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CLINICAL ARTICLE - FUNCTIONAL

Surgical adverse events of deep brain stimulation in the subthalamic nucleus of patients with Parkinson's disease. The learning curve and the pitfalls

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Abstract
Background Several surgical adverse events (SAEs) have been associated with Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) in Parkinson's Disease (PD) patients, leading to certain confusion about the risk/benefit ratio of this technique, and giving rise to the need of more and more extensive control studies over longer periods. The aim of this article is to identify and quantify the factors associated with the most frequent AEs from STN DBS in PD-diagnosed patients.
Methods The following variables were studied: aborted procedure, misplaced leads, intracranial haemorrhage, and seizures. This study was carried out in 233 patients diagnosed with PD, with 455 STN electrodes implanted and follow-up after 7 (8–14) years follow up.
Results A total amount of 56 SAEs occurred in 49 patients (11.76 % of total procedures, 12.31 % of implanted leads, 21.03 % of patients). SAEs were: five aborted procedures, 26 misplaced leads, ten intracranial haemorrhages, and 15 seizures. Of all the SAEs, long-term effects only happened in two cases of hemiparesis caused by intracranial haemorrhage; the other SAEs were reversible and didn't leave any long-term clinical consequences (0.42 % of procedures, 0.44 % of leads, and 0.86 % of patients).
Conclusions STN DBS in PD patients is a safe surgical procedure, with good risk/benefit ratios: procedure reliability/correct lead implantation in 95.59 %, 0 mortality/implanted lead, 0.12 morbidity/implanted lead, and 0.0043 neurological sequelae/implanted lead.

Keywords Deep brain stimulation · Parkinson's disease · Subthalamic nucleus · Surgical adverse events

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Introduction

Deep Brain Stimulation (DBS), it is a widely used technique to treat movement disorders such as Parkinson's Disease (PD) [26]. A better response to Subthalamic Nucleus (STN) DBS is achieved in levodopa-dependent patients with PD, either in those with treatment-derived motor complications, or those that do not respond to treatment [4]. Although DBS has been shown to be more effective than other treatments for PD, it may have surgical adverse events (SAEs), whose the frequency and severity could be crucial to determine whether or not the technique is indicated [1, 42].

A PubMed search with the keywords, "subthalamic nucleus", "Deep Brain Stimulation", "Parkinson's disease", "Adverse Events" and "Complications" only revealed a few articles involving a long-term evaluation of large patient populations numbers [14, 19, 21, 36, 39]. Another conclusion of this overview is the common understanding that the surgical team is a key factor when it comes to the number and severity of SAEs, which in turn, need to be communicated [14, 39]. Based on this information, the SAEs presented in this paper represent a larger number of PD diagnosed patients treated

with STN DBS treatment, using the same methodology, and treated using the same methodology, with follow-up occurring over longer time periods.

The aim of the study is to identify and quantify all factors involved with the most frequent SAEs for STN DBS in PD patients, as well as to define this technique's risk-benefit ratio .

Materials and methods

Patient population

There were 455 STN electrodes implanted in 233 patients through 476 procedures carried out between May 1998 (the first STN DBS implant in our hospital) and April 2012. Here, a procedure is defined as the surgical action performed to implant (or not) a DBS electrode in the STN area [27, 40]. The average follow-up period was seven years. All patients were selected according to the Core Assessment Program for Intracerebral Transplantations (CAPIT) [25], and only patients with a 35 % higher improvement on the Unified Parkinson's Disease Rating Scale (UPDRS) after levodopa or apomorphine administration [17] were included. Inclusion and exclusion criteria have been reported in a previous article [36].

Study variables

SAEs directly related to the surgical procedure were selected as the variables for this study: aborted procedures, misplaced leads, intracranial haemorrhage and seizures.

Surgical procedure

The surgical procedure has previously been described [36, 37]. The Cosman-Roberts-Wells (CRW) (Radionics Inc., Burlington MA, USA) stereotactic frame was used first, from May 1998 to December 2007, and followed by the Leksell stereotatic frame (Elekta, Stockholm, Sweden), from January 2008 to April 2012. The target location was determined using an indirect technique (related to the intercomissural line).

With the aim to define the STN somatosensory region as precisely as possible, the target point was obtained after a minimum amount of three neurophysiological microelectrode recordings (MER) series. Control Computed Tomography (CT) was carried out on every patient right after the surgical procedure, with the stereotactic frame in place, as well as a three days post-op Magnetic Resonance Imaging (MRI), in order to check the implanted DBS leads' coordinates with respect to the intercomissural midpoint. Antibiotic prophylaxis was prescribed from the date of surgery up to three days after the pulse generator (IPG) was implanted. Either Soletra® or Kinetra® IPGs (Medtronic Inc., Minneapolis MN, USA) were used.

Patient follow-up took place one, three, six and 12 months post-surgery, and on a yearly basis afterwards.

Definitions of some complications

An aborted procedure involves the abandonment of a procedure for intraoperative or perioperative reasons, except in the case of failure to locate the STN by means of MER.

Misplaced leads are defined as follows: a) a failure to locate the STN by MER during the surgical process, b) any situation requiring the lead(s) relocation due to a suboptimal position in the control MRI, and a clinical response under 30 % according to UPDRS part III, six months after surgery [24].

The intracranial haemorrhages were classified according to their location, (extra-axial, intraparenchymal or intraventricular) and size: mild/moderate (1–5 ml volume) and severe (volume>5 ml).

Statistic analysis

All data were analysed using the SPSS 18.0 (SPSS Inc., Chicago IL, USA) software application. As a descriptive study, continuous variables are presented as the mean and standard deviation (SD), with discontinuous variables as percentages. Fisher's test was used to compare variables by category. Also continuous variable averages such as age and number of trajectories were compared, according to different complications, using the Student's *t*-test and U-Mann–Whitney test for small samples. In all cases, the $p<0.05$ was considered statistically significant. Finally the chi-square test was applid to measure the relationship between dichotomous variables.

Results

Those studied were 122 males (52 %) and 111 females (48 %) with an average age of 61.09 years (36–74; *SD*=7.8. The average period from PD diagnosis until surgery was 11.28 years (2–23: *SD*=4.17). According to the Unified Parkinson's Disease Rating Scale (UPDRS) [17], the patients' average motor score before surgery was 34 (14–59) and a levodopa dose of 1186.55 mg (100–1,900). (Table 1).

The 455 leads were implanted during 476 procedures and 2,271 MERs were taken. The average patient post-surgery follow-up was 7.09 years (0.8–12; *SD*=3.72).

A total of 56 SAEs occurred in 49 patients (11.76 % of total procedures, 12.31 % of implanted leads, 21.03 % of patients). The SAEs were: five aborted procedures, 26 misplaced leads, ten intracranial haemorrhages and 15 seizures. Out of all the SAEs, the only long-term effects were two hemipareses from intracranial haemorrhage; the other SAEs were reversible and left no clinical consequences over time (0.42 % of procedures,

Table 1 Patient's statistics

Age	61.09(37–74; *SD*=7.82)
#Male	122
#Female	111
Average time PD diagnosed/surgery (years)	11.28 (2–23: *SD*=4.17)
Unified Parkinson's disease rating scale(UPDRS) before surgery	34(14–59)
Levodopa dose before surgery	1186.55 mg (100–1,900)

0.44 % of leads, and 0.86 % of patients). The mortality rate was zero during the first five years. Seventeen patients died from causes unrelated to the surgical procedure in the following years. There were 432 IPG replacements required throughout the entire period. Table 2. Figure 1.

All patients showed unilateral or bilateral pneumocephalus in the postoperative CT, depending on whether the procedure was unilateral or bilateral, and the average distance between the frontal bone's inner table and cerebral cortex was 0–8 mm (0.4–11.1; *SD*=3.063). This event was not considered an SAE, given it was a typical consequence of the surgical procedure.

Aborted procedures

In total, there were five aborted procedures (1.05 % of procedures and 1.09 % of implanted leads). (Table 2. Fig. 2).

Statistical analysis did not show any significant differences when it came to the amount of aborted procedures and patient's age or gender.

Misplaced leads

In total, there were 25 misplaced leads, 16 through a lack of STN location, and ten suboptimal lead locations (5.25 % within the total amount of procedures and 5.49 % of the implanted leads). (Table 2. Fig. 3).

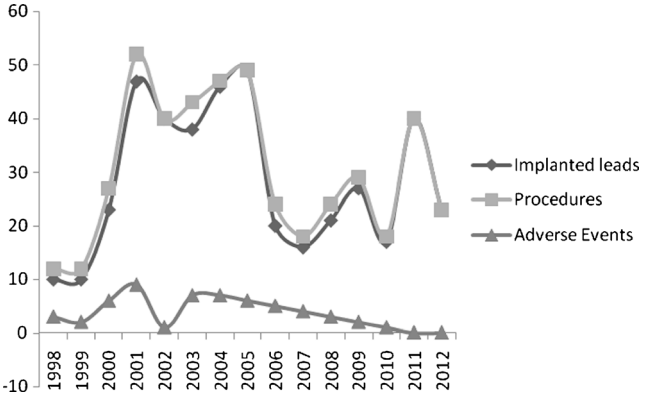

Fig. 1 Ratio #surgical adverse events vs #procedures and released. (%)

The statistical analysis did not show significant differences when it came to the number of misplaced leads and the remaining variables or the patients' age or gender.

Intracranial haemorrhages

A total of ten intracranial haemorrhages in ten patients occurred (2.1 % of procedures, 2.20 % of leads and 4.29 % of patients), with nine intraparenchymal and one intraventricular.

In 1998, one patient presented moderate subcortical venous haemorrhage and confusion. In 2000, one patient had moderate intraventricular haemorrhage and confusion, and another moderate had thalamic haemorrhage with impairment of consciousness, which led to an emergency CT and abortion of the surgical procedure. Both cases also presented moderate brain swelling. In 2001, two patients presented moderate cortical venous hemorrhagic infarction, one with moderate swelling and the other one with a large amount of swelling, and both patients also suffered seizures. In 2003, one patient suffered moderate right thalamic haemorrhage along with moderate brain swelling and seizures. In 2004, one patient presented moderate frontal intraparenchymal haemorrhage with brain swelling and seizures. In 2005, one patient showed a severe intraparenchymal haemorrhage leading to an emergency

Table 2 Number of surgical adverse events and released. Total number of procedures (476) = total number of implanted lead (455) + aborted procedures (5) + no STN location (16)

Year	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total
Procedures	12	12	27	52	41	46	49	33	45	21	25	30	20	40	28	476
Leads	10	12	25	47	41	42	48	33	43	19	23	29	20	40	23	455
Aborted procedures	0	0	1	1	0	1	0	0	2	0	0	0	0	0	0	5
Misplaced leads	2	2	3	4	0	4	1	0	2	2	3	2	1	0	0	26
Intracranial haemorrhages	1	0	2	2	0	1	1	2	0	1	0	0	0	0	0	10
Seizures	0	0	0	2	1	1	5	4	1	1	0	0	0	0	0	15
Total adverse events	8	2	6	9	1	7	7	6	5	4	3	2	1	0	0	56
Adverse event/procedure in %	25	16.67	22.22	17.30	2.44	15.21	14.29	18.18	11.11	19.04	12	6.66	5	0	0	11.76
Misplaced leads/procedures	16.66	16.66	11.11	7.69	0	8.70	2.04	4.44	4.44	9.52	12	6.66	5	0	0	7.49

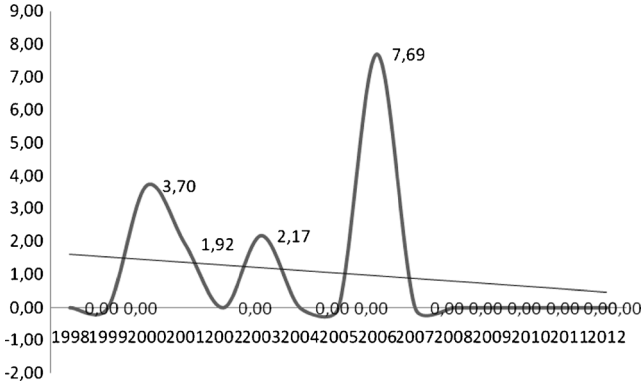

Fig. 2 Ratio #aborted procedures vs #procedures and released by year (%)

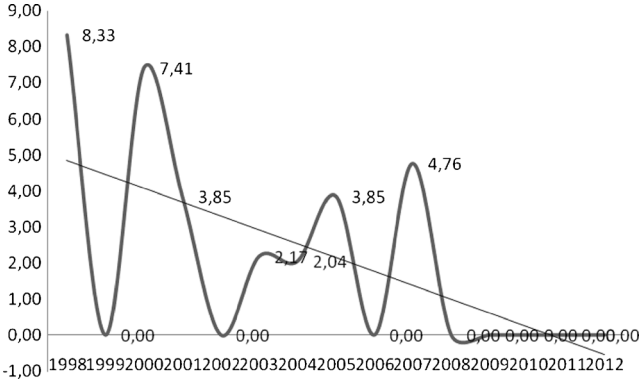

Fig. 4 Ratio # intracranial haemorrhage vs #procedures and released. (%)

evacuation without lead removal. As a consequence of the haematoma, the patient presented residual hemiparesis. This patient also suffered from large amounts of brain swelling on the hemorrhagic side, with moderate swelling on the contralateral side. In the same year, another patient presented moderate mesencephalic haemorrhage and seizures. Lastly, in 2007, another patient suffered severe intraparenchymal haemorrhage with bilateral moderate brain swelling which caused seizures and residual hemiparesis. Table 2. Fig. 4.

In the statistical comparison of intracranial haemorrhage and the rest of the studied variables, a statistically significant relationship between intracranial haemorrhage and seizures (p=0.002) was shown. We also observed that patients with intracranial haemorrhages are usually older (68.60 years; SD= 5.10) than those that did not present this complication (60.48 years; SD=7.83) (p<0.001).

Seizures

Fifteen patients presented seizures, six with intracranial haemorrhage and brain swelling, and five with brain swelling alone. Only four patients presented seizures on a normal postoperative CT. These patients presented a single tonic-clonic generalised seizure episode within the first 12 h post-surgery (3.15 % of procedures, 3.30 % of implanted leads and 6.44 % of patients). Table 2. Fig. 5.

In the statistical analysis carried out comparing seizures and the rest of studied variables, we only observed a significant relationship with intracranial haemorrhage (p=0.002). No statistical difference related to age, gender or number of MERs was found.

Discussion

Aborted procedures and misplaced leads

With this methodology, aborted procedures represented 1.05 % of the total amount of procedures, while previous published data range from 0.9 % to 4.9 % for this kind of SAE [14]. The causes were confusion and haemorrhage during surgery (2000), mechanical failure of the register system (2001), stereotactic frame misalignment (2003), a panic attack (2006), and a brain shift during the second lead implant procedure (2006). Unlike other authors [27], we have not included the procedures involving our team's failure to decide on an STN location in this section, because we consider that these procedures fit more appropriately in the misplaced leads

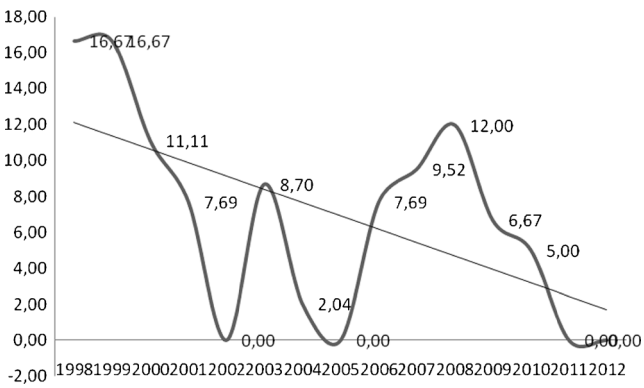

Fig. 3 Ratio #misplaced leads vs #procedures and released by year (%)

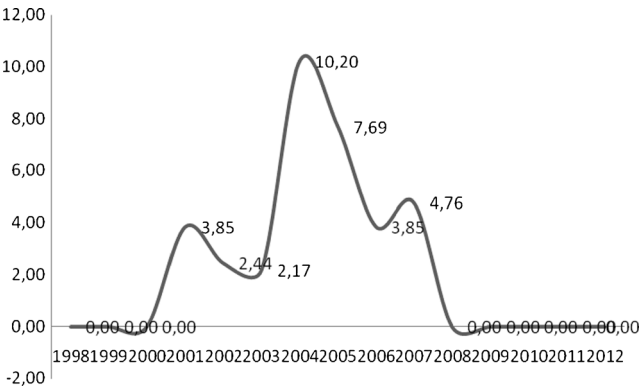

Fig. 5 Ratio # seizures vs #procedures and released. (%)

section, since the same methodological philosophy is involved.

Misplaced leads

Cases involving a failure to locate the STN with MERs are included in this section, given that we consider the reasons for this type of SAE are similar to those influencing a suboptimal positioning of the DBS lead in the STN.

From a total of 26 misplaced leads, 16 (61.54 %) were caused by failure to locate the STN, and ten (38.46 %) by a suboptimal position of the DBS electrode.

For the 16 cases in which we chose not to implant the DBS lead, it was decided that there was not enough representative STN activity in the MER recordings, leading to cancellation of the procedure, rather than leaving the DBS lead in a structure that had not been fully identified. The most common reasons against implantation of the DBS lead in the STN are: intrinsic errors of the stereotactic frame, CT or MRI, errors attributed to the observer (surgeon or radiologist), STN size, shape and spatial disposition variability, brain shift during the procedure, and lack of accuracy when the DBS lead is introduced without a cannula [13, 22, 27, 28, 32]. We think that pneumocephalus has little influence on brain shift, although it is an indirect sign of cerebrospinal fluid (CSF) loss and/or redistribution [2]. Precisely when CSF loss is higher than 20 mm^3, approximately 2 mm brain shift occurs in the anterior commissure [15]. If we assume that pneumocephalus volume is similar to the volume of CSF loss during the surgical procedure, the volume was always below 20 cm^3 for all misplaced leads cases, other than with one procedure in which we failed to correctly locate the STN, precisely due to brain shift during the second lead implant.

In normal studies, 35 % of initial radiological targets did not correlate to the final neurophysiological targets [38]. In the literature, the suboptimal implants rate varies between 2.2 % and 9 %, and in even up to 46.34 % of patients, with brain shift and intrinsic problems between the rigid cannula and the DBS [11, 27, 30], as the most common causes.

The average amount of MERs in procedures where the STN could not be located was 6.83 (4–12; *SD*=1.49), and 4.73 (3–7; *SD*=1.53) and 4.65 (3–7; *SD*=1.49) for the remaining misplaced lead procedures and DBS leads, respectively. Taking into account that a good recording and good clinical response to stimulation is the gold standard for the appropriate placement of the lead in the STN, along with neurophysiological STN identification by MERs, lead implantation using local field potentials (LFPs) were employed in 2009. Therefore, we believe that precision during DBS leads implants in the STN with MER and LFPs increases the number of non-implants but significantly decreases the number of misplaced leads, enhancing the implanted DBS lead efficiency, which provides us with a procedure reliability percentage of 95.59 %.

Although a misplaced lead is a complication that is ever-present, aside from the last two years of this study, we have observed one peak, concentrated between 1998 and 1999. This statistically significant, higher complication rate may be attributable to the learning curve with respect to the procedure.

Intracranial haemorrhage

Intracranial haemorrhage is the most severe complication of stereotactic surgeries and, although the consensus is that the incidence of symptomatic intracranial haemorrhage is below 2 %, its recurrence during movement disorder surgery varies between 0 % and 34 % [8, 10, 31, 35, 43]. This large variation is mainly due to target variability, the use of different surgical techniques, the use of different criteria for haemorrhage assessment, whether or not postoperative radiological controls are carried out, the differences in methodology from those in the published scientific articles, and the experience of the surgical team [5, 7, 9, 11, 18, 40].

While the bleeding risk is 0.7–2.9 % in some large series [6, 29], ten intracranial haemorrhages occurred in our study, corresponding to 2.10 % of procedures, 2.20 % of implanted leads and 4.29 % of patients, with these SAEs mainly occurring in 1998 (8.33 % of procedures) and 2000 (7.40 % of procedures).

If we take two time periods (1998–2004 and 2005–2012) and assess the recurrence of intracranial haemorrhage during these two periods, we observe that the incidence of intracranial haemorrhage per procedure was 2.93 and 1.27 % in the first and second periods, respectively, and, therefore, no statistically significant difference is observed. There is a downward trend in the incidence of intracranial haemorrhage per procedure, with a figure of 0 % in the last 138 procedures (Fig. 4). Since nine out of ten intracranial haemorrhages happened in the proximity of the lead pathway, we believe that these events occur because of a direct vascular lesion caused by the advance of the lead/guide tube system [3, 6]. All the patients who suffered intracranial haemorrhage presented clinical symptoms.

On the other hand, the recurrence of permanent neurological deficit produced by intracranial haemorrhage varies between 0.6 % and 6 % [16], with a figure of 0.42 % of procedures in our study (two residual hemipareses).

The relationship between the use of MER and intracranial haemorrhage rate is still a delicate topic. Some authors believe that there is a direct relationship with the amount of MERs and the risk for intracranial haemorrhage, whereas others do not find any significant difference [6, 16]. In our study, we compared the number of MERs between 1998–2004 and 2005–

2011. There were 4.0 (SD 3.32) and 4.50 MERs (SD 2.71) in the first and second period, respectively, and, therefore, there is no statistical difference between the two periods. These data supports the theory that the number of MERs is not related to the probability of intracranial haemorrhage, and the risk of bleeding was 0.005 per MER undertaken.

Similarly, an important correlation between the proximity of the lead entry point to a cerebral sulcus and the risk of intracranial haemorrhage has been described. This risk is often hard to avoid, since brain shift occurs on arachnoid opening, which may alter the cortical anatomy turning a projected gyrus into an actual sulcus trajectory [37]. In order to avoid pathways that may traverse cerebral sulci, we insert the lead in the cerebral cortex by direct vision, and if there is a sulcus in the craniotomy hole, MERs are undertaken—even when they are not parallel— across the same cortex entry point, with the aim of avoiding the sulcus. In cases where it is impossible to avoid the sulcus, a new burr hole should be made. Gologorsky et al. [20] published that 20 % of trajectories traversed a lateral ventricle, but this could only be verified in seven patients in our study. A low incidence of lateral ventricle crossing may be caused, in our opinion, by the entry angles used on all our patients from the outset: α (lateral) angle: 10–20º and β (anteroposterior): 50–60º [14].

As with other studies [5, 6, 22, 35, 39, 41, 43], statistical comparison of intracranial haemorrhage rate with its predictive risk factors (age, gender, MER use, number of MERs, the use of a cannula for lead introduction, arterial hypertension) was undertaken, and no significant statistical correlation was found, other than with age ($p<0.001$), given patients with intracranial haemorrhage were older than those without: 68.60 years (SD 5.10) versus 60.48 years ($SD=7.,83$) respectively. Finally, we also observed a significant relationship between intracranial haemorrhage and seizures ($p=0.002$).

Seizures

Meta-analysis have given rise to the claim that approximately 2.4 % (range: 0–13 %) of patients presented seizures after DBS surgery, 75 % of which occur during the lead implant procedure, with intracranial haemorrhage being the most common reason for their occurrence [7, 12]. In our series, the seizure rate was 6.44 % of patients, and consisted of a single tonic-clonic generalised episode that occurred during the first 12 h post-implantation, and no patients required anticonvulsant treatment after the hospital discharge.

If we compare the number of seizures during the 1998–2004 and 2005–2012 periods, we observe nine and six cases during the first and second period, respectively, with no statistically significant relationship between them. It is important to highlight that 60 % of seizures happened during the 2004–2005 period, possibly due to the lead-guide tube advance across the brain, as explained in the previous section. Seizures appeared to be associated to intracranial haemorrhage in 40 % of the cases conducted using our methods. No seizure events occurred during our last 138 procedures.

Statistical analysis comparing seizures and age, gender, total amount of MERs, MERs across the caudate nucleus, and surgery duration, showed no statistical difference ($p>0.05$). However, we did find a statistically significant relationship between seizures and intracranial haemorrhages ($p=0.002$).

Finally, although pneumocephalus was predicted to be a factor in seizures, as with the Pouratian et al., study, we didn't find a statistically significant relationship in our study [33].

The learning curve

Due to the complexity and great need for precision with STN DBS surgery in patients with PD, the learning curve is slow and long, which makes both complication and consequence rates highly dependent on the surgical team's experience [8, 11, 14, 39], and, although the efficacy has been proven, the risk/benefit ratio depends on the frequency and severity of SAEs [9, 34].

We found misplaced leads (46.43 %) to be the most common SAE, with highest incidence during 1998 and 1999, indicating a relationship with the learning curve.

If we compare the SAE rate per procedure/year, we observe that 1998 (25 %) and 2000 (22.22 %) were the years with the highest SAE rate, and 2011 and 2012 (0 %) were the lowest. If we now compare different time periods, 1998–2004 and 2005–2012, the SAEs varied from 14.64 to 8.86 % of procedures. In the end, we observed a significant drop in the SAE rate from 2007 (19.04 %) to 2011 (0 %). This shows a clear downward trend, indicating a relationship with the learning curve (Table 2).

In the analysis of the years with higher and lower numbers of procedures compared to the baseline, there was a higher average of misplaced leads when less than 30 procedures were carried out per year ($t_0=2.537$; $df=13$; $p=0.025$).

While neurological consequences could reach up to 6 % in the literature [23], only two intracranial haemorrhage derived hemipareses were considered as consequences (0.42 % of procedures, 0.44 % of implanted leads and 0.86 % of patients) in this study, given that all other complications were reversible. Finally, although the peak mortality rate is around 4.4 % in some series [8], we did not record any deaths during the procedure.

This study has the same limitations as any retrospective analysis. A prospective analysis may help to confirm the data.

Conclusions

- STN DBS in PD patients is a safe surgical procedure and features a good risk/benefit ratio: 95.59 % reliability/correct lead implantation for the procedure, 0 mortality/implanted lead, 0.12 morbidity/implanted lead and 0.0043 neurological sequelae/implanted lead.
- There is a two years learning curve for STN DBS on PD patients, and complications such as lead misplacement are less frequent after that time period.
- Intracranial haemorrhage was the highest morbidity SAE, and a statistically significant relationship exists between this issue and seizures.
- Age is correlated to intracranial haemorrhage rates.
- The number of MERs does not affect intracranial haemorrhage occurrences.

Conflict of interest None.

References

1. Baizabal JF, Simpson R, Jankovic J (2011) Diagnosis and treatment complications related to deep brain stimulation hardware. Mov Disord 28:1398–1406
2. Bakay RAE, Daniluk S, Davies KG, Novak P, Vu T, Nazzaro JM, Ellias SA (2009) Isolation of the brain-related factor of the error between intended and achieved position of deep brain stimulation electrodes implanted into the subthalamic nucleus for the treatment of Parkinson's disease. Neurosurgery 64(ONS Suppl 2):374–384
3. Benabid AL, Binder DK, Rau GM, Starr PA (2005) Risk factors for haemorrhage during microelectrode-guide deep brain stimulator implantation for movement disorders. Neurosurgery 56:722–732
4. Benabid AL, Chabardes S, Mitrofanis J, Pollak P (2009) Deep brain stimulation of the subthalamic nucleus for the treatment of Parkinson's disease. Lancet Neurol 8:67–81
5. Ben-Haim S, Asaad WF, Gale JT, Eskandar EN (2009) Risk factors for haemorrhage during microelectrode-guided deep brain stimulation and the introduction of an improved microelectrode design. Neurosurgery 64:754–763
6. Binder DK, Rau GM, Starr PA (2005) Risk factors for haemorrhage during microelectrode-guide deep brain stimulator implantation for movement disorders. Neurosurgery 56:722–732
7. Boviatsis E, Stavrinou L, Themistocleous M, Kouyialis A, Sakas D (2010) Surgical and hardware complications of deep brain stimulation. A seven-year experience and review of the literature. Acta Neurochir 152:2053–2062
8. Bronstein JM, Tagliati M, Alterman RL, Lozano AM, Volkmann J, Stefani A, Horak FB, Okun MS, Foote KD, Krack P, Pahwa R, Henderson JM, Hariz MI, Bakay RI, Rezai A, Marks WJ, Moro E, Vitek JL, Weaver FM, Gross RE, DeLong MR (2011) Deep brain stimulation for Parkinson's disease. An expert consensus and review of key issues. Arch Neurol 68:165–171
9. Burdik A, Fernández H, Okum M, Chi Y, Jacobson C, Foote K (2010) Relationship between higher rates of adverse events in deep brain stimulation using standardised prospective recording and patient outcomes. Neurosurg Focus 29(2):E4
10. Chabra V, Sung E, Mewes K, Bakay RA Abosch A, Gross RE (2010) Safety of magnetic resonance imaging of deep brain simulator systems: a serial imaging and clinical retrospective study. Clinical article. J Neurosurg 112:497–502
11. Chan DTM, Zhu XL, Yeung JHM, Mok VCT, Wong E, Lau C, Wong R, Lau C, Poon WS (2009) Complications of deep brain stimulation: a collective review. Asian J Surg 32:258–263
12. Coley E, Farhadi R, Lewis S, Whittle IR (2009) The incidence of seizures following deep brain stimulating electrode implantation for movement disorders, pain and psychiatric conditions. Br J Neurosurg 23:179–183
13. Daniluk S, Davies KG, Novak P, Vu T, Nazzaro JM, Ellias SA (2009) Isolation of the brain-related factor of the error between intended and achieved position of deep brain stimulation electrodes implanted into the subthalamic nucleus for the treatment of Parkinson's disease. Neurosurgery 64(ONS Suppl 2):374–384
14. Doshi P (2011) Long-term surgical and hardware-related complications of deep brain stimulation. Stereotact Funct Neurosurg 89:89–95
15. Elias WJ, Fu K-M, Frysinger RC (2007) Cortical and subcortical brain shift during stereotactic procedures. J Neurosurg 107:983–988
16. Elias WJ, Sansur CA, Frysinger RC (2009) Sulcal and ventricular trajectories in stereotactic surgery. J Neurosurg 110:201–207
17. Fahn S, Elton RL, the members of the Unified Parkinson's disease Rating Scale (1987) Recent developments in Parkinson's disease. Vol 2. Florham Park NJ. In: Fahn S, Marsden CD, Calne CB, Goldstein M (eds) MacMillan healthcare information., pp 153–163
18. Falowski S, Ooi YC, Smith A, Metman LV, Bakay RAE (2012) An evaluation of hardware and surgical complications with deep brain stimulation based on diagnosis and lead location. Stereotact Funct Neurosurg 90:173–180
19. Follet KA, Weaver FM, Stern M, Hur K, Harris CL, Luo P, Marks WJ, Rothlind J, Sagher O, Moy C, Pahwa R, Burchiel K, Hogarth P, Lai EC, Duda JE, Holloway K, SAmii A, Horn S, Bronsteins JM, Stoner G, Starr PA, Simpson R, Baltuch G, De Salles A, Huang GD, REda DJ, CSP 468 Study Group (2011) Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. N Engl J Med 362:2077–2091
20. Gologorsky Y, Ben-Haim S, Moshier E, Godbold J, Tagliati M, Weisz D, Alterman R (2011) Transgressing the ventricular wall during subthalamic deep brain stimulation surgery for Parkinson's Disease increases the risk of adverse neurological sequelae. Neurosurgery 69:294–300
21. Goodman RR, Kim B, McClelland S III, Senatus PB, Winfield LM, Pullman SL, Yu Q, Ford B, McKhann GM (2006) Operative techniques and morbidity with subthalamic nucleus deep brain stimulation in 100 consecutive patients with advanced Parkinson's disease. J Neurol Neurosurg Psychiatry 77:12–17
22. Krack P, Batir A, Van Blercom N, Chabardes S, Fraix V, Ardouin C, Koudsie A, Limousin PD, Benazzouz A, Le Bas JF, Benabid AL, Pollak P (2003) Five-year follow up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. N Engl J Med 349:1925–1934
23. Hu X, Jiang X, Zhou X, Liang J, Wang L, Cao Y, Liu J, Jin A, Yang P (2010) Avoidance and management of surgical and hardware-related complications of deep brain stimulation. Stereotact Funct Neurosurg 88:296–303
24. Lang AE, Widner H (2002) Deep brain stimulation for Parkinson's disease: patient selection and evaluation. Mov Disord 7:94–101
25. Langston JW, Gotees CG, Brooks D, Fahn S, Freeman T, Watts R (1992) Core assessment program for intracerebral transplantations. Mov Disord 7:2–13
26. Limousin P, Pollak P, Benazzouz A, Hoffmann D, Le Bas JF, Broussolle E, Perret JE, Benabid AL (1995) Effect on parkinsonian signs and symptoms of bilateral subthalamic nucleus stimulation. Lancet 345:91–95
27. Lyons KE, Wilkinson SB, Overman H, Pahwa R (2004) Surgical and hardware complications of subthalamic stimulation. A series of 160 procedures. Neurology 63:612–616

28. Miyagi Y, Shima F, Sasaki T (2007) Brain shift: an error factor during implantation of deep brain stimulation electrodes. J Neurosurg 107: 989–997
29. Oh MY, Abosch A, Kim SH, Lang A, Lozano A (2002) Long-term hardware-related complications of deep brain stimulation. Neurosurgery 50:1268–1276
30. Okun MS, Tagliati M, Pourfar M, Fernández HH, Rodríguez RL, Alterman RL, Foote KD (2005) Management of referred deep brain stimulation failures; a retrospective analysis from 2 movement disorders centres. Arch Neurol 62:1250–1255
31. Patel NK, Plaha P, Gill SS (2007) Magnetic resonance imaging-directed method for functional neurosurgery using implantable guide tubes. Neurosurgery 261:358–366
32. Patel NK, Khan S, Gill SS (2008) Comparison of atlas and magnetic-resonance-imaging based stereotactic targeting of the subthalamic nucleus in the surgical treatment of Parkinson's disease. 86:153–161
33. Pouratian N, Reames DL, Frysinger R, Elias WJ (2011) Comprehensive analysis of risk factors for seizures after deep brain stimulation surgery. J Neurosurg 115:310–315
34. Rodríguez-Oroz MC, Obeso JA, Lang AE, Houeto JL, Pollak P, Rehncrona S, Kulisevsky J, Albanese A, Vokmann J, Hariz MI, Quinn NP, Speelman JK, Guridi J, Zamarbide I, Gironell A, Mollet J, Pascual-Sedano B, Pidoux B, Bonnet AM, Agid Y, Xie J, Benabid AL, Lozano AM, Saint-Cyr J, Romito L, Contarino MF, Scerrati M, Fraix V, Van Blercom N (2005) Bilateral deep brain stimulation in Parkinson's disease: a multicentre study with 4 years follow-up. Brain 128:2240–2249
35. Sansur Ch A, Frysinger RC, Pouratian N, Fu K-M, Bittl M, Oskouian RJ, Laws E, Elias J (2007) Incidence of symptomatic haemorrhage after stereotactic electrode placement. J Neurosurg 107:998–1003
36. Seijo F, Alvarez-Vega MA, Gutierrez JC, Fernández F, Lozano B (2007) Complications in subthalamic nucleus stimulation surgery for treatment of Parkinson's disease. Review of 272 procedures. Acta Neurochir (Wien) 149:867–876
37. Seijo F, Lozano B, Santamarta E, Fernández F, Sainz A (2009) In deep brain stimulation: applications, complications and side effects. In: Rogers MH, Anderson PB (eds) Common questions and answers to deep brain stimulation surgery. Nova Science Publishers, Inc, New York, pp 1–29, ISBN: 978-1-60692-895-0
38. Tasker RR (1998) Deep brain stimulation is preferable to thalamotomy for tremor suppression. Surg Neurol 49:145–154
39. Vergani F, Landi A, Pirillo D, Cilia R, Antonini A, Sganzerla E (2010) Surgical, medical, and hardware adverse events in a series of 141 patients undergoing subthalamic deep brain stimulation for Parkinson's disease. World Neurosurg 4:338–344
40. Videnovic A, Metmann LV (2008) Deep brain stimulation for Parkinson's disease: prevalence of adverse events and the need for standardised reporting. Mov Disord 15:343–349
41. Voges J, Waerzeggers Y, Maarouf M, Lehrke R, Koulousakis A, Lenartz D, Sturm V (2006) Deep-brain stimulation: long-term analysis of complications caused by hardware and surgery-experiences from a single centre. J Neurol Neurosurg Psychiatry 77:868–872
42. Weaver FM, Follett K, Stern M, Hur K, Harris C, Marks WJ, Rothling J, Sagher O, REda D, MOy CS, Pahwa R, Burchiel K, Hogarth P, Lai EC, Duda JE, Holloway K, Samii A, Horn S, Bronstein J, Stoner G, Heemskerk J, Huang GD (2009) Bilateral deep brain stimulation vs. Best medical therapy for patients with advanced Parkinson's disease: a randomised controlled trial. JAMA 301:63–73
43. Zrinzo L, Foltynie MR, Limousin P, Hariz M (2012) Reducing hemorrhagic complications in functional neurosurgery: a large case series and systematic literature review. J Neurosurg 116:84–94

Comments

Complications following Deep brain stimulation (DBS) surgery are relatively common and are generally either procedural related or hardware related.

Procedura; complications such as ICH, electrode misplacement, aborted procedures etc are closely related with the overall volume of cases done and have a clear relation with the single surgeon learning curve. Procedural complications are less common in high volume centre where there is a well-established DBS program; the authors clearly stated this point in their discussion. Is there a minimal volume of DBS procedure per year that make a centre safe on the procedural point of view ?In the UK a minimum of 10 DBS per year has been considered the cut off number to receive accreditation, I still consider this number too low, possibly 35-50 DBS procedures are the number that a DBS centre should be performing to minimize procedural risks.

Another important issue is infection in DBS which can be either associated with the implantation or with the hardware revisions.

Reduction of infections could be achieved with antibiotics impregnated hardware (as has been developed for shunt hardware) and close collaboration with the manufacture is necessary to improve the infection profile of DBS.

In this interesting paper the authors reported a relatively high rate of ICH, is this possibly associated with MER and multiple trajectories. The jury is still out regarding the necessity of MER but there is definitively an increased risk with this technique. Delayed ICH/strokes are potentially devastating complications and as for brain biopsies can occur in DBS, early post-operative CT may give a false sense of security.

The functional neurosurgical community should work harder to reduce the rate of complications both procedural and hardware related, in the future national and international registry will allow to identify potential solvable problems in DBS surgery.

References

Risks of common complications in deep brain stimulation surgery: management and avoidance.

Fenoy AJ, Simpson RK Jr. J Neurosurg. 2014 Jan;120(1):132-9.

Deep brain stimulation of the subthalamic nucleus in Parkinson's disease: surgical technique, tips, tricks and complications.

Kocabicak E, Temel Y. Clin Neurol Neurosurg. 2013 Nov;115(11):2318-23.

Cerebral venous infarction: a potentially avoidable complication of deep brain stimulation surgery.

Morishita T, Okun MS, Burdick A, Jacobson CE 4th, Foote KD. Neuromodulation. 2013 Sep;16(5):407-13.

One-step tunneling of DBS extensions–a technical note. Linhares P, Carvalho B, Vaz R. Acta Neurochir (Wien). 2013 May;155(5):837-40;

Deep brain stimulation hardware complications in patients with movement disorders: risk factors and clinical correlations.

Baizabal Carvallo JF, Mostile G, Almaguer M, Davidson A, Simpson R, Jankovic J. Stereotact Funct Neurosurg. 2012;90(5):300-6

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