HHS Public Access

Author manuscript

Mov Disord. Author manuscript; available in PMC 2022 January 14.

Published in final edited form as:

Mov Disord. 2014 April ; 29(4): 532–538. doi:10.1002/mds.25816.

Predictive factors of speech intelligibility following subthalamic nucleus stimulation in consecutive patients with Parkinson's disease

Elina Tripoliti, **Patricia Limousin**, **Tom Foltynie**, **Joseph Candelario**, **Iciar Aviles-Olmos**, **Marwan I Hariz**, **Ludvic Zrinzo**

UCL, Institute of Neurology, Sobell Department, Unit of Functional Neurosurgery, Queen Square, London, WC1N 3BG

National Hospital for Neurology and Neurosurgery, Queen Square, London, WC1N 3BG

Corresponding author: Elina Tripoliti, Unit of Functional Neurosurgery, UCL Institute of Neurology, box 146, Queen Square, London, WC1N 3BG, UK, phone: +44 2034488729, fax: +44 2034488642, e.tripoliti@ucl.ac.uk.

Authors' degrees and financial disclosure

Mr Ludvic Zrinzo MD PhD FRCS

Consultant Neurosurgeon and Senior Lecturer

LZ is partly funded by the Department of Health National Institute for Health Research Biomedical Research Centres funding scheme. The Unit of Functional Neurosurgery, UCL Institute of Neurology, is supported by the Sainsbury Monument Trust and Parkinson's Appeal for Deep Brain Stimulation. LZ has received travel expenses and honoraria from Medtronic and St Jude Medical for speaking at meetings.

T Foltynie, MB BS, PhD, MRCP

Consultant Neurologist and Senior Lecturer

Dr Foltynie has received grant support from Michael J Fox Foundation, Parkinson's UK, Cure Parkinson's Trust and Brain Research trust. He has received honoraria for speaking at meeting from Medtronic, St Jude Medical, Abbvie, Novartis and Genus Pharmaceuticals. He has sat on advisory boards for Oxford Biomedica and Abbvie Pharmaceuticals.

Professor Patricia Limousin MD, PhD

Consultant Neurologist and Professor in Clinical Neurology

Professor Limousin has received funding from Parkinson's UK, Medtronic and NIH. The Unit of Functional Neurosurgery, UCL Institute of Neurology, is supported by the Sainsbury Monument Trust and Parkinson's Appeal for Deep Brain Stimulation. Professor Limousin has received travel expenses and honoraria from Medtronic and St Jude Medical for speaking at meetings.

Dr Elina Tripoliti PhD, MRCSLT

Consultant Speech and Language Therapist,

Dr Tripoliti has received travel expenses from Medtronic.

Joseph Candelario BSc

Clinical Nurse Specialist in deep brain stimulation

Mr Candelario has received travel expenses from Medtronic and St Jude.

Dr Iciar Aviles-Olmos, MD PhD

Dr Aviles-Olmos has received travel expenses from Medtronic and St Jude.

Professor Marwan Hariz, MD, PhD

Simon Sainsbury Chair of Functional Neurosurgery

The unit of Functional Neurosurgery is supported by the Parkinson Appeal UK, and the Monument Trust. MH has received travel expenses and honoraria from Medtronic and St Jude Medical for speaking at meetings.

Authors' roles

Elina Tripoliti: conception, organisation and execution of the research project, design and execution of the statistical analysis and writing of the manuscript.

Tom Foltynie: execution, review and critique of the statistical analysis and review and critique of the manuscript.

Ludvic Zrinzo: review and critique of the manuscript.

Joseph Candelario: review and critique of the manuscript.

Iciar Aviles-Olmos: review and critique of the manuscript.

Marwan I. Hariz: review and critique of the manuscript.

Patricia Limousin: Conception of the research project and review and critique of the manuscript.

All co-authors have contributed to the patients' care and data collection.

Abstract

Background—Speech changes following bilateral subthalamic nucleus deep brain stimulation (STN-DBS) can be variable, with the majority of patients experiencing speech deterioration over time. The aim of this study was to describe the perceptual characteristics of speech following chronic STN-DBS and to analyse clinical and surgical factors that could predict speech change.

Method—Fifty-four consecutive patients (34 male, mean age 58.8±6.3years, mean disease duration 12.5±4.7years, mean levodopa equivalent 1556±671mg/day, UPDRS-III off-medication 48.1±17.9 range 20–89, UPDRS-III on medication 12.4±7.8 range 2–31) participated in this study. They were assessed before and at one year following surgery using the Assessment of Intelligibility for the Dysarthric Speech, the perceptual scale from Darley et al and the UPDRS-III.

Results—Speech intelligibility deteriorated on average by 14.4% (p=0.0006) after one year of STN-DBS when off-medication and by 12.3% (p=0.001) when on-medication. The effect on speech was not linked to age at surgery, unlike the effect on motor outcome. The most significant predictive factors for deterioration of speech intelligibility when patients were off-medication/on-stimulation were a lower pre-operative speech intelligibility on-medication, a longer disease duration and medially placed left hemisphere active electrode contact.

Conclusion—Speech change following STN-DBS is variable and multifactorial. Consistent pre-operative speech evaluation would help inform patients on the possible effects of surgery. Appropriate consideration of speech deficits might assist surgical targeting, particularly of the left electrode.

Keywords

speech; deep brain stimulation; Parkinson’s disease; predictive factors

Introduction

Speech in people with Parkinson’s disease (PD) can be adversely affected[1] at any stage of the disease process[2]. Medical and surgical treatments can have variable effect on speech[3,4], regardless of their beneficial effects on other motor symptoms of the disease.

Deep brain stimulation in the subthalamic nucleus (STN-DBS) is an effective treatment for patients with PD who develop motor fluctuations[5,6]. Clinical predictive factors for motor improvement have been clearly described. Patients with good pre-operative levodopa response tend to enjoy greater motor benefits[6,7,8,9]. Speech disturbance is a frequent and disabling side effect of stimulation[10,8,6,4,11]. In their qualitative study, Ahlberg and colleagues[12] discussed the need for patients to be better informed before surgery regarding possible side effects on speech, in order to facilitate adjustment to the new speech condition.

In our previous study[4] we investigated the relationship of clinical and surgical factors on speech response to stimulation. Of the surgical factors, contacts positioned medially in the left STN area, abutting on, or into the medial zona incerta and prelemniscal radiations (Raprl) had more detrimental effect on speech intelligibility than contacts within the MRI defined STN borders, confirming results from other studies[13,14]. We have also demonstrated

a strong relationship between amplitude of stimulation in the left hemisphere and poorer speech intelligibility[4,15]. However, studies on the predictive value of pre-operative clinical factors on speech after bilateral STN-DBS are lacking.

This study aimed to analyse in greater detail the perceptual speech changes following bilateral STN-DBS and the clinical and surgical factors that could predict speech change.

Patients and methods

Fifty-four consecutive patients who underwent bilateral STN DBS between 2005 and 2007 participated in this study (Table 1). They were assessed before and at one year following surgery.

The study was approved by the National Hospital for Neurology and Neurosurgery and the Institute of Neurology joint Research Ethics Committee (ref nr: 03/NI38).

Surgical procedure and contact localisation were performed as previously described[16,17,18,4]: The subthalamic target was visualized on preoperative stereotactic MRI at 1.5T using T2-weighted, fast-acquisition sequences in all patients. Postoperative stereotactic MR images using an identical sequence were imported into the planning software allowing 3-dimensional reconstruction of the images along the electrode trajectory (FrameLink, Medtronic). Stereotactic localization of the four electrode contacts was performed using a template superimposed on the electrode artifact[47]. The coordinates of each contact were transposed onto the preoperative stereotactic MRI. Two neurosurgeons (LZ, MH) blinded to the results of STN-DBS on speech, independently assessed and agreed on the anatomic position of each contact in relation to the visualized STN in the axial and coronal planes.

Patient evaluation

At baseline, patients were assessed after overnight withdrawal of medication (off-medication) and on-medication. One-year after bilateral STN-DBS patients were assessed off-medication/on-stimulation and on-medication/on-stimulation. Evaluations for each patient were carried out on the same day and in the same order. The on-medication assessment took place one hour after the administration of a suprathreshold dose of levodopa. Speech assessment consisted of the Assessment of Intelligibility for Dysarthric Speech (AIDS)[19] and a 60-second monologue.

Data analysis

A native English speaking Speech and Language Therapist, independent to the study and blinded to the conditions, rated the 22 sentences from AIDS using the scale of Darley and colleagues[20] scale (henceforth “DAB scale”). The 35 speech dimensions listed by Darley et al[20] were grouped under six clusters as described in Plowman-Prine and colleagues[21]. Each speech cluster was assessed on a seven-point interval scale, where one represented the greatest deviation from normal speech and seven represented normal speech. Mean speech ratings were calculated individually for each of the six speech clusters (articulation, respiration, resonance, phonation, prosody and rate) and collectively for the whole scale across medication and stimulation settings. All perceptual analysis was performed in the

same quiet speech laboratory with identical equipment so as to minimize variability across listening tasks. Assessment of overall speech intelligibility was always determined first in order to eliminate familiarity effects from rereviewing a given sample. After the speech intelligibility rating, each sample of the AIDS sentences was played up to six times so that the rater could listen to the sample once while rating the particular speech cluster with the specific speech dimensions. Speech intelligibility was assessed using the sentence task of the AIDS as previously described[19,4,15]. Sound pressure level (dB SPL) for the read sentences was extracted using the Computerised Speech Lab (Pentax, USA) software program[4]. Speaking rate was obtained by dividing the total number of words (220) by the duration of the sentence sample in minutes, as instructed in the AIDS manual[19] (p 11).

Statistical analysis

Primary outcomes were the change in speech intelligibility and perceptual rating (total of the DAB scale) from baseline to one-year off-medication (one-year off-medication/on-stimulation minus baseline off-medication), and on-medication (one-year on-medication/on-stimulation minus baseline on-medication). Secondary outcomes were the loudness measures and the subscores of the DAB scale (respiration, articulation, phonation, resonance, prosody and rate). To assess the impact of STN-DBS and medication on acoustic and perceptual data across times we used one-way ANOVA with post hoc tests using Bonferroni adjustment for multiple comparisons.

We then used a series of univariate regression models to identify pre-operative and operative factors, which had a significant impact on speech outcome. Pre-operative factors of interest were selected a priori, based on the literature, and included pre-operative speech intelligibility off- and on-medication, pre-operative UPDRS-III score off- and on-medication, disease duration and age at surgery. Pre-operative factors surviving the univariate analyses were then evaluated using multivariate regression models with left active contact as a covariate. The latter was identified as significant in speech change from previous analysis of the anatomical localisation and STN segment[4]. Interactions between the significant factors were sought. The outcome variables for the regression were the change in speech intelligibility (in %) after one year of STN-DBS (one year off-medication/on-stimulation minus baseline off-medication) and the change in the total perceptual scale (/42).

Statistical analysis was performed on SPSS-18 for Mac and Prism 5 for Mac (Graphpad software, Inc). STATA version 8.0 was used for all regression analyses.

Results

Effects of STN-DBS on speech intelligibility and perceptual speech features at one year (N=54)

Speech intelligibility deteriorated on average by 14.4% (p=0.0006) after one year of STN-DBS when the patients were off medication and by 12.7% (p=0.001) when the patients were on-medication. In terms of perceptual ratings the total of the DAB scale (with a score of 42 marking near normal speech) deteriorated by 5.1 points (p=0.001) off-medication and by 6 points (p=0.0001) on-medication. When comparing on-medication conditions, analysis

of the perceptual subscales scores showed a more significant decline in the subscale of articulation (mean decline of 1.2 points, p=0.0001), followed by prosody (mean decline of 1.18 points, p=0.001), phonation (mean decline of 1.01, p=0.0001), respiration (mean decline of 0.94, p=0.001), rate (0.90, p=0.001) and finally resonance (0.76, p=0.05). When comparing off-medication conditions, analysis of the perceptual subscales showed a more significant decline in the subscale of articulation (mean decline of 1.5 points, p=0.0001), followed by respiration (mean decline 0.92, p=0.001) and then rate of speech (mean decline 0.86, p=0.01) and resonance (mean decline 0.6, p=0.01). There was no significant decline for the subscales of prosody and phonation when off-medication (Table 2).

Predictive value of clinical and surgical data

The univariate regression analyses demonstrated that pre-operative speech performance, disease duration and UPDRS-III off-medication were each predictive of speech outcome after one year, whereas age was not predictive of any speech outcome (Table 3).

We then analysed the significant variables from the univariate regression with left hemisphere active contact position as a covariate using a multivariate regression (Table 4). The most significant predictive factors for deterioration of speech intelligibility when off-medication/on-stimulation were a poorer pre-operative speech intelligibility on-medication, a longer disease duration and medially placed left hemisphere active contact. Only the poor pre-operative speech off-medication was a significant factor for the speech intelligibility deterioration when on-medication/on-stimulation (Table 4).

Interactions were sought between ‘left contact location’, ‘pre-operative speech intelligibility’ and ‘duration of PD’, and the outcome variable ‘intelligibility change’, using multivariate regression models including the covariates listed in Table 4. A significant interaction was found between ‘left contact location’ and ‘duration of PD’ (p=0.002) but not between ‘left contact location’ and ‘pre-operative speech intelligibility’ (p=0.318). This was a consistent finding regardless of whether the outcome variable was intelligibility change in the “on-medication” or in the “off-medication” state.

This suggests that a location of the active electrode medial to the left STN is of particular importance, affecting speech negatively particularly in patients with a longer history of PD. Additionally, medially placed left brain electrodes have similar negative effects on speech outcome across all patients regardless of baseline speech intelligibility.

Discussion

Impact of electrode positioning on speech outcome

It is clear from the data analysis that electrode positioning in the left hemisphere is critically important for speech especially if the electrode is located medially to the STN. The critical role of electrode positioning has been recently emphasised[22, 23].

Our results on speech outcome are in agreement with the literature[13, 24, 25] namely that speech deterioration can be a significant side effect of bilateral STN stimulation when the left active contact is positioned medial to the STN, in the adjacent medial zona

incerta and the pre-lemniscal radiations (in between the red nucleus and the subthalamic nucleus). According to Morel[26] cerebellothalamic and pallidothalamic tracts correspond to Hassler's pre-lemniscal radiation ("ra.prl") and to the prerubral field or Field H of Forel. The involvement of the cerebellothalamic and pallidothalamic tracts in speech deterioration could explain the delayed onset of speech problems and the non-parkinsonian perceptual characteristics of speech after bilateral STN-DBS[27].

The significant role of the left rather than the right electrode contact on speech deterioration after bilateral[28] and unilateral[29] STN-DBS has been previously documented. Our data adds to the imaging evidence on the preponderance of the left hemisphere supporting speech articulation[30,31,32]. Sowman and colleagues[33] used Transcranial Magnetic Stimulation on the cortical M1 area and found left lateralisation for control of facial muscles during speech production (as opposed to non-speech isometric tasks), with greater excitability change in the left hemisphere.

Perceptual characteristics of speech following one year of STN-DBS

In our cohort of 54 consecutive patients we used the DAB scale to identify the perceptual changes on speech after one year of STN-DBS. In their original studies of 1969, Darley et al[20] analysed the speech of 32 non-medicated PD patients, using the same scale, and they described the characteristics of hypokinetic dysarthria (p 257).

In our study patients pre-operatively without medication seem to present with similar characteristics, i.e. more severely affected prosody, followed by phonation, and respiration (Table 2). However the pattern was different one-year after STN-DBS, pointing towards a treatment-specific rather than disease-progression effect. The characteristics that seemed to deteriorate more significantly when patients were off-medication/on-stimulation were articulation, followed by respiration (which reflects patients' subjective complaint of tighter breathing). There is no effect of stimulation alone on phonation and prosody. When in the on-medication/on-stimulation condition however, the pattern changes and the impact on articulation, prosody and phonation become significant. This reflects again the more severe overall deterioration of speech when on-medication/on-stimulation. Patients complained of imprecise articulation mainly affected by reduced lip and tongue movements ("thick tongue effect") and difficulty controlling voice volume, which is usually explosive but more often reduced and breathy. Voice often sounds more nasal and it becomes strained-strangled with prolonged speaking. These speech characteristics are more common in spastic-pseudobulbar dysarthria, following bilateral cortical lesions[34]. The possibility of electrical stimulation in the subthalamic nucleus area spreading and affecting other areas involved in speech motor control has been explored before mainly in relation to the corticobulbar[35] and cerebellothalamic[27] tracts debate. Whichever basal ganglia-cortical pathway used, our results imply a delayed cortical involvement: the cortical control of articulation is mediated primarily by the ventral half of the lateral sensorimotor (Rolandic) cortex (vSMC)[36]. There is increasing clinical and imaging evidence of the links between basal ganglia and SMC in the area of speech motor control[37,38,39].

Pre-operative predictive factors

One of the main aims of this study was to provide clinicians and patients with information on the possible effects of STN-DBS on their speech prior to surgery. Unlike motor outcome, the effect on speech was not linked to age at surgery or pre-operative motor scores[7,9,40,41,42]. It was however linked to disease duration and medially placed active contact in the left hemisphere. Disease duration has been linked to speech and swallowing deterioration: “In the vast majority of paralysis agitans disorders of speech become obvious as the disease advances”[43]. Merola and colleagues[42] reported that the median duration of disease at the time of onset of speech difficulties was 29.16 years. Contrarily Metter and Hanson[2] report no link between disease duration and degree of speech impairment. The reason why longer disease duration would be predictive of poorer speech outcome may also be related to the severity of speech problems pre-operatively. There is no longitudinal study on speech progression to provide more conclusive data.

The strongest clinical predictive factor for speech deterioration when off-medication / on-stimulation was the residual speech problem when on-medication pre-operatively. Thus, the better the speech on-medication pre-operatively, the better the outcome one year post, off-medication/on-stimulation. Or inversely, the fact that the severity of the residual parkinsonian speech score when on-medication was predictive of a poor post-operative outcome is probably explained by the presence of non-dopaminergic lesions within the basal ganglia[44] which would not respond to medication and thus stimulation. Additionally the only predictor of poor speech outcome at the on-medication/on-stimulation condition was the pre-operative off-medication speech. This could reflect the residual ability to compensate and mediate the combined effects of medication and stimulation on the motor control of speech following STN-DBS. The role of dopaminergic neuromodulation in normal speech motor control remains unknown and is based largely on indirect clinical evidence, from pathological processes such as PD, spasmodic dysphonia and stuttering. There is evidence of the critical role of dopamine on learned vocal expression in songbirds[45]. More recently Simonyan and colleagues[46] used PET, fMRI and DTI to investigate the extent of striatal dopamine release and its influence on the organisation of functional striatal speech networks during production of meaningful English sentences. They found that “in the associative striatum speech-induced dopamine release established a significant relationship with neural activity and influenced the left-hemispheric lateralization of striatal functional networks”. This is the first evidence for the neurochemical underpinnings of hemispheric dominance of human speech and language control. However the fact that parkinsonian speech does not respond to dopaminergic therapy or indeed to deep brain stimulation shows a different mechanism for speech motor control in PD.

Conclusion

To the best of our knowledge, this is the first study on a large consecutive cohort of patients to systematically examine the perceptual speech changes and the predictive value of clinical and surgical factors on speech response to bilateral STN-DBS. It confirms the clinical impression that compromised pre-operative speech is a predictor of poor outcome. Age at surgery was not predictive factor for speech outcome, but disease duration was. Additionally,

medially placed left hemisphere electrodes have equally negative effects on speech outcome across all patients regardless of baseline speech intelligibility.

There is a need however to further examine the large variability in speech response to STN-DBS and the so far unexplained delay in the onset of speech difficulties after bilateral STN DBS.

References

1. Logemann JA, Fisher HB, Boshes B, Blonsky ER. Frequency and co-occurrence of vocal tract dysfunctions in the speech of a large sample of Parkinson patients. J Speech Hear Disord. 1978; 43: 47–57. [PubMed: 633872]
2. Metter EJ, Hanson WR. Clinical and acoustical variability in hypokinetic dysarthria. J Commun Disord. 1986; 19: 347–366. [PubMed: 3490498]
3. Pinto S, Ozsancak, Tripoliti E, Thobois S, Limousin-Dowsey P, Auzou P. Treatments for dysarthria in Parkinson's disease. The Lancet Neurology. 2004; 3: 547–556. [PubMed: 15324723]
4. Tripoliti E, Zrinzo L, Martines-Torres I, et al. Effects of subthalamic stimulation on speech of consecutive patients with Parkinson disease. Neurology. 2011; 76: 80–86. [PubMed: 21068426]
5. Limousin P, Krack P, Pollak P. Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease. N Engl J Med. 1998; 339: 1105–1111. [PubMed: 9770557]
6. Kleiner-Fisman G, Fisman DN, Zamir O, et al. Subthalamic nucleus deep brain stimulation for parkinson's disease after successful pallidotomy: clinical and electrophysiological observations. Mov Disord. 2004; 19: 1209–1214. [PubMed: 15390008]
7. Welter ML, Houeto JL, Tezenas du MS. Clinical predictive factors of subthalamic stimulation in Parkinson's disease. Brain. 2002; 125: 575–583. [PubMed: 11872614]
8. Krack P, Batir A, Van BN, et al. Five-year follow-up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. N Engl J Med. 2003; 349: 1925–1934. [PubMed: 14614167]
9. Charles PD, Van BN, Krack P. Predictors of effective bilateral subthalamic nucleus stimulation for PD. Neurology. 2002; 59: 932–934. [PubMed: 12297584]
10. Hariz MI, Johansson F, Shamsgovara P, Johansson E, Hariz GM, Fagerlund M. Bilateral subthalamic nucleus stimulation in a parkinsonian patient with preoperative deficits in speech and cognition: persistent improvement in mobility but increased dependency: a case study. Mov Disord. 2000; 15: 136–139. [PubMed: 10634253]
11. Piboolnurak P, Lang AE, Lozano AM, Miyasaki JM, Sait-Cyr JA, Poon YY, Hutchison WD, Dostrovsky JO, Moro E. Levodopa response in long-term bilateral subthalamic stimulation for Parkinson's disease. Mov Disord. 2007; 22: 990–7. [PubMed: 17443692]
12. Ahlberg E, Laakso K, Hartelius L. Perceived changes in communication as an effect of STN surgery in Parkinson's disease: a qualitative interview study. Parkinson's dis. 2011; 2011: 540158. [PubMed: 21876840]
13. Plaha P, Ben-Shlomo Y, Patel NK, Gill SS. Stimulation of the caudal zona incerta is superior to stimulation of the subthalamic nucleus in improving contralateral parkinsonism. Brain. 2006; 129: 1732–1747. [PubMed: 16720681]
14. Paek SH, Han JH, Lee JY, Kim C, Jeon BS, Kim DG. Electrode position determined by fused images of preoperative and postoperative magnetic resonance imaging and surgical outcome after subthalamic nucleus deep brain stimulation. Neurosurgery. 2008; 63: 925–936. [PubMed: 19005383]
15. Tripoliti E, Zrinzo L, Martinez-Torres I, et al. Effects of contact location and voltage amplitude on speech and movement in bilateral subthalamic nucleus deep brain stimulation. Mov Disord. 2008; 23: 2377–283. [PubMed: 18785648]
16. Hariz MI, Krack P, Melvill R, et al. A quick and universal method for stereotactic visualization of the subthalamic nucleus before and after implantation of deep brain stimulation electrodes. Stereotact Funct Neurosurg. 2003; 80: 96–101. [PubMed: 14745216]

17. Holl EM, Petersen EA, FOltynie T, Martinez-Torres I, Limousin P, Hariz MI, Zrinzo L. Improving targeting in image-guided frame-based deep brain stimulation. Neurosurgery. 2010; 67: 437–447. [PubMed: 21099570]
18. Nakajima T, Zrinzo L, Foltynie T, Olmos IA, Taylor C, Hariz MI, Limousin P. MRI-guided subthalamic nucleus deep brain stimulation without micro-electrode recording: can we dispense with surgery under local anaesthesia? Stereotact Funct Neurosurg. 2011; 89: 318–325. [PubMed: 21921673]
19. Yorkston, KM, Beukelman, DR. Assessment of Intelligibility of Dysarthric Speech. CC Publications; Tigard Oregon: 1984.
20. Darley, FL, Aronson, AE, Brown, JR. Motor Speech Disorders. Philadelphia: W.B. Saunders Company; 1975.
21. Plowman-Prine EK, Okun MS, Sapienza CM, Shrivastav R, Fernandez HH, Foote KD, Ellis C, Rodriguez AD, Burkhead LM, Rosenbek JC. Perceptual characteristics of parkinsonian speech: a comparison of the pharmacological effects of levodopa across speech and non-speech motor systems. NeuroRehabilitation. 2009; 24: 131–44. [PubMed: 19339752]
22. Wodarg F, Herzog J, Reese R, et al. Stimulation site within the MRI-defined STN predicts postoperative motor outcome. Mov Disord. 2012; 27: 874–879. [PubMed: 22517070]
23. Witt K, Granert O, Daniels C, Volkmann j, falk D, van Eimeren T, Deuschl G. Relation of lead trajectory and electrode position to neuropsychological outcomes of subthalamic neurostimulation in Parkinson's disease: results from a randomised trial. Brain. 2013; 136: 2109–2119. [PubMed: 23801735]
24. Velasco F, Jimenez F, Perez ML. Electrical stimulation of the prelemniscal radiation in the treatment of Parkinson's disease: an old target revised with new techniques. Neurosurgery. 2001; 49: 293–306. [PubMed: 11504105]
25. Paek SH, Lee Jy, Kim HJ, et al. Electrode position and the clinical outcome after bilateral subthalamic nucleus stimulation. J Korean Med Sci. 2011; 26: 1344–1355. [PubMed: 22022189]
26. Morel, A. Stereotactic Atlas of the Human Thalamus and Basal Ganglia. NewYork, NY 10016: Informa Healthcare; 2007.
27. Astrom M, Tripoliti E, Hariz MI, Zrinzo l, Martinez-Torres I, Limousin P, Wardell K. Patient-specific model-based investigation of speech intelligibility and movement during deep brain stimulation. Stereotact Funct Neurosurg. 2010; 88: 224–33. [PubMed: 20460952]
28. Santens P, De Letter M, Van Borsel J, De Reuck J, Caemaert J. Lateralised effects of subthalamic nucleus stimulation on different aspects of speech in Parkinson's disease. Brain Lang. 2003; 87: 253–258. [PubMed: 14585294]
29. Wang E, Verhagen ML, Bakay R, Arzbaecher J, Bernard B. The effect of unilateral electrostimulation of the subthalamic nucleus on respiratory/phonatory subsystems of speech production in PD: a preliminary report. Clin Linguist Phon. 2003; 17: 283–289. [PubMed: 12945603]
30. Riecker A, Ackermann H, Wildgruber D, DOgil G, Grodd W. Opposite hemispheric lateralization effects during speaking and singing at motor cortex, insula and cerebellum. Neuroreport. 2000; 11: 1997–2000. [PubMed: 10884059]
31. Wildgruber D, Ackermann H, Grodd W. Differential contributions of motor cortex, basal ganglia, and cerebellum to speech motor control: effects of syllable repetition rate evaluated by fMRI. Neuroimage. 2001; 13: 101–109. [PubMed: 11133313]
32. Simonyan K, Ostuni J, Ludlow CL, Horwitz B. functional but not structural networks of the human laryngeal motor cortex show left hemispheric lateralization during syllable but not breathing production. J Neurosci. 2009; 29: 14912–14923. [PubMed: 19940187]
33. Sowman PF, flavel SC, McShane CL, Sakuma S, Miles TS, Nordstrom MA. Asymmetric activation of motor cortex controlling human anterior digastrics muscles during speech and target-directed jaw movements. J Neurophysiol. 2009; 102: 159–166. [PubMed: 19420123]
34. Duffy, JR. Motor Speech Disorders. Mosby; 2007.
35. Tommasi G, Krack P, Fraix V, Le Bas JF, Chabardes S, Benabid AL, Pollak P. Pyramidal tract side effects induced by deep brain stimulation of the subthalamic nucleus. J Neurol Neurosurg Psychiatry. 2008; 79: 813–819. [PubMed: 17928327]

36. Bouchard KE, Mesgarani N, Johnson K, Chang EF. Functional organization of human sensorimotor cortex for speech articulation. Nature. 2013; 495: 327–332. [PubMed: 23426266]
37. Watkins KE, Smith SM, Davis S, Howell P. Structural and functional abnormalities of the motor system in developmental stuttering. Brain. 2008; 131: 50–59. [PubMed: 17928317]
38. Simonyan K, Ludlow CL. Abnormal structure-function relationship in spasmodic dysphonia. Cereb Cortex. 2012; 22: 417–425. [PubMed: 21666131]
39. Riecker A, Mathiak K, Wildgruber D, Erb M, Hertrich I, Grodd W, Ackermann H. fMRI reveals two distinct cerebral networks subserving speech motor control. Neurology. 2005; 64: 700–706. [PubMed: 15728295]
40. Guehl D, Cuny E, Benazzouz A, et al. Side-effects of subthalamic stimulation in Parkinson's disease: clinical evolution and predictive factors. Eur J Neurol. 2006; 13: 963–971. [PubMed: 16930362]
41. Fasano A, Romito LM, Daniele A, Piano C, Zinno M, Bentivoglio AR, Albanese A. Motor and cognitive outcome in patients with Parkinson's disease 8 years after subthalamic implants. Brain. 2010; 13309: 2664–76.
42. Merola A, Zibetti M, Angrisano S, et al. Parkinson's disease progression at 30 years: a study of subthalamic deep brain stimulation patients. Brian. 2011; 134: 2074–2084.
43. Selby G. Cerebral atrophy in Parkinsonism. J Neurol Sci. 1968; 6: 517–59. [PubMed: 4885324]
44. Agid Y. Parkinson's disease: pathophysiology. Lancet. 1991; 337: 1321–1324. [PubMed: 1674304]
45. Simonyan K, Horwitz B, Jarvis E. Dopamine regulation of human speech and bird song: a critical review. Brain and Language. 2012; 122: 142–150. [PubMed: 22284300]
46. Simonyan K, Herscovitch P, Horwitz B. speech-induced striatal dopamine release is left lateralized and coupled to functional striatal circuits in healthy humans: A combined PET, fMRI and DTI study. Neuroimage. 2013; 70: l21–32.
47. Yelnik J, Damier P, Demeret S, Gervais D, Bardinet E, Bejjani B-P, et al. Localization of stimulating electrodes in patients with Parkinson disease by using a three-dimensional atlasmagnetic resonance imaging coregistration method. J Neurosurg. 2003; Jul; 99 (1) 89–99. [PubMed: 12854749]

Table 1

Patient characteristics (N=54)

Baseline patient characteristics	
Male/Female	34/20
Age mean ± SD (range)	58.8 ± 6.3 (42 to 69)
Disease duration mean ± SD (range)	12.5 ± 4.7 (6 to 25)
Levodopa equivalent daily dose (LEDD) (mg/day)	1556 ± 671
UPDRS-III off medication	48.1 ± 17.9 range 20–89
UPDRS-III on-medication	12.4 ± 7.8 range 2–31

Table 2

Changes in intelligibility (% of words understood) and perceptual speech characteristics (as per Darley, Aronson & Brown, 1975) in 54 consecutive PD patients following one year of bilateral STN-DBS (mean ± SD).

	Baseline off-medication	Baseline on-medication	one year off-medication/on-stimulation	one year on-medication/on-stimulation
Speech intelligibility	98% (4.3)	97% (7.7)	83.9% (28)	84.3% (26.6)
dB max reading	69.3 (6.9)	73.4 (7)	74.8 (6)	76.2 (6.5)
Rate (words per minute)	149.3 (26.8)	147 (26)	150.2 (36.3)	140.5 (37.9)
Total				
perceptual score (/42)	32.4 (4.6)	32.5 (5.2)	27.3 (8.8)	26.5 (8.9)
articulation (/7)	5.9 (0.8)	5.6 (1.3)	4.4 (1.9)	4.4 (1.9)
respiration (/7)	5 (1)	4.9 (1.1)	4.1 (1.6)	3.9 (1.7)
resonance (/7)	5.6 (1)	5.6 (0.8)	4.9 (1.6)	4.9 (1.3)
phonation (/7)	4.8 (1)	5.1 (1)	4.4 (1.5)	4.1 (1.6)
prosody (/7)	4.9 (1.5)	5.3 (1.4)	4.1 (1.8)	4.1 (2)
Rate control (/7)	6 (0.9)	5.8 (1.3)	5.2 (1.6)	4.9 (1.7)

Table 3

Univariate analysis of pre-operative clinical predictive factors on speech intelligibility change off- and on-medication and perceptual rating (DAB scale) change one year after STN-DBS (N=54).

Outcome Variable	*Predictive Variable*	*B-coefficient*	*P<*
Change in speech intelligibility AIDS pre-off to one year off/on	**AIDS pre-on**	−1.8	0.0001
	AIDS pre-off	−2.5	0.01
	UPDRS-III pre-on	0.75	0.23
	UPDRS-III pre-off	0.78	0.004
	Duration of PD	2.77	0.001
	Age at surgery	0.08	0.87
Change in speech intelligibility AIDS pre-on to one year on/on	AIDS pre-on	0.31	0.52
	AIDS pre-off	−3.99	0.0001
	UPDRS-III pre-on	0.68	0.24
	UPDRS-III pre-off	0.51	0.03
	Duration of PD	1.99	0.004
	Age at surgery	0.30	0.51
Change in DAB scale pre-off to one year off/on	**AIDS pre-on**	−0.43	0.001
	AIDS pre-off	−0.99	0.41
	UPDRS-III pre-on	0.23	0.18
	UPDRS-III pre-off	0.23	0.001
	Duration of PD	0.47	0.042
	Age at surgery	0.02	0.86
Change in DAB scale pre-on to one year on/on	AIDS pre-on	0.13	0.2
	AIDS pre-off	−0.94	0.0001
	UPDRS-III pre-on	0.32	0.025
	UPDRS-III pre-off	0.16	0.007
	Duration of PD	0.43	0.014
	Age at surgery	−0.05	0.63

Table 4

Multivariate regression of pre-operative clinical predictive factors with left electrode contact anatomical description (medial versus inside) as covariate, on speech intelligibility change off- and on- medication and perceptual rating (DAB scale) change one year after STN-DBS (N=54)

Outcome variable	Predictive variable	B-coefficient	P<
Change in speech intelligibility AIDS pre-off to one year off/on	**AIDS pre-on**	−1.73	0.001
	AIDS pre-off	−0.74	0.398
	UPDRS-III pre-on	−0.28	0.614
	UPDRS-III pre-off	0.00	0.990
	Duration of PD	2.35	0.002
	Left active contact position	9.25	0.006
Change in speech intelligibility AIDS pre-on to one year on/on	AIDS pre-on	0.67	0.147
	AIDS pre-off	−3.05	0.002
	UPDRS-III pre-on	−0.88	0.172
	UPDRS-III pre-off	0.29	0.360
	Duration of PD	1.33	0.060
	Left active contact position	6.65	0.063