Neuropsychological effects of bilateral STN stimulation in Parkinson disease

A controlled study

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Abstract—*Objective:* To evaluate the cognitive and behavioral effects of bilateral subthalamic nucleus (STN) stimulation in patients with Parkinson disease (PD). *Methods:* The authors included 103 patients; 99 patients were evaluated 6 months after surgery. A control group of 39 patients with PD was formed and 36 patients were evaluated 6 months later. At baseline and at follow-up we administered neuropsychological tests of language, memory, visuospatial function, mental speed, and executive functions. A depression rating scale, a quality of life scale, self and proxy ratings of memory and dysexecutive symptoms, and a neuropsychiatric interview were also administered. *Results:* Six months after surgery, the STN group showed a larger decline than the control group on measures of verbal fluency, color naming, selective attention, and verbal memory. Moreover, the STN group showed a decrease in positive affect, and an increase in emotional lability and cognitive complaints. On the other hand, the STN group showed an increase in quality of life and a slight decrease in depressive symptoms. Nine percent of the STN patients had psychiatric complications (vs 3% of controls). *Conclusions:* Bilateral subthalamic nucleus stimulation has an adverse effect on executive functions with implications for daily life of the patients and their relatives.

NEUROLOGY 2006;66:1830–1836

Bilateral subthalamic nucleus stimulation (STN) can reduce parkinsonian symptoms in patients with advanced Parkinson disease (PD).[1-3] However, studies on the neuropsychological effects of bilateral STN stimulation show inconsistent results.[4] The only controlled study[5] reported mildly affected attention and verbal fluency. A study with a large patient group[6] found that bilateral STN stimulation did not lead to global cognitive deterioration in the long term. Some smaller studies found little effect on cognition.[7,8] However, in older patients, a decrease of performance in memory, mental speed, and fluency was found.[9] Moreover, it was reported that STN stimulation can induce overall cognitive decline or behavior changes in some patients.[10]

Several other studies reported behavior changes,[11] with case studies on depression,[12,13] mania,[14,15] aggression,[16] pseudobulbar crying,[17] and mirthful laughter.[18]

In view of the paucity of controlled studies and the conflicting findings of the uncontrolled research into possible side effects of STN stimulation, we conducted a prospective, controlled, multicenter follow-up study. We determined the cognitive effects of bilateral STN stimulation after 6 months using a comprehensive neuropsychological battery. Possible behavioral changes were registered with scales that measure depression, dysexecutive problems, and other neuropsychiatric symptoms. Finally, the impact of bilateral STN stimulation on quality of life was taken into account.

Additional material related to this article can be found on the *Neurology* Web site. Go to www.neurology.org and scroll down the Table of Contents for the June 27 issue to find the title link for this article.

Methods. *Patients.* Twenty patients in the STN group have been previously described.[19] The other patients were recruited between June 2001 and June 2005 from three participating Dutch hospitals experienced in STN stimulation for PD. Eligible patients had idiopathic PD with an unequivocal reduction in off phase symptoms on levodopa, and despite optimal pharmacologic treatment at least one of the following symptoms: severe response fluctuations, dyskinesias, dystonia, tremor, or bradykinesia. Exclusion criteria were predominantly unilateral symptoms without severe response fluctuations, severe brain atrophy on CT or MRI scans, Hoehn and Yahr stage 4 or 5 in the best on phase, Dementia Rating Scale score of less than 120, psychosis or depression at inclusion, or surgical contraindications.

Alongside the STN group, we formed a control group of patients who had had idiopathic PD for more than 5 years. They

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Supported by a grant from the Prinses Beatrix Fonds and the Parkinson patiëntenvereniging.

Disclosure: J.D. Speelman acts as an independent consultant for Medtronic Ltd. (Minneapolis). He has received travel grants from Medtronic Ltd. For the other authors no financial interests or other potential conflicts are involved.

Received November 14, 2005. Accepted in final form April 17, 2006.

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were recruited from the outpatient clinic of the AMC and from two other hospitals in the region: the Kennemergasthuis in Haarlem and the Vrije Universiteit Medical Center. Exclusion criteria were identical to those of the STN group. The medical ethics committees of the participating hospitals approved the study.

Surgical procedure. Within 3 months after baseline assessment, the STN group underwent stereotactic surgery,[2] using ventriculography, MRI, or a CT scan to determine the position of the target structure. Microelectrode recording was used in 37 of the 100 patients. After macroelectrode test-stimulation a four contact electrode (model DBS-3389, Medtronic, Minneapolis) was implanted. The electrodes were connected to the implantable pulse generator (Itrel II, Soletra, or Kinetra, Medtronic, Minneapolis) under general anesthesia. We could not systematically perform MRI postoperatively, because this is not allowed in the Netherlands.

Assessments. Neuropsychological examination was completed in the mornings, while patients were at their optimal status. The examination was suspended whenever a patient indicated that he or she went into "off." A board-certified neuropsychologist or a supervised test technician administered the tests. Follow-up assessment was done 6 months after surgery for the STN group and 6 months after baseline for the control group. Neuropsychological protocol was identical for the experimental and the control group.

Standardized motor scoring was done at baseline and follow-up with Unified Parkinson's Disease Rating Scale (UPDRS) part three and Hoehn and Yahr staging for the experimental group in the on and off phases. For the control group, standardized on/off evaluations were not available. UPDRS part three and Hoehn and Yahr staging was done when patients indicated "on" phase.

Neuropsychological tests. We selected a battery of tests to evaluate cognitive functions often affected in PD. To minimize practice effects we used alternate forms where available in a balanced order across patients. If available, parallel forms were used at follow-up. The following tests were administered: Dementia Rating Scale (DRS); Category fluency[20]: score is raw number correct in 2 minutes; Controlled Oral Word Association Test (COWAT)[21]: score is raw number correct in 3 minutes; Alternating fluency: score is raw number correct in 4 minutes[22]; Dutch Adult Reading Test (DART)[23]: the DART is the Dutch counterpart of the National Adult Reading Test (NART)[24]; Paced Auditory Serial Addition Task (PASAT): speed 3.2 seconds per digit,[25] maximum score is 60; Auditory Verbal Learning Test (AVLT)[26]; Groningen Intelligence Test: Visuospatial reasoning, a subtest of a Dutch Intelligence Test[20]; Stroop Color Word Test[27]; Odd Man Out Test (OMO)[28]; Trail Making Test parts A and B[29]; Boston Naming test (BNT).[30]

Mood and behavior rating scales. The DEX Questionnaire of the Behavioral Assessment of the Dysexecutive Syndrome[31] and the Memory Assessment Clinic ratings (MAC)[32,33] were completed by the patient and a proxy. The DEX is a 20-item questionnaire for rating dysexecutive symptoms such as apathy, distractibility, lack of social awareness, and planning problems. High scores indicate executive dysfunction. The MAC scales measure a wide range of everyday memory abilities and amnesic symptoms. In this study we used only the ability subscale (21 items). High scores indicate good memory abilities.

To assess neuropsychiatric changes a Dutch translation of the Neuropsychiatric Inventory (NPI) was used.[34] The NPI is not specifically constructed for repeated measures. At baseline and follow-up we asked for changes in behavior compared to previous behavior.

The NPI consists of the following 12 items: Delusions, Hallucinations, Agitation/Aggression, Dysphoria, Anxiety, Euphoria, Apathy, Disinhibition, Irritability/Lability, Aberrant Motor behavior, Night time behavior, Appetite/Eating behavior. The version of the NPI available at the time did not provide some items relevant to the purpose of this study. We therefore constructed 5 extra items based on the Frontal Behavioral Inventory (FBI).[35] These items are Disgust; Negligence; Sexual interest; Language and Speech; and Cognitive changes (appendix E-1 on the *Neurology* Web site at www.neurology.org).

During the test session a combined version of the abbreviated Profile of Mood States (POMS)[36] and the Positive Negative Affect Scale (PANAS)[37] was completed by the patient. This is a list of 60 adjectives by which subjects describe their mood during the week preceding the assessment. For the POMS, the adjectives are clustered in five subscales (depression, anger, fatigue, vigor, and tension), and for the PANAS, the adjectives are clustered into positive and negative affects. The Montgomery & Åsberg Depression scale (MADRS)[38] was also administered. This is a 10-item depression rating scale. High scores indicate depression. Also, the PD quality of life (PDQL)[39] was administered. High scores indicate low quality of life.

Table 1 *Demographic and disease characteristics of the patient sample at baseline*

	STN (n = 99)	Control (n = 36)
Men/women, n	58/41	21/15
Age, y	57.9 (8.1)	63.0 (9.1)
Education, y	11.0 (2.9)	12.4 (3.0)
DART-IQ	102.6 (13.4)	106.3 (10.3)
Disease duration, y	13.7 (6.1)	10.4 (4.6)
UPDRS part 3 "off"	43.6 (12.5)	
UPDRS part 3 "on"	21.2 (9.2)	25.4 (13.8)
Hoehn & Yahr "off"	3.7 (0.9)	
Hoehn & Yahr "on"	2.7 (0.6)	2.7 (0.7)
Medication in LEU preop	899.3 (498.0)	629.6 (304.9)

Values are mean (SD).

STN = subthalamic nucleus stimulation; DART = Dutch Adult Reading Test; UPDRS = Unified Parkinson's Disease Rating Scale; LEU = levodopa equivalent units.

Statistical analyses. We compared the STN group with the control group on all measures. In view of the unequal subgroup sizes and the nature of the data, nonparametric tests were used (Mann-Whitney *U* test).

Change scores were calculated as the score at follow-up minus the score at baseline. *p* Values of less than 0.05 (one-tailed) were accepted as significant. We did not correct the level of significance for multiple comparisons to reduce the probability of type I error because we were mainly interested in detecting adverse effects of the surgical intervention. Under this circumstance, type II error (failure to detect an effect when it actually exists) is more serious than type I error (considering an effect to be real when it is not).[40]

We computed effect sizes according to Cohen's d. Effect size is defined as the difference between the mean change scores of both groups divided by the pooled SD of the scores. An effect of 0.2 reflects a small effect, 0.5 a medium, and 0.8 a large effect.[41]

With Pearson's r, we analyzed the associations between the change scores of the neuropsychological measures and the levodopa test at baseline, the changes in LEU, and changes in motor scores.

Results. A total of 103 patients were included in the STN group (table 1). The control group consisted of 39 patients with PD. After 6 months, four patients from the STN group were lost to follow-up (two missing, two refused). Three patients from the control group were lost to follow-up (one deceased, one because of a broken hip, one refused). There were no significant differences between patients who attended the follow-up and patients who were lost with respect to medical, demographic, or cognitive characteristics at baseline. Data from 99 patients of the STN group and 36 of the control group were analyzed.

Although the STN group had fewer years of education, the estimation of the premorbid intelligence by the National Adult Reading Test was not significantly different from that of the control group. Patients from the STN group had PD for about 2 years longer, and used more levodopa medication. There were no differences in score on UPDRS part 3 and Hoehn and Yahr score in "on" phase. Comparison of motor functioning in "off" phase could not

Table 2 *Cognitive test scores at baseline and change scores at 6 months follow-up for STN and control groups*[*]

Test	STN	Control	*p* Values	Cohen d
Dementia Rating Scale total	136.1 (5.4)	137.0 (5.4)		
Change score	–2.3 (6.8)	–0.4 (4.6)	0.06	–0.4
Category fluency	38.9 (9.8)	40.5 (7.9)		
Change score	–5.6 (6.7)	–0.8 (6.7)	0.000	–0.5
COWAT letter fluency	35.1 (13.1)	36.6 (11.1)		
Change score	–4.2 (8.8)	–0.1 (9.3)	0.01	–0.3
Alternating fluency	46.2 (13.6)	48.4 (11.1)		
Change score	–7.3 (10.4)	–0.1 (7.8)	0.000	–0.6
AVLT total score	39.2 (9.5)	37.3 (9.2)		
Change score	–0.8 (9.7)	1.6 (7.0)	0.11	–0.3
AVLT delayed recall	8.1 (2.8)	7.0 (2.8)		
Change score	–0.8 (3.2)	0.5 (2.2)	0.02	–0.5
Stroop word seconds	50.9 (13.6)	48.6 (10.3)		
Change score	2.1 (11.1)	1.0 (7.7)	0.27	–0.1
Stroop color seconds	65.7 (15.0)	65.4 (11.8)		
Change score	6.3 (14.2)	–0.3 (6.6)	0.000	–0.5
Stroop color word seconds	128.3 (53.1)	128.8 (41.1)		
Change score	17.0 (62.9)	–13.8 (32.1)	0.000	–0.6
Trailmaking A seconds	49.3 (18.3)	47.1 (19.1)		
Change score	0.3 (19.0)	–2.6 (15.6)	0.08	0.2
Trailmaking B seconds	135.0 (78.2)	113.1 (50.8)		
Change score	19.3 (91.8)	8.7 (42.4)	0.37	–0.3

Values are mean (SD). Negative change scores indicate decline in performance except for speeded test variables; *p* = level of significance Mann-Whitney *U* test; the effect size (Cohen's d) is negative if in the direction of decline on this variable for the STN group or positive if it is in the direction of improvement on this variable.

* See table E-1 for complete overview of results.

STN = subthalamic nucleus stimulation; COWAT = Controlled Oral Word Association Test; AVLT = Auditory Verbal Learning Test.

Table 3 *Scores on questionnaires at baseline and change scores at 6 months follow-up for STN and control groups*[*]

Questionnaire	STN	Control	*p* Values	Cohen d
Montgomery Asberg Depression Rating scale	6.8 (4.7)	5.8 (4.6)		
Change score	–0.3 (6.7)	–0.7 (5.3)	0.46	–0.1
POMS depression	5.8 (6.0)	4.5 (5.4)		
Change score	–0.1 (6.7)	0.6 (4.8)	0.08	0.1
POMS anger	4.3 (4,4)	4.1 (4.7)		
Change score	0.3 (5.3)	0.8 (4.7)	0.24	0.1
POMS fatigue	8.3 (5.7)	6.1 (5.5)		
Change score	–1.3 (6.8)	–0.03 (5.8)	0.11	0.2
POMS vigor	11.6 (4.4)	11.1 (4.2)		
Change score	–0.8 (4.5)	0.3 (3.1)	0.09	–0.3
POMS tension	9.3 (5.2)	6.4 (5.5)		
Change score	–2.2 (4.9)	–0.1 (3.9)	0.02	0.4
PANAS positive affect	32.7 (9.1)	30.3 (11.9)		
Change score	–2.6 (10.2)	2.2 (6.6)	0.01	–0.6
PANAS negative affect	20.4 (11.3)	15.6 (10.7)		
Change score	–1.6 (12.6)	0.8 (10.8)	0.07	0.2
Parkinson Quality of Life	101.1 (20.9)	86.4 (24.3)		
Change score	–16.6 (22.2)	–1.8 (14.6)	0.000	0.7
NPI irritability/lability	0.7 (1.3)	0.8 (1.8)		
Change score	0.7 (2.1)	–0.3 (1.8)	0.01	–0.7
NPI sleep disorder	2.7 (2.5)	2.9 (2.9)		
Change score	–0.4 (2.6)	–1.2 (2.3)	0.04	–0.3
Sexual changes	0.9 (1.9)	1.0 (2.3)		
Change score	0.0 (1.4)	–0.4 (1.5)	0.14	–0.4
Language/speech changes	3.8 (2.8)	3.3 (2.5)		
Change score	–0.1 (3.3)	–0.4 (1.9)	0.42	–0.1
Cognitive changes	1.7 (2.0)	1.9 (2.2)		
Change score	1.3 (3.1)	–0.4 (1.9)	0.01	–0.8

Values are mean (SD). The effect size (Cohen's d) is negative if in the direction of decline on this variable for the STN group or positive if it is in the direction of improvement on this variable.

* See table E-2 for complete overview of results.

STN = subthalamic nucleus stimulation; POMS = Profile of Mood States; PANAS = Positive Negative Affect Scale; NPI = Neuropsychiatric Inventory.

be performed, because motor scores in "off" phase were not available for the control group.

The cognitive test scores of the groups are shown in table 2 (see table E-1 for complete overview of cognitive tests results). The table provides the mean scores at baseline, the mean change at follow-up, and the effect sizes. The STN and control group were not significantly different at baseline except for a lower score at the delayed verbal recall in the control group and a worse score for the STN group on the Odd Man Out. Results of the mood and behavioral questionnaires are presented in table 3 (see table E-2 for complete overview of results of questionnaires). At baseline the STN group showed significantly more symptoms of tension and fatigue on the POMS, significantly more negative affect on the PANAS, and significantly less quality of life compared to the control group.

Follow-up. Patients from the STN group were seen about 1 month later for follow-up than the control group. This was due to the delay between baseline assessment and surgery.

The STN stimulation had a clear positive effect on motor functions. Six months after surgery the STN group showed a large decrease on the UPDRS part 3 in "off" phase (mean 34%). Decrease on the UPDRS was significantly correlated with the levodopa test at baseline (r = –0.34), with a high levodopa test score at baseline corresponding with a large improvement in motor functioning after surgery. There was a large reduction in levodopa medication (LEU) in the STN group, whereas the medication dose in the control group hardly changed (mean change in LEU in STN group: –212.6 SD 454.3, mean change in LEU in control group 27.1 SD 59.4, $p < 0.001$). This reduction was significantly correlated with the decrease on the UPDRS part 3 both in off (r = 0.24) and in on phase (r = 0.26).

On the cognitive tests, patients from the STN group showed a significant decline compared to the control group on all verbal fluency measures. Moreover, the STN group showed a significant decline compared to the control group on the subtests Attention and Initiation/Perseveration of the Dementia Rating Scale, on the delayed recall of the Auditory Verbal Learning test, on the Stroop Color Card and the Stroop Color Word Card.

On the mood and behavior rating scales, the STN group reported significantly fewer signs of tension on the POMS compared to baseline than the control group. On the

PDQL, the STN group showed a larger increase in quality of life compared to the baseline than the control group. The STN group showed a significantly larger decline in positive affect on the PANAS than the control group. On the NPI, family members reported an increase on irritability/lability and a lower decrease in sleep disturbances for the STN group compared to the control group. Also, they reported significantly more changes in cognition for the STN group.

As the groups were not equal at baseline with respect to LEU and disease duration, we wondered if differences in change on the neuropsychological variables after 6 months were due to surgery or to these baseline differences in LEU and disease duration. We therefore conducted analyses of variance with change scores as the dependent variables and years of education and LEU on baseline as covariates. This covariance analysis showed the same pattern of significant differences on the cognitive variables.

When we correlated the significant variables with medical variables, we found that a decrease on the Dementia Rating Scale and a decrease on the delayed recall of the AVLT were significantly correlated with a low levodopa test at baseline ($r = 0.23$ and $r = 0.25$). There were no significant associations between cognitive variables and changes in motor scores or change in LEU.

The electrodes were displaced in two patients. In one patient, electrode was in the genu of the internal capsule. In the other patient, the right electrode was at the border of the internal and external globus pallidum; this was probably caused by brain shift due to a perioperative subdural accumulation of air after CSF leakage through the burr hole. The left electrode was at target. Both patients developed a dementia syndrome after surgery. Another patient had a left sided occipital hemorrhage a few days after surgery caused by resuming anticoagulation. Afterward she had vascular dementia. Still another patient had a right subcortical hemorrhage a day after surgery. Afterwards his wife noticed evident behavior changes (i.e., impulsivity and self-centered behavior). Repeating all analyses after exclusion of those four patients did not change the results, apart from the difference in change score on the AVLT delayed recall, which no longer reached significance.

Anticholinergics are regularly prescribed for symptomatic treatment of PD, but are notorious for their negative side effects on cognition. Twenty patients of the STN group and 10 patients of the control group used anticholinergic medication at baseline or follow-up. Repeating all analyses after exclusion of the patients who used anticholinergics showed the same significant differences, with again the exception of the change score on the AVLT delayed recall, which no longer reached significance. Instead, the difference in change score on the PASAT was now significant, with the STN group showing a slight decline in score and the control group an improvement.

After surgery we noted several psychiatric events in the STN group. Transient psychosis occurred in two patients, in one followed by a suicide attempt. This patient also showed sexual disinhibition. Another patient had a relapse of earlier treated voyeurism. In still another patient pathologic gambling appeared. Mania occurred in one patient and depression in three patients. Finally one patient had increased aggressive and self-centered behavior. Taken together, 9 of the 99 STN patients (9%) had psychiatric events that needed extra care. Six months after surgery the psychiatric problems were still evident, although in some cases they had become less severe. Transient psychosis had resolved by then. In the control group of 36 patients, one patient (3%) developed depression.

Discussion. Six months after surgery the STN group showed a clear improvement of motor functioning. However, compared to a control group, the STN group showed a significant decline in verbal fluency, on the speed of naming colors, on selective attention, and on delayed verbal recall. Furthermore, patients of the STN group reported a decrease in positive affect compared to the control group. Moreover, the proxies of the STN group reported significant increases in cognitive complaints and in irritability/lability. Nonetheless, the STN group showed an obvious increase in quality of life and a slight decrease in tension. The significant changes on the cognitive and behavioral measures are, except for the decline of verbal memory, not merely due to negative events following surgery, faulty placement of electrodes, or use of anticholinergics. The sizes of the negative effects (Cohen's d) were large on cognitive complaints, and medium on category fluency, alternating fluency, color naming, delayed verbal recall, selective attention, irritability, and positive affect. The positive effect sizes were medium on quality of life and tension, and only small on mood measures.

The most parsimonious explanation for the decrease in verbal fluency and selective attention, and to a lesser extent for the decrease in verbal recall and color-naming speed, seems to be executive dysfunction. The changes on behavioral measures, i.e., the flattening of positive affect, the increased irritability/lability, and cognitive complaints, are compatible with this line of thought. In our study we see flattening of positive affect and also improvement in quality of life, while usually improvement in quality of life is related to improvement in mood. However, improvement in quality of life after bilateral STN stimulation can be related to only physical aspects.[42]

Neuropsychological decline was not associated with improvement in motor scores. This implies that patients who did not show much improvement in motor functioning were not necessarily the ones who showed cognitive decline. A low levodopa test at baseline and consequently low expectations on improvement in motor scores after bilateral STN stimulation was related to decline in a cognitive screening test. Although this was not supported by other test results, it emphasizes the importance of the preoperative screening of motor functioning.

The findings of our study are comparable to the results of the controlled study, which also found mildly impaired attention and verbal fluency, even in a smaller group of patients.[5] Changes in verbal fluency, attention, and verbal memory have been described earlier, in uncontrolled studies on bilateral STN stimulation,[9] but those negative side effects were particularly seen in older patients. A recent

uncontrolled study in a large series of patients concluded that STN stimulation does not lead to global cognitive deterioration.[6] Because we were also interested in the small changes, we used a more lenient significance level. When we apply our level of significance to its results, a significant change in frontal score and in the subtest of initiation and attention of the Mattis' DRS can be detected. This is in line with our findings of neuropsychological decline, especially in executive function. Moreover, the study did mention an increase in apathy and several psychiatric events after surgery, adding up to 24% of its patient sample. It seems to us that this study underestimates the changes in cognition and behavior, which affect at least one out of four patients after bilateral STN stimulation. Even if those changes are indeed transient, impact on daily life and postoperative management will be notable.

A study in which bilateral STN was compared with subcutaneous continuous infusion of apomorphine[43] also found that the STN group showed a moderate worsening on verbal fluency and Stroop naming, which is comparable to our results. They concluded that the neuropsychological changes in the STN group did not have consequences for regular activities. However, they did not appropriately measure these activities. Using a standard questionnaire, we found that relatives complained more about the cognitive status of the patient after bilateral STN stimulation.

Finally, we could not confirm previous observations of a high risk for suicide after deep brain stimulation.[44] Within 6 months after surgery, there was only one suicide attempt in the experimental group of 99 patients.

It is not clear how executive dysfunction after bilateral STN stimulation could be explained in terms of brain functioning. A PET study found that poor verbal fluency during STN stimulation was related to decreased activation of the inferior frontal cortex.[45] The spread of electrical current from the stimulator is probably not restricted to the sensorimotor part of the STN. Given its small size the current may also affect the limbic and cognitive-associative part,[45] as well as the medial forebrain bundle, zona incerta, lateral hypothalamus, and other regions that have extensive limbic connections.[46] Another hypothetical explanation may be that stimulation disconnects the basal ganglia, and cortically based processing has taken over but cannot compensate completely for those functions normally subserved by basal ganglia.[47]

Furthermore, the lowering of the levodopa dose after bilateral STN stimulation is often suggested to cause apathy, and consequently, a decline in neuropsychological measures, which require mental effort.[48] In our study the decline of some neuropsychological measures was not related to levodopa reduction.

A major shortcoming of our study is that it is not a randomized trial. At the time we planned our study, randomization between surgery and a waiting list control condition was not considered to be an ethical option, because of the proven efficacy of the DBS procedure. Differences between the groups on neuropsychological variables could be due to differences in demographic or disease characteristics. In our study the STN group had slightly longer disease duration and used more levodopa medication at baseline, implying more severe PD symptomatology. However, these variables did not explain a significant portion of the variance of the neuropsychological change scores. Statistically controlling for these baseline differences did not affect the results.

Secondly, we cannot determine whether the effects on executive functioning are due to the surgical intervention or to the deep brain stimulation, because we did not systematically compare cognitive functioning in on and off stimulation. Studies that have done so until now suggest subtle, differential effects on executive function with the stimulator turned on and off.[7,49-51] We only have incidental observations at our disposal. One patient in our clinic improved greatly after switching off the stimulator (Smeding et al., in preparation). Thus, direct cognitive-behavioral stimulation effects are possible, and detrimental cognitive effects cannot exclusively be attributed to the surgical intervention.

Furthermore, we did not know the exact location of the STN electrodes because we were unable to obtain postoperative MRI scans due to Dutch legislation. We suspected an electrode displacement because of side effects in two cases. This was proven in one patient by CT scan and in the other, recently, by fusion of the postoperative CT scan with perioperative MRI scan. When we excluded these patients from the data analysis, results did not change. The favorable motor improvement of the other patients indicated that the electrodes were well placed.

A minor point is that we did not include patients with a possible early dementia. It is assumed that a dementia syndrome is a risk factor for bilateral STN stimulation,[9,52] although this has only been studied in case reports.[9,53,54] From clinical experience we know that some patients with obvious cognitive deficits did not develop a dementia syndrome after surgery, while they improved profoundly in motor functioning and quality of life. By excluding surgical candidates with obvious cognitive impairments beforehand, we may have deprived them from a last option of improvement in motor functioning. Future studies should be directed to this problem.

A final consideration concerns the question whether the obvious motor benefits of bilateral STN stimulation still outweigh the adverse cognitive effects. When we spoke to patients and their relatives in the office, we noticed that in the majority of the cases they evidently do. Cognitive decline, if apparent, was of concern to the patients, but the advantages in daily life resulting from the improved motor functioning usually made up for it. Conversely, in some of our patients cognitive or emotional changes led to an evident step backwards in daily life. If they had known this beforehand, they would not have

decided positively for surgery. This was more often expressed by relatives than by the patients themselves. Even in a case where a patient had obvious personality change and cognitive decline after surgery, the patient was happy with the results on motor functioning and would do it again. However, this could also suggest impairment in adequate judgment. Even if neuropsychological changes do not seem to outweigh the motor benefits, they do have consequences for daily life, and patients have to be informed about them. Therefore, we need to establish predictors that will tell which patients are at risk for cognitive or emotional decline after bilateral STN stimulation.

Acknowledgment

The authors thank M. Hoogman, A. Rienstra, R. ten Dijke, and E. Wijnalda (psychologists) for neuropsychological testing of several patients. They also thank M. Postma (Parkinson nurse AMC), R.M.A. de Bie, R. Esselink (neurologists AMC), and A. Portman (neurologist UMCG) for scoring motor functioning of the patients, M. Vermeulen (neurologist) for advice on study design, and J. Kuster (neurologist from Kennemer Gasthuis Haarlem) and J. Zijlmans (neurologist Vrije Universiteit Amsterdam) for recruitment of patients with PD for the control group.

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Neuro*Images*

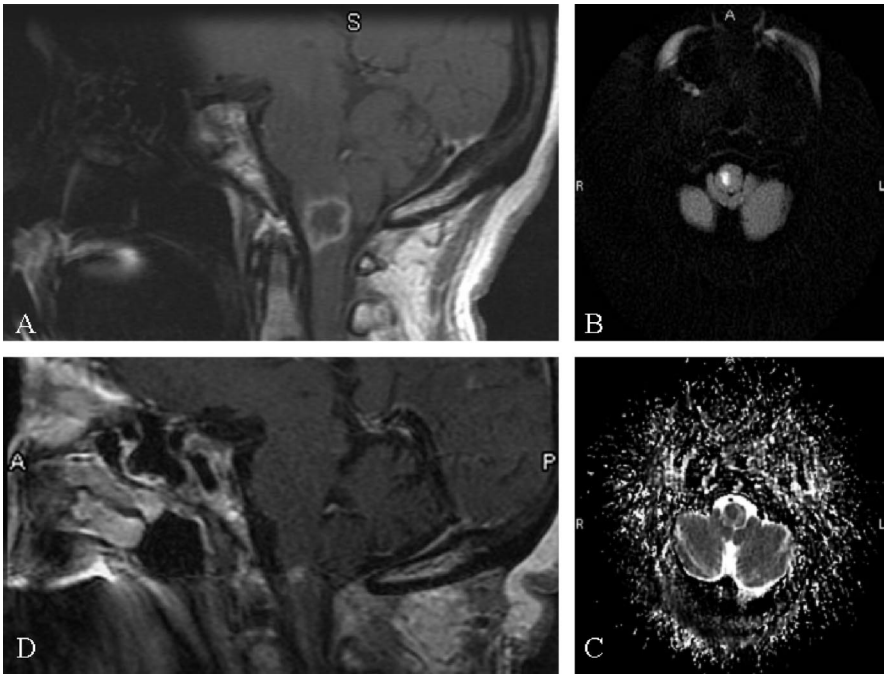

Figure. (A) A 1.8 × 1.4 cm peripherally enhancing mass expanding the cervicomedullary junction on MRI. (B) An area of restricted diffusion (C) with a corresponding low apparent diffusion coefficient is shown within the center of the lesion. (D) Five months after treatment, the lesion had improved significantly.

Solitary pyogenic abscess of the medulla oblongata: Survival after aspiration and antibiotics

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A 69-year-old woman presented with 2 days of nausea and gait ataxia, without other neurologic findings or laboratory abnormalities. Needle aspiration of a medulla oblongata lesion (figure) by lateral craniotomy grew *Streptococcus pneumoniae*; no source was found. Postoperatively, she required a tracheotomy. Antibiotics were started; 5 months later there was dramatic improvement of the lesion and functional independence was regained.

This unusual site for a pyogenic abscess has a poor outcome.[1] Brainstem symptoms are absent due to longitudinal expansion of the abscess. Restricted diffusion on MRI with corresponding low ADC is classic.[2] However, aspiration is necessary to distinguish other ring-enhancing lesions.

Disclosure: The authors report no conflicts of interest.

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Neurology 2006;66;1836
DOI 10.1212/01.wnl.0000210495.56520.5a