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Incidence and Management of Hardware-Related Wound Infections in Spinal Cord, Peripheral Nerve Field, and Deep Brain Stimulation Surgery: A Single-Center Study

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Keywords
Deep brain stimulation · Spinal cord stimulation · Peripheral nerve field stimulation · Infection · Surgical management · Antimicrobial treatment · Neuromodulation

Abstract
Introduction: Neuromodulation using deep brain stimulation (DBS), spinal cord stimulation (SCS), and peripheral nerve field stimulation (PNFS) to treat neurological, psychiatric, and pain disorders is a rapidly growing field. Infections related to the implanted hardware are among the most common complications and result in health-related and economic burden. Unfortunately, conservative medical therapy is less likely to be successful. In this retrospective study, we aimed to identify characteristics of the infections and investigated surgical and antimicrobial treatments. ***Methods:*** A retrospective analysis was performed of patients with an infection related to DBS, SCS, and/or PNFS hardware over an 8-year period at our institution. Data were analyzed for type of neurostimulator, time of onset of infection following the neurosurgical procedure, location, and surgical treatment strategy. Surgical treatment of infections consisted of either a surgical wound revision without hardware removal or a surgical wound revision with partial or complete hardware removal. Data were further analyzed for the microorganisms involved, antimicrobial treatment and its duration, and clinical outcome. ***Results:*** Over an 8-year period, a total of 1,250 DBS, 1,835 SCS, and 731 PNFS surgeries were performed including de novo system implantations, implanted pulse generator (IPG) replacements, and revisions. We identified 82 patients with infections related to the neurostimulator hardware, representing an incidence of 3.09% of the procedures. Seventy-one percent of the patients had undergone multiple surgeries related to the neurostimulator prior to the infection. The infections occurred after a mean of 12.2 months after the initial surgery. The site of infection was most commonly around the IPG, especially in DBS and SCS. The majority

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(62.2%) was treated by surgical wound revision with simultaneous partial or complete removal of hardware. Microbiological specimens predominantly yielded *Staphylococcus epidermidis* (39.0%) and *Staphylococcus aureus* (35.4%). After surgery, antimicrobials were given for a mean of 3.4 weeks. The antimicrobial regime was significantly shorter in patients with hardware removal in comparison to those who only had undergone surgical wound revision. One intracranial abscess occurred. No cases of infection-related death, sepsis, bacteremia, or intraspinal abscesses were found. ***Conclusion:*** Our data did show the predominance of *S. epidermidis* and *S. aureus* as etiologic organisms in hardware-related infections. Infections associated with *S. aureus* most likely required (partial) hardware removal. Aggressive surgical treatment including hardware removal shortens the duration of antimicrobial treatment. Clear strategies should be developed to treat hardware-related infections to optimize patient management and reduce health- and economic-related burden.

Introduction

The field of neuromodulation to treat diverse neurological, psychiatric, and pain disorders is quickly growing. Among the most common techniques used for the last decades in neuromodulation are deep brain stimulation (DBS), spinal cord stimulation (SCS), and peripheral nerve field stimulation (PNFS). Improvement in quality of life in medically refractory neurological, pain, and neuropsychiatric patients has led to a rapidly growing interest, acceptance, and increasing numbers of surgery. The hardware used for neuromodulation in every different technique consists of surgically implanted leads and a subcutaneously implanted pulse generator (IPG), which will deliver electrical stimulation to various parts of the central and peripheral nervous system. Many systems include extension cables connecting both parts.

DBS is a widely accepted treatment for movement disorders, such as Parkinson's disease, essential tremor, and dystonia, with long-lasting clinical benefit [1–3]. DBS has also proven to be effective in the fields of psychiatry, pain, and epilepsy [1, 4–7]. SCS has been used for the treatment of diverse pain disorders, which requires the implantation of a lead in the spinal epidural space in order to deliver electrical pulses to the dorsal columns, roots, and horns of the spine [8]. These electrical pulses aim to provide pain relief by modulating the passage of nociceptive signals from the affected area to subcortical and cortical areas of the brain [9, 10]. Most SCS-treated patients suffer from failed back surgery syndrome with neuropathic components. Other indications include complex regional pain syndrome, degenerative spine disorders, angina pectoris, post-amputation pain syndromes, chronic limb ischemia, and post-viral pain syndromes, among others [8]. PNFS is a type of neuromodulation that requires the placement of leads in the vicinity of affected nerves right at the subcutaneous space [11]. It is believed that the generated action potentials in afferent axons will transmit into the spinal cord in order to activate the synapses and modulate pain signals [10, 12].

The global market for implantable neurostimulators has grown rapidly over the last decade and is expected to advance faster over the next years [1, 13, 14]. For instance, recent calculations show that around 208,000 patients worldwide have received DBS implants for neurological and neuropsychiatric disorders [15]. Furthermore, pain and pain-related disorders form an increasingly growing problem worldwide with a significant global burden of disease and disability [16, 17]. This contributes to an increased interest and demand for neuromodulation techniques to treat chronic pain syndromes. More than a decade ago in the USA alone, more than 27,000 SCS devices were already implanted each year [14] and have grown since. The expansion has also been observed in the field of PNFS surgery [13].

The procedures related to neurostimulators are well tolerated, and the rate of surgical complications is generally relatively low. In previous studies, the rate of complications directly related to the surgery, like hemorrhage, lead malposition, or infections, in DBS was around 8–12% [18, 19] and for SCS and PNFS around 4–18% [20]. A device-related infection is among the most common complications. Reported infection rates for DBS, SCS, and PNFS are quite similar for the different devices. Generally, infection rates are reported between 2.5 and 5%, but infection rates have been described as high as 10–15% for individual centers [21–23]. Infections can lead to unscheduled hospital admissions, additional surgeries, hardware removal, therapeutic setbacks by discontinuation of stimulation and reoccurrence of debilitating symptoms and also result in an additional economic burden [24]. Conservative medical treatment of such infections has demonstrated a low success rate [22]. There are guidelines in neuromodulation regarding infection prevention with unspecific recommendations to infection treatment [25]. Strategy is mainly based on best medical practice and experience of the treating centers and health professionals.

In this study, we investigated the surgical strategies and medical approaches of hardware-related infections in our center. We aimed to identify the most common infectious agents and which surgical strategy and antibiotic treatment could be successfully used to treat them. We also aimed to compare the length of the antibiotic treatments based on the surgical strategy and the detected bacteria.

Materials and Methods

We retrospectively analyzed digital medical records of patients who underwent DBS, SCS, or PNFS surgery at the Department of Stereotactic and Functional Neurosurgery of the University Hospital of Cologne, Germany, from January 2012 to December 2019. ICD-10 codes were used to identify patients with complications related to the implants. Inclusion criteria included a documented postoperative clinical infection related to the hardware. A postsurgical infection was identified by classical symptoms such as wound swelling, redness, local heating, and pain, potentially accompanied by (purulent) secretion, fever, malaise, elevated inflammatory markers, and visually exposed hardware. Excluded were patients with noninfectious skin erosions with negative microbiological cultures or eubacterial PCR, noninfectious hardware-related problems (e.g., pain along subcutaneous cables), stimulation-related problems, and infections related to other types of implanted devices (e.g., intrathecal medication pumps). Patients with nonspecific wound irritation and without confirmed infection as specified above were not included for analysis.

From digital records, we extracted patient (gender, age, comorbidities), disease characteristics, type of hardware (DBS, SCS, PNFS), location of the infection, infectious agent, surgical procedure, and antimicrobial treatment. The infection latency was calculated as the period of time between the most recent surgery and onset of infection. We divided our cohort into early infections that occurred within the first three postoperative months and late infections that occurred after 3 months [26]. We also documented whether the infection occurred after a first neurostimulator implantation or after a scheduled hardware revision or replacement (e.g., IPG replacement). The included patients ultimately underwent a surgical procedure. Based on the surgical procedure, we created two groups: (i) surgical wound revision without hardware removal, (ii) surgical wound revision with hardware removal. For further analysis, we also specified whether hardware was removed partially or completely. Patients who underwent multiple surgeries for the infection were stratified in the group with the most aggressive type of surgery, for example, a patient who had a local wound revision without hardware removal but required hardware removal later on was included in the group of surgical wound revision with hardware removal. Finally, clinical outcome was assessed by the occurrence of major complications related to infection as death, sepsis, bacteremia, osteomyelitis, intracranial and/or intraspinal abscess.

Data were statistically tested using the Prism 8 software (GraphPad Software LLC, 2020). To evaluate the duration of antimicrobial treatment after surgical wound revision with and without hardware removal, we used the unpaired *t* test. After this analysis, we further divided the group that required hardware explantation into a group with partial and a group with complete hardware removal. Differences in the duration of the antimicrobial regime between the three groups were analyzed with a one-way ANOVA analysis with Tukey's post hoc test. We also analyzed for differences in the duration of antimicrobial treatment based on identified bacteria (*S. epidermidis* vs. *S. aureus*), for which we used the unpaired *t* test. A p value <0.05 was considered as statistically significant. Data are expressed as mean ± SEM.

Results

Patient Demographics

From January 2012 to December 2019, we found 137 patient records with potential postoperative neurostimulator-related infections. A total of 55 patients were excluded due to noninfectious pain related to the hardware (n = 19), other implanted devices (n = 16), hardware-related complications (e.g., noninfectious skin erosion; n = 9), stimulation-related complications (n = 7) and due to a lack of data (n = 4). Ultimately, 82 patients were included in the final analysis (Fig. 1) who underwent a total of 118 revision surgeries to treat the infection.

The average age at the time of infection was 57.7 years (±1.8 years; range, 20–89 years). The gender ratio was 1.22 male to 1 female (male n = 45, female n = 37). Demographic data and most common comorbidities are displayed in Table 1. According to the type of neurostimulator, 46 patients had a DBS system (n = 46/82; 55.6%) followed by SCS (n = 21/82; 25.6%), PNFS (n = 12/82; 14.6%), and some patients had both SCS and PNFS systems implanted (n = 3/82; 3.7%) (Table 1).

Over an 8-year period, a total of 1,250 DBS surgeries were performed, including 560 de novo system implantations, 644 IPG replacements, and 46 revision surgeries. 1,835 SCS surgeries were performed with 1,196 system implantations, 126 battery replacements, 394 revision surgeries, and 119 explanations. 731 PNFS surgeries were performed from 2012 till 2019, including 415 implantations of test electrodes, 266 implantations of whole PNFS systems, 22 battery replacements, and 28 revision surgeries. The implanted DBS, SCS, and PNFS devices were specifically designed for the particular mode of neuromodulation, and no hardware or electrode was used for off-label stimulation.

In total, 118 revision surgeries were performed for infections, representing an overall incidence of 3.05% of the cases. This resulted in a reported infection rate of 5.7% for DBS (n = 71/1,250), 1.7% for SCS (n = 32/1,835), and 2.1% for PNFS (n = 15/731).

The most common indication for DBS patients was Parkinson's disease (n = 32/46; 69.6%) followed by dystonia (n = 4/46; 8.7%), essential tremor (n = 3/46; 6.5%),

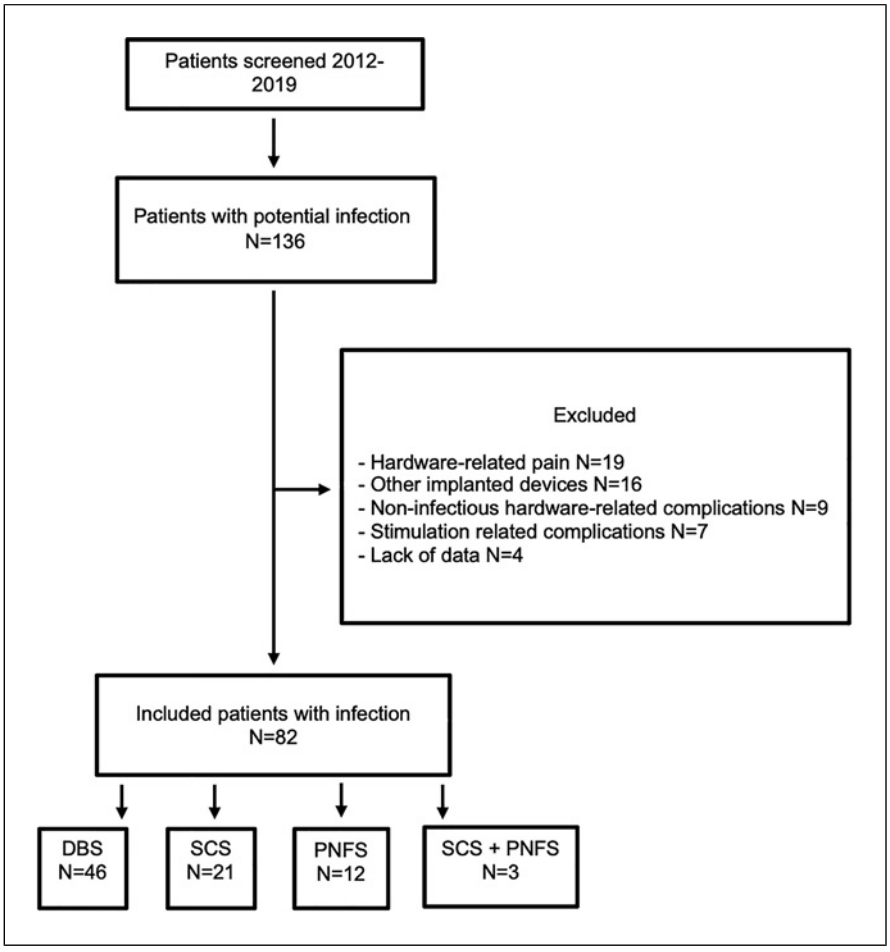

Fig. 1. Flowchart of retrospective patient selection from January 2012 until December 2019 for final data analysis.

Tourette syndrome (n = 3/46; 6.5%), obsessive-compulsive disorder (n = 3/46; 6.5%), and Alzheimer's disease (n = 1/46; 2.2%). Depending on the indication, DBS system implantations were either performed under general anesthesia or analgesic sedation. According to the internal standards of our hospital, all patients received prophylactic antibiotic medication with cefazoline prior to surgery, which was continued for 2 days postoperatively. In case of penicillin allergy, patients received clindamycin. Battery replacements were mostly performed under analgesic sedation, unless it was contraindicated. In case of IPG replacements, patients only received prophylactic antibiotics prior to surgery. The vast majority of patients with implanted SCS systems were treated for chronic back and leg pain (n = 19/21; 90.5%), followed by chronic bladder and bowel problems (n = 1/21; 4.8%) and polyneuropathy (n = 1/21; 4.8%). PNFS patients included patients with chronic back pain (n = 6/12; 50.0%), chronic cervical pain (n = 2/12; 16.7%), postsurgical neuropathies (n = 2/12; 16.7%), migraine (n = 1/12; 8.3%), and phantom pain (n = 1/12; 8.3%). SCS or PNFS electrode implantations or explanations and battery replacements were performed by default under analgesic sedation and local anesthetics, unless it was contraindicated. De novo battery implantations were performed under general anesthesia. All patients received prophylactic antibiotics, either cefazoline or clindamycin, prior to surgery. All patients with both SCS and PNFS systems implanted were treated for chronic back pain (n = 3/3) (Table 1).

Time of Infection

Infections predominantly occurred in patients who had undergone multiple surgeries (71%), for example, scheduled IPG replacement, in comparison to patients who underwent a de novo hardware implantation (29%). The average number of surgeries related to the implanted neuromodulation system before the infection occurred was 2.6 (±2.2). Unfortunately, in 4 patients, who had several prior interventions, we could not retrace the exact number

Table 1. Patient demographic data including age (years ±SD), gender, comorbidities, diagnosis, type of neurostimulator

Demographics	
Mean age, years	57.7±1.8
Gender ratio (♂:♀)	1.22:1 (♂ *n* = 45:♀ *n* = 37)
Comorbidities, *n* (%)	
Obesity (total)	30 (36.6)
Mildly obesity (BMI: 30–34.99)	22 (26.8)
Moderate obesity (BMI: 35–39.99)	6 (7.3)
Adipositas permagna (BMI above 40)	2 (2.4)
Nicotine abuse	20 (24.4)
Type 2 diabetes	7 (8.5)
Arterial hypertension	25 (30.5)
Diagnosis	
DBS, *n* = 46, *n* (%)	
Parkinson's disease	32 (69.6)
Dystonia	4 (8.7)
Essential tremor	3 (6.5)
Tourette syndrome	3 (6.5)
Obsessive-compulsive disorder	3 (6.5)
Alzheimer's disease	1 (2.2)
SCS, *n* = 21, *n* (%)	
Chronic back and leg pain	19 (90.5)
Chronic bowel and bladder problems	1 (4.8)
Neuropathy	1 (4.8)
PFNS, *n* = 12, *n* (%)	
Chronic back pain	6 (50.0)
Chronic cervical pain	2 (16.7)
Neuropathy	2 (16.7)
Migraine	1 (8.3)
Phantom pain	1 (8.3)
SCS + PFNS, *n* = 3, *n* (%)	
Chronic back pain	3 (100.0)

of surgeries because they were performed in other hospitals. Postoperative infections occurred after an average of 12.2 months (12.2 ± 1.7 months), with a range between 1 and 95 months (7.9 years) after the last surgery. We observed that most infections (59.0%) occurred later than 3 months after the most recent surgery with a mean of 19.6 ± 2.5 months. In cases where the infection occurred within the first three postoperative months, the mean delay after surgery was 1.5 ± 0.1 months. With respect to the type of neurostimulator, we observed a similar trend among DBS patients with 67.6% of their infections typically developing later than 3 months after surgery. However, SCS patients more often had an early infection within the first three postoperative months (57.1%). There was no difference in infection timing in PNFS (50% within 3 months postoperatively) and SCS+PNFS (50% within 3 months postoperatively) treated patients.

Table 2. Distribution of the infection site along the implanted hardware for the entire group as well as according to the type of neurostimulator expressed in percentages (%)

	Infection site		
	IPG, %	Leads and extensions, %	both, %
Overall	**44.0**	34.1	21.9
DBS	**45.7**	26.1	26.7
SCS	**47.6**	38.1	14.3
PNFS	25	**58.3**	16.7
SCS + PNFS	**66.7**	33.3	–

The most common infection site for each type of neuromodulation is highlighted.

Location of Wound Infection

Infections were mainly located at the site where the IPG was implanted (*n* = 36/82; 44.0%), followed by infections along the leads and extension cables (*n* = 28/82; 34.1%) and both locations simultaneously (*n* = 18/82; 21.9%) (Table 2). After differentiating for the type of neurostimulator, DBS and SCS patients had a higher rate of infection at the site of the IPG (45.7% DBS, 47.6% SCS), followed by the leads (26.1% DBS, 38.1% SCS) and both locations simultaneously (28.3% DBS, 14.3% SCS). On the other hand, in PNFS patients, the infection was most likely to be located around the leads (58.3%).

Surgical Treatment Strategy

From the entire cohort of 82 patients, 37.8% underwent surgical wound revision without hardware removal (*n* = 31/82) and 62.2% received surgical wound revision with partial or complete hardware removal (*n* = 51/82) (Fig. 2). In both cases, a wound debridement was performed, and the wound was washed out with iodine and/or hydrogen peroxide solution. Antibiotic irrigations were not used. In 8 patients where the hardware was not removed, the IPG was relocated in close proximity to the original IPG pocket. Infections that were managed without hardware removal were mainly located at the IPG (68%). In 32% of patients, the infection involved the tissues near the leads and extension cables. Wound revision with hardware removal was slightly more common for infections around the leads and extension cables (50.6%) than IPG-related infections (40.3%). In the remaining 9.1%, infections occurred simultaneously at the IPG as well as the leads and extension cables.

In total, the 82 patients underwent 118 surgeries for the management of their infections. One-third of the

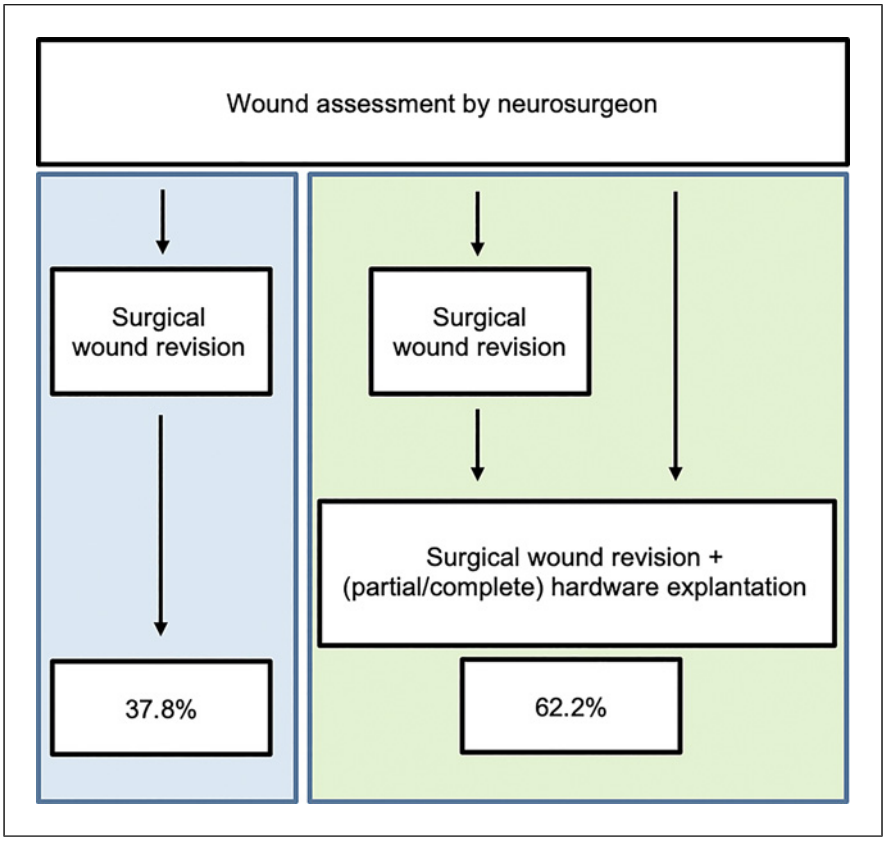

Fig. 2. Flowchart of the surgical strategies to treat the infected wounds which were related to the neurostimulator hardware.

Table 3. The strategy of choice with surgical wound revision with partial/complete hardware removal according to the type of neurostimulator expressed in percentages (%)

	Surgical wound revision + hardware removal, %
DBS	52.2
SCS	76.2
PNFS	66.7
SCS + PNFS	100

patients required multiple surgical revisions to treat the infection (n = 26/82, 31.7%), with most of them requiring hardware removal (n = 21/26; 80.7%). More specifically, in 10 cases, multiple revision surgeries were necessary in patients who primarily had a wound revision but required second surgery with hardware removal due to persisting or new infection (47.6%). Furthermore, some patients who underwent an initial partial hardware removal procedure eventually required a secondary procedure to completely remove the system (n = 7/21; 33.3%).

In patients who were managed with repeated surgical revision without hardware removal, the average time to the subsequent surgery was 8.5 (±8.8) months. If the hardware was removed in a subsequent surgery, on average, the second surgery was performed 5.5 (±4.7) months after the initial revision surgery.

Surgical Treatment by Neurostimulator

In DBS, 47.8% of patients were treated by surgical wound revision alone (n = 22/46) and 52.2% underwent a surgical wound revision with hardware removal (n = 24/46). Differently, surgical wound revision with hardware removal was predominant among the other groups, 76.2% in SCS patients (n = 16/22), 66.7% in PNFS patients (n = 8/12), and 100% in patients with simultaneous SCS and PNFS systems (n = 3/3) (Table 3).

Microbiological Cultures

A wide variety of bacteria were obtained from the microbiological samples (Table 4). The most frequently found bacteria were *S. epidermidis* and *S. aureus* with

Table 4. Species distribution of microbiological cultures from intraoperatively obtained samples expressed in both numbers and percentages (%), with the predominant presence of *S. epidermidis* and *S. aureus* in the infected wounds

	Surgical wound revision, n = 31, n (%)	Surgical wound revision + hardware removal, n = 51, n (%)	Total, n = 82, n (%)
Staphylococcus epidermidis	**17** (**54.8**)	15 (29.4)	**32** (**39.0**)
Staphylococcus aureus	4 (12.9)	**25** (**49.0**)	**29** (**35.4**)
Klebsiella oxytoca	1 (3.2)	2 (3.9)	3 (3.7)
Cutibacterium acnes	2 (6.5)	–	2 (2.4)
Corynebacterium spp.	–	2 (3.9)	2 (2.4)
Streptococcus dysgalactiae	–	1 (2.0)	1 (1.2)
Escherichia coli	1 (3.2)	–	1 (1.2)
Enterobacter aerogenes	–	1 (2.0)	1 (1.2)
Pseudomonas aeruginosa	–	1 (2.0)	1 (1.2)
Finegoldia magna	1 (3.2)	–	1 (1.2)
Serratia marcescens	–	1 (2.0)	1 (1.2)
Inconclusive	3 (9.7)	3 (5.9)	6 (7.3)
Wrong/no probe	2 (6.5)	–	2 (2.4)

The most common infection site for each type of neuromodulation is highlighted.

39.0% (n = 32/82) and 35.4% (n = 29/82), respectively. Only one case of methicillin-resistant *S. aureus* infection was documented in this group.

In general, the surgical treatment strategy followed in *S. epidermidis* and *S. aureus* infections was contrastingly different. Approximately half of the patients with *S. epidermidis* were treated with a wound revision procedure (53%) and almost the other half with hardware removal (47%). On the other hand, most patients with *S. aureus* infections underwent a revision with hardware removal (86.2%).

The predominance of *S. epidermidis* or *S. aureus* was observed in patients irrespective of the type of neurostimulator implanted. In DBS patients, we found 37% (n = 17/46) *S. epidermidis* versus 32.6% (n = 15/46) *S. aureus*, 33% (n = 7/21) versus 38% (n = 8/21) in SCS, and 50% (n = 6/12) versus 42% (n = 5/12) in PNFS patients, respectively. The 3 patients with both SCS and PNFS combined implantations had two infections with *S. epidermidis* (66.6%; n = 2/3) and one infection with *S. aureus* (33.3%; n = 1/3).

Antimicrobial Management

Antimicrobial treatment was given for an average of 3.4 weeks (±0.3 weeks) across all patient groups. Patients who solely received a wound revision were treated significantly longer with antimicrobials than patients who underwent surgery with hardware removal (4.2 ± 0.6 weeks vs. 3.0 ± 0.2 weeks; $p < 0.05$). In particular, patients with complete removal of the neurostimulator were treated significantly shorter with antimicrobials than patients with solely wound revisions (2.5 ± 0.2 weeks vs. 4.2 ± 0.6 weeks; $p < 0.05$; Fig. 3). Partial hardware removal did not show a significant difference in antimicrobial treatment duration when compared to the other groups (3.5 ± 0.4 weeks; $p > 0.05$; Fig. 3). The duration of antimicrobial treatment in patients with infections caused by *S. epidermidis* versus *S. aureus* was similar (3.3 ± 0.4 weeks vs. 3.7 ± 0.4 weeks; $p > 0.05$). In 52.4% of the cases, antimicrobials of the lincosamide (28.0%) or penicillin (24.4%) class were administered. Alternatively, fluoroquinolone (11.0%), cephalosporin (9.8%), or sulfonamide (7.3%) antimicrobials were given. Rarely, a glycopeptide (1.2%) or nitroimidazole (1.2%) was administered. To treat staphylococcal biofilms around the device, rifampicin was added in 24.6% of patients with confirmed staphylococcal infection (n = 15/61). Of those patients, 53.3% (n = 8/15) were successfully treated with surgical wound revision alone, leaving the hardware in situ. In 13.3% (n = 2/15), partial hardware removal was performed, and in 33.3% (n = 5/15), complete removal of the neurostimulator was performed.

Clinical Outcome

All patients were followed for at least 1 year after the last intervention. One patient developed an intracranial abscess (1.2%; n = 1/82). No cases of sepsis, bacteremia,

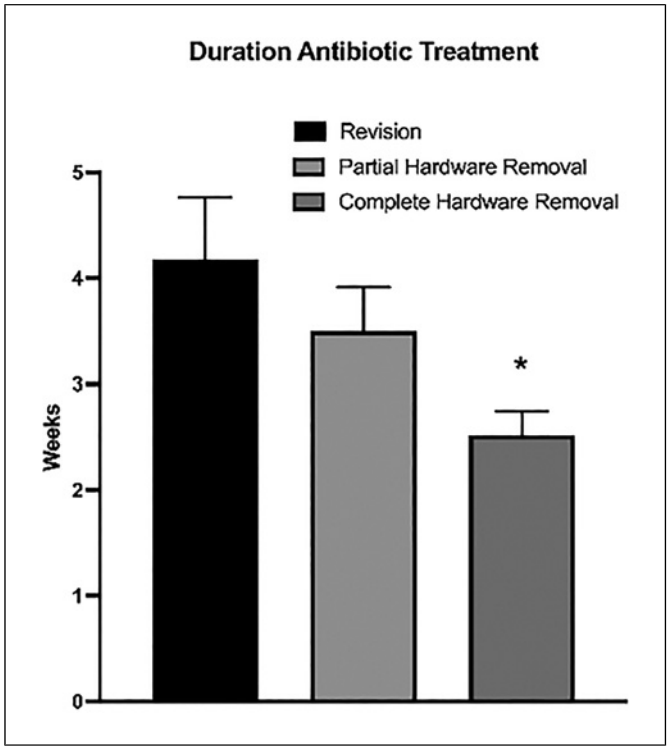

Fig. 3. Analysis of mean duration of antimicrobial treatment after surgery between surgical wound revision without hardware removal (black), surgical wound revision with partial hardware removal (light gray), and surgical wound revision with complete hardware removal (dark gray). One-way ANOVA; means with SEM (weeks); *$p < 0.05$ surgical wound revision without hardware removal vs. surgical wound revision with complete hardware removal.

osteomyelitis, intraspinal abscesses, or death associated with the hardware infection were found. No infection-related death occurred in our cohort.

Discussion

In this retrospective single-center study, we describe the prevalence of neurostimulator-related infections, the responsible microbiological agents, as well as the surgical approaches and antimicrobial regimens used for their treatment. Our infection rate of 5.7% for DBS procedures is in accordance with most studies [21, 27, 28]. SCS (1.7%) and PNFS (2.1%) related infection rates are relatively low compared to 2.5–5% reported in the literature [23, 29–32]. Furthermore, we found only one case of intracerebral abscess in a DBS patient. Other severe clinical events related to hardware infections such as sepsis, bacteremia, osteomyelitis, or death did not occur.

The infections that we investigated were surgically treated with either a wound revision or a wound revision with simultaneous hardware removal. DBS-related infections were almost equally treated by both surgical strategies, whereas infections related to SCS or PNFS predominantly required hardware removal. Interestingly, we found that most infections (59%) in our study occurred more than 3 months after surgery. Some reports corroborate our findings with a similar delay [27], while other studies primarily observed early infections [22, 33].

The area surrounding the IPG was the most frequent infection location in our study. We also observed that the majority of infections (72%) occurred after an IPG replacement or other type of revision procedure, which is in line with other studies [22, 23, 33]. Replacement of a non-rechargeable IPG is generally considered to be a minor procedure, but infections and other possible complications including wound erosions, hematoma, and hardware malfunction appear in circa 9% of the cases [34]. Moreover, it has been estimated that infection rates after IPG replacement are three times higher than after a complete new DBS implantation [33]. In our cohort, the reported infection rate after IPG replacement or other revision surgeries was 3.8% versus 1% after de novo system implantation in DBS, SCS, and PNFS combined. These factors may favor the implantation of rechargeable IPGs from an infection point of view [35].

Infections treated successfully with a wound revision without hardware removal were mainly located around the IPG (68%). On the other hand, hardware removal was predominantly performed (59.7%) in cases with lead and cable infections or extended infection with leads, cables, and IPG affected simultaneously. This may be explained by closer proximity of leads and cables to the central nervous system or extend of the infection. An intracranial or spinal abscess should be avoided at all costs. Since the IPGs are remotely located from the active leads, it can be argued that these infections may benefit from surgical wound revision without losing the clinical benefits of neurostimulation. Treatment escalation with hardware explantation is always possible.

The infectious agents *S. epidermidis* and *S. aureus* were most frequently found in microbiological cultures. These are common in hardware-related infections [22, 23, 28, 36, 37]. The complete surgical removal of a device has been advocated as a general principle [37]. However, reoccurrence of neurological and psychiatric symptoms after neurostimulator removal requires individualized decision-making based on the burden for patients and their families and should be kept to a minimum.

Interestingly, we observed a difference in surgical strategy for both bacteria. In the case of *S. epidermidis*,

53% were treated with wound revision, whereas 47% required a wound revision with hardware removal. In contrast, *S. aureus* infections required removal of hardware in most patients (86%) to control the infection. This is supported by experimental studies of *S. aureus* infections in spinal implants demonstrating insufficiency of antimicrobial treatment and infection recurrence [38]. Biofilm formation around the hardware is likely to be key, causing infection persistence and antimicrobial tolerance [39]. Bacteria embedded in biofilm are less susceptible to antimicrobial treatment, due to lower rates of bacterial growth within the biofilm and decreased antimicrobial activity [37, 40]. If an implant has been left in situ combination therapy with rifampicin is generally recommended [37]. Coagulase-negative staphylococci are generally less pathogenic, and local surgical revision may therefore be sufficient.

Guidelines to prevent or lower the risk of infection in neuromodulation have provided recommendations regarding management of preexisting conditions, surgical preparation, surgical technique, and postoperative care; however, these do not differ from other surgical procedures [25]. Implementing strategies that reduce infection risk by nasal screening for *S. aureus* and preoperative decolonization with nasal mupirocin and chlorhexidine soap for 5–7 days have shown to be effective in general deep surgical infections [41], as well as in DBS procedures [36]. There is a wide consensus on preoperative intravenous antimicrobial prophylaxis, for example, administration of cephalosporins 30–60 min before incision. Some authors have suggested additional administration of antimicrobials into the wounds by injection or washing or the usage of antimicrobial envelopes [25, 42, 43], but this remains controversial. In case of an infection, there is no consensus on duration of antimicrobial treatment. This has been generally based on best medical practice, clinical condition, and inflammatory markers. In our study, patients were treated with antimicrobials for an average of 3.4 weeks after the revision procedure. In comparison, infections in cardiac pacemakers and defibrillators are typically treated for 2 weeks with antimicrobials after hardware removal [37]. However, major complications such as sepsis or bacteremia may prolong the treatment up to 6 weeks [37].

The main limitations of this study can be attributed to its retrospective study design. Unfortunately, it was not always possible to reproduce why a certain treatment strategy was followed. The applied antimicrobial treatment was also very heterogenous, which made comparisons difficult. Prospective controlled studies would be necessary to identify criteria based on which the decision between local wound revision and hardware removal could be made.

Conclusion

Infections related to neurostimulators are predominantly caused by *S. epidermidis* and *S. aureus*. In case surgical intervention of infection is required, *S. aureus*-related infections required hardware removal, whereas *S. epidermidis* infections could also be treated by local wound revision in half of the cases. Hardware removal leads to shortened antimicrobial treatment.

Guidelines should be developed with recommendation regarding administrated antimicrobials and surgical strategies, depending on the time of the infection and the detected pathogens. These should take potential consequences of halted stimulation in consideration after hardware explantation, which is burdensome and, in some cases, even dangerous for the patient.

Statement of Ethics

This study was registered and approved by the Local Ethical Committee, Ethics Commission of Cologne University's Faculty of Medicine, under the registration number 23-1372-retro. Written informed consent from the participants was not required for this retrospective study in accordance with local/national guidelines.

Conflict of Interest Statement

G.M. is a consultant for Boston Scientific and Medtronic. V. V.-V. is a member of advisory boards and has received speaker's honoraria from Medtronic, Boston Scientific, and Abbott. PA has received honoraria for lecturing fees and educational activities from Boston Scientific and Medtronic. None of the researchers received funding directly related to this study.

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Author Contributions

Conceptualization: I.K., J.W., G.M., V. V.-V., and P.A.; investigation: I.K., P.H., S.K.H.T., and P.A.; methods: I.K., S.K.H.T., H.S., and P.A.; writing – original draft: I.K., S.K.H.T., and P.A.; writing – review and editing: I.K., S.K.H.T., P.H., J.W., G.M., H.S., V. V.-V., and P.A.; and visualization: I.K., P.H., and P.A.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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