A multicentre study on suicide outcomes following subthalamic stimulation for Parkinson’s disease

Valerie Voon,1,2,* Paul Krack,3 Anthony E. Lang,2 Andres M. Lozano,2 Kathy Dujardin,4 Michael Schüpbach,5 James D’Ambrosia,1 Stephane Thobois,6 Filippo Tamma,7 Jan Herzog,8 Johannes D. Speelman,9 Johan Samanta,10 Cynthia Kubu,11 Helene Rossignol,3 Yu-Yan Poon,2 Jean A. Saint-Cyr,2 Claire Ardouin3 and Elena Moro2

1National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA, 2University of Toronto, UHN, Toronto, ON, Canada, 3University Joseph Fourier, Grenoble, 4Lille University Hospital, Lille, 5National Institute of Health and Medical Research (INSERM), Hôpital de la Pitié-Salpêtrière, Paris, 6Université Lyon I, Hospital Neurologique Pierre Wertheimer, Lyon, France, 7Neurological clinic, Ospedale San Paolo, Italy, 8Christian-Albrechts-Universität Kiel, Kiel, Germany, 9Academic Medical Center of Amsterdam, Amsterdam, The Netherlands, 10University of Arizona, Phoenix, AR and 11The Cleveland Clinic Foundation, OH, USA

*Present address: National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA

Correspondence to: Dr Valerie Voon, National Institute of Neurological Disorders and Stroke, National Institutes of Health, 10 Center Drive, Bldg 10, Rm 5S213, Bethesda, MD 20892-1428, USA
E-mail: voonv@ninds.nih.gov

Subthalamic nucleus deep brain stimulation improves motor symptoms and quality of life in advanced Parkinson’s disease. As after other life-altering surgeries, suicides have been reported following deep brain stimulation for movement disorders. We sought to determine the suicide rate following subthalamic nucleus deep brain stimulation for Parkinson’s disease by conducting an international multicentre retrospective survey of movement disorder and surgical centres. We further sought to determine factors associated with suicide attempts through a nested case-control study. In the survey of suicide rate, 55/75 centres participated. The completed suicide percentage was 0.45% (24/5311) and attempted suicide percentage was 0.90% (48/5311). Observed suicide rates in the first postoperative year (263/100 000/year) (0.26%) were higher than the lowest and the highest expected age-, gender- and country-adjusted World Health Organization suicide rates (Standardized Mortality Ratio for suicide: SMR 12.63–15.64; P < 0.001) and remained elevated at the fourth postoperative year (38/100 000/year) (0.04%) (SMR 1.81–2.31; P < 0.05). The excess number of deaths was 13 for the first postoperative year and one for the fourth postoperative year. In the case-control study of associated factors, 10 centres participated. Twenty-seven attempted suicides and nine completed suicides were compared with 70 controls. Postoperative depression (P < 0.001), being single (P = 0.007) and a previous history of impulse control disorders or compulsive medication use (P = 0.005) were independent associated factors accounting for 51% of the variance for attempted suicide risk. Attempted suicides were also associated (P < 0.05) with being younger, younger Parkinson’s disease onset and a previous suicide attempt. Completed suicides were associated with postoperative depression (P < 0.001). Postoperative depression remained a significant factor associated with attempted and completed suicides after correction for multiple comparisons using the stringent Bonferroni correction. Mortality in the first year following subthalamic nucleus deep brain stimulation has been reported at 0.4%. Suicide is thus one of the most important potentially preventable risks for mortality following subthalamic nucleus deep brain stimulation for Parkinson’s disease. Postoperative depression should be carefully assessed and treated. A multidisciplinary assessment and follow-up is recommended.

Keywords: suicide; deep brain stimulation; Parkinson’s disease; depression; subthalamic stimulation

Abbreviations: ICDs = impulse control disorders; LEDD = Levodopa equivalent daily dose; SMR = standardized mortality ratio; STN DBS = subthalamic nucleus deep brain stimulation; UPDRS = Unified Parkinson’s Disease Rating Scale

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Suicidal outcomes following STN DBS

Introduction
Parkinson’s disease is a neurodegenerative disorder characterized by motor, cognitive, behavioural, autonomic and other non-motor symptoms. The disorder can be treated by dopamine replacement therapy or neurosurgical therapies. Subthalamic nucleus deep brain stimulation (STN DBS) is a well-established surgical treatment effective for the motor symptoms and quality of life in advanced Parkinson’s disease (Deuschl et al., 2006). However, postoperative neurobehavioural symptoms have been reported. These include depression (1.5–25%), (Houeto et al., 2002; Troster et al., 2003) hypomania/mania (4–15%), emotional reactivity (75%), postoperative confusion (0–25%), apathy (8–51%) (Czernicki et al., 2005; Castelli et al., 2006; Ory-Magne et al., 2007) and social difficulties (75%) (Schupbach et al., 2006) (for review see Voon et al., 2006). These neurobehavioural symptoms are possibly related to individual preoperative vulnerability, dopaminergic medication withdrawal, medication interacting with stimulation, postsurgical and stimulation effects, Parkinson’s disease itself and psychosocial changes (Voon et al., 2006). However, the majority of these symptoms are transient and manageable.

Suicide rates following any significant life-altering events tend to be elevated. For instance, a recent meta-analysis of 11 epilepsy surgery studies reported a postoperative suicide rate of 1% which is 31 times higher than that of the general population (Pompili et al., 2006). The suicide rate following DBS for a range of movement disorders was reported at 4.3% (Burkhard et al., 2006). However, the suicide rate following STN DBS at 0–1% (Krack et al., 2003; Albanese et al., 2005; Soulas et al., 2008), was marked as a small proportion of the variance in risk and lacks specificity (Oquendo et al., 2006). Known suicide risk factors in the general population include psychiatric disorders and, in particular, depression, gender, age, marital status, comorbid physical illness and previous suicide attempts (Kessler et al., 1999; World Health Organization, 2006) (for review see Maris, 2002). In a recent study investigating risk factors in two completed and four attempted suicides from 200 STN DBS Parkinson’s disease patients, suicidal behaviours were associated with postoperative depression and impaired impulse regulation (Soulas et al., 2008).

We performed a multicentre retrospective study with the following two objectives: (i) to determine the rate of postoperative attempted and completed suicides after STN DBS for Parkinson’s disease and (ii) to determine factors associated with attempted suicides using a nested case-control follow-up study. Parkinson’s disease patients having undergone DBS in other targets were not surveyed as the markedly smaller number of surgeries would have biased any comparisons.

Method
Study design
For the first objective to assess suicide rate, movement disorder and neurosurgical centres were contacted by phone and e-mail to ask if they would participate with contact attempted a minimum of three times. Inclusion criteria included centres with either a history of publications on DBS for Parkinson’s disease or likely completion of more than 100 STN DBS surgeries. The number of STN DBS surgeries completed up to April 2005, the number of preoperative (while on the wait list) and postoperative attempted and completed suicides and the number of months the event occurred after surgery were requested.

For the second objective to assess factors associated with suicide attempts, centres with more than one event were asked if they would take part in a retrospective chart review using a specific questionnaire. Charts were reviewed either by a neurologist, psychologist, nurse or research assistant, who were part of the neurosurgical clinical or research team. Inclusion criteria for identified cases included either a reported completed suicide or attempted suicide. For each identified case, two Parkinson’s disease controls without suicidal behaviours who had undergone STN DBS surgery immediately prior to and immediately after the identified case at the same centre were selected. All centres in the case-control study adhered to the commonly accepted selection criteria for surgery (Lang et al., 2006). Rates were compared to country-specific general population suicide rates (World Health Organization, 2006).

Suicide risk factors questionnaire
The following factors were compared between Parkinson’s disease patients with suicide attempts and Parkinson’s disease controls: gender, age, marital status, psychiatric disorders (pre-and postoperative depression were assessed categorically and dimensionally), previous suicide attempts, motor status, dopaminergic dose change and cognitive status.

The multiple-choice survey requested the following information:

(i) known suicide risk factors in the general population (Kessler et al., 1999; World Health Organization, 2006); for review see Maris (2002);
(ii) patient characteristics;
(iii) motor surgical outcome was assessed as percentage of postoperative motor improvement (last follow-up available) using the Unified Parkinson’s Disease Rating Scale (UPDRS) motor score (Fahn et al., 1987), calculated as |([preoperative UPDRS motor score off-medication — postoperative UPDRS motor score off-medication/on stimulation]) / preoperative UPDRS motor score off-medication) | × 100. This variable
was assessed to determine if motor efficacy of the surgical intervention was associated with suicide attempts;

(iv) electrical parameters (i.e. amplitude, frequency, pulse widths, contact polarity) and postoperative brain MRI for electrode placement confirmation were assessed to determine if DBS parameters or electrode placement was associated with attempts;

(v) preoperative and postoperative medication (at the time of the event) type and dose. Levodopa equivalent daily dose (LEDD) (Hobson et al., 2002) percent change was calculated as (preoperative LEDD−postoperative LEDD)/preoperative LEDD. This variable was assessed to determine if a decrease in dopaminergic dose along with a potential dopaminergic withdrawal state was associated with attempts;

(vi) preoperative psychiatric status. To standardize preoperative depression reporting, a history of past depression included only patients on antidepressants at appropriate doses at the time of preoperative assessment. Preoperative depression assessment was based on Beck Depression Inventory (cut-off 14/15) (Visser et al., 2006) or Montgomery Asberg Depression Rating Scale (cut-off 14/15) (Leentjens et al., 2000) scores using Parkinson’s disease-specific optimal cut-off scores. The Beck Depression Inventory is a 21-item patient-rated scale (score range 0–63) which has been validated in Parkinson’s disease depression (Visser et al., 2006). The Montgomery Asberg Depression Rating Scale is a 10-item clinician-rated scale (score range 0–70) which has been validated in Parkinson’s disease depression (Leentjens et al., 2000). The Parkinson’s disease-specific optimal cut-off scores were used to dichotomize patients into depressed or not depressed in order to systematically assess for the presence or absence of depression as categorical variables. Impulse control disorders (ICDs) diagnosis was based on a history of clinician-diagnosed pathological gambling or hypersexuality. Symptoms of other ICDs such as binge eating or shopping had not been routinely assessed pro-operatively;

(vii) cognitive measures included the Mattis Dementia Rating Scale, Frontal Scores (Pillon et al., 1986) and Mini Mental Status Exam scores were assessed to determine if cognitive status was associated with attempts. The Mini Mental Status Exam is a 30-point clinician-administered questionnaire that assesses for cognitive status. The Mattis Dementia Rating Scale is a clinician-rated instrument (range 0–144) for the assessment of cognitive status. The measures were compared as continuous variables;

(viii) postoperative behavioural symptoms included depression requiring antidepressant treatment, apathy, hypomania/mania, psychotic symptoms and hypersexuality recorded in the chart at any time after surgery. The symptoms of apathy, hypomania/mania, psychosis and hypersexuality were determined by clinical impression documented in the chart;

(ix) duration between last assessment and event; and

(x) outcomes included psychiatric treatment, type of treatment and degree of improvement.

All centres that participated in the data submission and chart review obtained approval or followed patient protection laws according to guidelines of their local hospital ethics boards.

Statistical analysis

The completed and attempted suicides were compared with age- and gender-matched country-specific suicide rate data from the WHO (World Health Organization, 2006) using Chi-Square test. To adjust for gender and age, the proportion of males undergoing DBS was presumed to be 65% (Hariz et al., 2000) and the only the age ranges of 35–64 were considered. The highest and lowest expected number of suicides weighted per country were calculated as follows: Lowest expected number of age-, gender- and country-adjusted suicides per 100 000/year = \( \frac{[(0.65 \times \text{lowest suicide rate per 100 000 for men ages 35–64 per country}) + 0.35 \times \text{(lowest suicide rate per 100 000 for women ages 35–64 per country})] \times \text{(number of surgeries per country–number of suicides from previous postoperative year per country)}/\text{total number of surgeries}] \) The same calculation was applied to determine the highest expected number of age-, gender- and country-adjusted suicides per 100 000/year. Both the highest and lowest expected number of suicides were reported. The observed number of suicides was calculated as follows: observed number of suicides per 100 000/year = observed number of suicides per year/total number of surgeries−number of postoperative suicides in previous year × 100 000. The weighted standardized mortality ratio (SMR) was calculated as follows: SMR = \( \frac{\text{[(observed number of suicides per country year/expected number of suicides per country year) \times \text{(number of surgeries per country)}/\text{total number of surgeries}]}}{\text{(lowest suicide rate per 100 000 for men ages 35–64 per country)}/\text{total number of suicides per country}] \} \) The excess number of suicides per year was calculated as follows: excess number of suicides = \( \text{[(observed number of suicides per country–expected number of suicides per country)]} \)

The Mann–Whitney U-test for continuous variables and the Chi-Square test for discrete variables were used to compare associated factors between attempters and controls, completers and controls, postoperative depressed and non-depressed and postoperative apathetic and non-apathetic patients. Logistic regression analysis was used to determine independent risk factors for attempted suicide. For the comparison between factors associated with attempters and controls, a stringent correction for multiple comparisons was applied using the Bonferroni corrected \( P \leq 0.003 \). Statistics were calculated using SPSS 12.0.

Results

Suicide rates

Fifty-five centres completed the survey on suicide rates from 75 centres contacted (73%). Five thousand three hundred and eleven STN DBS patients were included. Nineteen North American (2189), 30 European (2787), one South American (110) and five Asian centres (225) participated.

The completed suicide percentage was 0.45% (24/5311) and attempted suicide percentage was 0.90% (48/5311). Centres had been performing STN DBS for mean 6.5 ± 1.7 years (range: 3–12). Three completed and three attempted suicides occurred on the wait list of patients approved for surgery; the total number of patients on the waiting list was not assessed. The mean wait list duration was 6.6 ± 7.8 months. The mean number of months after surgery of all events was 17.8 months (95% CI: 11.2–34.4) (range: completed suicides 1–48 months; attempted suicides 0.25–100 months). Fifty per cent of cases occurred by
10 months and 75% by 17 months. The first postoperative year suicide rate (263/100 000/year) (0.26%/year) was significantly higher than the age- and gender-matched country-specific rates [SMR for suicide (based on the lowest and highest expected age- gender- and country-specific WHO suicide rates): SMR 12.63–15.64; P < 0.0001] and remained elevated at the fourth postoperative year (38/100 000/year) (0.04%) (SMR 1.81–2.31; P < 0.05) (World Health Organization, 2006) (Table 1 and Fig. 1). The excess number of deaths was 13 for the first postoperative year and one for the fourth postoperative year. Participating countries were dichotomized into countries with high and moderate rates according to age-matched WHO suicide rates (World Health Organization, 2006). Countries with high baseline rates (>13/100 000/year) had a percentage of 0.59% (12/2037) and the countries with moderate baseline rates (6–13/100 000/year) had a percentage of 0.37% (12/3274). Postoperative percentages per country and country-specific suicide rates were not correlated (Pearson correlation coefficient = 0.30; P = 0.31).

**Associated factors**

Ten centres were involved in the case-control study on associated factors. Twenty-seven attempted suicides and nine completed suicides were compared to 70 controls (Table 2). Attempted suicides were associated with being single, previous history of impulse control disorders or compulsive medication use, and postoperative depression. Attempted suicides were also more weakly associated with being younger, earlier Parkinson’s disease onset, previous suicide attempt and percent LEDD change. Using logistic regression analysis, postoperative depression (P-value on model entry: P = 0.001), being single (P = 0.001), history of impulse control disorders (P = 0.002) were independent factors accounting for 51% attempted suicide risk variance with an 82.5% prediction accuracy. Following correction for multiple comparisons, only postoperative depression remained significantly associated with attempted and completed suicides.

Almost half of patients verbalized suicidal ideation prior to attempts or completed suicides (Table 3).

Postoperative depression and apathy were the two behaviours seen most frequently at the time of suicide

![Fig. 1](https://example.com/figure1.png)

**Table 1** Standardized mortality ratios per postoperative year for suicides following STN DBS for Parkinson's Disease

<table>
<thead>
<tr>
<th>Postop year</th>
<th>Observed suicides per year</th>
<th>Observed suicides per 100 000/year</th>
<th>Expected suicides per 100 000 year</th>
<th>Weighted standardized mortality ratio</th>
<th>95% CI</th>
<th>P-values</th>
<th>Excess number of suicides</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>263.60</td>
<td>16.44</td>
<td>15.64</td>
<td>(9.81–26.32)</td>
<td>&lt;0.0001</td>
<td>13.12</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>113.27</td>
<td>16.44</td>
<td>6.91</td>
<td>(4.14–11.33)</td>
<td>&lt;0.0001</td>
<td>5.13</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>18.90</td>
<td>16.44</td>
<td>1.16</td>
<td>(0.61–2.22)</td>
<td>0.38</td>
<td>0.13</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>38.1</td>
<td>16.44</td>
<td>2.31</td>
<td>(1.30–4.09)</td>
<td>0.004</td>
<td>1.31</td>
</tr>
</tbody>
</table>

One patient not included as duration after surgery was not reported.

- **Observed number of suicides per 100 000 year** = (Observed number of suicides per year / (Total number of surgeries — Number of suicides in previous years)) × 100 000.
- **Expected suicides per 100 000 year** = (number of suicides from previous postoperative year per country)/total number of surgeries. The same calculation was applied to determine the highest expected number of age-, gender- and country-adjusted suicides per 100 000 year.
- **Weighted standardized Mortality Ratio (SMR)** = (Observed number of suicides per country per year)/Expected number of suicides per country year) × (number of suicides per country)/total number of surgeries). P-values and 95% CI were obtained using chi-square analysis for the odds ratio or SMR.
- **Excess number of suicides** = (Observed number of suicides per country — Expected number of suicides per country).
attempt (Table 3). Postoperative depressed patients ($n=48$) as a group had a greater frequency of preoperative antidepressant use ($n=39$) (32/48 versus 9/39; $P=0.03$) with a trend towards more frequent preoperative suicide attempts (7/47 versus 1/39; $P=0.07$). Postoperative apathetic patients ($n=15$) as a group had a greater frequency of postoperative depression (13/15 versus 33/70; $P=0.009$), preoperative history of impulse control disorders and compulsive medication use (6/15 versus 9/66; $P=0.03$), and greater percent LEDD change [mean (SD): 72.5% (19.1) versus 59.4% (30.2); $P=0.04$].

### Discussion

#### Suicide rates

In this multicentre international retrospective survey involving 55 centres and 5311 patients, the percentage of patients committing suicide following STN DBS surgery for Parkinson’s disease was 0.5% and that of attempted suicide was 0.9%. STN DBS had been performed at these centres between 3 and 12 years. Seventy-five percent of events occurred within the first 17 postoperative months. The age-matched SMR for suicide in the first postoperative year was 12.6–15.6 and decreased to 2.31–1.81 by the fourth...
postoperative year. This rate is considerably lower than the 4.3% (6/140) reported following DBS for a range of movement disorders at a centre that had performed DBS for 9 years (Burkhard et al., 2006). Four of six patients with completed suicides in this previous study were STN DBS Parkinson’s disease patients. Within the general population suicide attempts are 20 times more frequent than completed suicides (World Health Organization, 2006). That the attempt rate was only twice that of the completed rate suggests either under-reporting or a greater proportion of successful attempts.

As further comparison, the suicide rate following epilepsy surgery is 1% or 31 times higher than the general population (Pompili et al., 2006). However, whereas the baseline epilepsy suicide rate is eight times higher than the general population (Pompili et al., 2005), baseline Parkinson’s disease suicide rates range from the same as to as much as 10 times lower than the general population (Myslobodsky et al., 2001; Juurlink et al., 2004), despite the presence of a chronic medical illness, comorbid psychiatric disorders and psychosocial losses. Thus, the relative postoperative suicide rate may be greater for Parkinson’s disease than for epilepsy. Furthermore, postoperative mortality from other causes (e.g., haemorrhage, infection) in the first year following STN DBS for Parkinson’s disease was reported at 0.41% (3/737) (Hamani et al., 2005). Thus, suicide in the first postoperative year (0.26%) represents one of the highest potentially modifiable risks for mortality following DBS for Parkinson’s disease.

Limitations of our study include its retrospective nature, differential followup at centres, lack of systematic diagnostic criteria and sample size in the case-control study. However, the use of rating scales, appropriate Parkinson’s disease-specific cutoff scores for depression severity and a definition of clinical severity of depression based on need for treatment limited subjective reporting. The inclusion of centres was restricted based on criteria that would capture centres with adequate postoperative follow-up to ensure a valid reporting of postoperative suicide rates. However, we note that this may create a sampling bias since highly subspecialized centres with adequate follow-up would have lower suicide rates. Furthermore, the dropout rate during follow-up is a significant issue, which is not quantified in this paper. Finally, events occurring in the later postoperative years were likely under-reported. Thus, the rates reported in this study are likely an underestimate of the actual rate.

That the Parkinson’s disease suicide rate is similar or lower than the general population allows for the general population baseline suicide rate to be used as a comparator. However, we note that suicide rates are likely higher in those presenting for surgery as reflected in the observed events on waiting lists (three attempted and three completed suicides). Patients presenting for surgery likely have different motivations for surgery, coping strategies, age and disease burden. For instance, a history of repeated surgeries was previously identified as a risk factor (Burkhard et al., 2004). A wait-list control group would be more appropriate control (Voon et al., 2006).

**Associated factors**

The primary risk factors associated with suicide attempts in this study were related to known general suicide risk factors and postoperative behavioural states (summarized in Table 4). A trend of greater changes in postoperative dopaminergic medication dose \( (P = 0.05) \) was observed with suicide attempts. Attempts were not associated with motor outcome. Missing data may contribute to biases.

Completed suicides in the general population are associated with a psychiatric disorder, particularly depression (World Health Organization, 2006). In this study, postoperative depression was associated with both completed and

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**Table 3 Characteristics and outcomes of attempted and completed suicides following STN DBS for Parkinson’s disease**

<table>
<thead>
<tr>
<th>Attempted suicide</th>
<th>Completed suicide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbalized suicidal ideation</td>
<td>45.0 (9/20)</td>
</tr>
<tr>
<td>Mean duration between last assessment and event in days (SD)</td>
<td>89.8 (200.5)</td>
</tr>
<tr>
<td>&lt;1 week</td>
<td>26.0 (6/23)</td>
</tr>
<tr>
<td>1–3 months</td>
<td>21.7 (5/23)</td>
</tr>
<tr>
<td>3–6 months</td>
<td>391 (9/23)</td>
</tr>
<tr>
<td>&gt;6 months</td>
<td>4.3 (1/23)</td>
</tr>
<tr>
<td>Stressors</td>
<td></td>
</tr>
<tr>
<td>Separation/divorce</td>
<td>26.3 (5/19)</td>
</tr>
<tr>
<td>Social isolation</td>
<td>10.5 (2/19)</td>
</tr>
<tr>
<td>Placement</td>
<td>10.5 (2/19)</td>
</tr>
<tr>
<td>Psychiatric diagnosis at time of attempt</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>16.7 (4/24)</td>
</tr>
<tr>
<td>Depression</td>
<td>45.8 (11/24)</td>
</tr>
<tr>
<td>Psychotic symptoms</td>
<td>16.7 (4/24)</td>
</tr>
<tr>
<td>Hypomania</td>
<td>4.2 (4/24)</td>
</tr>
<tr>
<td>Apathy</td>
<td>41.7 (10/24)</td>
</tr>
<tr>
<td>Levodopa withdrawal</td>
<td>8.3 (2/24)</td>
</tr>
<tr>
<td>Generalized anxiety</td>
<td>20.8 (5/24)</td>
</tr>
<tr>
<td>or panic attacks</td>
<td></td>
</tr>
<tr>
<td>Adjustment disorder</td>
<td>20.8 (5/24)</td>
</tr>
<tr>
<td>Treatments following events</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>12.0 (3/25)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>60.0 (15/25)</td>
</tr>
<tr>
<td>Dopaminergic medication change</td>
<td>20.0 (5/25)</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>16.0 (4/25)</td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>32.0 (8/25)</td>
</tr>
<tr>
<td>Current status</td>
<td></td>
</tr>
<tr>
<td>Not improved</td>
<td>4.3 (1/23)</td>
</tr>
<tr>
<td>Somewhat improved</td>
<td>26.1 (6/23)</td>
</tr>
<tr>
<td>Moderately improved</td>
<td>17.4 (4/23)</td>
</tr>
<tr>
<td>Significantly improved</td>
<td>47.8 (11/23)</td>
</tr>
</tbody>
</table>

Reported in % (N) unless specified.
attempted suicides after STN DBS. These findings are in keeping with the observation that postoperative depression following STN DBS has a greater effect on quality of life than motor outcomes (Troster et al., 2003). Postoperative depression can be related to the psychosocial changes, the neurobiology of Parkinson’s disease, the dopaminergic withdrawal state or individual vulnerabilities. This finding is consistent with a recent study demonstrating that suicidal behaviours was associated with postoperative depression (Soulas et al., 2008). Our ability to identify risk factors for completed suicides was limited by the small sample size.

Attempted suicides in the general population are associated with depression, substance abuse, divorce and being female (World Health Organization, 2006). In this current study, postoperative suicide attempts were associated with postoperative depression, being single, and a history of impulse control disorders or compulsive medication use. Other weaker associations included younger age, younger Parkinson’s disease onset and preoperative suicide attempts. There were no significant associations with gender or preoperative depression. Eighty percent had postoperative psychiatric diagnoses. Forty-seven percent had a major relationship or residential change or were socially isolated. These findings are in keeping with recent studies focusing on psychosocial issues suggest a high proportion of marital difficulties (75%) following STN DBS surgery (Schupbach et al., 2006). Expectations, identity changes, more subtle relationship changes and other psychosocial losses were not assessed.

Medication-induced impulse control behaviours and compulsive dopaminergic medication use can be improved by STN stimulation and medication decreases in well-selected Parkinson’s disease patients (Ardouin et al., 2006).

However, new onset pathological gambling has been reported after STN DBS (Smeding et al., 2007). Our study suggests Parkinson’s disease patients with a history of these behaviours may be at greater risk for postoperative suicide attempts.

Although country-specific baseline suicide rates differ, there was no significant association with country-specific suicide rates and STN DBS suicide outcomes. However, the cultural willingness to report suicide outcomes and the acceptance of ‘rational suicide’ may be confounders.

Patients with preoperative depression and antidepressant use or previous suicide attempts were more likely to develop postoperative depression, thus highlighting the importance of obtaining a preoperative psychiatric history (Houeto et al., 2002). Although postoperative depression and apathy were correlated, the behaviours were dissociable in this study. Whereas postoperative depression was associated with markers of preoperative depression, apathy was associated with a history of impulse control disorders and greater dopaminergic dose decrease.

Finally, a greater LEDD decrease was weakly associated with suicide attempts suggesting that the relative LEDD change may unmask underlying behavioural states or mediate dopaminergic withdrawal symptoms leading to postoperative depression or apathy.

High lethality suicide attempts in the general population have been associated with impairments in the Stroop interference task (a measure of the ability to suppress irrelevant responses and a marker of impulsivity) (Keilp et al., 2001) and in verbal fluency (Keilp et al., 2001), both of which can be impaired by STN stimulation (Voon et al., 2006). However, rather than specific impairments, higher lethality suicide attempts have been suggested to be associated with greater generalized executive impairments.

Table 4 Summary of factors associated with attempted suicides following STN DBS for Parkinson’s disease

<table>
<thead>
<tr>
<th></th>
<th>Probably associated (P &lt; 0.01)</th>
<th>Possibly associated (P &lt; 0.05)</th>
<th>Not associated (P &gt; 0.05)</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative individual factors</td>
<td>Hx of impulse control disorders or compulsive medication use</td>
<td>Previous attempt Younger age Younger Parkinson’s disease onset</td>
<td>Gender Preoperative cognitive status</td>
<td>Family history of suicide</td>
</tr>
<tr>
<td>Postoperative state</td>
<td>Postoperative depression* Postoperative apathy</td>
<td>Motor efficacy Stimulation parameters Postoperative cognitive changes</td>
<td>Interaction of stimulation with impulse control</td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Percent LEDD decrease**</td>
<td>Country-specific suicide rates</td>
<td>Dopaminergic withdrawal state</td>
<td></td>
</tr>
<tr>
<td>Psychosocial factors</td>
<td>Single</td>
<td>Expectations Identity changes Relationship changes Supports Other stressors</td>
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</table>

*Postoperative depression remains significant following Bonferroni correction.

**P = 0.05.
et al. 2001) and decreased prefrontal cortical activity (Oquendo et al., 2003). In our study, general measures for executive and cognitive scores did not differ between attempters and controls. Specific tests for verbal fluency and the Stroop task were not systematically conducted.

Impulsive suicide attempts have also been considered a form of impulsive behaviour. Impulsive behaviour can be subdivided into three different forms: motoric impulsivity (or the inability to inhibit a prepotent motor response), the tendency to rapid decision making without adequate evaluation of choices or impulsive choice (or the tendency to devalue delayed rewards). The effects of STN DBS on the first two factors have been assessed. STN stimulation has been demonstrated to improve both choice reaction time and response inhibition as measured using the stop-signal task (van den Wildenberg et al., 2006). The authors suggest that the results are due to the overall improvement of parkinsonian symptoms rather than a specific effect of STN stimulation on response selection and inhibition. However, Hershey et al. (2004) demonstrated that motor response inhibition was impaired with a go/no-go task in the context of higher cognitive demand. Several, but not all, studies have demonstrated STN stimulation induced impairments in a task that requires response inhibition and response selection during high conflict (Stroop word–colour interference task) (reviewed in Voon et al., 2006). Frank et al. (2007) further demonstrated that STN stimulation in Parkinson’s disease patients results in faster reaction times to high conflict rewarding choices rather than the expected slowing of decision making. This effect was not seen with high conflict punishment choices. Thus, the literature suggests that STN stimulation does not affect motor impulsivity but impairs decision making under conditions of high conflict rewarding choices. However, as decision making in suicidal outcomes is likely associated with conflicting choices involving punishment avoidance, it is not clear if the cognitive impairments observed with STN stimulation are necessarily related to suicidal behaviours.

In conclusion, postoperative suicide is one of the most important and potentially preventable risks for mortality following STN DBS for Parkinson's disease. We demonstrate that the risk is significantly elevated in the first postoperative year and remains elevated in the fourth postoperative year. Our data are likely an underestimate of the true risk particularly in the late postoperative years. The risk, like that in the general population, is multifactorial. No single factor is sufficient to predict risk or should serve as a surgical contraindication. Postoperative depression should be followed and managed. Subjects with a history of impulse control disorders or compulsive medication use and are single may be at higher risk for suicide attempts and should be carefully assessed and followed. Patients should be encouraged to be open during preoperative assessment with the understanding that the assessment is multifactorial with the goal to identify factors requiring management and closer follow-up. Patients and family members should be warned of this potential outcome. Clinicians should actively inquire about suicidal ideation and promote awareness that the symptom is treatable. Suicidal ideation should be taken seriously. A multidisciplinary assessment and follow-up is encouraged.

References


Appendix
The prevalence rates were presented at an oral session at the American Academy of Neurology, San Diego, USA, 2006. The associated factors were presented at an oral session at the Movement Disorders Congress, Kyoto, Japan, 2006.

The following Investigators participated in the study: