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Deep Brain Stimulation for Parkinson's Disease: What Is the Role of the Anesthesiologist?

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Stem Case and Key Questions Content

A 66-year-old, 73 Kg man presents for bilateral subthalamic nucleus (STN) deep brain stimulator (DBS) implantation. You are scheduled to provide anesthesia care for this procedure. The patient's past medical history is remarkable for longstanding Parkinson's disease (PD) manifested by severe resting tremor, lower extremity rigidity, and dyskinesia. Fourteen years ago, when initially diagnosed, he was started on Sinemet (levodopa/carbidopa) which helped to stabilize his symptoms for several years. However, during the past year, his symptoms worsened and side effects of L-dopa, in form of dyskinesia, motor fluctuations, and nausea were noted.

His other medical problems include diet controlled diabetes and hypertension treated with hydrochlorothiazide.

1. What sort of procedure is DBS for PD? Who are the candidates for this procedure? What are the surgical steps? How does it work? How effective is DBS?
2. How would you assess this patient preoperatively?
3. Would you stop the anti -Parkinson medication before the surgery?
4. What is the influence of different anesthetic drugs on microelectrode recording (MER)?
5. What are the anesthetic goals for this case? Is there a routine technique? Is general anesthesia precluded? If the patient becomes restless during the testing, what are your options to alleviate his discomfort, without interfering with the procedure itself?

On the day of surgery, in the MRI suite, a stereotactic head frame is placed under local anesthesia. After the imaging study is done, the patient is brought to the operating room, where the care is taken over by you, the anesthesiologist.

6. How would you like to monitor this patient?

The head frame is attached to the operating room table, and the patient is placed in the supine beach-chair position. All pressure points are padded, and patient comfort confirmed.
The vital signs are: heart rate 90 bpm; blood pressure 175/84 mmHg; SpO2 98% on 3L/min oxygen administered via nasal prongs; respiratory rate 14/min, and end-tidal CO2 30 mmHg.

7. Is this blood pressure acceptable to proceed? What are your concerns and what treatment options would you consider?

While prepped and draped, the patient complains of claustrophobia and anxiety, and requests sedation. You start the sedation regimen as selected during the PBLD session.

The surgery commences. Local anesthetic is infiltrated for burr hole access in the frontal bone. The patient tolerates well the left burr-hole access but soon after the right burr-hole is drilled, the patient coughs and becomes agitated. The O2 saturation decreases to 88% and respiratory rate increases to 30/min. Because coughing has dislodged the end-tidal CO2 monitor from the nasal prong, reading is unavailable. Otherwise the patient seems conscious, with stable hemodynamics, and unchanged ECG. However the cough continues and the O2 saturation drops to 78%. While you are frantically trying to improve the oxygenation and reattach the CO2 monitor, the surgeon starts to infuse saline into the burr-hole.

8. So, what's happening? Is the surgeon's action justified? Explain.
Now the sedation is discontinued to allow patient's cooperation during neuronal microelectrode recording (MER). During the manipulation of the electrode, the patient becomes disoriented, and within seconds unresponsive to verbal stimuli. Then, he develops generalized tonic-clonic seizures followed by loss of consciousness and respiratory arrest.
9. How would you manage this situation? If the airway needs to be secured, how will you accomplish it?
The patient recovers with no neurological deficit, and the procedure continues. After 6 hours when the final DBS electrode is tested, the patient develops decreased level of consciousness, dysarthria and facial droop.
10. How do you explain the neurological deterioration in this patient? Is there any way to prevent this complication?
The patient slowly recovers apparently with no gross neurologic sequelae.
Once the MER has been completed, the surgeon informs you that after this challenging case he would like to insert the generator under general anesthesia (GA) sometime next week.
11. About 1-year following DBS implantation, the patient returns for an Open Prostatectomy under GA. What precautions, if any should be taken to keep the patient and his DBS safe during the surgery?

Model Discussion Content

Parkinson's disease- pathology and management options

Parkinson's disease is the most common movement disorder, affecting approximately 1.5-3% of the adult population with an annual incidence of 20/100,000. It has been estimated that there is a cumulative lifetime risk of 1 in 40 for developing PD [1]. Although the exact etiology of the disease is unknown, it was hypothesized that progressive neurodegeneration is induced by genetic, environmental, neurotoxic, or infectious factors contributing to the loss of dopaminergic neurons in the substantia nigra. The decrease in dopaminergic (inhibitory) activity allows a relative increase in cholinergic (excitatory) activity and may account for some of the symptoms, such as rigidity, tremor, brady or akinesia [2]. Medical treatment is directed primarily toward correcting the dopamine-acetylcholine imbalance and restoring dopamine levels in the basal ganglia by the administration of levodopa and other drugs. However, the side effects of these drugs are multiple and include nausea, hypotension, cardiac arrhythmias, and movement disorders. Dyskinesia is the most disabling feature and a limiting factor in the use of levodopa therapy. Stereotactic surgical interventions such as pallidotomy, thalamotomy, and recently deep brain stimulation (DBS) represent new options for patients with intractable symptoms or for those who developed medication related side effects. Placement of a neurostimulator (DBS) in the subthalamic nucleus (STN) or globus pallidus is the most common and least invasive of the neurosurgical procedures. Electrical stimulation of these nuclei blocks the abnormal neuronal

activity in the basal ganglia and ameliorates the symptoms of PD. A recent meta-analysis of the available literature, which included data from 34 studies/924 patients, showed that the long-term improvement with DBS could be dramatic. Average reduction in dyskinesia was 70%; average reduction in L-dopa requirement was 60%; improvement in quality of life was 34.5%. [3]. DBS insertion is a complex process, and involves multiple steps: the first step into the procedure requires attachment of a stereotactic frame to the skull and CT/MRI-guided imaging for precise localization of the brain structures responsible for the symptoms. The second step takes place in the operating room, when microelectrodes are implanted through small burr holes into the area previously identified by radio imaging. Intraoperative microelectrode recording (MER) and macro- stimulation are used to determine the best possible location for the DBS electrode (usually the STN). The testing involves highly sophisticated neurophysiologic recording and neurological examination during the recording. The goal is optimal reduction in symptoms such as improvement in tremor, bradykinesia, and rigidity and avoidance of adverse effects such as dysarthria, eye deviation, and tonic contractions. Then, during the final step, the pulse generator is implanted in the subclavicular region and connected to the DBS wires subcutaneously. Postoperatively, the optimal stimulation settings and antiparkinsonian medication are progressively adjusted according to the patient's response.

Preoperative considerations
Preoperative evaluation is very important and should provide information on disease severity, associated disorders, drug therapy and complications of therapy [4]. The main area of concern for the anesthesiologist is the respiratory and cardiovascular system. Dysphagia and upper airway dysfunction is common in patients with PD increasing the risk of perioperative aspiration and airway obstruction. If aspiration prophylaxis is considered, avoid metoclopramide, a dopamine antagonist that may induce itself Parkinson’s disease [2, 5]. Autonomic dysfunction and levodopa therapy may lead to orthostatic hypotension. If vasopressors are needed, direct acting agents, such as phenylephrine should be considered [5]. Finally, assessment of patient’s ability to cooperate in whom MAC is planned and thorough explanation about each step of the surgery are absolutely necessary. The only absolute contraindication to this technique is an uncooperative patient. Patients with obstructive sleep apnea, the very obese, and those with uncontrolled HTN all pose potential problems and increase the risk of the surgery. Anti-parkinson medications should be withheld 12-24 hours before surgery. The goal is to induce an “off-period” and arouse the “target” symptoms (tremor, rigidity), and then intraoperatively observe the direct effect of stimulation, e.g. improvement in motor symptoms. It is worth noting that cessation of L-dopa medication may result in rebound hypertension and arrhythmias; thus administration of antihypertensive medication is highly recommended.

Anesthetic considerations
The impact of different anesthetic drugs on MER recording is not well known. Commonly used anesthetic drugs, especially those with GABA-ergic activity, may modify neuronal activity of the basal ganglia from which micro recordings are made, and thus interfere with the localization of STN. In addition, drugs such as barbiturates, BDZ’s, and opioids, have been shown to suppress tremor and involuntary movement typical of PD, imposing difficulties in interpreting and observing changes in symptoms during the stimulation period [2, 6]. There are reports of muscle rigidity and dystonia after the administration of fentanyl and alfentanil [2]. Controversy exists over the role of propofol in ameliorating or exacerbating tremor and abnormal movements. The occurrence of severe dyskinesia during DBS placement was recently reported by Deogaonkar et al. and attributed to low-dose propofol infusion [7]. They speculated that propofol through its

interaction with the GABA neurotransmitter system, may potentiate GABA-ergic responses in the nucleus pallidus, area that seems to be responsible for causing dyskinesia in PD patients. In addition, several other drugs used in anesthesia practice are know to interact adversely with PD or potentiate its symptoms: in patients taking selegiline, a MAO inhibitor, administration of meperidine has been associated with fatal reactions, including hyperthermia, rigidity, coma, and death. Drugs with anti-dopaminergic activity (droperidol, metoclopramide, etc) may induce or enhance extrapyramidal symptoms, so their use is absolutely contraindicated [2, 5].
Anesthetic options for DBS are rather limited and subordinated to the main goal of the procedure: to have an awake, cooperative patient during intracranial electrode placement. The reasons are obvious: maximal preservation of neuronal firing during MER, ability to monitor stimulation-induced improvement in symptoms, such as rigidity and tremor, or assess unwarranted neurologic/psychological side effects. Ideally, local anesthesia with minimal or no sedation should be used for the entire procedure, apart from pulse generator placement. However, the procedure tends to be lengthy, positioning in head frame uncomfortable, off-drug induced exacerbation in motor symptoms distressing, and creation of burr-hole painful. All of these may compromise patients' tolerance and jeopardize the success of the procedure. Thus, a suitable anesthetic plan, previously discussed with the surgeon and patient, is essential. In some institutions, sedation will be allowed for the "silent" part of surgery which includes stereotactic frame application and burr-holing. As this represents the shortest part of the procedure, is imperative to choose a drug with short context-sensitive half time and favorable emergence characteristics. In this context, propofol would be particularly appealing, however as described previously, its unpredictable effects on target neuronal activity and on PD motor symptoms are concerning. Propofol in combination with remifentanil is frequently administered for awake craniotomies with asleep-awake-asleep technique. Except for a short communication by Gray et al, there are no reports about its use for DBS implantation [8]. To avoid muscle rigidity, a well-documented effect of opioids in PD, the authors used very low infusion rates of 0.05-0.15 mcg/kg/min with good results. Currently, dexmedetomidine (dex) is emerging as a promising sedative agent in the DBS setting [9]. Dex is a clinically versatile α2-receptor agonist that provides cooperative sedation, anxiolysis and analgesia without respiratory suppression. It has been proven particularly useful in awake craniotomies allowing successful mapping of the eloquent brain areas and neurophysiologic testing [5]. Meanwhile, the experience with this drug for DBS is limited, and based only on case reports. Nevertheless, a recent report suggests that patient cooperation, PD symptoms, and the quality of MER were preserved by IV sedation with dex during DBS implant in 11 cases [9]. In the case report by Deogaonkar, propofol induced dyskinesias during DBS have been effectively controlled by dex. Dosing of dex varies, some protocols start with a bolus of 0.5 to 1 mcg/kg and then an infusion of 0.2 to 0.7 mcg/kg/hour. However, data from new studies suggest that low doses of 0.1- 0. 4 mcg/kg/hour are advisable, as higher doses may interfere with MER [10]. In conclusion, in the absence of randomized controlled studies relating to the "best" sedative/anesthetic for DBS placement, we have to rely on personal experience and surgeon's preference in providing good results. Regardless of the drug chosen, the level of sedation is of crucial importance, since oversedation results in an unresponsive patient and respiratory depression. As the patient's head is fixed via the frame to the operating table, airway maintenance may be extremely challenging. Communication with the surgeon and rapid removal of the stereotactic frame might be lifesaving in this scenery. General anesthesia (GA) is rarely used routinely and reserved for patients who cannot tolerate the surgery being awake or lightly sedated. In fact, the adverse effects of GA on PD patients are well documented in the anesthesia literature. These side effects are not benign and consist of respiratory compromise including airway obstruction and aspiration, hemodynamic impairment,

and exacerbation of neurological symptoms. As well, it is believed that optimal targeting of the SN under GA may be compromised if not impossible. In a recently published study, Maltete et al [11] found that targeting of the SN was less accurate in 15 patients under GA compared with the control group under LA. Although there have been reports of satisfactory MER for DBS under GA, these results apply only to a very small number of patients [12]. Further, large-scale studies will be needed in order to define the role of GA for DBS cases.

At our institution, patients are brought to the operating room after having the stereotactic frame applied in the MRI suite with local anesthesia or minimal sedation with midazolam. On arrival to the operating room, ASA standard monitors are placed. Because anti-Parkinson medications have been withheld, patients may exhibit exaggerated tremors that can interfere with monitoring. Sometimes the non-invasive BP cuff may be placed on the leg (fewer tremors). In addition to routine monitors, some anesthesiologists (the author) will use an arterial line for accurate monitoring of BP and blood sampling.

Intraoperative complications

• Hypertension

High BP (systolic > 140 mmHg) may pose a real danger and should be addressed immediately, as HTN has been associated with increased risk of intracerebral hemorrhage (ICH) [13, 14, 15]. The management will depend on the precipitating factors, including: anxiety→ administer sedative/analgesic as planned; cessation of antihypertensive/ anti-Parkinson medication→ any antihypertensive drug IV by preference and careful titration except central-acting β-blockers, which suppress tremor activity in target neurons. It is prudent not to start surgery until BP is under control.

• Venous air embolism

In each procedure when the surgical site is above the heart, air can entrain into the circulation and occlude the blood flow. Venous air embolism is a rare but well documented complication of awake craniotomies, as well DBS surgeries [15,16,17]. Risk factors include: semi sitting or sitting position, relative hypovolemia, and open dural veins. In addition, is important to remember that spontaneous breathing generates a negative intrathoracic pressure and thus promotes the passage of air into the venous circulation. In awake and spontaneously breathing patients the presenting symptoms of VAE are: coughing, tachypneea/dyspneea, chest pain, desaturation, and if monitored, decrease in end-tidal CO2. The pathogenesis of cough is not quite elucidated; reflex bronchoconstriction due to cytokine release and complement activation seems to play a major role. The treatment is aimed to reduce further air entry by flooding the surgical field with saline, sealing the burr-holes with bon vax, tilting table to the left, and placing the patient in steep Trendelenburg position. Oxygenation should be maintained, and if necessary blood pressure supported by administration of fluids and vasopressors. Early diagnosis of VAE is essential for successful treatment. For this reason, some authors recommend the use of precordial Doppler as a sensitive, non-invasive monitoring device for early detection of VAE during DBS surgery. Since clinically significant VAE has never been reported, most institutions including ours do not routinely place precordial Doppler for these cases. Nevertheless, the occurrence of sudden and continuous cough or tachypnea in a patient undergoing DBS placement could indicate the possibility of evolving VAE.

• Seizure

Among the neurologic complications of the DBS procedures, seizures are frequently observed. In a recent retrospective review of 178 patients scheduled for DBS implantation under monitored anesthesia care, seizures occurred in 8 patients (4.5%), mostly during stimulation

and testing [14]. Five patients developed focal seizures and did not require treatment; 3 patients had a tonic-clonic form that responded to small doses of midazolam and/ or propofol IV. No one of the patients needed general anesthesia or airway control with intubation. Khatib et al [15] in their review of perioperative events during DBS placement (258 procedures) concluded that the most common neurologic complications (3.6%) were ICH and seizure. As we can see, seizures are often focal and self-limited; if treatment is needed use IV midazolam, thiopental or propofol in small doses and titrated to effect. However, grand mal seizures should be managed aggressively to prevent musculoskeletal injury, hypoxemia, and aspiration of gastrointestinal contents. While the surgeon applies iced saline irrigation into the burr hole, the anesthesiologist role is to maintain an open airway, adequate oxygenation, and administer drugs to terminate the seizure.

• Airway management

Airway management may be extremely challenging in patients with the head restrained into a frame! Although laryngeal mask is always an option, in the case of intractable seizures one should be prepared to induce general anesthesia and endotracheal intubation. Prior to surgery, the anesthesiologist should have clear knowledge on how to remove the frame rapidly in an urgent situation. Alternatively, a fiberoptic bronchoscope or blind nasal intubation might be helpful in securing the airway . Intracerebral hemorrhage (ICH) is the most feared perioperative complication of DBS surgery. It is estimated to occur in 1- 4% of patients and lead to permanent neurological deficit in 0.6-0.7%.

• Intracerebral hemorrhage (ICH)

Systemic HTN is a well-recognized risk factor for the development of ICH during stereotactic surgery. A recent retrospective study in 259 patients (DBS was performed in 167 procedures) found that HTN was the most significant risk factor to ICH (incidence 1.2%) and hypertensive patients suffered hemorrhagic complications eight times more frequently [18]. In another large study, Gorgulho et al [19] reported five cases of hemorrhage (2.02%) during DBS placement. The mean maximum intraoperative BP was 157/83 in hypertensive patients who experienced hemorrhage and 158/85 in nonhypertensive patients who experienced hemorrhage. This data suggests that chronic as well as acute intraoperative HTN may have the same impact on ICH; for that reason intensive monitoring and aggressive control of BP should be of major concern for the neuroanesthetist. Although not based on randomized controlled studies, current recommendations are to keep MAP at, or preferably, somewhat below normal for that patient. According to the data from Gorgulho's article, at our institution we opted to maintain a SBP below 140 mmHg. To control systemic hypertension we prefer to use a continuous infusion of nicardipine or esmolol rather than bolus medications. Although controversial, some institutions use dex to achieve hemodynamic control and reduce the need for antihypertensive medications. Any intraoperative sudden change in the patients' level of consciousness and/or onset of a new neurological deficit should alert to the possibility of ICH. If the event is severe, acute resuscitation of the patient such as removing the stereotactic frame and securing the airway may be needed. Also, the patient may need to be urgently taken to the CT or MRI unit for scanning and back to the operating room for emergent craniotomy.

Post-operative management of patients with DBS

The DBS neurostimulator can be affected by or adversely affect medical devices such as cardiac pacemakers, cardioverter/defibrillators (ICD), electrocautery, ECG, as well as interfere with procedures like MRI, lithotripsy, or electroconvulsive therapy (ECT). [20]. Electrocautery used to achieve surgical hemostasis during Prostatectomy or other surgical procedures may cause thermal injury to the brain tissue or damage the device itself. The ECG may show

artifacts and make rhythm interpretations difficult. These problems led our department to develop general guidelines (based on literature review and Medtronic recommendations) for the safe intraoperative management of patients with DBS:
1) Have patient bring their remote controller for the DBS device which allows him/her or the neurologist to turn the device on/off
2) Turn the DBS device off just after induction and before electrocautery is used, (when the device is on it may interfere with the ECG).
3) Use bipolar cautery if possible, at the lowest effective power settings
4) If not possible to use bipolar cautery, then place the grounding pad of the unipolar cautery as far away as possible from the neurostimulator (typically found on the anterior chest wall) and leads. Make sure that the DBS and leads are not placed between the grounding pad and the surgical site.
5) Once electrocautery use has ceased, the device may be turned back on. Failure to turn the DBS back on may result in return of severe Parkinson's symptoms such as hypoventilation, brady/akinesia, prolonged emergence, etc.

For further information regarding the management of patients with DBS, please refer to the DBS manufacturer Medtronic website at: www.medtronic.com/patients/parkinsons-disease/therapy/index.htm<br Summary comment: all of these complications underscore the fact that, although this procedure requires little to no anesthesia, there is a need for the presence of a vigilant anesthesiologist to deal with the medical emergencies and positively influence patients' outcome.

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