Attempted and completed suicides after subthalamic nucleus stimulation for Parkinson’s disease

T Soulas,1,2 J-M Gurruchaga,1 S Palfi,1 P Cesaro,2 J-P Nguyen,1 G Fénelon2

ABSTRACT
A higher than expected frequency of suicide has been reported among patients undergoing subthalamic nucleus deep brain stimulation (STN DBS) for advanced Parkinson’s disease (PD). We conducted a retrospective survey of 200 patients with PD who underwent STN DBS. Two patients (1%) committed suicide and four (2%) attempted suicide, despite clear motor improvements. Suicidal patients did not differ from non-suicidal patients with respect to age, disease duration or preoperative amplitude analysis. Scores on the Mattis Dementia Rating Scale (MDRS, maximum score 144) and the Montgomery–Asberg Depression Scale (MADRS, maximum score 60) were compared with a t test between suicidal patients and the last 75 consecutive non-suicidal patients who had undergone the same preoperative assessment of depression. All patients who attempted suicide were interviewed by a psychologist (TS).

RESULTS
Two patients (1%) committed suicide and four patients (2%) attempted suicide, a mean 12.0 (7.2) months after surgery, despite fair to excellent motor improvement. Attempted and completed suicides occurred between 2002 and 2006. Details of the six suicidal patients are given in table 1. No suicides occurred among waiting list patients. Compared with the 75 non-suicidal patients, the suicidal patients did not differ significantly with respect to age (61.6 (7.8) vs 60.7 (7.5) years), disease duration (13.0 (4.5) vs 11.7 (4.5) years), MDRS score (133.7 (6.9) vs 135.0 (4.5)) or MADRS score (9.5 (5.7) vs 11.4 (3.9)). No link was found between suicide and recent changes in stimulator settings. Three of the four patients who attempted suicide did not really endanger their life, and all tended to minimise their actions. These three patients took a drug overdose while under considerable mental pressure, and none had a history of compulsive medication or overdose. Two illustrative cases are described.

METHODS
We reviewed the files of all 200 patients with PD (127 men and 73 women; mean age 61.8 (8.6) years; disease duration 14.8 (4.8) years) who underwent bilateral STN DBS in our centre between 1997 and 2006. During the study period, 24 patients died. There were two suicides, two deaths in undetermined circumstances and one death by defenestration 3 days after surgery. This latter patient was in a postoperative confusional state and the stimulator had not yet been switched on; we considered that death was more likely accidental than intentional and did not include this case among the suicides. Six patients were monitored in other centres, for geographic reasons, and 12 patients were lost to follow-up (possibly following unreported death). At the end of the study period, all of the remaining 158 patients were followed-up in our centre by the same neurologist (J-MG). STN DBS was performed under local or general anaesthesia. STN coordinates were calculated from preoperative MRI and intraoperative ventriculographic data and were confirmed by intraoperative recording of neuronal activity with semi-microelectrodes and turn

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direction of a nearby beach. His spouse alerted the police but his body was discovered 1 h later on the beach; he had died from drowning.

Case No 5 (attempted suicide)
Prior to surgery this patient had episodes of hypersexuality (including undisclosed paedophile behaviour), pathological gambling and a tendency to L-dopa addiction. These impulse control disorders improved after a reduction in dopaminergic treatment. A few months after surgery the patient developed a depressive state. He also had several abrupt reactions, such as running home from our ward while the stimulation parameters were being set. He attempted suicide 15 months after surgery, which was located not within the STN but in the substantia nigra"e, suggesting that, at least in patients with pre-DBS mood disorder, dopaminergic drugs should not be abruptly reduced postoperatively. Finally, DBS itself may have a direct effect on mood. Severe but reversible depression has been noted on activating the stimulator, when the stimulating plot was located not within the STN but in the substantia nigra or the zona incerta. STN DBS has also been followed by onset of mania or hypomania in the months following surgery. Postoperative depression does not appear to explain the observed rate of suicide, however. Firstly, as already mentioned, although depression is frequent in PD, the rate of suicide is low; secondly, some suicides after STN-DBS are not clearly associated with depression, as in our patient Nos 2 and 5, and in other series (patient No 4 in Burkhard and colleagues). Other potential risk factors include altered impulse regulation and/or an inability to control emotions. Increased impulsiveness was probably a major factor in the suicidal behaviour of some of our patients, as illustrated by case No 1. The possible impact of STN DBS on impulse control is not clearly established. In some cases, impulse control disorders such as pathological gambling and dopaminergic drug addiction can be improved by STN DBS, probably through the reduction in dopaminergic treatment. Lhomme and colleagues found that, in patients with PD off medication, STN DBS did not globally induce impulsiveness in the Rogers decision making test or on the Barratt self-rating

discussion
The prevalence of completed (1%) and attempted (2%) suicide after STN DBS was higher than expected in this series. The prevalence rate of suicide in the French population of the same age (between 45 and 74 years) is approximately 16/105 for women and from 37 to 50/105 for men. The two completed suicides observed here both involved drowning, whereas the most frequent methods recorded in the general French population of the same age are shooting and hanging. Other cases of attempted and completed suicide have been reported following STN DBS. In a recent large prospective multicentre study of 9025 patients undergoing STN DBS, the rates of completed and attempted suicide were 0.4% and 0.9%, which are again far higher than in the general population.

Suicide is commonly associated with depression in patients with PD after STN DBS, as in the general population. Four of our six suicidal patients were depressed. Voon and colleagues found that postoperative depression after STN-DBS was a major risk factor for suicide. Transient or chronic depression has been reported to affect up to 25% of patients following STN DBS. The origin of this postoperative depression is unclear and may be multifactorial. Risk factors may include a history of mood disorders, and psychological factors such as poor tolerance of the adverse effects of STN DBS (hypoesthesia, eyelid apraxia, etc), disappointment with the results of STN DBS or difficulties adjusting to familial or socio-professional life. A reduction in dopaminergic treatment may also play a part (our case No 2, see Houéto and colleagues), suggesting that, at least in patients with pre-DBS mood disorder, dopaminergic drugs should not be abruptly reduced postoperatively. Finally, DBS itself may have a direct effect on mood. Severe but reversible depression has been noted on activating the stimulator, when the stimulating plot was located not within the STN but in the substantia nigra or the zona incerta. STN DBS has also been followed by onset of mania or hypomania in the months following surgery.

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Table 1 Characteristics of the suicidal patients

<table>
<thead>
<tr>
<th>Completed suicides</th>
<th>Attempted suicides</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient No 1</strong></td>
<td><strong>Patient No 2</strong></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>M</td>
</tr>
<tr>
<td><strong>Age at DBS (y)</strong></td>
<td>67</td>
</tr>
<tr>
<td><strong>PD duration at DBS (y)</strong></td>
<td>8</td>
</tr>
<tr>
<td><strong>UPDRS III (score)</strong></td>
<td>33/23 (30)</td>
</tr>
<tr>
<td><strong>Levodopa equivalent daily dosage (mg)</strong></td>
<td>2400/455 (61)</td>
</tr>
<tr>
<td><strong>Parameters of stimulation</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Contact (right/left)</strong></td>
<td>2/6</td>
</tr>
<tr>
<td><strong>Voltage (V, right/left)</strong></td>
<td>2.8/2.1</td>
</tr>
<tr>
<td><strong>Frequency (Hz, right/left)</strong></td>
<td>160/160</td>
</tr>
<tr>
<td><strong>Pulse width (µs, right/left)</strong></td>
<td>90/90</td>
</tr>
<tr>
<td><strong>Time between DBS and suicidal behaviour (months)</strong></td>
<td>5</td>
</tr>
<tr>
<td><strong>Pre-DBS psychiatric features</strong></td>
<td>–</td>
</tr>
<tr>
<td><strong>Family history</strong></td>
<td>PD, suicides</td>
</tr>
<tr>
<td><strong>Pre-DBS suicide attempts</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Psychiatric features at time of suicide</strong></td>
<td>Depression, delusions</td>
</tr>
<tr>
<td><strong>Setting/apparent trigger</strong></td>
<td>Home/mild annoyance</td>
</tr>
<tr>
<td><strong>Method of suicide</strong></td>
<td>Drowning</td>
</tr>
</tbody>
</table>

*Post-DBS data from the last evaluation before suicide.

DBS, deep brain stimulation; PD, Parkinson’s disease; UPDRS III, Unified Parkinson’s Disease Rating Scale, part III (motor examination).
scale, although it did induce premature responses in the interference part of the Stroop test, suggesting defective executive inhibition. However, Frank et al recently showed that STN DBS selectively interferes with the normal ability to slow down when faced with decision conflict. In contrast, impulse control disorders such as pathological gambling and hypersexuality may occur de novo following surgery. Impulsive aggressive behaviours have also been reported following STN DBS, as well as aggressive behaviour induced by intraoperative stimulation of the posterior hypothalamic area. Our patients did not display such aggressive behaviours but, in keeping with previous observations, some of them had stronger emotional reactivity (case Nos 1, 3 and 4). A possible effect of STN DBS on impulsivity suggests that these patients need careful postoperative setting of the electrical parameters, along with close psychiatric follow-up.

Finally, it should be emphasised that suicides have also been reported following pallidal or thalamic DBS in patients with PD and other conditions, such as dystonia. This further suggests that an induced disturbance of the basal ganglia circuitry, presumably in the limbic component, may induce mood disorders and/or suicidal ideas.

The main limitation of our study is its retrospective nature. We cannot rule out the possibility that some suicide attempts were not spontaneously disclosed by the patients or their caregivers, especially during the early years of the study period, before attention was drawn to the risk of postoperative behavioural changes. It is also possible that some patients who were lost to follow-up attempted suicide. However, the effect of such biases would be to underestimate the real prevalence of suicide in this setting, and would thus reinforce the main conclusions of our study.

In conclusion, suicidal behaviour is a serious potential hazard of STN DBS. Although postoperative depression is a clear risk factor, other factors such as increased impulsiveness may play a part. This risk calls for careful preoperative assessment and for close postoperative psychiatric and behavioural follow-up.

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REFERENCES

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