Appendix e-1

Suicidal patients

Case 1. A 50-year-old woman with primary generalized dystonia (DYT-1 mutation, disease duration of 22 years) committed suicide (medication overdose and suffocation) 4 years after bilateral GPi DBS. She had a family history of psychiatric difficulties (MDD, OCD, anorexia, cyclothymia) and a previous history of alcohol and sexual abuse. Her BFMDRS motor score at baseline was 60/120. She was diagnosed with bipolar affective disorder at the baseline assessment; she received an additional borderline personality disorder diagnosis after surgery. She was married. Preoperative psychiatric treatment included fluoxetine 20 mg/day, topiramate 200 mg/day, clonazepam 1.5 mg/day, and temazepam 30 mg/day. After surgery, following a suicide attempt (8 months before her suicide) carbolithium was started at 300 mg/day. At her last psychiatric assessment (1 months before the suicide), the diagnosis was unchanged; the antidepressant and BDZ treatment was increased (fluoxetine 30 mg/day, topiramate 300 mg/day, zoplicon 7.5 mg/day, clonazepam 3 mg/day, temazepam 45 mg/day, lorazepam 1 mg/day). At the last DBS follow-up, 3 months before the suicide, the motor BFMDRS score was 19/120 and stimulation parameters were: right GPi, case+, 6-7-, 2.0V/60 microsec/180Hz; left G Pi, case+, 2-, 2.0V/60 microsec/180Hz. Cognitive functions were conserved before and after surgery.

Case 2. A twenty-nine years old woman with post-traumatic segmental dystonia (disease duration of 24 years) had a new postoperative diagnosis of major depressive episode. She committed suicide 2 years after unilateral right thalamic ventralis intermedius nucleus (Vim) and GPi DBS, by means of narcotic overdose and gun shooting. She was involved in police investigation for drug trafficking and completed suicide 48 hours after sentencing to 2 years of house arrest. She had a family history of alcohol and drug use. There were no preoperative psychiatric issue, including suicidal ideation, identified. She did not take any
antidystonia or psychiatric medications before surgery. No cognitive deterioration was present before or after surgery. She had a partner who committed suicide 1 year prior to her. At baseline motor assessment BFMDRS motor and disability scores were respectively 16/120 and 3/30. At the last psychiatric assessment 3 months before suicide, medications included venlafaxine 150 mg, amitriptyline 10 mg, pregabalin 450 mg, clonazepam 4 mg. At last DBS visit, three months before suicide, the BFMDRS motor and disability scores were 8/120 and 2/30 respectively and the stimulation parameters were Vim DBS: 3-0+/ 3.6 V/90 microsec/135 Hz and Gpi DBS: 1-2-0+/3.9 V/210 microsec/135 Hz.
Medication changes

a. Primary segmental and generalized dystonia

Before surgery

At baseline, twenty patients (77%) received treatment with BDZ, eight patients (30.8%) with other antidystonia drugs (triexyphenidyl, baclofen), three (11.5%) with tetrabenazine and eight patients (30.7%) with antidepressant therapy (SSRI, NSRI, TCA). Only one patient (3.8%) was in preoperative treatment with antipsychotic drugs.

Analgesic therapy (non steroidal anti-inflammatory drugs and/or opioids) concerned seven patients (27%).

After surgery

Sixteen patients (61.5%) were in BDZ treatment: it was stopped in four cases and reduced in six cases, mostly because of the motor improvement.

Five patients (19.2%) took other antidystonia medications (triexyphenidyl, baclofen). These were stopped in three patients secondary to motor benefit following surgery. Also tetrabenazine was stopped in two patients secondary to dystonia improvement after DBS.

Antidepressant therapy was present in ten patients (38.4%). It was stopped in one patient. However, three patients started an antidepressant: sertraline was started in two patients (for worsening of anxiety secondary to BDZ reduction after surgery in one case with GAD diagnosis, unchanged after surgery, and in the other one for depressive symptoms onset in the context of a new postoperative diagnosis of alcohol abuse); fluoxetine was started for worsening of anxiety in one patient with diagnosis of SA, unchanged after surgery.

Antipsychotic drugs were unchanged in the one patient compared to baseline.

Two patients (7.7%) received analgesic therapy post-operatively. Analgesics were stopped in five patients.
b. Primary CD

Before surgery
At baseline, 15 patients (75%) were treated with BDZ, ten patients (50%) with antidepressant therapy, eight (40%) with analgesics (non steroidal anti-inflammatory drugs and/or opioids) and four patients (20%) with antidystonia medications (triexyphenidyl, baclofen). Two patients (10%) received antipsychotic drugs.

After surgery
Sixteen patients (80%) took BDZ. No patients were able to stop BDZ therapy, (indeed one patient added a second BDZ for insomnia), but four patients were able to reduce the daily dose secondary to motor benefit. One patient started BDZ therapy for anxiety symptoms in the context of alcohol dependence.

Five patients (25%) were on antidepressant therapy: it was stopped in six cases, whereas in one patient duloxetine was started de novo for MDD onset.

Three patients (15%) had analgesic treatment. One patient started it after surgery.

Other antidystonia meds were taken only by two patients (10%) after surgery.

One (5%) received antipsychotic treatment.

c. Secondary Dystonia

Before surgery
At baseline, four patients (44%) received treatment with BDZ, three patients (33.3%) with tardive dystonia were taking antipsychotic medications, and two patients (22.2%) antidepressant medications.

Only one (11.1%) patient was on therapy with triexyphenidyl at baseline and one patient (11.1%) was on analgesic treatment (non steroidal anti-inflammatory drugs).

After surgery
Six patients (66%) were on BDZ therapy; it was reduced in two patients due to improvement of anxiety after surgery. However, in two cases BDZ therapy was started, for insomnia and anxiety symptoms worsening (BAD).

Three patients (33.3%) were on antidepressant therapy: it was unchanged in two patients but started de novo in the suicidal patient for major depressive episode onset.

Antipsychotic therapy was stable in the three patients (33.3%). The one patient with triexyphenidyl stopped it after surgery, while one patient (11.1%) started baclofen.

The one patient on analgesic treatment was able to stop it after surgery.

**Parameters of stimulation**

At the last DBS follow-up, right/left mean ± SD amplitude, pulse width and frequency of stimulation were: in primary segmental/generalized dystonia 2.3 ± 0.2/ 3.3 ± 0.1 V; 91.3 ± 8.9/107.5 ± 10.9 µsec; 157.1 ± 8.3/162.1 ± 5.5 Hz; in primary CD: 2.74 ± 0.9/2.9 ± 0.9 V; 81.0 ± 39.1/79.5 ± 8.0 µsec; 145.5 ± 42.5/147.0 ± 42.5 Hz; in secondary dystonia: 1.8 ± 1.7/2.5 ± 1.7 V; 51.8 ± 60.1/49.1 ± 24.3 µsec; 86.8 ± 76.2/113.6 ± 72.6 Hz.