obtained during the years of providing cZi DBS has had a great impact on the neuropsychological methods we now use at our unit. Since continuous performance tests measuring attention involve a motor component, such as the integrated visual and auditory (IVA) continuous performance tests (CPTs) CPT-3 or IVA++, we decided not to include these kinds of tests for the assessment of attention. However, the use of the PASAT has its own set of challenges, and it is well known that performance on this test is easily affected by stress.²⁹ The use of auditory-based tests for attention, such as the dichotic listening test, might at first seem to solve this problem, but the problem of hearing loss in an elderly population gives rise to a new set of challenges when interpreting the results. This can make the use of similar auditory-based tests practically impossible since the patients cannot distinguish various sounds due to a slight loss of hearing, which at times may not even be detected by the patient.

Conclusions

This study indicates that the cZi is a safe DBS target from a cognitive perspective. We did not find any major negative effects on the tests of cognitive function included, other than a slight decline of semantic verbal fluency.

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Disclosures

Dr. Blomstedt is a consultant for Abbott, Boston Scientific, and Medtronic and is a stockholder in Mithridaticum AB. Dr. Hariz has received honoraria and travel expenses from Medtronic and Boston Scientific for speaking at meetings.

Author Contributions

Conception and design: Philipson, Jahanshahi. Acquisition of data: Philipson. Analysis and interpretation of data: Philipson. Drafting the article: Philipson, Jahanshahi. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Philipson. Statistical analysis: Philipson. Study supervision: Blomstedt, Hariz, Jahanshahi. Primary surgeon: Blomstedt.

Correspondence

Johanna Philipson: University Hospital of Umeå, Sweden. johanna.philipsson@umu.se.