**The effect of deep brain stimulation on impulse control related disorders in Parkinson’s disease – a 10-year retrospective study of 137 patients**

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Dear Editor,

Up to 15% of patients with Parkinson’s Disease (PD) experience impulse control and related behaviours (ICRBs), though it is not fully understood why (1). Dopamine agonists (DA) and high total dose of levodopa have been associated with development of ICRBs, with the reduction or withdrawal of a DA often improving these symptoms. Subthalamic nucleus deep brain stimulation (STN-DBS) can be used as a tertiary therapy for PD in order to reduce DA dosage (2, 3), however, the effect of STN-DBS on ICRBs is unclear (4, 5, 6).

Reports into STN-DBS have shown conflicting results. Kim et all (2018) (7) found that all pre-operative ICRBs (n=8) resolved following DBS, with 7 patients experiencing new and persistent ICRBs at 7 years of follow up without any significant change to medication. This suggests an independent effect of STN-DBS on ICRBs, but with both positive and negative outcomes seen. A similar independent DBS effect on ICRBs is suggested by other studies (8), with both improvement and worsening of symptoms seen. Literature suggests mixed outcomes post-DBS on pre-existing ICRBs, as well as de novo ICRBs appearing in approximately 15% of cases reported (9). Hypotheses exist that STN-DBS treatment itself could be a risk factor for ICRBs, or that de novo ICRB cases may have specific risk factors independent to DBS treatment, e.g. PD symptom duration prior to DBS insertion, or total PD symptom duration (7, 10).

We performed a retrospective study of patients collated over 10 years, examining 137 PD patients who had bilateral STN-DBS under the care of The Walton Centre NHS Foundation Trust. We aimed to review any clinical or demographic factors correlating with ICRBs before and after STN-DBS.

We retrospectively assessed patients for the presence of ICRBs who were treated with STN-DBS for PD between 2010 and 2020. Pre- and post-operative electronic documentation, clinic letters and written notes were reviewed and anonymised. Table 1 demonstrates our definition of ICRBs. All patients had a clinical diagnosis of PD and were on PD medications prior to STN-DBS insertion. The following information were collected: patient demographics, age of PD diagnosis, date and type of DBS insertion, any reference to ICRB, type of ICRB, date of first ICRB documentation, medications at the time of ICRB onset, and clinical assessment of ICRBs over time. Pre-operative Unified Parkinson’s Disease Rating Scale (UPDRS) and Minnesota impulsive disorders interview (MIDI) scores were noted when available. Patients with incomplete data were excluded. The lowest dose of medication was assumed when a dose was not referenced.

We classified patients as having pre-operative ICRBs if they were present before surgery, and ‘de novo’ ICRBs, if developed after surgery. An estimated levodopa equivalent daily dose (LEDD) was calculated at onset of ICRB.

 Mann-Whitney U test was used to compare the clinical characteristics of patients with pre-existing ICRB with de novo ICRB cases All data analyses were done with SPSS version 25 package (IBM Corp. Released 2017. IBM SPSS Statistics for Macintosh, Version 25.0. Armonk, NY: IBM Corp.)

Among the 141 patients initially included in the study, 4 were excluded due to insufficient data. A total of 137 patients with PD were reviewed. 70% were men, the mean age for diagnosis of PD was 49 years. The mean duration of PD before DBS insertion was 10 years in men, and 11 years in women (Table 2). The mean follow up time from PD diagnosis was 17 years (SD +/-7.01) and mean follow up from DBS insertion was 6.95 years (SD +/-4.86).

Pre-implantation objective assessments were carried out 122/141 patients. Reasons for exclusion include implantation prior to record keeping, implantation elsewhere, or incomplete data. Analysis of UPDRS and MIDI scores can be found in Table 3.

47/137 patients had a documented ICRB. Ten were excluded due to insufficient medication data making the ICRB cohort 37 (Table 3). 24/37 (64.8%) suffered from one ICRB type with hypersexuality being to most highly reported (Figure 1 A).

The LEDD at ICRB diagnosis was calculated for the ICRB cohort. 3/37 had estimates used for medication doses. At onset of ICRB, 16/37 (43%) were taking a dopamine agonist with a total LEDD average of 1194.63 (+/- 609.26) mg/day. 21/37 (57%) were not taking a DA, with a total LEDD average of 1048.57 (+/- 721.31) mg/day. ,

27/37 ICRB patients (75%) demonstrated preoperative clinical improvement or resolution with reduction of DA or LEDD and did not recur with STN-DBS insertion. 5/37(13.5%) had ICRBs that persisted or recurred following STN-DBS. 5/37 (13.5%) developed de novo ICRB (Figure 1 B).

The de novo group had a PD diagnosis for twice as long as patients with pre-operative ICRBs (p>0.05). All clinical characteristics between the pre-operative ICRBs and de novo cohorts failed to meet significance (Table 4, Figure 1B). Mean duration of DBS before development of ICRBs was 3.5years. All de novo ICRBs demonstrated qualitative clinical improvement with reduction of DA or LEDD.

In conclusion, of the 37/137 patients who experienced ICRB related to their PD, 27% experienced them after STN-DBS insertion, with 13.5% occurring de novo. These results reflect the literature. There were no significant clinical discriminators found to suggest risk factors for developing ICRBs after STN-DBS, however, duration of PD diagnosis should be focussed on in further studies.

The study’s strength is that it was a single centre study of patients who underwent bilateral STN-DBS, it had a large sample size and a long duration of follow-up. Our research has some limitations. Patients in our study were followed under a prospective protocol, ICRBs were investigated retrospectively. Therefore, some cases of preoperative ICRB might have been resolved postoperatively without being reported due to recall bias. Our reliance on clinical documentation resulted in exclusion of patients due to incomplete data, and longitudinal objective assessment of ICRBs through scoring systems would be beneficial for future work. Future studies should consider analysis of electrode contacts in ICRB development and to evaluate pre-operative neuropsychological and neuropsychiatric testing.

 **FIGURE LEGEND**

**Figure 1 A:** A bar chart demonstrating the frequency of ICRB types reported

**Figure 1 B:** Box plot demonstrating duration of PD symptoms at ICRB diagnosis, comparing de novo ICRB cases (green) to pre-existing ICRB cases (red)

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