

Anesthetic Management of Parkinson's Patients Undergoing Deep Brain Stimulation

Research Article

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Abstract

Surgical treatment for Parkinson's disease has evolved from permanent removal of parts of the brain to minimally invasive surgical techniques such as deep brain stimulation. Ample evidence supports the efficacy and safety of DBS giving rise to its use in other clinical settings such as benign tremors, dystonia, epilepsy and other neuropsychiatric disorders. Anesthetic and surgical techniques for DBS may vary among institutions and physicians. Indirect surgical technique such as frame-based imaging, is used to target brain structures even though frameless stereotactic techniques (direct technique) involving magnetic resonance imaging (MRI) have been described. Local, general anesthesia, and combined anesthetic techniques have been used. Although local anesthesia seems to offer better intraoperative evaluation of the neurological responses, it may be associated with intraoperative complications such as anxiety, hypertension and hemorrhage. General anesthesia is a common practice for the insertion of generator and tunneling of leads. No standardized guidelines for anesthesia management of Parkinson's patient undergoing DBS have been described and clinical findings regarding ideal anesthetic technique are controversial.

Keywords: Deep Brain Stimulation; Parkinson's Disease; Microelectrode Recordings; Neurodegenerative Disorders; General Anesthesia; Local Anesthesia.

Introduction

Deep Brain Stimulation (DBS), the procedure of placing stimulating electrodes into targeted brain structures, was first introduced in 1987 [1, 2]. There are several theories explaining the efficacy of DBS [3-6], but ample evidence exists on the safety and efficacy of DBS in Parkinson's disease (PD), leading to expanded indications for DBS including benign tremors, dystonia, epilepsy and other neuropsychiatric disorders [7, 8]. Prior to the introduction of DBS, surgical treatment for PD traditionally involved permanent removal of parts of the brain – thalamotomy, pallidotomy, and cingulotomy [9]. Side effects of lesions in deep brain structures include, but are not limited to, paresis, confusion, hypersalivation, dysarthria, and gait disturbances [10-11]. DBS is now used in place of surgical lesioning, and deep brain targets vary depending on the underlying disorder [7-8]. The deep brain targets in the treatment of PD include the ventralis intermedius

nucleus, the subthalamic nucleus, and the globus pallidus [8].

DBS is a multi-step procedure that incorporates intracranial electrodes inserted surgically, a programmable pulse generator implanted under the clavicle or in the abdomen, and an extension cable that passes subcutaneously connecting the two [3, 12-16]. There is currently no consensus on surgical or anesthetic approach to DBS and techniques vary between institutions and physicians. Generally, local analgesia or a regional block is used to place patients securely in a headframe. Frame-based imaging is used to target brain structures and plan coordinates of surgery. A burr hole is made in the skull for electrode placement, usually under local anesthesia or conscious sedation. Microelectrode recordings (MER) guide the placement of electrodes; additionally, macrostimulation is used to ensure the area stimulated helps improve the movement disorder with minimal side effects. Macrostimulation involves a series of physical manipulation and

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mental tasks performed with the patient awake to assess the degree of response to the DBS. Their speech pattern, musculoskeletal range of motion, and the occurrence of paresthesia, occur during this phase of the procedure. This testing influences the permanent placement of the electrodes. The remaining steps in DBS involve internalization of leads and implantation of the impulse generator into the chest or abdomen [4, 9, 12-16].

The order in which surgical steps occur and the length of time between them may vary. Most commonly, electrode placement occurs first, and several days to weeks later, the impulse generator is implanted. Anesthetic techniques include local anesthesia, conscious sedation, and general anesthesia [3]. The complexity of DBS makes anesthetic considerations very important. Anesthetic considerations include, but are not limited to, the need for patient cooperation, optimization of patient comfort, difficulty of airway access when the patient is positioned in the headframe and away from the anesthesia care provider, facilitation of intraoperative neuromonitoring, and the potential interference of anesthesia with MERs [3, 4, 9]. To date, no guidelines to standardize DBS anesthesia protocols have been developed. This review intends to categorize the variety of anesthetic techniques currently present in the literature in the hopes of identifying gaps where future studies can be designed to create a standardized and optimized DBS anesthesia protocol.

Methods

An extended literature search was conducted to explore anesthetic management and outcomes in patients undergoing DBS for Parkinson's disease. Search keywords included "deep brain stimulation," "anesthesia," "neurodegenerative disorders," and "Parkinson's." Focus was placed on recent literature published in the last five years.

Discussion

Patients undergoing DBS for Parkinson's disease may receive anesthetic care in the form of: local anesthesia, general anesthesia, or monitored anesthesia care (MAC). The following sections will discuss these techniques and their outcomes, including Unified Parkinson's Disease Rating Scale part III (UPDRS III) improvement, and anesthetic-related complications such as hemodynamic instability, perioperative cognitive changes, and respiratory depression.

Local Anesthesia

A purely local anesthesia technique with long acting agents such as bupivacaine may be administered for intracranial insertion of the leads. This technique avoids complications associated with moderate to deep sedation, such as transient mental changes, hemodynamic liability, nausea, vomiting, or restlessness. A partial scalp nerve blockade, usually including the supraorbital and greater occipital nerves, is used most often as an alternative to widespread subcutaneous local infiltration. In fact, Watson and Leslie concluded that nerve blocks were less painful compared to the subcutaneous infiltration of local anesthesia, but neither technique was superior in preventing pain associated with pin placement [17]. Similarly, Gazoni et al., found that the use of ropivacaine for skull blockade prior to pin placement did not

significantly improve patient pain scores in patients receiving maintenance anesthesia with remifentanyl [18]. It should be noted, however, that cardiotoxicity or neurotoxicity might result from high levels of local anesthetics [19, 20].

Among the benefits of using local anesthesia are the lack of pharmacological interference with microelectrode recordings (MERs) or macrostimulation testing, as well as shorter anesthesia and surgical time [21, 22]. MERs help guide the placement of electrodes, so their accuracy is critical for the success of procedures and interference may occur with intravenous anesthetics, such as propofol [22]. In addition to MERs, macrostimulation testing is very important. Since the goal of DBS is to treat the symptoms of Parkinson's, it is helpful to see intraoperatively if stimulation of the targeted brain region alters the characteristic tremors, rigidity, and bradykinesia of PD. Some medications can interfere with these symptoms, thus interfering with macrostimulation testing. For example, remifentanyl is known to cause rigidity [23]. In a recent retrospective study, Lange et al. found that length of surgery was significantly increased ($p < 0.001$) in a group receiving propofol and remifentanyl anesthesia (330 minutes) compared to a group receiving local anesthesia with psychological guidance (245 minutes) [21].

Although local anesthetics provide good outcomes due to excellent MER quality, it should be noted that local anesthesia is usually only practical to the burr-hole craniotomy and electrode insertion stage of the DBS procedure. A general anesthetic is common practice for insertion of generator and tunneling of leads.

In a randomized prospective study by Sassi et al., they looked at the impact of sedation with dexmedetomidine. There was a control group ($n=10$) which did not receive any dexmedetomidine sedation. Two of the controls (20%) developed agitation and required abortion of the procedure. After discovering the apparent ability of dexmedetomidine to ease anxiety, Sassi et al. terminated the randomization protocol after enrolling 23 patients [24].

Anxiety is not only a concern for the patient's overall comfort, but may also induce a severe hypertensive state with the potential risk of intracranial hemorrhage. Yamada et al. noted a case in which anxiety-induced hypertension developed under local anesthesia and the surgery had to be completed under general anesthesia [25]. Furthermore, Glossop and Dobbs were the first to report two cases of coronary artery vasospasm (one of which was a Parkinson's patient) in DBS under local anesthesia [26]. It is of interest that details regarding the specifics of local anesthetic technique and the impact of awake surgery on patient anxiety were not included.

The development of perioperative hypertension is a particular concern in Parkinson's patients who exhibit hemodynamic instability due to their disease [3, 27, 28].

Some of the reviewed studies using local anesthesia reported hemorrhages, and although unspecified, it is possible that anxiety may have played some role in that outcome. For example, Deuschl et al., found one case (0.64%) of perioperative cerebral hematoma and two cases (1.3%) of asymptomatic mild intracerebral hematoma [29]. Limousin et al., also reported one case (5%) of

intracerebral hematoma [30]. These values do not differ greatly from reported values in large retrospective reviews of DBS complications. Fenoy et al., reviewed 1356 DBS procedures and found an intraoperative complication rate of 3.4% asymptomatic intraventricular hemorrhage (IVH), 1.1% symptomatic intracerebral hemorrhage (ICH), and 0.5% asymptomatic ICH [31]. Furthermore, Khatib et al., found a 2.8% intracranial hemorrhage rate in a retrospective study of 258 DBS procedures at the Cleveland Clinic using different anesthetic techniques [12]. Interestingly, an age greater than 64 has been reported as an independent risk factor for intracranial hemorrhage during DBS [12, 32].

Whether patients older than 64 should be excluded or not from receiving local anesthesia due to risk of perioperative hemorrhage, might be investigated in order to develop guidelines for DBS anesthetic management.

General Anesthesia

Several studies have investigated PD patient outcomes in DBS under general anesthesia. Patients often undergo general anesthesia when they are unable to tolerate awake surgery due to anxiety, chronic pain, coughing, or severe movement disorders [3, 33]. General anesthesia is also commonly used in pediatric DBS for dystonia [34, 35]. Therefore, the use of general anesthesia extends the inclusion criteria for patients receiving DBS.

There are some potential advantages of general anesthesia use in DBS patients. This type of technique allows the anesthesiologist to be in full control of the patient's physiology, including the respiratory system. Endotracheal intubation ensures a secure airway, which is a significant concern for the anesthesiologist because the stereotactic headframe limits access to the airway in emergency situations, such as unplanned conversions to general anesthesia. General anesthesia may also lower surgical and anesthetic time compared to conscious sedation. After reviewing craniotomy cases with an awake anesthetic protocol using dexmedetomidine, Dreier et al., found that general anesthesia significantly shortened surgery time when compared to the conscious sedation technique [36].

Some major anesthetic concerns regarding general anesthesia management, including the effect on MER and unwanted anesthetic side effects, should be considered. Several studies have shown altered neurophysiology with anesthetics, including unidentifiable widening of the background noise and decreased neuronal spiking [22, 28, 37]. In addition, macrostimulation testing cannot be performed and intraoperative complications may be not be easily detected. For example, venous air embolism is often identified when an awake patient begins to cough vigorously after burr-hole placement [39].

Conversely, there is literature to support the theory that a general anesthetic does not affect the ability to effectively elicit MEPs and result in a successful DBS placement [28, 40, 42]. Specifically, desflurane has been shown to provide adequate intraoperative MER [42-44]. Tsai et al., successfully identified neuronal spiking in the dorsolateral subthalamic nucleus using desflurane as a general anesthetic alongside median nerve stimulation [42]. Furthermore, Lettieri et al., found no significant difference in neurophysiological data (mean frequency, burst index, pause

index, and detected spike number) between local anesthesia and a general anesthesia protocol with ketamine and remifentanyl [41].

There are reported complications of intraoperative seizures and perioperative cognitive changes believed to be related to the use of general anesthesia for DBS placement. Herrick, et al., reported that 41% of 17 patients receiving droperidol and fentanyl experienced intraoperative seizures [45]. Another study has reported a 1.2% rate of intraoperative seizures using general anesthesia with propofol and remifentanyl [28]. Interestingly, this side effect was not mentioned in any of the reviewed literature regarding local anesthesia use. In addition, rates of 3.7% and 10% of transient post-operative confusion were encountered in patients undergoing general anesthesia [40, 44]. Hertel et al., associated general anesthesia with transient mental changes, including cognitive decline and disorientation in 22.2% of patients [38].

Lange, et al., found that deep sedation is linked to a significantly increased risk of intraoperative delirium (IOD). In this study, patients receiving propofol and remifentanyl (group I) as part of the asleep-awake-asleep (AAA) technique experience IOD at a rate of 7.9%, whereas patients receiving psychological guidance with local anesthetics (group II) did not. Overall, their data supports the hypothesis that opioid use increases the risk of IOD; however, a large randomized prospective study is necessary to confirm these results [21]. Other adverse events related to general anesthesia include post-operative nausea and vomiting. According to a 2013 study by Hocking et al., nausea and vomiting are a major concern for patients and thus, it is important to consider these side effects when determining the best management for DBS [46].

Thus, general anesthesia may be compatible with MER, but larger randomized controlled studies are needed to develop specific guidelines. It should be noted that image-guided electrode placement with computed tomography or magnetic imaging may also be used as an alternative to MER, but MER will likely prevail as an opportunity to learn more about the neurophysiology behind deep brain stimulation [47, 48].

Monitored Anesthesia Care (MAC)

MAC appears to be a popular management method, consisting of patient sedation without total annihilation of intraoperative MERs. Propofol and dexmedetomidine are the two most popular medications used in this technique. MAC using dexmedetomidine and opioids is the recommended management for DBS patients, although this recommendation is not specific to Parkinson's patients [49].

Compared to general anesthesia, MAC produces less MERs interference. Propofol is often stopped prior to intraoperative testing due to concerns of decreased interaction during the macro testing phase. Propofol has an advantage because of its relatively short half-life and it takes approximately 9 minutes for recordings to return to pre-propofol levels [22].

In contrast, dexmedetomidine sedation has been successfully continued throughout intraoperative testing, easing patient anxiety alongside quality recordings [34, 50]. Dexmedetomidine, in particular, provides some benefits when used in awake neurosurgery, such as hemodynamic stability, control of violent

dyskinesias, and reduced post-operative pain [24, 51, 52]. Benzodiazepines should be avoided entirely, as they interfere with MERs [49].

The MAC technique appears advantageous but there are associated potential risks involving poor airway control, respiratory depression or obstructive sleep apnea, requiring emergent intubation. This is of particular concern in the Parkinson's population, which is significantly affected by obstructive apnea and pulmonary disease [3, 53]. Unfortunately, the stereotactic headframe makes airway access incredibly difficult. In such emergent situations, the patient may have to be taken out of the stereotactic headframe, therefore interrupting the flow of the surgery.

Herrick et al., found that 25% of awake craniotomy patients receiving propofol developed respiratory depression [45]. Fábregas et al., concluded that a plasmatic propofol concentration of 0.35µg/ml reached during stereotactic surgery for Parkinson's disease patients minimized the risk of respiratory depression and provided adequate sedation. This concentration was determined based on a Target Controlled Infusion (TCI) model [54].

Although Dreier et al., and Jani et al., reported no respiratory complications using dexmedetomidine [36, 50], Rozet et al., found two cases (9%) of respiratory complications generated by a dexmedetomidine dose higher than 0.6mcg/kg/h in Parkinson's patients [55].

Comparing the Different Management Types: Future Directions

A few studies have directly compared the use of local anesthesia and general anesthesia in managing PD patients undergoing DBS. In a comparative cohort study, Chen et al., observed 52 PD patients receiving bilateral STN DBS, 33 of who received general anesthesia. The remaining 19 patients received local anesthesia. UPDRS III post-operative improvement was 46.9% and 49.6% for general and local anesthesia, respectively. Rates of sialorrhea (24.24%) and dysarthria (18.18%) in the general anesthesia group significantly differed from the local anesthesia group (5% sialorrhea and 0% dysarthria). The authors concluded that overall anesthetic management did not significantly affect UPDRS III outcomes, but use of desflurane as a general anesthetic contributed to more significant cognitive decline, sialorrhea, and dysarthria [43].

In 2007, Yamada et al., reviewed 25 Japanese PD patients receiving DBS under general (n=15) and local (n=10) anesthesia. UPDRS III scores improved 72.7% and 84.50% using an inhalational general anesthetic and local anesthetic, respectively. Although the local anesthetic shows a greater percentage of improvement, Yamada et al., concluded that the difference between local and general anesthetic management was not significant [25]. Lefaucher et al., similarly reported no statistically significant difference in patient outcomes when general anesthesia was used compared to local anesthesia [56].

The reviewed literature supports similar UPDRS outcomes regardless of anesthetic management (local versus general). To our knowledge, no randomized control trial has addressed DBS outcomes in patients undergoing local versus general anesthesia. Recently, Van Horne et al., proposed a staging reversal of DBS,

traditionally done in the following sequence: burr-hole drilling and electrode placement followed by pulse generator placement under general anesthesia. Van Horne et al. reversed the staging order of DBS in over 140 patients with movement disorders, including Parkinson's. The authors noted that placing the pulse generator and drilling the burr holes under general anesthesia reduced patient anxiety due to lack of awareness of the drilling process. The second stage in this reversed model includes microelectrode recording and macrostimulation testing under local anesthesia [57]. Further investigation of this technique could show promise in the future of DBS staging and anesthetic management.

DBS and MRI

During the last decade, magnetic resonance imaging (MRI) has been used to identify the subthalamic nucleus (STN) for electrodes implantation in DBS surgery.

Currently, indirect technique for STN targeting is well known. This technique is based on the use of stereotactic and anatomical landmarks, usually corroborating MER with intraoperative stimulation. Direct technique with MRI is becoming an interesting alternative to recognize anatomically the STN, avoiding possible errors associated with the former such as lack of precision and complications linked to the trajectory of the leads [58].

Chabardes et al., described the surgical implantation of leads using MRI guidance in 2 patients with PD. Both patients underwent DBS surgery under general anesthesia and no surgical complications were found. They emphasized the clinical improvement in the immediate post-operative period and after 1 year follow-up for patient 1 and 2, concluding that frameless stereotactic procedures with MRI guidance seemed to be more accurate than indirect procedures [58].

Cheng et al., evaluated 39 patients with PD using 1.5T MR imaging in 16 patients, and 3T MR imaging in 23 patients for leads implantation in STN. They found no difference between clinical outcomes in both groups even though 3T MRI improved resolution for direct STN targeting [59].

Financial Considerations

Standardizing the anesthetic management of DBS for Parkinson's disease may have significant financial benefits. DBS is an expensive procedure with an approximate average initial surgery cost of \$65,000 [60]. For anesthesia alone in subthalamic DBS, McClellan et al. found the mean cost to range from \$3000 - \$6000 depending on the laterality of electrode placement. The same research team identified the financial burden of the MER technique, covering over 40% of anesthesia-related expenses [61].

As DBS expands as a treatment option for Parkinson's patients due to changes in inclusion criteria or technological advances, it is critical to consider the potential financial burden on the healthcare system.

Conclusion

Currently, there are no standardized guidelines for the anesthetic management of Parkinson's patients undergoing DBS. General

anesthesia has extended the inclusion criteria for DBS, but may not be ideal due to potential MER interference and neurological complications. Local anesthesia is a cheaper option that avoids MER interference, but concerns still remain for patient comfort and anxiety-induced hypertension.

A purely local anesthesia technique remains an option that avoids MER interference, but concerns still remain for patient comfort and anxiety-induced hypertension. Additionally, a general anesthetic will remain an essential aspect to placement of the generator at some point in the staging.

MAC shows great promise for the anesthetic management of patients undergoing DBS, but airway management and possible conversion to general anesthesia must be considered by the anesthesiologist.

Further research is necessary to directly compare Parkinson's patient outcomes using these different techniques, especially since many of the reviewed studies considered a low sample size and were retrospective in their design. Future large, randomized prospective studies will decide the best anesthetic management for Parkinson's patients and lead to standardized guidelines.

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