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Deep Brain Stimulation Hardware-related Infections: Ten-year Experience at a Single Institution

Kingsley O. Abode-Iyamah, M.D.[1], **Hsiu-Yin Chiang, Ph.D.**[2], **Royce W. Woodroffe, M.D.**[1], **Brian Park, B.Sc.**[3], **Francis J. Jareczek, B.S., B.A.**[3], **Yasunori Nagahama, M.D.**[1], **Nolan Winslow, M.D.**[3], **Loreen Herwaldt, M.D.**[2,4,5], **Jeremy D.W. Greenlee, M.D.**[1]

[1]Departments of Neurosurgery, The University of Iowa Carver College of Medicine, Iowa City, IA 52242, USA

[2]Internal Medicine, The University of Iowa Carver College of Medicine, Iowa City, IA 52242, USA

[3]The University of Iowa Carver College of Medicine, Iowa City, IA 52242, USA

[4]Program of Hospital Epidemiology, University of Iowa Hospitals and Clinics, Iowa City, IA 52242, USA

[5]Department of Epidemiology, The University of Iowa College of Public Health, Iowa City, IA 55242, USA

Abstract

Objective: Deep brain stimulation (DBS) is an effective surgical treatment for managing some neurologic and psychiatric disorders. DBS hardware infection causes significant morbidity: hardware explantation may be required; initial disease symptoms such as tremor, rigidity, and bradykinesia may recur; and the medication requirements for adequate disease management may increase. These morbidities are of particular concern given that published DBS infection rates have been as high as 23%. To date, however, the key risk factors and potential preventive measures for these infections remain largely uncharacterized.

Methods: We performed a retrospective cohort study of patients undergoing primary DBS implantation at a single institution from December 2005 through September 2015 to identify possible risk factors for surgical site infection (SSI) and assess the impact of preoperative and intraoperative prophylactic antibiotics on the SSI rate. We also assessed the effect of a change in the National Healthcare Safety Network's definition of SSI on the number of SSI detected. Statistical analyses were performed using the two-sample t-test, the Wilcoxon rank-sum test, the Chi-square test, the Fisher's exact test, or logistic regression as appropriate for the variables examined.

Results: Two hundred forty-two adult patients had 464 electrodes placed during 245 primary procedures (most patients underwent bilateral electrode implantation) over approximately 10.5 years. Among these 245 procedures, nine infections (3.7%) occurred within 90 days and 16 (6.5%)

Corresponding Author: Jeremy D.W. Greenlee, M.D., Department of Neurosurgery, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, Iowa City, IA, 52242, Phone: 319-356-2771, jeremy-greenlee@uiowa.edu.

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occurred within one year of DBS placement. Gram-positive bacteria were the most common etiological microorganisms. The majority of patient- and procedure-related characteristics did not differ between patients that acquired SSI and those that did not. The rate of SSI among patients who received intra-wound vancomycin powder was only 3.3% compared to 9.7% among patients who did not receive topical vancomycin powder, and intra-wound vancomycin powder was associated with a decreased risk of SSI (odds ratio 0.32; 95% confidence interval [0.10 – 1.02]; P = 0.04). SSI rates were similar after staged and unstaged implantations.

Conclusions: While most patient and procedure-related factors assessed in this study did not appear to affect the incidence of SSI, the data suggest that intra-wound vancomycin powder may help reduce SSI risk after DBS implantation. Furthermore, given the implications of SSI after DBS and the frequency of infections occurring greater than 90 days after implantation, continued follow-up for at least 1 year after these procedures is prudent to establish the true burden of these infections and to properly treat them when they do occur.

Keywords

DBS complication; vancomycin powder; risk factors; prophylaxis

Introduction

Bekhtereva et al. introduced implantation of deep brain stimulators (DBS) into clinical practice in 1963.[5,23] Subsequently, DBS has been proven to be an effective surgical treatment for some movement[14,17,32,47,48,55] and psychiatric disorders,[26,34,36,38,40,42,51,54] and implantation of DBS is becoming increasingly common,[37] with estimates of more than 100,000 systems implanted world-wide. However, placement of DBS systems can be associated with significant complications, including stroke, death, and hardware-related infection.

Infections of DBS systems are common, and patients with these infections may require additional hospitalizations and surgical procedures to eradicate infections through complete or partial hardware removal and prolonged antibiotic therapy.[7–10,16,18–20,25,29,44,45,49,53] Estimates of infection rates following DBS procedures differ but have been reported to be as high as 23%.[7–10,16,19,20,25,29,44,45,49,53] Reported rates may vary in part due to discrepancies in the definition of surgical site infection (SSI), which may be affected by the duration of surveillance, whether reoperation is required, and whether or not superficial incisional infections are considered SSI.[7–10,16,19,20,25,29,44,45,49,53] This surveillance period is guided in part by the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN), which in January 2013 decreased the duration of surveillance for SSI after hardware placement from one year to 90 days.[1,31]

Despite the significance of this clinical problem and the availability of various preventive measures, a surprising paucity of literature examines either risk factors for DBS-related infections or means of infection prevention.[6,39] One recent report documents the beneficial effect of preoperative antiseptic skin wash on reducing SSI after DBS implantation.[29] Prophylactic antibiotics are recommended for DBS implantation; however, few studies have assessed whether certain antimicrobial agents are more effective than others.[6] While some

investigators have found that intra-wound topical vancomycin powder (VP) is associated with lower SSI rates after spine operations[13,33,43,50,52,56] and after craniotomy,[2] to our knowledge, only one has assessed whether intra-wound VP is associated with lower SSI rates after DBS placement procedures.[46]

To address this knowledge gap, we conducted a single-center retrospective cohort study to identify possible risk factors for DBS infections. We investigated the effect of patient characteristics and operative factors, including the number of procedures used to implant the DBS system, the antibiotic used for perioperative prophylaxis, and the placement of intra-wound VP on SSI rates after DBS implantation.

Methods

Study design

We conducted a retrospective cohort study of all adult patients (≥ 18 years old) undergoing primary DBS electrode implantation procedures between December 1, 2005 and September 30, 2015 at the University of Iowa Hospitals and Clinics (UIHC). Patients were identified using UIHC's electronic medical record (EMR). We reviewed each patient's EMR to obtain data on demographics, patient characteristics, procedural factors, and SSI. We included only those patients receiving DBS implants for the first time, whether the devices were implanted during a single "unstaged" procedure (i.e., concurrent implantation of lead[s], extension[s], and implanted pulse generator[s] [IPG]) or during staged procedures (i.e., lead[s] implanted during one procedure and extension[s] and IPG[s] implanted during a subsequent procedure). We excluded patients undergoing revision procedures or isolated IPG replacements. Data were collected to evaluate the incidence of SSI using both the current NHSN definition, which requires surveillance for only 90 days after implantation, and the prior NHSN SSI definition, which required surveillance for one year after DBS implantation.[1,31] Infections were independently identified by an infection preventionist. Consistent with the NHSN definitions, we did not consider stitch abscesses or cellulitis to be SSI. This study was approved by The University of Iowa Institutional Review Board (IRB# 201203774).

Surgical technique

Single stage ("unstaged") implantation: The techniques for lead placement are the same for both unstaged and staged implantations. After a patient was deemed an appropriate candidate for DBS implantation, a movement disorder neurologist selected the appropriate target nucleus: typically the subthalamic nucleus (STN) or globus pallidus interna (GPI) for patients with Parkinson's disease, the ventralis intermedius (VIM) for patients with essential tremor, and the GPI for patients with dystonia. Indirect targeting was utilized for these patients and intraoperative electrophysiology (microelectrode recording for GPI and STN targets and macrostimulation for VIM targets) was used to determine the final lead position. A small subset of patients, identified by psychiatric experts, underwent DBS implantation for medically refractory obsessive-compulsive disorder (OCD). For these patients, MRI-based direct targeting was used to place leads in the ventral capsule and ventral striatum

(VC/VS). All lead implantations were performed under local and monitored anesthesia except three patients who required general anesthesia because of significant anxiety.

Frame-based stereotaxy was used for all lead placements, and trajectories and entry points were chosen to avoid prominent sulci, the ventricles, and the caudate nucleus. Hair was clipped only around the areas to be incised, and two-stage skin preps were done with either alcohol swabs or chlorhexidine/alcohol combination sponges (Chloraprep, BD, Inc., Franklin Lakes, NJ) followed by povidone-iodine gel. Povidone-iodine adhesive skin drapes (Ioban, 3M, St. Paul, MN) were applied.

All patients received prophylactic antibiotics intravenously 30–60 minutes before their incisions. Intracranial leads were placed under monitored anesthesia care. Standard stereotactic techniques were used for lead placement, and plastic caps (StimLoc, Medtronic, Inc., Minneapolis, MN) were used to secure the leads. For bilateral lead placements, one lead was tunneled subgaleally to the contralateral side of the head to facilitate placement of a single, dual channel IPG (e.g., Activa PC, Medtronic, Minneapolis, MN). The distal lead ends were capped and coiled in a subgaleal or subperiosteal pocket around the burr hole cap. The wounds were irrigated copiously with a bacitracin and saline solution. A subset of patients had approximately 200–250 mg of VP placed into their incisions before wound closure.

For single stage procedures, the stereotactic frame was removed after both frontal incisions were closed. The patient was subsequently placed under general endotracheal anesthesia for implantation of the lead extensions and the IPG. The scalp, neck, and chest were prepped and draped. Incisions were made in the infraclavicular and retroauricular regions, and the frontal burr hole incision ipsilateral to the planned generator site was reopened. The DBS hardware was placed. A subset of patients had approximately 400 mg of VP distributed among the frontal, retroauricular, and infraclavicular incisions before closure. All patients were admitted to the hospital after lead placements and intravenous (IV) prophylactic antibiotics were continued for 24 hours postoperatively.

Staged implantation: Most patients underwent two-stage implantation procedures. The first procedure involved placement of intracranial leads under monitored anesthesia care as described above. Postoperatively, patients were admitted to the hospital overnight and received intravenous prophylactic antibiotics for 24 hours. The second procedure typically occurred seven to ten days after lead implantation, and was performed under general endotracheal anesthesia in an outpatient surgery setting. Each patient received prophylactic intravenous antibiotics prior to incision. A subset of patients had VP placed in the three incisions before wound closure during the second stage procedure. Thus, some patients received VP in their incisions during both procedures. Patients also received oral antibiotics for 24 hours after the second stage procedure.

Peri-operative antibiotics

During the study period, we implemented several changes in perioperative antibiotic administration. From January 1, 2005 to May 31, 2011, all patients without penicillin allergies received intravenous nafcillin. On June 1, 2011, we began administering cefazolin

perioperatively based on data from a study of neurosurgical spine procedures at our hospital[28] and an update in clinical practice guidelines.[12] Patients who were allergic to penicillin received either vancomycin or clindamycin based on the surgeon's preference. Recent work in the surgical and neurosurgical literature has demonstrated the efficacy of topical vancomycin in preventing SSI;[13,33,43,50,52,56] as such, starting March 1, 2012, all patients who were not allergic to vancomycin had VP placed into their surgical incisions.

Statistical analysis

Statistical analysis was performed using SAS v9.3. We used the two-sample t-test for normally distributed continuous variables or the Wilcoxon rank-sum test for continuous variables that were not normally distributed. For categorical variables, we used the Chi-square test or the Fisher's exact test and computed the odds ratio (OR) and P-value when applicable. Given the independent association of gender with SSI rate (see results below), we performed logistic regression to control for gender when determining the associations between vancomycin powder use or IV cefazolin prophylaxis and SSI. All statistical tests were two-tailed. P-values less than 0.05 were considered significant.

Results

Number of DBS procedures and rate of SSI

During the 10.5-year study period, we identified 242 patients who received 464 new electrode placements during 245 primary DBS implantation procedures. Nine SSI (3.7%) were detected within 90 days of DBS placement and 16 (6.5%) were detected within one year. The median time to the onset for all 16 SSI was 79 days (range 30 to 244 days); for the nine SSI that occurred fewer than 90 days after the procedure, the median time to onset was 50 days. Eleven infections (68.8%) affected scalp wounds and five (31.2%) affected chest wounds.

Culture results demonstrated a heterogeneous group of microorganisms (Table 1). Gram-positive bacteria, including *Propionibacterium acnes* (N = 7; 43.8%) and *Staphylococcus aureus* (N = 6; 37.5%) alone or in combination with other organisms, were the most common etiologic agents. Gram-negative organisms alone or in combination with *P. acnes* caused two SSI (12.5%). Five of seven patients (71.4%) with SSI occurring after 90 days had polymicrobial infections, all of which included *P. acnes*. Among the nine patients with SSI occurring before 90 days, only three (33.3%) had polymicrobial infections; however, given the small numbers of SSI, the proportion of polymicrobial SSI was not found to be statistically different between the two time groups. Infections with more virulent organisms did not exhibit shorter time to SSI.

Postoperative readmission rates differed between patients with and without SSI. All 16 patients with SSI were readmitted compared to only eight (3.5%) patients without SSI ($P < 0.0001$). DBS hardware was removed from seven (43.8%) patients with SSI. Of these seven patients, six (85.7% of those whose hardware was removed; 37.5% of all infected patients) had hardware re-implanted.

Comparison of patient, procedure, and other factors between patients with and without SSI

Patients with SSI and patients without SSI were similar with respect to age, body mass index (BMI), preoperative glucose level, American Society of Anesthesiologists (ASA) score, preoperative diagnosis, procedure laterality, anatomic target, procedure duration, and the antibiotic used for perioperative intravenous antimicrobial prophylaxis (Table 2). Male patients were less likely than female patients to acquire SSI (OR = 0.28; 95% CI [0.10 – 0.80]; P = 0.01) after DBS procedures. Although the antibiotic used for prophylaxis was not significantly associated with the incidence of infection, none of the 17 patients given vancomycin developed SSI. Twelve of 124 patients (9.7%) who did not receive intra-wound VP had SSI while only four of 121 patients (3.3%) receiving topical VP later went on to develop an infection. Approximately half of patients without SSI, compared to 25.0% of patients with SSI, had received intraoperative topical VP (OR = 0.32; 95% CI [0.10 – 1.02]; P = 0.04). After controlling for gender, the association between VP and decreased SSI risk remained but no longer reached the predefined level of significance (adjusted OR = 0.32; 95% CI [0.10 – 1.03]; P = 0.06). Wound dehiscence was observed in more patients with SSI than those without (25.0% compared to 2.2%; OR = 14.9; 95% CI [3.5 – 62.9]; P < 0.01). There was no difference in wound dehiscence rates between the VP and non-VP groups.

Comparison of patient, procedure, and other factors between staged and unstaged implantations

Overall, 17 (6.9%) procedures were unstaged implantations and 228 (93.1%) were staged. The median time between the first stage and the second stage was 10 days (Table 2). Patients who underwent staged implantation were more likely to have ASA scores ≥ 3 and have a diagnosis of Parkinson’s disease (Table 3). Those with staged procedures were less likely to be undergoing DBS to treat essential tremor and were thus less likely to have the VIM targeted during surgery. Unilateral DBS placement was overrepresented in those undergoing unstaged procedures (94.1% compared to 4.4%). The SSI rate was similar between those with staged and unstaged procedures (6.6% compared to 5.6%). The rates of other complications, such as wound dehiscence and post-operative seroma, did not differ between the staged and unstaged groups.

Discussion

This retrospective cohort study of 245 DBS implantations conducted over a 10.5-year period at a single institution was designed to assess patient- and procedure-related factors associated with SSI after DBS implantation. Surprisingly, the only patient-related factor associated with SSI was gender; males were less likely to have SSI compared to females. Other patient-related factors such as age, BMI, and preoperative blood glucose levels did not differ between patients with and without SSI. These two groups also did not differ with regard to most procedure-related factors, including staged versus unstaged operations and operation duration. However, a greater proportion of patients without SSI had received intra-wound topical vancomycin powder during their procedure, suggesting that the use of topical VP may be a practice critical for reducing the rates of SSI after DBS implantation.

Number of DBS procedures and rate of SSI

In our cohort, we report an overall SSI rate after DBS implantation of 3.7% and 6.5% at 90 days and one year, respectively. These findings are consistent with a review of the literature on hardware-related complications of DBS conducted by Hamani *et al.* in 2006, who identify a mean SSI rate of 6.1%.[30] A closer examination of individual studies, including several published more recently, demonstrates heterogeneity in reported SSI rates, which may range from 0% to 23%[7,9–11,16,19,20,25,29,44,45,49,53] This heterogeneity is most likely related to a number of factors, such as inconsistent definitions of SSI (e.g., including or excluding superficial infections) or variable durations of follow-up. Furthermore, considerable differences exist in the duration of postoperative monitoring for infectious complications, as illustrated in this study: when procedure-related SSIs are defined as those occurring within 90 days of surgery, the SSI rate is 3.7%. When this time frame is extended to one year, more SSIs are detected, and the infection rate increases to 6.5%. As such, the shorter duration of the current NHSN guidelines, which limit the definition of SSI to include only the proximate postoperative period (i.e., 90 days), may result in underestimation of a true risk of SSI. However, while it is important that the long term infectious complications of DBS implantation be identified, SSIs occurring after 90 days are not likely to be associated with procedure-related factors and would be more apt to arise from wound complications or extensions of infection from other sources. Thus, the rate of delayed SSI is unlikely to be affected by interventions targeted at periprocedural factors such as surgical technique or preoperative antibiotic administration.

Most microorganisms isolated from the SSI in this study population were gram-positive bacteria commonly found on the skin, with methicillin-sensitive *Staphylococcus aureus* and *Propionibacterium acnes* present in the majority (68.8%) of cases. These findings are consistent with those reported in the literature.[16,21,25] Interestingly, *P. acnes* is overrepresented here compared to other studies of DBS-related SSI, though it is a known opportunistic pathogen in the setting of neurosurgical procedures. Recent observational studies note that postoperative infections with *P. acnes* tend to have an indolent course and present with delayed SSI.[27,41] Our data also support these observations: the median time to SSI in *P. acnes*-containing infections was 156 days, compared to 56 days in infections with organisms other than *P. acnes*. The implications of this delayed presentation are two-fold: clinicians must be aware that infectious complications of DBS implantation may occur well outside the immediate postoperative period, and the definition of SSI may need to be expanded to include potentially late-presenting SSI.

Comparison of patient, procedure, and other factors between patients with and without SSI

Of the multiple patient-related factors analyzed in this study, gender was the only variable associated with SSI, such that male patients were less likely to acquire SSI than female patients (OR = 0.28; 95% CI [0.10 – 0.80]; P = 0.01). Occurrence of SSI was not associated with age, BMI, preoperative blood glucose level, ASA score, or diagnosis. These data are consistent with several other studies that find no relationship between SSI and patient demographics[7,11,45] or diagnosis for which DBS was indicated.[45,49] The lack of an association with ASA score, a proxy measure of patient comorbidities, was somewhat

surprising. Others have described an increased prevalence of comorbidities among patients with SSI compared to those without;[7] however, this finding was not replicated in our study.

The apparently protective influence of male gender is interesting, but the reason for this association is not readily apparent. Other reports describe procedure-specific differences in SSI rates among men and women. One large study documents higher rates of SSI in men compared to women after abdominal surgeries but lower rates after cardiac surgeries.[35] These authors also find that the microorganisms isolated from the SSI are gender-specific: coagulase-negative *Staphlococcus* were more commonly cultured from SSI in men while MSSA and *Pseudomonas aeruginosa* were more commonly cultured from SSI in women. Other studies that do not distinguish among types of surgery find higher rates of SSI in men.[15] The underpinning reasons for the discrepant SSI rates are unclear but may be influenced by differences in propensity for skin colonization, immune system responses, and the impact of hormones.

We also found no associations between procedure-related factors, e.g., elements such as the anatomic target and the operative time, and the incidence of SSI. This observation is also consistent with the literature[11,25,45,49] and suggests that interventions specifically targeting the procedure itself may not have a significant impact on reducing SSI postoperatively.

The choice of perioperative antibiotic may influence the rates of and microorganisms responsible for SSI. While the interaction between perioperative antibiotic and SSI rate did not reach statistical significance in this study, we did observe that none of the 17 patients who received perioperative prophylactic IV vancomycin later developed an SSI. Bhatia *et al.* report a similar finding in which patients receiving vancomycin for prophylaxis had a lower incidence of SSI compared to those receiving cefuroxime.[6] We (Table 1) and others[6,16,21,25,46] have demonstrated that the majority of SSI are caused by gram-positive bacteria; as such, the selection of an antibiotic with good gram-positive coverage is important. However, we did observe infections secondary to gram-negative bacteria in a small subset of our patients. The very low frequency of gram negative infections reported across studies may obviate the need for prophylactic gram-negative coverage. This argument is supported by Bhatia and colleagues' finding that combined vancomycin and gentamycin did not lead to a significant decrease in SSI rate when compared to vancomycin alone.[6] However, the importance or impracticality of adding prophylactic gram-negative coverage cannot be determined definitively by our retrospective study, and a large multicenter trial may be required to address that issue in a more definitive manner.

Importantly, intra-wound topical VP led to a lower rate of SSI (3.3% compared to 9.7%) among our cohort and was associated with a lower risk of SSI compared with standard treatment. The use of locally applied antibiotics for SSI prevention has only recently become more commonplace in some sectors of the neurosurgical field. Intra-wound VP generates supratherapeutic antibiotic concentrations locally[4] while reducing the risk of toxicities seen with systemic delivery.[22] Since the first reports of efficacy in the late 2000s,[39] many groups have established the ability of intra-wound VP to reduce SSI after spinal procedures,[2,4,13,24,33,43,50,52,56] and the use of topical VP has begun to expand to other neurosurgical procedures such as craniotomy and cranioplasty.[2,3] One objective of our study

was to determine whether intra-would VP was similarly effective at reducing SSI rates after DBS implantation.

To date, only one other report has described the use of VP to reduce SSI after DBS implantation.[46] Rasouli and Kopell recently found that the use of 1000 mg intra-wound VP resulted in a SSI rate of only 1.3% (four of 297 patients), which is slightly lower than the rate reported here (3.3%, four of 121 patients). This discrepancy may in part be explained by the higher dose of VP used by these authors (1000 mg, compared to ~200 – 400 mg per wound used in this study) but is also likely related to the choice of perioperative prophylactic antibiotic. As we also observed, the majority of SSI in the Rasouli and Kopell study were caused by gram-positive organisms (three of four, 75%, all *Staph spp.*); thus, strong antibiotics with good gram-positive coverage would be of most benefit for reducing rates of infection. All patients in the Rasouli and Kopell study received a combination of 1000 mg IV vancomycin and 1500 mg IV cefuroxime preoperatively and continued to receive both antibiotics 24 hours postoperatively. As noted previously, none of the 17 patients in our study that received IV vancomycin for perioperative prophylaxis later went on to develop SSI. Thus, the use of IV vancomycin for antibiotic prophylaxis may also significantly contribute to the lower rate of SSI observed by Rasouli and Kopell.

The optimal VP dose for preventing SSI after DBS implantation is not known. Due to the depth of incision and subcutaneous wounds after spinal operations combined with use of wound drains, most surgeons apply 1000 mg or more of VP for SSI prevention during these procedures.[43,52] Rasouli and Kopell similarly applied 1000 mg intra-wound VP in their recent study of SSI after DBS implantation.[46] Because the incisions and subcutaneous wound depths are significantly smaller for DBS procedures than those for spinal operations, we elected to use a lower dose of VP (200 – 400 mg) for SSI prevention in our patient population. This lower dose also reduced the risk of SSI after DBS implantation; however, the rate of SSI in our study was not as low as that observed by Rasouli and Kopell. While this observation may suggest that the ability of intra-wound VP to reduce SSI is dose-dependent, the difference in perioperative prophylactic antibiotic administration between these two studies limits our ability to draw conclusions about the optimal dose of VP.

Comparison of patient, procedure, and other factors between staged and unstaged implantations

We found that several patient- and procedure-related factors were associated with the staging of DBS implantation. Patients who underwent staged implantation were more likely to have ASA scores ≥ 3 and were more likely to undergo DBS to treat Parkinson's disease. Given that Parkinson's disease was the most common indication for DBS implantation and that > 90% of procedures were staged, this latter association is likely due to the high co-occurrence of staged procedures and PD. The association between ASA score and staged implantation may be related to patient diagnoses: more unstaged DBS procedures were performed in managing essential tremor, a condition treated with DBS in relatively younger patients who do not suffer from as many comorbidities. Given that patients with essential tremor were less likely to undergo staged operations, the VIM, the anatomical target for DBS therapy of essential tremor, was also underrepresented among staged procedures. Unilateral

implantations were more likely to be completed in unstaged operations while bilateral implantations were more likely to be completed in staged operations, an observation that may mirror the somewhat lower complexity of unilateral compared to bilateral electrode implantation.

Our study is one of few to compare SSI rates after staged and unstaged DBS implantation. Importantly, we found that the SSI rate did not differ between the two groups, and no association was identified between type of procedure and SSI. The few available data comparing SSI rates between staged and unstaged procedures are inconsistent, with some studies reporting increased rates of SSI after staged procedures[16] but other studies finding no differences.[49] In their recent report describing the use of VP to reduce SSI risk after DBS implantation, Rasouli and Kopell performed only staged procedures and found infection rates to be less than 2%;[46] however, the use of VP in all patients and the absence of a patient group with unstaged procedures precludes the ability to draw conclusions about the impact of procedure type on SSI rates. Of note, the number of unstaged DBS implantations in our study was low (17 of 245 or 6.9% of all procedures), and the SSI rate determined here may not accurately reflect the true incidence of SSI in a larger population.

Implications of these data for clinical practice

Not only does hardware-related infection following DBS placement tax the healthcare system, but it may also significantly burden the individual suffering from SSI though the financial and time costs associated with required follow-up care, neither of which is well defined. Surgical site infections associated with DBS instrumentation can be challenging to treat, and failed medical management of the SSI may lead to complete or partial removal of the DBS system. In these cases, patients must undergo additional surgical procedures, spend several extra days in the hospital, and are likely to suffer from the return of the motor or psychiatric symptoms for which they had received DBS placement.[18] The return of symptoms can be particularly debilitating for those patients who have become reliant on their DBS for symptom management.

The optimal means of addressing the burden of these infections is to prevent them before they happen. It is therefore prudent to identify major risk factors associated with DBS infection and to design and implement measures to reduce the risk of SSI. In this study, we have presented our institutional experience with SSI after DBS placement and have identified patient- and procedure-related factors associated with SSI. We found that surprisingly few patient- and procedure-related factors were predictive of SSI. Importantly, the duration of the procedure and whether the operation was completed in a staged or unstaged manner did not impact the incidence of SSI. While we did not have the statistical power to detect an association between choice of perioperative prophylactic antibiotics and SSI, we did find that the application of intra-wound topical VP led to a decreased rate of SSI among our patients. Similar data exist for the use of VP during spinal procedures; however, to our knowledge, this is the first report comparing SSI rates after DBS implantation between patients who received intra-wound VP and those who did not. Our data suggest that the use of intra-wound topical VP will reduce the incidence of SSI after DBS placement,

which will in turn decrease the associated morbidity and significant burden on patients that are produced by these infections.

This study had several strengths. Although retrospective cohort studies can be subject to selection bias and recall bias, we attempted to minimize these potential biases by collecting objective data from patient charts. All procedures were performed by a single neurosurgeon at a single institution, which minimizes inconsistencies in procedural technique and reduces some of the heterogeneity in the studied patient group. Cases of SSI were identified and confirmed with the assistance of experts in infectious disease and hospital epidemiology, improving the sensitivity and specificity of case identification. In contrast to the recent report by Rasouli and Kopell,[46] this study included both patients who had received topical VP during their procedure and those who did not, allowing us to directly compare and evaluate the association between VP use and incidence of SSI.

It should be noted that this study also had some important limitations. First, this retrospective cohort study is inherently subject to known limitations of this study type, such as potentially poor data quality, e.g., due to incomplete documentation in the medical record. A relatively small proportion of patients underwent unstaged DBS placement and may not be fully representative of this group of patients; thus, the conclusions drawn about patient- and procedure-related factors associated with unstaged procedures must be interpreted with caution. Finally, as this study was performed at a single institution, the results may not be generalizable to all patients undergoing DBS implantation.

Several future directions could be explored to expand upon the findings presented here. Our study was not designed to assess the differential efficacy of perioperative prophylactic intravenous antibiotics; however, we did note that none of the patients receiving intravenous vancomycin for prophylaxis later went on to develop SSI. Future studies should assess whether systemic intravenous vancomycin is the most effective antibiotic for perioperative prophylaxis in patients undergoing DBS implantation. A prospective cohort study would be helpful to further evaluate the efficacy of VP identified here, though given the small numbers of SSI, it is likely that a large cohort of patients would be required to achieve sufficient power.

Conclusion

Here we reported the factors associated with DBS hardware-related infections over ten years at a single institution. Hardware-related surgical site infection rate after DBS implantation was 3.7% within 90 days and 6.5% within one year of surgery, which is comparable to the reported rates in the literature. The majority of patient-related (e.g., age, diagnosis) and procedure-related (e.g. staged versus unstaged DBS, operative time) factors do not appear to impact SSI. Importantly, we found that the use of intra-wound vancomycin powder was associated with significantly lower SSI rates after DBS placement. To our knowledge, this is the first comparison of SSI rates after DBS procedures between patients who did and did not receive intra-wound VP, and it thus provides an important contribution to the growing literature documenting the efficacy of topical VP in reducing SSI associated with neurosurgical procedures.

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Table 1.

Organisms cultured from surgical site infections after deep brain stimulator implantation

SSI organism	N (%)	Days to SSI
MSSA	6 (37.5%)	
MSSA alone	4 (25.0%)	51, 56, 97, 119
MSSA, *Propionibacterium acnes*	1 (6.3%)	156
MSSA, GPR suggestive of diphtheroids	1 (6.3%)	76
P. acnes	6 (37.5%)	
P. acnes alone	1 (6.3%)	32
P. acnes, GPR suggestive of diphtheroids	1 (6.3%)	207
P. acnes, Pseudomonas aeruginosa	1 (6.3%)	30
P. acnes, methicillin-resistant CoNS, *Staphylococcus epidermidis*	1 (6.3%)	195
P. acnes, Enterobacter cloacae	1 (6.3%)	114
P. acnes, Staphylococcus lugdunensis	1 (6.3%)	244
Gram-positive cocci	1 (6.3%)	36
Methicillin-resistant *S. epidermidis*	1 (6.3%)	82
Serratia marcescens	1 (6.3%)	38
Mixed skin flora	1 (6.3%)	50
All infections	16 (100%)	30 – 244

CoNS: coagulase-negative staphylococci; GPR: gram-positive rods; MSSA: methicillin-susceptible *Staphylococcus aureus*

Table 2.

Characteristics of patients and procedures stratified by the presence or absence of a surgical site infection

Variable	All patients (N = 245)	Non-SSI (N = 229)	SSI (N = 16)	Odds ratio for SSI (95% CI)	P-value
Patient-related factors					
Age at time of surgery (years, mean ± SD)	62.9 ± 11.3	62.7 ± 11.5	65.6 ± 6.7	-	0.13
Male gender	162 (66.1%)	156 (68.1%)	6 (37.5%)	**0.28 (0.10 – 0.80)**	**0.01**
BMI (kg/m^2, mean ± SD)	29.2 ± 6.3	29.2 ± 6.4	30.3 ± 4.6	-	0.49
Blood glucose[1] (mg/dL, mean ± SD)	104.9 ± 34.1 (N = 244)	105 ± 33.6 (N = 228)	104.1 ± 40.9	-	0.92
ASA ≥ 3	125 (51.2%) (of N = 244)	119 (52.2%) (of N = 228)	6 (37.5%)	0.55 (0.19 – 1.56)	0.26
Diagnosis					
Dystonia	13 (5.3%)	12 (5.2%)	1 (6.3%)	1.21 (0.15 – 9.90)	0.59
Essential tremor	94 (38.4%)	86 (37.6%)	8 (50.0%)	1.66 (0.60 – 4.59)	0.32
OCD	6 (2.4%)	6 (2.6%)	0 (0%)	-	1.00
Parkinson's disease	131 (53.5%)	124 (54.2%)	7 (43.8%)	0.66 (0.24 – 1.83)	0.42
Post-stroke thalamic pain syndrome	1 (0.4%)	1 (0.4%)	0 (0%)	-	1.00
Procedure-related factors					
Side					
Bilateral	219 (89.3%)	204 (89.1%)	15 (93.8%)	1.84 (0.23 – 14.5)	1.00
Left	12 (4.9%)	12 (5.2%)	0 (0%)	-	1.00
Right	14 (5.7%)	13 (5.7%)	1 (6.3%)	1.11 (0.14 – 9.09)	1.00
Anatomical target					
GPI	48 (19.6%)	45 (19.7%)	3 (18.8%)	0.94 (0.26 – 3.45)	1.00
STN	98 (40.0%)	93 (40.6%)	5 (31.3%)	0.66 (0.22 – 1.98)	0.46
VC/VS	6 (2.4%)	6 (2.6%)	0 (0%)	-	1.00
VIM	93 (38.0%)	85 (37.1%)	8 (50.0%)	1.69 (0.61 – 4.68)	0.30
Staged procedure	228 (92.7%)	213 (92.6%)	15 (93.8%)	1.13 (0.14 – 9.08)	1.00
Time to second stage (day, median (range))	10 (0 – 346) (N = 228)	10 (0 – 84) (N = 213)	9 (7 – 346) (N = 15)	-	0.61
Operation duration[2] (minutes, mean ± SD)	168.3 ± 46.9 (N = 244)	167.6 ± 47.0 (N = 228)	178.3 ± 44.5	-	0.38
Other factors					
Antimicrobial prophylaxis					
Cefazolin	151 (61.4%)	140 (61.1%)	11 (68.8%)	1.40 (0.47 – 4.16)	0.54
Nafcillin	52 (21.1%)	48 (21.0%)	3 (18.8%)	0.87 (0.24 – 3.18)	1.00
Vancomycin	17 (6.9%)	17 (7.4%)	0 (0%)	-	0.61
Other	26 (10.6%)	24 (10.5%)	2 (12.5%)	1.22 (0.26 – 5.70)	0.68
Topical vancomycin powder	121 (49.2%)	117 (51.1%)	4 (25.0%)	**0.32 (0.10 – 1.02)**	**0.04**

Variable	All patients (N = 245)	Non-SSI (N = 229)	SSI (N = 16)	Odds ratio for SSI (95% CI)	P-value
Postoperative seroma	1 (0.4%)	0 (0%)	1 (6.3%)	-	0.07
Wound dehiscence	9 (3.7%)	5 (2.2%)	4 (25.0%)	**14.9 (3.5 – 62.9)**	< **0.01**

[1]Blood glucose was recorded during a preoperative assessment occurring within the month preceding the procedure.

[2]For staged procedures, overall duration was defined as the sum of the time from incision to wound closure for each stage.

ASA: American Society of Anesthesiologists; BMI: body mass index; GPI: globus pallidus interna; Kg/m^2: kilograms/meter squared; mg/dL: milligrams/deciliter; OCD: obsessive-compulsive disorder; SD: standard deviation; STN: subthalamic nucleus; SSI: surgical site infection; VC/VS: ventral capsule/ventral striatum; VIM: ventralis intermedius

Table 3.

Characteristics of patients and procedures stratified by staged and unstaged implantation

Variable	Staged (N = 228)	Unstaged (N = 17)	Odds ratio for staged (95% CI)	P-value
Patient-related factors				
Age at time of surgery (years, mean ± SD)	63.0 ± 11.0	60.8 ± 14.2	-	0.43
Male gender	150 (65.8%)	12 (70.6%)	0.80 (0.27 – 2.36)	0.69
BMI (kg/m^2, mean ± SD)	29.3 ± 6.4	28.6 ± 4.8	-	0.70
Blood glucose[1] (mg/dL, mean ± SD)	105.6 ± 34.9 (N = 227)	95.6 ± 18.0	-	0.05
ASA ≥ 3	121 (53.1%)	4 (25.0%) (N = 16)	**3.39 (1.06 – 10.83)**	**0.03**
Diagnosis				
Dystonia	13 (5.7%)	0 (0%)	-	0.61
Essential tremor	83 (36.4%)	11 (64.7%)	**0.31 (0.11 – 0.88)**	**0.02**
OCD	5 (2.2%)	1 (5.9%)	0.36 (0.04 – 3.26)	0.35
Parkinson's disease	127 (55.7%)	4 (23.5%)	**4.09 (1.29 – 12.92)**	**0.01**
Post-stroke thalamic pain syndrome	0 (0%)	1 (5.9%)	-	0.07
Procedure-related factors				
Side				
Bilateral	218 (95.6%)	1 (5.9%)	**348.8 (42.0 – 2898.3)**	**< 0.01**
Left	5 (2.2%)	7 (41.2%)	**0.03 (0.01 – 0.12)**	**< 0.01**
Right	5 (2.2%)	9 (52.9%)	**0.02 (0.01 – 0.07)**	**< 0.01**
Anatomical target				
GPI	47 (20.6%)	1 (5.9%)	4.15 (0.54 – 32.1)	0.21
STN	95 (41.7%)	3 (17.7%)	3.33 (0.93 – 11.9)	0.05
VC/VS	5 (2.2%)	1 (5.9%)	0.36 (0.04 – 3.26)	0.35
VIM	81 (35.5%)	12 (70.6%)	**0.23 (0.08 – 0.67)**	**< 0.01**
Operation duration[2] (minutes, mean ± SD)	168.4 ± 47.6	167.0 ± 35.9 (N = 16)	-	0.91
Other factors				
Antimicrobial prophylaxis				
Cefazolin	141 (61.8%)	10 (58.8%)	1.13 (0.42 – 3.09)	0.81
Nafcillin	47 (20.6%)	4 (23.5%)	0.84 (0.26 – 2.71)	0.76
Vancomycin	15 (6.6%)	2 (11.8%)	0.53 (0.11 – 2.53)	0.33
Other	25 (11.0%)	1 (5.9%)	1.97 (0.25 – 15.50)	1.00
Topical vancomycin powder	113 (49.6%)	8 (47.1%)	1.11 (0.41 – 2.97)	0.84
Postoperative seroma	1 (0.4%)	0 (0%)	-	1.00
Wound dehiscence	9 (4.0%)	0 (0%)	-	1.00
Surgical site infection	15 (6.6%)	1 (5.9%)	1.13 (0.14 – 9.08)	1.00

[1] Blood glucose was recorded during a preoperative assessment occurring within the month preceding the procedure.

[2] For staged procedures, overall duration was defined as the sum of the time from incision to wound closure for each stage.

ASA: American Society of Anesthesiologists; BMI: body mass index; GPI: globus pallidus interna; kg/m^2: kilograms/meter squared; mg/dL: milligrams/deciliter; OCD: obsessive-compulsive disorder; SD: standard deviation; STN: subthalamic nucleus; SSI: surgical site infection; VC/VS: ventral capsule/ventral striatum; VIM: ventralis intermedius