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## Staphylococcus aureus screening and decolonization reduces the risk of surgical site infections in patients undergoing deep brain stimulation surgery

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1 *Staphylococcus aureus* screening and decolonization reduces the risk  
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20 Nasal *S. aureus* screening before DBS

21  
22 Keywords: deep brain stimulation; *Staphylococcus aureus*; screening; surgical site infection.

**23 Summary**

24 In a controlled before-and-after study in a single-center, we assessed whether identification of  
25 *Staphylococcus aureus* (SA) nasal carriers followed by nasal mupirocin ointment and  
26 chlorhexidine soap reduced surgical site infections (SSI) among 182 patients undergoing deep  
27 brain stimulation. 119 patients were included in the control group and 63 in the screening  
28 group. There was a significant SSI decrease from 10.9% to 1.6% between the two groups  
29 ( $p < 0.04$ ; relative risk: 0.13; 95% confidence interval: 0.003-0.922). There were eight SSI  
30 involving SA in the control group and none in the screening group. No specific risk factors for  
31 SSI were identified.

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## 49 **Introduction**

50 Deep brain stimulation (DBS) is a major surgical treatment in neurological diseases  
51 resistant to medical treatment such as Parkinson's disease, essential tremor, primary dystonia  
52 or Tourette's syndrome.<sup>1</sup> This procedure is safe, effective and well tolerated by patients but  
53 surgical site infection (SSI) remains a major problem with rates up to 15%.<sup>2</sup> DBS system  
54 device includes intracranial electrodes, subcutaneous wire extensions and internal pulse  
55 generators (IPG).<sup>2,3</sup> When SSI occurs, partial or total removal of the system device is  
56 generally necessary, along with antibiotic therapy. However, superficial SSIs may sometimes  
57 be treated conservatively with antibiotics alone.

58 *Staphylococcus aureus* (SA) is the most frequent bacterium identified in SSIs after  
59 DBS procedures, accounting for 36% to 57% of infections; nasal carriage is known to be a  
60 direct risk factor for nosocomial SA infections, including SSI.<sup>2-4</sup> Three approaches for the  
61 eradication of SA exist: preoperative systemic antibiotics, bacterial interference and local  
62 application of antibiotics. In the latter case, mupirocin nasal ointment is widely used.<sup>4,5</sup> In  
63 2010, a randomized, double-blind, placebo-controlled and multicenter trial showed that  
64 screening and decolonization of nasal carriers of SA using nasal mupirocin and chlorhexidine  
65 soap reduced SA nosocomial infection, in particular deep SSI.<sup>6</sup> To our knowledge, this  
66 method has never been studied among patients undergoing a DBS procedure.

67 The aim of our study was to assess the effectiveness of screening and decolonization  
68 of SA on SSI rate in patients undergoing DBS implantation at our center.

## 69 **Patients and Methods**

### 70 *Study design*

71 A controlled before-and-after study was used. From January 2008 to December 2012,  
72 we included in the control group 119 patients admitted for DBS procedure. From January  
73 2013 through June 2015, screening for nasal carriage of SA of 63 patients began at their  
74 preoperative consultation; these patients constituted the screening group. The primary  
75 outcome of the study was the occurrence of SSI in each group. Written informed consent was  
76 obtained from each participant and the study was conducted in accordance with the  
77 Declaration of Helsinki.

78 To screen patients for SA carriage, a dry, sterile rayon swab was rotated twice in each  
79 nostril then placed in 100 µl of Trypticase Soy Broth. Patients who were nasal carriers of SA  
80 received protocol instructions: during the five days before surgery application of 2%  
81 mupirocin nasal ointment three times a day, and a daily shower with 4% chlorhexidine soap.  
82 Patients in the control or the negative screening groups showered with 4% povidone-iodine  
83 soap the evening before surgery and on the morning of surgery. Skin preparation immediately  
84 before the operative procedure consisted of cleaning with 4% povidone-iodine soap then a  
85 thorough rinse, drying with sterile paper towels and application of 5% povidone-iodine-  
86 alcohol. From 2010, in accordance with the recommendations of the French Society of  
87 Anaesthesiology, preoperative antibiotic prophylaxis by cloxacillin was replaced by  
88 cefazolin.<sup>7</sup>

### 89 *Surgical procedure and SSI surveillance*

90 The DBS procedure was performed after the patient had been weaned off therapeutic  
91 drugs on the day prior to surgery. Under local anaesthesia, and with the patient conscious, one  
92 or two electrodes (Medtronic Inc., Minneapolis, MN) were inserted into the basal ganglion  
93 nuclei, as indicated by the underlying pathology. Finally, under general anaesthesia, one or  
94 two IPG (Medtronic, Inc., Minneapolis, MN) were implanted in the subclavicular area or in  
95 the anterior abdominal wall and connected to the intracranial electrodes with subcutaneous  
96 wire extensions. Patients were sometimes operated on on two different sessions if electrode  
97 implantation took too long to allow implantation of the IPG the same day. After implantation,  
98 electrodes were externalized during two days, and wire extensions and the IPG were  
99 implanted three days later. Since 2011, a research protocol meant that patients undergoing  
100 subthalamic nucleus (STN) DBS had intracranial local field potentials (LFP) recordings to  
101 explore the STN local neural activity.

102 Patients underwent outpatient review one month postoperatively, and were then  
103 hospitalized in the Neurology Department at three, six and 12 months post-operatively to  
104 adapt device settings. A prospective monitoring protocol for SSI surveillance was used for  
105 every patient operated on since 2008.<sup>8</sup> SSIs were classified as superficial (grade I), deep  
106 incisional (grade II) and organ-space (grade III).<sup>9</sup> Total or partial removal of the infected  
107 device was decided on a case-by-case basis.

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109 *Statistical analysis*

110 Clinical and microbiological data were analyzed using SPSS statistics software,  
111 version 17. For univariate analyses, Chi-squared or Fisher's exact test was used to compare  
112 categorical variables, and Student's t-test or Mann-Whitney U-test to compare continuous  
113 variables.  $P < 0.05$  was considered statistically significant.

114 **Results**

115 Results demonstrated significant differences between the two groups: one SSI  
116 occurred in the screening group (1.6%) due to *Enterobacter aerogenes* and 13 infections in  
117 the control group (10.9%) ( $P = 0.04$ ; relative risk 0.13; 95% confidence interval, 0.003-0.922)  
118 (Table I). SSIs in the control group were due to SA in eight patients (61.5%); *Escherichia*  
119 *coli*, *Micrococcus* sp. and *Propionibacterium acnes* accounted for one case each and in two  
120 cases, no bacterium was identified.

121 The two patient groups were comparable in terms of age, sex, neurological  
122 pathologies, underlying disorders and American Society of Anaesthesiology (ASA) score  
123 (Table II). In the screening group, total duration of surgery and electrode implantation was  
124 significantly shorter than in the control group. Procedures were more frequently completed  
125 during a single day in the screening group. There were four (3.4%) patients with LFP  
126 recordings in the control group and 15 (23.8%) in the screening group. Only one patient from  
127 the control group with LFP recordings had a SSI.

128 In the screening group, nasal screening of SA was positive in 23 (36.5%) patients and  
129 negative in 34 (54%) patients. Screening was not performed in six (9.5%) patients.

130 Removal of the infected device was performed in 11 control group cases (eight grade  
131 II and three grade III). The last two cases, involving grade I SSI, were treated with antibiotics  
132 only. In the screening group, the IPG of the infected patient was removed. No patient had a  
133 recurrence of infection. Among the 12 patients undergoing device removal, re-implantation  
134 was done in six cases in the control group and in the case of the screening group. The patients  
135 who did not undergo re-implantation were all offered, but declined, the procedure.

136 Analysis of infected vs uninfected patients showed that duration of hospitalization was  
137 significantly longer for infected patients than for uninfected patients ( $P = 0.017$ ). No risk  
138 factors for SSI were identified.

## 139 Discussion

140 This study showed that detection of SA nasal carriage followed by decolonization with  
141 mupirocin nasal ointment and chlorhexidine gluconate soap significantly reduced the risk of  
142 SSI in DBS patients. In a study of 6 771 patients in internal medicine, cardiothoracic,  
143 vascular, orthopedics, gastrointestinal or general surgery departments, Bode *et al* reduced the  
144 deep SSI rate of 79% using screening and decolonization of SA nasal carriers admission or  
145 the week before admission.<sup>6</sup> Our data are consistent with the experience of Bode *et al* in  
146 another patient group, and support the value of SA decolonization prior to DBS to prevent SSI  
147 by SA.

148 During the two periods, the patient groups were comparable. However, probably  
149 owing to the greater experience of the neurosurgeon, procedures in the screening group were  
150 significantly shorter than in the control group, more frequently being completed in a single  
151 day. While there were more LFP recordings in the screening group, there was no increased  
152 risk of SSI. Hospitalization lasted longer in the group of infected patients because five SSIs  
153 occurred before patients discharge. In the control group, the higher number of IPG implanted  
154 and the longer total length of the procedures might have increased the risk of SSI, but within  
155 the control group there was no significant correlation between surgical factors and the  
156 occurrence of SSIs (data not shown). Our study was a relatively small single-centre study, and  
157 caution is therefore required in interpreting our results. In particular, although we identified  
158 no statistically significant risk factors for SSI, our study was not powered to detect differences  
159 related to sex, age, ASA score, neurological pathology, underlying diseases and surgical  
160 management.<sup>2,3</sup>

161 The prevalence of SA carriage in our study was 36.5% (23 patients), which is  
162 consistent with previously published carriage rates of 12% to 70%.<sup>4</sup> Decolonization of SA  
163 carriers appears to be effective in reducing the risk of post-operative infections, especially  
164 superficial and organ/space SSI (Grade I: 0 vs 2; Grade III: 0 vs 3). A major benefit of  
165 avoiding infection is avoiding the removal of any part of the DBS system device; as well as  
166 the financial and social costs of managing infections suspending stimulation can be  
167 troublesome for patients, being associated with severe worsening of disease symptoms.

168 Mupirocin and chlorhexidine are relatively safe, and none of our patients reported  
169 serious adverse effects of the treatment. In 2012, Courville *et al.* assessed the cost-  
170 effectiveness of such treatment in preventing SSI in patients undergoing hip and knee

171 arthroplasty and concluded of its interest.<sup>10</sup> Although a cost-benefit analysis of SA screening  
172 and decolonization before DBS surgery has not yet been reported, we believe that the  
173 interventions are likely to be cost-effective. We plan to undertake a future cost-effectiveness  
174 analysis in the future..

## 175 **Conclusion**

176 This is the first study, to our knowledge, to demonstrate the association between  
177 screening and decolonization of SA nasal carriage and a decreased risk of SSI in DBS  
178 patients. The preoperative protocol was safe and easy to apply, and was well-tolerated, by  
179 patients. We also found that LFP recordings did not increase the SSI risk.

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182 language.

183 **Conflicts of interest:** none.

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**Table I**

Post-operative infections in patients undergoing a deep brain stimulation procedure during the periods before and after implementation of a regimen of pre-operative *Staphylococcus aureus* screening and decolonization

	Screening group N=63	Control group N=119	P Value	RR <sup>1</sup>
SSI <sup>2</sup> — no. (%)				
All bacteria	1 (1.6)	13 (10.9)	<b>0.04</b>	<b>0.13 (0.003-0.922)</b>
<i>S. aureus</i>	0	8 (6.7)	-	-
Mean ( $\pm$ SD <sup>3</sup> ) time to onset (days)	33	49.3 ( $\pm$ 68.8)	-	-
Site of infection - no. <sup>4</sup> (%)				
IPG <sup>5</sup> only	1	1	-	-
wire extension only	0	1	-	-
electrode only	0	1	-	-
IPG + wire extension	0	3	-	-
wire extension + electrode	0	2	-	-
diffuse	0	5	-	-
Grade of infection - no. (%)				
I	0	2	-	-
II	1	8	-	-
III	0	3	-	-

<sup>1</sup>RR, relative risk; <sup>2</sup>SSI, surgical site infection; <sup>3</sup>SD, standard deviation; <sup>4</sup>No., number; <sup>5</sup>IPG, internal pulse generator.

**Table II**

Characteristics of the 182 patients operated on for deep brain stimulation before and after implementation of a regimen of pre-operative *Staphylococcus aureus* screening and decolonization

Variables	Screening-group (N=63)	Control-group (N=119)	p Value
Mean ( $\pm$ SD <sup>1</sup> ) age — year	54.4 ( $\pm$ 13.5)	53.1 ( $\pm$ 15.4)	0.59
Male sex — no. <sup>2</sup> (%)	40 (63.5)	66 (55.5)	0.3
Mean ( $\pm$ SD) duration of hospitalisation — days	18.8 ( $\pm$ 5)	16.3 ( $\pm$ 5.7)	<b>&lt;0.01</b>
Mean ( $\pm$ SD) duration of follow-up — months	16.2 ( $\pm$ 6)	47.9 ( $\pm$ 20.9)	<b>&lt;0.01</b>
Neurological pathologies — no. (%)			
Parkinson disease	40 (63.5)	69 (58)	0.47
Essential tremor	13 (20.6)	23 (19.3)	0.83
Dystonia	8 (12.7)	17 (14.3)	0.77
OCD <sup>3</sup>	0	5 (4.2)	-
Tourette's syndrome	2 (3.2)	5 (4.2)	0.73
ASA <sup>4</sup> score - no. (%)			
1	3 (4.8)	12 (10.1)	0.21
2	56 (88.9)	98 (82.4)	0.29
3	4 (6.3)	9 (7.5)	1
Underlying disorder — no. (%)			
Diabetes mellitus	0 (0)	8 (6.7)	-
Smoking	8 (12.7)	7 (5.9)	0.15
Alcoholism	0 (0)	1 (0.8)	-
Obesity	3 (4.8)	4 (3.4)	0.7
Corticosteroids therapy	0 (0)	1 (0.8)	-
Surgical management — no. (%)			
1 day	47 (74.6)	68 (57.1)	<b>0.02</b>
2 days	16 (25.4)	51 (42.9)	<b>0.02</b>
LFP <sup>5</sup> recordings — no. (%)	15 (23.8)	4 (3.4)	<b>&lt;0.01</b>
Number of electrode per patient — no. (%)			
One (unilateral)	17 (27)	35 (29.4)	0.73
Two (bilateral)	46 (73)	84 (70.6)	0.73
Number of IPG <sup>6</sup> per patient and position — no. (%)			
One (unilateral)	59 (93.7)	60 (50.4)	<b>&lt;0.01</b>
Two (bilateral)	4 (6.3)	59 (49.6)	<b>&lt;0.01</b>
Subclavicular	59 (93.7)	117 (98.3)	0.18
Abdominal	4 (6.3)	2 (1.7)	0.18
Mean ( $\pm$ SD) duration of the surgical phases – min <sup>7</sup>			
Total procedure	241.7 $\pm$ 80.4	295 $\pm$ 96.5	<b>&lt;0.01</b>
1 electrode implanted	110.6 $\pm$ 29.6	153.2 $\pm$ 64.8	<b>0.01</b>
2 electrodes implanted	223.3 $\pm$ 51.2	263 $\pm$ 56.9	<b>&lt;0.01</b>
1 IPG implanted	46.2 $\pm$ 15.5	44 $\pm$ 12.1	0.39
2 IPG implanted	87.5 $\pm$ 19.4	87.3 $\pm$ 24.4	0.98

<sup>1</sup>SD, standard deviation; <sup>2</sup>No., number; <sup>3</sup>OCD, obsessive compulsive disorder; <sup>4</sup>ASA, American Society of Anesthesiology; <sup>5</sup>LFP, local field potentials; <sup>6</sup>IPG, internal pulse generator; <sup>7</sup>min, minutes.