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Short communication

# Cognitive outcome of pallidal deep brain stimulation for primary cervical dystonia: One year follow up results of a prospective multicenter trial

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ABSTRACT

*Background:* Pallidal deep brain stimulation (DBS) is effective in alleviating motor symptoms of medication refractory cervical dystonia, but little is known about effects on cognitive functions.
*Methods:* As part of the first randomized, sham-controlled multicenter trial on DBS in medication-refractory primary cervical dystonia (ClinicalTrials.gov, number NCT00148889), a subgroup of 13 patients aged 39 to 69 underwent prospective neuropsychological long-term follow-up assessments. Various cognitive domains (memory, executive functions, attention, visual perception, mental arithmetic and verbal intelligence) were examined before and after 12 months of continuous DBS.
*Results:* Only the number of produced words in a verbal fluency task which included alternating categories decreased after stimulation ($p = 0.020$). All other cognitive domains remained unchanged.
*Conclusions:* These findings indicate that long-term pallidal DBS for the treatment of primary cervical dystonia seems to be safe regarding global cognitive functioning.


## 1. Introduction

Primary cervical dystonia, also called spasmodic torticollis, is the most common form of focal dystonia characterized by involuntary repetitive movements or abnormal postures of the head, associated with pain and depression [1,2]. The neuropsychological status of patients suffering from primary dystonia seems to be relatively intact, apart from selective deficits in semantic verbal fluency and attentional functions [3,4].

Chronic deep brain stimulation (DBS) of the globus pallidus pars interna (GPi) has proved to be effective at reducing symptoms of primary cervical dystonia refractory to medical treatment [5–7]. Potential neuropsychological side-effects of pallidal DBS for cervical dystonia have been mentioned only in two smaller case series using non-standardized measurements with tests differing from patient to patient [5,6]. These studies detected significant declines in verbal fluency in one patient and in verbal memory in another [6], or reported no relevant cognitive deteriorations [5].

As part of the first randomized, sham-controlled, multicenter trial on DBS in primary medication-refractory cervical dystonia [7] we evaluated the impact of chronic pallidal deep brain stimulation on neuropsychological outcome parameters during a one-year clinical follow-up.

## 2. Methods

### 2.1. Study design and patients

The complete description of the parent study can be found

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**Table 1**
Clinical characteristics, movement scores and medication of patients at baseline and 12 months after surgery.

| Case | Gender | Disease duration | Age | TWSTRS baseline (change to baseline[a] after 1 year of GPi-DBS) | | | | | | | | CDQ-24 | | BDI | | Medication | | Adverse events |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Severity | | Pain | | Disability | | Total | | Pre-Op | 1 year | Pre-Op | 1 year | Pre-Op | 1 year | |
| 1 | m | 6 | 39 | 21 | (85.7%) | 15 | (93.3%) | 14 | (100.0%) | 50 | (92.0%) | 42 | 1 | 13 | 0 | AG, Anti-Ch, Anti-D, Anti-SP, BZD | | |
| 2 | m | 7 | 42 | 17 | (47.1%) | 10 | (60.0%) | 8 | (100.0%) | 35 | (62.9%) | 23 | 13 | 2 | 0 | | | |
| 3 | m | 9 | 46 | 20 | (−10.0%) | 14 | (7.1%) | 12 | (−8.3%) | 46 | (−4.3%) | 50 | 32 | 9 | 5 | | | Hemiparesis or stroke (resolved)[b] |
| 4 | f | 16 | 44 | 20 | (45.0%) | 14 | (−7.1%) | 12 | (−8.3%) | 46 | (15.2%) | 58 | 63 | 16 | 15 | Anti-D, BZD, DA | AG, Anti-D, BZD | |
| 5 | m | 16 | 69 | 19 | (57.9%) | 12 | (−8.3%) | 15 | (6.7%) | 46 | (23.9%) | 27 | 27 | 3 | 7 | AG, Anti-D, Anti-SP, BZD, Hypnotic | | Exchange of extension cable[b] |
| 6 | f | 19 | 37 | 20 | (95.0%) | 14 | (50.0%) | 19 | (89.5%) | 53 | (81.1%) | 72 | 20 | 14 | 6 | Anti-SP, BZD | | |
| 7 | m | 13 | 67 | 22 | (54.5%) | 15 | (100.0%) | 20 | (70.0%) | 57 | (71.9%) | 78 | 20 | 9 | 4 | Anti-D, BZD | BZD | Tethering of extension cable[b] |
| 8 | f | 27 | 45 | 21 | (66.7%) | 7 | (100.0%) | 17 | (88.2%) | 45 | (80.0%) | 44 | 41 | 11 | 11 | AG | | |
| 9 | f | 17 | 66 | 26 | (34.6%) | 13 | (30.8%) | 23 | (52.2%) | 62 | (40.3%) | 57 | 50 | 4 | 9 | Anti-D, BZD | Anti-D, BZD | |
| 10 | f | 7 | 55 | 15 | (80.0%) | 6 | (100.0%) | 4 | (100.0%) | 25 | (88.0%) | 27 | 2 | 2 | 0 | | | Dyskinesia due to DBS |
| 11 | f | 34 | 69 | 23 | (13.0%) | 0 | (0.0%) | 13 | (61.5%) | 36 | (30.6%) | 49 | 48 | 11 | 14 | BZD | | Worsening of Dystonia due to DBS |
| 12 | m | 4 | 57 | 24 | (45.8%) | 13 | (53.8%) | 19 | (57.9%) | 56 | (51.8%) | 43 | 47 | 7 | 9 | Anti-D | | |
| 13 | f | 16 | 64 | 28 | (10.7%) | 10 | (100.0%) | 11 | (−9.1%) | 49 | (24.5%) | 67 | 70 | 16 | 16 | | | |
| | Mean | 14.69 | 53.85 | 21.2 | (48.2%) | 11.0 | (52.3%) | 14.4 | (53.9%) | 46.6 | (50.6%) | 49.0 | 33.4 | 9.0 | 7.4 | | | |
| | SD | 8.64 | 12.16 | 3.5 | (30.7) | 4.4 | (44.1) | 5.2 | (43.9) | 10.0 | (31.2) | 17.3 | 22.0 | 5.1 | 5.6 | | | |

Table 1 summarizes the characteristics of patients by basic demographic variables as well as their medication and their disease symptoms as measured by the Toronto Western Spasmodic Torticolli Rating Scale (TWSTRS), with higher scores indicating more severe symptoms. In addition, Beck Depression Inventory (BDI) and patients' disease-specific, health-related quality of life as measured with the Craniocervical Dystonia Questionnaire (CDQ-24) is presented, with lower scores indicating a higher quality of life.

[a] The percentage of change to baseline in the TWSTRS was calculated by: (Baseline Score - Follow-up Score)/Baseline Score. Accordingly, a change of 100% indicates a complete reduction of symptoms whereas a negative change indicates a worsening.

[b] A serious adverse event, an event which is life-threatening or requires or lengthens a stay in hospital. AG = Analgetic (as Morphine or Opioids); Anti-Ch = Anticholinergic (as Trihexyphenidyl or Biperiden); Anti-D = Antidepressant (as Mirtazapine or Trimipramine); Anti-SP = Anti-Spastics (as Baclofen); BZD = Benzodiazepine (as Clonazepam, Diazepam, Lorazepam, Nitrazepam or Tetrazepam); DA = dopaminergic drugs (L-Dopa and Dopa decarboxylase inhibitors); Hypnotic (as Zolpidem). m = male; f = female. SD = Standard Deviation.