Surgical and Hardware-Related Adverse Events of Deep Brain Stimulation

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Surgical and Hardware-Related Adverse Events of Deep Brain Stimulation: A Ten-Year Single-Center Experience

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ABSTRACT

Introduction: Although deep brain stimulation (DBS) is effective for treating a number of neurological and psychiatric indications, surgical and hardware-related adverse events (AEs) can occur that affect quality of life. This study aimed to give an overview of the nature and frequency of those AEs in our center and to describe the way they were managed. Furthermore, an attempt was made at identifying possible risk factors for AEs to inform possible future preventive measures.

Materials and Methods: Patients undergoing DBS-related procedures between January 2011 and July 2020 were retrospectively analyzed to inventory AEs. The mean follow-up time was 43 ± 31 months. Univariate logistic regression analysis was used to assess the predictive value of selected demographic and clinical variables.

Results: From January 2011 to July 2020, 508 DBS-related procedures were performed including 201 implantations of brain electrodes in 200 patients and 307 implantable pulse generator (IPG) replacements in 142 patients. Surgical or hardware-related AEs following initial implantation affected 40 of 200 patients (20%) and resolved without permanent sequelae in all instances. The most frequent AEs were surgical site infections (SSIs) (9.95%, 20/201) and wire tethering (2.49%, 5/201), followed by hardware failure (1.99%, 4/201), skin erosion (1.0%, 2/201), pain (0.5%, 1/201), lead migration (0.52%, 2/386 electrode sites), and hematoma (0.52%, 2/386 electrode sites). The overall rate of AEs for IPG replacement was 5.6% (17/305). No surgical, ie, staged or nonstaged, electrode fixation, or patient-related risk factors were identified for SSI or wire tethering.

Conclusions: Major AEs including intracranial surgery–related AEs or AEs requiring surgical removal or revision of hardware are rare. In particular, aggressive treatment is required in SSIs involving multiple sites or when *Staphylococcus aureus* is identified. For future benchmarking, the development of a uniform reporting system for surgical and hardware-related AEs in DBS surgery would be useful.

Keywords: Adverse events, complications, deep brain stimulation, hardware failure, infection

Conflict of Interest: The authors reported no conflict of interest.

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INTRODUCTION

Deep brain stimulation (DBS) is nowadays an established and widely applied treatment for several brain disorders, such as Parkinson disease (PD), tremor, epilepsy, and obsessive-compulsive disorder (OCD).[1–4] Although this neurosurgical treatment has shown to be effective in the short and long term, some patients may not experience an improvement in their quality of life because of undesired stimulation-induced side effects or adverse events (AEs).[5–8] The reported incidence of surgical and hardware-related AEs varies largely.[9] In a systematic analysis including 96 articles, the incidence of a variety of AEs related to hardware, including surgical site infections (SSIs) (5.12% [4.45–11.51]), lead migration (1.6% [0.72–3.04]), fracture or failure of the lead or other parts of the implant (1.46% [0.41–4.2]), and skin erosions without infection (0.48% [0.36–7.14]), was reported.[9] Interestingly, patients with indications such as Tourette syndrome (TS) and epilepsy were found to be more prone to undergo hardware-related SSIs than those with PD.[9,10] However, patient- or surgery-related factors associated with and the management of surgical and hardware-related AEs of DBS are not frequently described.[11–14]

In light of increased application of DBS in established and emerging indications and substantial resources required for DBS (ie, extensive programming, lifelong follow-up, and recurrent hardware costs), reporting current surgical and hardware-related AEs is essential for evaluating the risk-benefit ratio of this therapy. Here, we present a comprehensive analysis of the AEs that occurred following DBS-associated surgical procedures over a period of ten years in a single center. This study aimed to give an overview of the nature and frequency of those AEs in our center and to describe the way they were managed. Furthermore, an attempt was made at identifying possible risk factors to inform possible future preventive measures.

MATERIALS AND METHODS

Data Assessment and Follow-Up

This study involved a retrospective chart review of all patients receiving a DBS system or implantable pulse generator (IPG) replacement between January 2011 and July 2020 of a single academic center (Maastricht University Medical Center). Data were retrieved from chart records and included age, sex, diagnosis, and the presence of comorbidity. Details of the surgical sessions were documented, including the length of procedure and, if applicable, the time to internalization of external leads. All peri- and postoperative AEs related to DBS were recorded, including hematoma, pain, SSI, wound dehiscence, skin erosion, painful extension wire tethering, and migration or fracture of brain electrodes or extension wires. In addition to the demographic data, we documented the following risk factors potentially predisposing to DBS hardware-related AEs: surgical procedure duration, surgical experience, body mass index, smoking, diabetes mellitus, and postoperative wound leakage. Only patients with a minimum follow-up of six months were included, resulting in a mean follow-up time of 43 ± 31 months.

Ethical Statement

The work described was conducted in accordance with the Declaration of Helsinki. Approval by an institutional review board and patient consent are not required by law in the case of research with patient data collected in the course of routine clinical care if the data are made anonymous and nonidentifiable (indicated on the website of the Dutch Central Committee on Research Involving Human Subjects: https://english.ccmo.nl/investigators/legal-framework-for-medical-scientific-research/your-research-is-it-subject-to-the-wmo-or-not).

Surgical Procedure

DBS Implantation

For a detailed description of our stereotactic DBS procedures, please refer to the previous publications.[15–18] In short, surgical procedures were performed under general anesthesia with remifentanil and propofol (n = 56) or under local and procedural sedation and analgesia (posterior subthalamic area with application of 1% lidocaine with epinephrine 1:100,000 at the scalp incision and pin sides; n = 145).[19] A total of 201 DBS implantations were performed by four surgeons (n = 74, n = 41, n = 71, and n = 14, respectively). All four surgeons had several years of experience before the defined period. A Leksell stereotactic frame (Model G, Elekta Instrument Stockholm, Stockholm, Sweden) was mounted on the skull, and a perioperative computed tomography scan of the head with frame was acquired and fused with the preoperative magnetic resonance images using the FrameLink software (Medtronic, Fridley, MN) or Brainlab iPlan (Brainlab, Feldkirchen, Germany). The planned target was defined in relation to the anterior and posterior commissures and adjusted on the basis of the patient's individual anatomy. Typically, the angles of approach were chosen to avoid the lateral ventricle and the caudate nucleus. In 194 patients, microelectrode recordings were performed. The techniques for lead placement were the same for both staged and single-stage implantations. For single-stage implantations, the stereotactic frame was removed after both frontal incisions had been closed. In the case of local anesthesia, the patient was placed under general endotracheal anesthesia for the implantation of the lead extensions. These were subsequently connected to an IPG in the infraclavicular or abdominal regions, where the abdominal location of the IPG is preferred to reduce tethering concerns and increase the distance from the brain electrode in case of SSI. For two-stage implantation procedures, fixed electrodes were connected to an externalized extension cable, and after a mean of five days, the electrodes were internalized.

IPG Replacement

IPG replacement surgical procedures were routinely performed under local anesthesia (1% lidocaine with epinephrine 1:100,000) by a stereotactic and functional neurosurgeon. For primary DBS implantation, surgical procedures were generally postponed if there was any relative contraindication to proceeding (ie, recent illness). Skin preparation was performed with a chlorhexidine solution (chlorhexidine digluconate 0.5% in alcohol 70%) or povidone-iodine. After disinfection, the surgical site was covered with an iodine-impregnated adhesive (Ioban; 3M, Saint Paul, MN) in participants without iodine intolerance. Implants were opened only right before insertion. Wound closure was typically done in multiple layers to prevent dead space formation.

Perioperative Sterile Techniques/Antibiotic Prophylaxis

Complete hair removal was abandoned in 2014.[20] Henceforth, for both single- and two-stage implantation procedures, the evening before lead placement, the hair was washed with povidone-iodine shampoo. Perioperative sterile techniques have been

described previously.[20] Prophylactic antibiotics were given to patients in single- and two-stage implantation procedures. Patients received 2 g of cefazolin one hour to 30 minutes preoperatively and, subsequently, 1 g every four hours followed by 1 g every six hours. Patients with penicillin or cephalosporin allergies typically received vancomycin (single 1000-mg dose). In addition, the cement which was used for fixation of the leads contained tobramycin or erythromycin (Stryker, Kalamazoo, MI). Before IPG replacement, patients received a single dose of intravenous (IV) antibiotics. After skin closure following both IPG replacement and primary DBS implantation, the surgical site was injected with several milliliters of a 20-mg/mL gentamicin solution; no vancomycin powder was applied.

Statistical Analyses

All statistical analyses were performed using IBM SPSS Statistics (version 20; IBM Corp, Armonk, NY). For categorical variables, we used the χ^2 test to compare proportions between the groups. The odds ratio and p value for each comparison were computed, when appropriate. To investigate the predictive power of comorbidity (described earlier in the text) and predictability of postoperative parameters, we either used univariate or binary regression analyses. The level of significance was set at $p < 0.05$ and Bonferroni corrected where appropriate. Unless otherwise indicated, results are displayed as mean ± SD.

RESULTS

Demographics

From January 2011 to July 2020, a total 386 leads were implanted in 200 consecutive patients, within 201 procedures. Patients were finally implanted with bilateral ($n = 185$) or unilateral ($n = 16$) electrodes from various models, including Model 3387 ($n = 45$), Model 3389 ($n = 146$) (Medtronic), and Abbot Infinity ($n = 10$) (Abbott, Abbott Park, IL), which were fixed in the burr hole with acrylic cement ($n = 172$) (Antibiotic Simplex, Stryker, Kalamazoo, MI) or with the device Stimloc ($n = 22$) (Medtronic) or Guardian ($n = 7$) (Abbott). The procedure was staged in 38 patients (19%).

The IPGs used for implantation were the Activa PC ($n = 177$), RC ($n = 4$), SC ($n = 10$) (Medtronic), or Infinity ($n = 10$) (Abbott). IPGs were implanted in the infraclavicular region and in the abdominal wall in 31 and 170 cases, respectively.

The diagnosis included PD ($n = 103$), epilepsy ($n = 35$), essential tremor ($n = 25$), dystonia ($n = 15$), OCD ($n = 13$), TS ($n = 8$), and pain ($n = 1$). Age at the time of surgery was 54 ± 16 years, ranging from 10 to 88 years. The mean follow-up time after surgery was 40 ± 29 months. Table 1 shows the patient characteristics of primary implantations.

Demographics IPG Replacement

Over the period from January 2011 to July 2020, 307 IPG replacements were performed in 142 unique patients. Two patients were excluded from further analyses because their brain electrodes were not implanted in our own center. Of note, the remaining 140 patients included 60 patients with primary lead implantations before January 2011. Of the remaining 82 patients who received brain electrodes in the defined period, the mean time to first IPG replacement was 1195 ± 506 days, and the mean IPG replacement per stimulation year was 0.5 ± 0.4 (Table 2), with no difference between indications.

Revision Surgery

Additional surgery for AEs or therapy revision was performed in 38 patients, of which 37 received brain electrodes in the defined period. Revision procedures could be categorized into surgery related to SSI (31 procedures in 20 patients), wire tethering ($n = 5$), skin erosion or wound dehiscence ($n = 4$), hardware failure ($n = 5$), loss of treatment benefit or stimulation-related AEs ($n = 6$), perioperative defects ($n = 2$), reimplantation or reinternalization ($n = 10$), abdominal hematomas ($n = 1$), and revision after lead ($n = 2$) or IPG ($n = 4$) migration or malposition.

Adverse Events

Overall, there were 57 AEs in 52 individuals, including 40 AEs in 40 patients occurring in the cohort receiving brain electrodes in the period from January 2011 to July 2020. Table 3 summarizes the number and nature of the hardware-related AEs after implantation. The numbers of AEs after IPG replacement are summarized in Table 4.

Perioperative Damage

Perioperative damage of the DBS lead was observed in one patient (1/386 electrode sites = 0.26%). In this case, the distal contact point of one brain electrode was broken, which was

Table 1. Patient Characteristics of DBS Implantations.

Indication	DBS implantation		Age	Sex		Target						
	N (%)	Nonstaged (%)	Mean ± SD	Female (%)	Bilateral (%)	STN	VC/VS	Vim/PSA	ANT	GPi	GPe	VP
PD	104 (52)	87 (84)	61 ± 8	33 (32)	98 (94)	90	0	9	0	5	0	0
Epilepsy	35 (18)	24 (69)	39 ± 12	12 (34)	35 (100)	0	0	0	35		0	0
ET	25 (12)	19 (76)	65 ± 13	8 (32)	17 (68)	0	0	25	0		0	0
Dystonia	15 (7)	15 (100)	37 ± 23	6 (40)	14 (93)	0	0	0	0	14	1	0
OCD	13 (6)	12 (92)	42 ± 12	8 (62)	13 (100)	0	13	0	0		0	0
TS	8 (4)	4 (50)	29 ± 10	3 (38)	8 (100)	0	0	0	0	8	0	0
Pain	1 (1)	0 (*)	79	0 (*)	0 (0*)	0	0	0	0		0	1
Total	201	161 (81)	54 ± 16	70 (35)	185 (92)	90	13	34	35	27	1	1

ANT, anterior nucleus of the thalamus; ET, essential tremor; GPe, globus pallidus externus; GPi, globus pallidus internus; STN, subthalamic nucleus; VC/VS, ventral capsule/ventral striatum; Vim/PSA, thalamic ventral intermediate nucleus/posterior subthalamic area; VP, ventral pallidum.
*One male patient received a unilateral electrode in a staged procedure.

Table 2. Patient Characteristics of IPG Replacements.

Indication	IPG replacements	Age	Sex	Replacements/stimulation year
	N (%)	Mean ± SD	Female (%)	Mean ± SD*
PD	160 (52)	68 ± 8.1	31 (19)	0.5 ± 0.4
Epilepsy	8 (3)	39 ± 5.7	3 (38)	0.3 ± 0.1
ET	58 (19)	67 ± 13	12 (21)	0.4 ± 0.2
Dystonia	8 (3)	52 ± 24	2 (25)	1.5 ± 1.1
OCD	13 (4)	49 ± 9	5 (38)	0.8 ± 0.2
TS	58 (19)	44 ± 12	2 (3)	0.8 ± 0.1
Pain	0	—	—	—
Total	305	61 ± 15	55 (18)	0.5 ± 0.4

ET, essential tremor.
*IPG replacements/stimulation year was calculated for the cohort receiving brain electrodes in the period between January 2011 and July 2020.

observed before internalization in a staged procedure. Perioperative damage of the extension cable occurred during IPG replacement in one patient (1/305 IPG replacement procedures = 0.33%). The damaged hardware was revised immediately in both patients.

Lead Migration

Routine imaging typically obtained several days postoperatively revealed lead migration in two patients (2/386 electrode sites = 0.52%), requiring immediate surgical revision of the electrode.

IPG Dislocation

Four patients reported (4/508 total procedures = 0.79%) a dislocated IPG, which occurred in two patients following initial implantation. Apart from one patient who was treated conservatively, all IPG dislocations required repositioning.

Hematomas

Two patients (2/386 electrode sites = 0.52%) developed a subdural hematoma (SDH) postoperatively. In one patient, an SDH was observed following an in-hospital fall, and another patient developed a symptomatic SDH several weeks after DBS implantation, corresponding to the location of direct post-DBS implantation pneumocephalus. Both patients required surgical drainage of the SDH. Four patients developed a hemorrhage around the IPG pocket following IPG replacement (3/305 IPG replacement procedures = 0.98%) or initial implantation of the hardware (1/201 initial implantations of the stimulation system = 0.50%). Three patients were treated conservatively with prophylactic antibiotics, and one patient required surgical revision because of significant normocytic anemia.

Wire Tethering

Extension cable tethering occurred in eight patients. Typically, patients had concerns of retro-auricular "bowstringing" (3) or pain around the IPG location (5). For the latter, there was an equal distribution between an abdominal and infraclavicular location (3 vs 2). Five patients developed concerns after initial implantation (5/201 implantation procedures = 2.49%), whereas three patients presented with concerns after IPG replacement (3/305 IPG replacement procedures = 0.98%). In three patients, conservative management, ie, push-up bra or tight undershirt, provided significant relief of their concerns. The remaining patients underwent successful surgical revision.

Hardware Failure

After a mean of 18 months, four patients underwent revision surgery because of hardware failure (4/201 implantation procedures = 1.99%) manifested as high impedances (3) or intermittent stimulation (1) and concomitant recurrent disease symptoms, requiring replacement of the relevant hardware. In one patient, the hardware failure occurred after trauma, although no hardware disconnection was found. In the remaining patients, the cause of malfunction could not be identified. There was no difference in the occurrence of hardware failure between the manufacturer ($p = 0.107$) or DBS indication ($p = 0.633$).

Pain

Two patients reported an excessive sensation of pain after surgery. One patient (1/386 electrode sites = 0.26%) had concerns of occipital neuralgia with the maximal point just cranial to the connection of the brain electrode to the extension cable one year after surgery. After ruling out structural causes or lead displacement by magnetic resonance imaging, the patient was treated with corticosteroid injection with good result. A second patient had concerns of persistent wound pain developing after multiple (+10) IPG replacements because of constant high-voltage stimulation settings (1/305 IPG replacement procedures = 0.33%). Fortunately, concerns resolved after conservative treatment, and the IPG was replaced by a rechargeable system.

Wound Dehiscence

Wound dehiscence, defined as any separation of approximated wound edges without any signs of infection, was observed in one patient following IPG replacement (1/305 IPG replacement procedures = 0.33%). The wound was closed with secondary intention and prophylactic antibiotics.

Skin Erosion Without Infection

Skin erosion of the IPG pocket (1) and cranial electrodes (2) was observed in three patients following initial implantation of the

Table 3. Frequency of AEs per Indication Following Initial Implantation.

Indication	*N*	Total no. of AEs (%)	SSI	Skin erosion	Wound dehiscence	Wire tethering	Perioperative damage	Hematomas	Hardware migration	Hardware failure	Pain
PD	104	22 (21)	10	1	0	5	1	2	1	1	1
Epilepsy	35	7 (20)	2	1	0	0	0	0	2	2	0
ET	25	6 (24)	4	0	0	0	0	1	0	1	0
Dystonia	15	5 (33)	4	0	0	0	0	0	1	0	0
OCD	13	0 (0)	0	0	0	0	0	0	0	0	0
TS	8	0 (0)	0	0	0	0	0	0	0	0	0
Pain	1	0 (0)	0	0	0	0	0	0	0	0	0
Total	201	40 (20)	20	2	0	5	1	3	4	4	1

ET, essential tremor.

Table 4. Frequency of AEs per Indication Following IPG Replacement.

Indication	*N*	Total no. of AEs (%)	SSI	Skin erosion	Wound dehiscence	Wire tethering	Perioperative damage	Hematomas	Hardware migration	Hardware failure	Pain
PD	160	8 (5)	4	1	0	2	0	0	1	0	0
Epilepsy	8	1 (13)	0	0	0	0	0	0	1	0	0
ET	58	2 (3)	0	0	0	0	1	1	0	0	0
Dystonia	8	1 (13)	0	0	0	1	0	0	0	0	0
OCD	13	1 (8)	0	0	1	0	0	0	0	0	0
TS	58	4 (7)	1	0	0	0	0	2	0	0	1
Pain	0	0	0	0	0	0	0	0	0	0	0
Total	305	17	5	1	1	3	1	3	2	0	1

ET, essential tremor.

hardware (2/201 implantation procedures = 1.00%). One incident of skin erosion was documented after replacement of the IPG (1/305 IPG replacement procedures = 0.33%). For management, one case of light erosion was treated conservatively without antibiotics. All other incidences of skin erosion were surgically revised with additional prophylactic antibiotic therapy.

Surgical Site Infection

SSI was the most commonly reported surgery-related AE. In the period from January 2011 to July 2020, 20 infections occurred after primary implantation of DBS hardware (20/201 implantation procedures = 9.95%). There was no difference in SSI incidence in nonstaged vs staged procedures (11% vs 5.0%, $p = 0.256$) or between different indications (Table 3). Furthermore, no difference in SSI incidence was observed before and after April 2014, when complete hair removal was abandoned (7% vs 11%, $p = 0.38$). The median time interval between operation and SSI was 85.9 days (range: 4–247), with 60% of the SSIs occurring within three months. Following primary DBS implantation, SSI occurred most frequently at the IPG site, and there was no difference between an infraclavicular ($n = 2$) and an abdominal ($n = 8$) location ($p = 0.694$). In three patients, the SSI involved multiple sites, ie, retro-auricular and abdominal. The most frequent pathogen was *Staphylococcus aureus* (31%).

Four patients with PD and one patient with TS developed an SSI following IPG replacement located in the infraclavicular (4) or abdominal (1) regions (5/305 IPG replacement procedures = 1.64%). The median interval between IPG replacement and SSI occurrence was 73 days (range: 18–178), with 80% of the SSIs occurring within three months.

A total of 25 patients presenting with an SSI were treated according to several treatment strategies (Table 5). Patients were initially treated with IV antibiotics ($n = 14$), in combination with wound revision ($n = 7$) or direct partial removal of the hardware ($n = 4$). In none of the cases was patients' hardware removed completely at the beginning of treatment. Patients who developed an SSI early after initial implantation/IPG replacement were more likely to receive IV antibiotics alone. Of the patients treated with antibiotics alone, 13 patients developed an SSI following initial implantation. In six patients (42.9%), this treatment with IV antibiotics was successful, with an antibiotic regime aimed at the causative pathogen for six weeks of IV antibiotics in ambulatory care, followed by six weeks of oral antibiotics. Most patients received flucloxacillin, with a mean follow-up of 18 ± 10 months. Of the remaining patients, eight required additional removal of the hardware. Of these, six had cultures positive for *S aureus*. In none of the three patients with a multiple site SSI (scalp and IPG site), was treatment with IV antibiotics successful. Four patients received initial partial removal of the hardware, comprising only the IPG (1) or removal of both the IPG and extension leads (3), which was successful in 75% of the cases. One of the patients receiving removal of both IPG and extension leads required complete removal of the hardware eventually. An SSI reoccurred after the partial removal of the DBS hardware, and subsequent reimplantation was performed after 43 and 214 days, respectively, in two patients necessitating complete removal of the hardware. When initial treatment was unsuccessful, the mean time to secondary treatment (partial or complete removal) was 64 days for the group that initially received antibiotics, 49 days for the wound revision group, and 499 days for partial removal.

Table 5. Management of Hardware-Related Infections.

Treatment	Mean time interval* (d)	Patients (N)	Infection site			Bacteriologic profile			Treatment successful	Secondary treatment (N)	Mean time interval‡ (d)	Infection site		
			IPG†	Scalp	Mixed	Pos	Neg	ng	na			IPG†	Scalp	Mixed
Antibiotics	58 (12–202)	14	6	5	3	8	0	4	2	42.9% (6/14)	Partial removal: 5 Complete removal: 3	64	5	0	3
Antibiotics + wound revision	102 (4–247)	7	4	3	0	4	1	2	0	85.7% (6/7)	Additional wound revision: 1	49	0	1	0
Antibiotics + partial replacement/removal	165 (60–213)	4	3	1	0	2	1	0	1	75% (3/4)	Complete removal: 1	499	0	1	0
Antibiotics + complete removal		0								—	—				

na, not available; ng, no growth; Neg, gram-negative (*Escherichia coli*, *Enterobacter cloacae*, *Serratia marcescens*); Pos, gram-positive (*S aureus*, *S capitis*, *S epidermidis*, group B beta-hemolytic streptococci).
*Mean time interval from procedure (initial implantation/IPG replacement) to infection occurrence.
†IPG site: infraclavicular/abdominal.
‡Mean time interval in days from initial treatment to secondary treatment (range).

Surgical Features and Risk of AEs

There were no differences between the incidence of total AEs and surgical features (Table 6) or surgeon ($p = 0.15$). For SSI and wire tethering, we further analyzed specific surgical features known for or more likely to cause these AEs. For staged and nonstaged procedures, there was no difference in incidence of SSI (11% [18/161] vs 5% [2/40], $p = 0.91$). There also was no difference in SSI requiring (partial) removal of the hardware following postoperative externalization of the DBS electrodes (50% [9/18] vs 50% [1/2], $p = 1.00$). Likewise, we did not identify a difference in SSI occurrence after fixation of the DBS electrodes with antibiotic-impregnated acrylic cement or with a device (eg, Stimloc) (11% [3/28] vs 11% [17/173], $p = 0.99$). SSI was more common in rechargeable than nonrechargeable IPGs (50% [2/4], $p = 0.007$). Nevertheless, this result was nonsignificant after correction for multiple testing (0.05/9). Considering concerns of wire tethering, no difference was observed for an infraclavicular (3% [1/31]) or abdominal (2% [4/170]) location of the IPG.

Risk Factors

A binary regression analysis was performed to identify risk factors for wire tethering and SSI following initial implantation of the hardware. None of the potential risk factors was significantly associated with these AEs. Infection risk on a per-patient basis was not predicted by age, indication, sex, diabetes mellitus, obesity, use of anticoagulation, and smoking.

Table 6. Surgical Features and Incidence of AEs.

Surgical characteristics	AE	*p* Value
Type of IPG		
Rechargeable	50% (2/4)	0.08
Nonrechargeable	17% (33/197)	
Microelectrode recordings		
MER	17% (33/194)	0.43
No MER	29% (2/7)	
Procedure		
Staged	8% (3/40)	0.07
Nonstaged	20% (32/161)	
Anesthesia		
General	19% (12/62)	0.73
Local	17% (23/137)	
IPG location		
Abdominal	19% (33/170)	0.80
Infraclavicular	7% (2/31)	
Target		
STN	20% (18/91)	0.74
VC/VS	15% (2/13)	
Vim/PSA	18% (6/33)	
GPi/ANT	12% (7/57)	
GPe	0% (0/1)	
VP	33% (2/6)	
Duration of procedure		
Duration < 4 h	13% (6/46)	0.40
Duration ≥ 4 h	16% (16/98)	
Location of electrodes		
Unilateral	13% (2/16)	0.59
Bilateral	18% (33/185)	
Fixation		
Burr hole cap	29% (8/28)	0.09
Cement	16% (27/173)	

ANT, anterior nucleus of the thalamus; GPe, globus pallidus externus; GPi, globus pallidus internus; MER, microelectrode recordings; STN, subthalamic nucleus; VC/VS, ventral capsule/ventral striatum; Vim/PSA, thalamic ventral intermediate nucleus/posterior subthalamic area; VP, ventral pallidum.

DISCUSSION

In this retrospective analysis, we documented the hardware- and surgery-related AEs related to 201 consecutive DBS system implantations and 305 IPG replacements. Overall, there were 40 AEs (20%) following initial implantation of DBS hardware, of which 37 required additional surgery, eg, wound revision (11) and (partial) hardware removal and revision (18). Reports documenting AEs following DBS surgery remain equivocal with AE incidence rates ranging between 2.5% and 30.4%.[11,12,21–23] As a consequence, an unambiguous reporting system was suggested on the basis of the following three categories: intracranial AEs including hemorrhages and other intracranial AEs; SSIs, erosions, and related AEs requiring partial or complete hardware removal; and lead revisions for various reasons.[24] Furthermore, Engel et al[24] proposed to report AEs, with the exclusion of intracranial AEs, in patient-years (mean follow-up × number of patients) rather than per electrode or implantation. As defined by the criteria in Engel et al,[24] we observed 2 (1%) intracranial AEs, 10 partial or complete hardware removals (1.5% per patient-years), and 8 lead revisions (1.2% per patient-years). When compared with the literature, the reported incidences are favorable—intracranial AEs, 3.8%; partial or complete hardware removal, 3.6%; and lead revisions, 4.1%.

The most common hardware-related AE following initial implantation was SSI (10%), which is higher than the mean SSI incidence described in large systematic reviews of literature (4.7%–5.12%) but within observed ranges (4.45–11.68; 0–15.2).[9,10,25] We found no association of selected variables, ie, obesity, smoking, and diabetes mellitus. Our data do not support previous reports of patients with new indications such as OCD, epilepsy, and TS being more prone to undergo hardware-related AEs than patients with PD.[9] In particular, we found no higher incidence of hardware-related SSI requiring hardware removal for patients with TS, which is in line with recent reports.[26] However, we recognize that a subset of these patients has a greater tendency to repetitively touch surgical wounds.[27] Furthermore, in line with recent studies suggesting that externalization of DBS electrodes does not increase the risk of SSI, we found no difference in the incidence of SSI following staged or nonstaged procedures.[13,28] In contrast with the literature, we were unable to associate a surgeon's experience with the incidence of SSIs or AEs altogether.

Although patients were not treated according to a specified protocol, SSI treatment was aimed at preserving the DBS system. Initially, 64% of the patients who developed SSI received initial treatment with antibiotics only, which was considerably higher than that reported in the literature (15%).[9] Patients who developed an SSI early after initial implantation were more likely to receive IV antibiotics alone, without the removal of the implanted devices. Here, we assume that this might be because of personal restraints of the treating clinician in withdrawing the patients from their newly gained, long-wanted therapy shortly after implantation. Our results support previous reports that stimulation-sparing management of *S aureus* may be ineffective because six of eight cultures of patients requiring additional (partial) removal of the stimulation after IV antibiotics were positive for *S aureus*.[29] *S aureus* screening

and subsequent decolonization may therefore be considered, because it has been shown to reduce DBS-associated SSI incidence.[30] Initial treatment with IV antibiotics of SSIs involving multiple sites failed. In these patients, surgical removal of the infected hardware may be a better strategy. Given that antibiotic therapy was successful in four patients presenting with an isolated SSI of the scalp, of which three occurred over the lead entry wounds and one in the retro-auricular area, we challenge the often-adapted notion that an SSI over the brain electrodes always necessitates removal of all hardware.[29]

AEs following IPG replacement are rare, with incidence rates of hematoma, wound dehiscence, displacement, and skin erosion varying around 1%.[31,32] Whether wire tethering concerns may be attributed to an IPG replacement is debatable. However, the three patients with traction concerns after IPG replacement specifically localized the IPG site as the source of their pain. Incidence rates of SSI following IPG replacement vary in the literature; Sillay et al[33] reported an SSI rate of 0.5% in 208 IPG replacements, whereas Pepper et al[34] reported a higher rate of 10% SSI in 80 patients.[35] A larger multicenter cohort comprising 1293 IPG replacements reported an SSI incidence of 2.3% per procedure, with possible underreporting of minor superficial SSI.[32] We observed five SSIs following 305 IPG replacements (1.64%), which required IPG removal in two patients (0.67%). The low rate of SSI following IPG replacement is remarkable given that a recent study found 32% sonication cultures (23/71 patients in whom an IPG was replaced) positive for low-virulent pathogens, ie, *Cutibacterium acnes*.[36] We could not confirm previous findings that multiple IPG replacements increase the SSI rate because all IPG infections occurred in patients receiving brain electrodes before 2011, and previous IPG replacements in these patients could not be confirmed.

Strengths and Limitations

The principal limiting factor of this study is its retrospective design, where chart review may have resulted in lower AE rates and lack of independent data monitoring. Prospectively and systematically recording AEs has been demonstrated to result in higher AE rates, with a recorded incidence rate of up to 60.1%.[37] Few studies systematically report AEs in clinical practice. The strengths of this study are its relatively large and unselected study population that includes the most common diseases treated by DBS.

CONCLUSION

The incidence of surgical and hardware-related AEs following initial implantation of DBS hardware was within the range reported in current literature, with a higher mean rate of SSI in our center, for which we found no clear explanation. We could not identify surgery- or patient-related factors that predisposed to developing surgical or hardware-related AEs. In particular, we found no differences following a staged or nonstaged procedure or between DBS indications. Most patients with SSI were treated with isolated antibiotic therapy, which was unsuccessful in 57% of the cases. We have decided to apply a more aggressive treatment approach to SSIs involving multiple sites or when *S aureus* is identified. When applying the three proposed categories for surgical and hardware-related DBS AEs, our incidence rates of AEs are lower than that reported in the literature. We support the need for a uniform reporting system for surgical and hardware-related AEs in DBS surgery, which is useful for benchmarking. However, although clearly defined, the proposed categories may not be useful for patient counseling because minor AEs will be underreported.

Authorship Statements

Tim A.M. Bouwens van der Vlis, Mégan M.G.H. van de Veerdonk, and Linda Ackermans designed and conducted the study, including patient recruitment, data collection, and data analysis. Tim A.M. Bouwens van der Vlis and Mégan M.G.H. van de Veerdonk prepared the manuscript draft with important intellectual input from Linda Ackermans, Albert F.G. Leentjens, Marcus L.F. Janssen, Mark L. Kuijf, Koen R.J. Schruers, Annelien Duits, Felix Gubler, Pieter Kubben, and Yasin Temel. All authors approved the manuscript.

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