Rubrospinal activation during asleep subthalamic nucleus deep brain stimulation: a false localizing sign. Illustrative case

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BACKGROUND Deep brain stimulation (DBS) can be a life-changing intervention for patients with Parkinson’s disease (PD), but its success is largely dependent on precise lead placement. The subthalamic nucleus (STN) is one of the most common surgical targets of DBS, but the close anatomical and physiological resemblance of the STN to the mediocaudal red nucleus renders these landmarks difficult to distinguish.

OBSERVATIONS We present an atypical case in which targeted localization of the STN resulted in symptoms pathognomonic of rubrospinal tract (RST) stimulation. A 79-year-old female with a 12-year history of right-hand resting tremor due to medically refractory PD presented for asleep bilateral STN-DBS surgery. Right STN intraoperative testing revealed left hand and elbow flexion contractures, initially suggestive of corticospinal tract activation, despite imaging studies demonstrating reasonable lead placement in the central dorsolateral STN. The lead was moved anteromedially near the medial border of the STN, but stimulation at this location revealed similar but more robust flexor hand and arm contractures, without any extraocular muscle involvement. Thus, activation of the RST was suspected.

LESSONS Isolated activation of the RST is possible during STN-DBS surgery. Its identification can help avoid false localization and suboptimal lead placement.

https://thejns.org/doi/abs/10.3171/CASE23100

KEYWORDS functional neurosurgery; Parkinson’s disease; deep brain stimulation; rubrospinal tract; subthalamic nucleus

Since its Food and Drug Administration approval in 1997, deep brain stimulation (DBS) has revolutionized the standard of care for Parkinson’s disease (PD)-related tremor in patients whose symptoms cannot be controlled adequately with medication. Among the most common surgical targets of DBS is the subthalamic nucleus (STN), with patients experiencing a 48% improvement in bradykinesia and 53% improvement in rigidity from baseline to 6 months postoperatively.1

During awake DBS surgery, intraoperative microelectrode recordings (MERs) and stimulation testing are the most reliable means to determine optimal lead placement. Stimulation-induced contralateral muscle contractions or dysarthria suggest lateral activation of the corticospinal tract (CST). Conversely, medial stimulation is associated with ipsilateral contractures of extracranial muscles innervated by cranial nerve (CN) III or autonomic changes generally associated with red nucleus (RN) activation.

Asleep DBS, as the term implies, is performed with the patient under sedation2,3 or full anesthesia.4,5 Thus, optimal lead placement is accomplished using intraoperative imaging. Macrostimulation testing after lead placement is possible during asleep DBS1 but is limited to motor responses only. Macrostimulation can induce peripheral muscle contractions suggesting CST activation or ipsilateral medial eye deviations suggestive of CN III activation.

The RN is a poorly understood, primitive structure located in the ventral midbrain. Anatomically, the RN receives input from the cerebellum and cerebral cortex. RN outputs include the rubrospinal tract (RST) and the inferior olivary nucleus. Prior studies involving STN-DBS–mediated activation of the RN during awake DBS surgery have shown autonomic changes (sweating, nausea, diplopia, malaise).6,7

The RST, when activated, causes a stereotyped flexor grasping reflex of the upper limbs, which is normally inhibited by higher order frontal brain regions. Inhibition of higher centers (by trauma or anesthesia)
can result in RST disinhibition, allowing the flexion reflex to be unimpeded. To date, isolated activation of the RST during STN-DBS has not been reported. We present a case of asleep STN-DBS that resulted in specific and isolated RST activation during macrostimulation of the most inferior contact that was localized to the inferomedial border of STN. This false localizing sign is important to recognize to prevent suboptimal lead implantation.

Illustrative Case

A 79-year-old female presented with a 12-year history of PD after initial presentation of right-hand resting tremor. Initial neurological and physical examination findings at that time were consistent with asymmetrical resting tremor, bradykinesia, and cogwheel rigidity. The Unified Parkinson's Disease Rating Scale Part III score was 46. Medication therapy with pramipexole, rasagiline, mirabegron, and carbidopa/levodopa was tried and failed. After a formal evaluation, bilateral STN-DBS was recommended (Fig. 1).

The patient underwent intubation by the anesthesia team using 1/2 minimum alveolar concentration sevoflurane and 120 mg succinylcholine 20 mg/mL. A direct targeting method was used to select initial target coordinates. The coordinates of the midcommissural point (MCP) and STN were determined utilizing intraoperative tomography merged with preoperative magnetic resonance imaging (MRI) sequencing. The target coordinates were then calculated based on the position of the STN relative to the MCP. Target coordinates were (12.1 mm lateral, 4.4 mm posterior, 4.6 mm inferior) to the MCP (Fig. 2).

Frame-based stereotaxy utilizing intraoperative tomography was merged with preoperative MRI sequences to visualize the STN for implantation. Medtronic StealthStation S8 software was used to confirm our calculations of the direct STN coordinates. The auto-merge was verified for accuracy, and manual adjustments were made intraoperatively based on calculated radial error as needed. Once the lead was implanted, intraoperative tomography confirmed its location at (12.4 mm, 3.6 mm, 4.3 mm; Fig. 3). A train of four was performed to ensure neuromuscular blockade was not active. Intraoperative bipolar stimulation was performed sequentially at contact pairings 1–4+, 2–4+, and 4–1+ while the patient was observed for signs of motor contractures in the face, tongue, arm, and leg. Pupillary changes and eye deviation were also assessed.

Right STN intraoperative testing through the DBS lead at bipolar configuration 1–4+ (130 Hz, 120 msec) resulted in left-hand flexor contractures starting at 3 mA. These contractures were re-demonstrated at higher contact 2–4+ but not at 4–1+. Based on macrostimulation findings, activation of the CST was falsely suspected. The lead was repositioned 2 mm in the antero-medial direction (Fig. 3). Macrostimulation at this location (1–4+, 130 Hz, 120 msec) revealed stereotypic flexor hand and arm contracture starting at 3 mA again. No contractures of the face, tongue, or lower extremity were noted. No activation of CN III or pupillary changes were noted either. Repeat intraoperative imaging confirmed the lead location along the medial border of the STN. Thus, activation of the RST medially or inferiorly was suspected.

The lead was repositioned back to the initial location but at 1.5 mm above the previous depth. The final lead location was at 12.6 mm, 3.2 mm, 2.8 mm (Fig. 3). Stimulation now revealed no motor or eye deviation findings up to 6 mA. Postoperative stimulation testing did not demonstrate any motor, sensory, or autonomic side effects up to 6 mA at all contacts tested.
to be within the volume of tissue activated by the STN-DBS lead. However, it is at this axial plane that the RST travels from the medial border to the RN inferiorly and is amenable to stimulation by a medially placed lead. As one travels further caudal along the axial plane, CN III exits the RN and comes close to the STN at its most inferior-ventral part, and it is at this more mediocaudal location that CN III activation is expected.

An additional consideration is the highly variable size and position of the STN, especially the anterior border; such differences have been shown to be considerably larger than errors associated with imaging techniques. As a result, consideration of the clinical signs is a critical tool in determining and, when necessary, adjusting the trajectory. In this case, the development of motor contractions suggested that the track was possibly too lateral, resulting in STN activation. This led us to believe that image registration was possibly off, so we considered an anteromedial move to deviate away from fibers of the CST.

To that end, it is also important to address the possibility of imaging registration and merging accuracy as sources of discrepancy. Although the auto-merge in this case was verified for accuracy, errors are inherent to the use of coregistration software for merging images, and this possibility cannot be neglected as a contributor to our findings. Nonetheless, the use of intraoperative computed tomography has been demonstrated to improve microelectrode targeting accuracy, so our use of this technique arguably decreases the likelihood that any errors in merging accuracy were significant.

Lessons

The inability to receive subjective, intraoperative feedback from patients is a limitation of asleep DBS as compared to awake. Intraoperative macrostimulation after lead placement in asleep DBS, when used, is limited, because it utilizes muscle contractions and variability in basic vital signs as a marker. In asleep STN-DBS surgery, the CST abuts the lateral and inferolateral border of the STN, whereas the medial and inferomedial borders are close to the RN. Thus, generalized peripheral muscle contractions of the extremities are presumed to reflect a more laterally placed lead, whereas unilateral eye deviation or pupillary size changes are associated with a medially placed lead. The present report demonstrates that it is possible to activate a motor pathway, specifically the RST, by an inferomedially placed lead. Activation of the RST should be considered as a false localizing sign during STN-DBS, especially asleep DBS, to prevent inadvertent lead repositioning.

References


Discussion

Observations

This report is the first to describe isolated activation of the RST during asleep STN-DBS. Although similar complications may be underreported, only three cases of DBS misplacement in the RN have been described in the literature, both occurring during awake DBS. One group demonstrated that both patients showed MER neuronal activity comparable to the STN and without notable side effects of microstimulation. However, macroelectrode implantation resulted in an array of side effects; the first patient reported a marked autonomic reaction; and the second, dysarthria, diplopia, ipsilateral ptosis, and dizziness. Such adverse effects allowed for directional correction. Similarly, another study described a case in which, despite MER demonstrating neuronal activity thought to be representative of the STN, the patient reported diplopia and dizziness on macroelectrode stimulation, indicating medial displacement of the target in the RN, which was subsequently corrected. Although these studies both reported RN electrophysiology and macrostimulation results secondary to lead displacement, neither described specific activation of the RST.

Given the intimate anatomical relationship between these structures, the lack of additional side effects beyond those suggestive of RST activation is rather puzzling. In the context of general anesthesia, it is possible that a lack of cortical inhibition to the RN rendered the RST susceptible to activation. Additionally, although we did not observe any pupillary dilation, other autonomic sensations such as nausea are not readily apparent during asleep DBS, also lending to the reasoning behind seemingly isolated RST activation.

Given the anatomical proximity, it is interesting to note the activation of RST without CN III activation, which is often used to demarcate the medial limits of STN-DBS lead placement. One possible explanation is the relative craniocaudal location of CN III in relation to the STN. Rostrally, at dorsolateral and mid-STN axial planes, CN III resides within the midportion of the RN and is henceforth less likely


Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Sani, Mitchell, Pearce. Acquisition of data: all authors. Analysis and interpretation of data: Sani, Mitchell, Pearce. Drafting the article: Mitchell, Pearce. Critically revising the article: Sani, Mitchell, Pearce. Reviewed submitted version of manuscript: Sani, Mitchell, Pearce. Approved the final version of the manuscript on behalf of all authors: Sani. Study supervision: Sani. Figure creation: King.

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