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Stereo-electroencephalography in the setting of a preexisting deep brain stimulation device: illustrative case

Stephen Jaffee, MD,[1] Navnika Gupta, MD,[2] Dallas Kramer, MD,[1] Dorian M. Kusyk, MD,[1] James Valeriano, MD,[2] Amanda Merkley, MS,[3] Trent Kite, BS,[1] Shaifali Arora, MD,[2] Pulkit Grover, PhD,[3] and Alexander C. Whiting, MD[1]

[1]Department of Neurosurgery, Allegheny Health Network Neuroscience Institute, Pittsburgh, Pennsylvania; [2]Department of Neurology, Allegheny Health Network Neuroscience Institute, Pittsburgh, Pennsylvania; and [3]Department of Electrical and Computer Engineering, Carnegie Mellon University, Pittsburgh, Pennsylvania

BACKGROUND Deep brain stimulation (DBS) and responsive neurostimulation are increasingly being used to treat drug-resistant epilepsy (DRE). However, patients who experience partial or limited improvement in seizure control could require additional surgical interventions or refinement of their epilepsy network characterization, including further stereo-electroencephalography (SEEG) investigations. SEEG in the setting of previously implanted hardware demonstrates a myriad of technical challenges. The authors present the first reported demonstration of SEEG electrode implantation with a preexisting DBS device.

OBSERVATIONS The patient was a 36-year-old male with a history of severe DRE with focal impaired awareness seizures beginning at 7 years of age. Despite having a bilateral DBS device for the anterior nucleus of the thalamus, he continued to have 1–2 seizures per day and was offered SEEG. The patient tolerated the surgery well without any morbidity, with a successfully improved definition of his epilepsy network. SEEG allowed the medical team to titrate stimulation settings while following intracranial electrographic response.

LESSONS SEEG in the setting of preexisting DBS can be performed safely without damage to functioning hardware, and the authors obtained characterization and localization of the epilepsy network. Further follow-up will be needed to assess the efficacy outcomes of additional intervention in this patient.

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KEYWORDS epilepsy; deep brain stimulation; stereo-electroencephalography; case report

Epilepsy affects millions of individuals in the United States, with roughly one-third of these patients experiencing drug-resistant epilepsy (DRE).[1,2] DRE is characterized by persistent seizures despite the use of multiple antiseizure medications (ASMs), posing a significant challenge in treatment management. For patients with DRE, surgical intervention offers a promising and effective therapeutic option, with the primary goal of achieving seizure freedom or controlling seizure frequency. Current surgical treatments for DRE include resective surgery, laser ablation, vagus nerve stimulation (VNS), deep brain stimulation (DBS), and responsive neurostimulation (RNS).[1] These interventions are selected based on the individual patient's epilepsy network and specific therapeutic objectives.

Neuromodulation techniques, such as VNS, DBS, and RNS, aim to modulate or disrupt the patient's epilepsy network, thereby restoring normal brain function or reducing susceptibility to seizures. DBS involves the stereotactic implantation of electrodes into deep brain structures. This procedure is performed through burr holes in the skull, with the electrodes connected via subcutaneous tunneling to an internal pulse generator implanted in the chest. DBS targeting the anterior nucleus of the thalamus (ANT) has shown promise in patients with focal epilepsy, particularly when the seizure activity is thought to involve the circuit of Papez.[3,4] The results from the SANTE (Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy) trial, a pivotal study investigating ANT-DBS, and its long-term follow-up study demonstrated median seizure reductions of 56% and 75% at 2 and 7 years, respectively, in patients with DRE.[3,5] Despite the efficacy of DBS in reducing seizure frequency, patients do not always achieve seizure freedom, and some patients might continue to experience disabling seizures.[6] A recent study by Yang et al. demonstrated that some patients with epilepsy who have already undergone placement of a

ABBREVIATIONS ANT = anterior nucleus of the thalamus; ASM = antiseizure medication; CTA = CT angiography; DBS = deep brain stimulation; DRE = drug-resistant epilepsy; EMU = epilepsy monitoring unit; MPRAGE = magnetization-prepared rapid acquisition gradient echo; RNS = responsive neurostimulation; SEEG = stereo-electroencephalography; VNS = vagus nerve stimulation.

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single DBS or RNS system benefited from additional neuromodulation surgery, which included either the simultaneous implantation of both DBS and RNS devices or a transition from one modality to the other.[7]

As the application of neuromodulation for epilepsy continues to expand, a growing number of patients who experience partial or limited improvement in seizure control could require additional surgical interventions or further refinement of their epilepsy network characterization. One such technique, stereo-electroencephalography (SEEG), involves the direct implantation of electrodes into the brain to map the epileptic network better, allowing for more precise surgical planning or targeted therapy. However, as neuromodulation technologies like DBS and RNS become more widely adopted, there might be an increasing need to perform SEEG in patients who already have implanted cranial devices, introducing a series of technical challenges.[2,8] SEEG electrode implantation in patients with previous DBS device implantation confers unique challenges and concerns regarding perioperative management, like the possibility of distorted imaging from device artifact on MRI, increased infection risk from previous hardware, the presence of scar formation, and the possibility of electrical damage to the DBS device.

To our knowledge, we report the first documented case of SEEG electrode implantation in a patient with a preexisting DBS system. Our case illustrates the process of further characterizing the patient's epilepsy network and evaluating the potential for subsequent surgical interventions aimed at reducing seizure burden. In this report, we outline the decision-making process, considerations for safety, device compatibility, and operative technique used.

Illustrative Case

We present the case of a 36-year-old male with severe DRE with seizure onset at the age of 7 years. His seizure semiology was predominantly characterized by focal impaired awareness seizures. Despite treatment with multiple ASMs including carbamazepine, cenobamate, and topiramate, his seizures remained poorly controlled (greater than 3 seizures per day). The patient had previously undergone surgical intervention with a local surgeon involving a limited bilateral depth electrode implantation for invasive monitoring. The implantation sampled from the bilateral temporal lobes and posterior superficial frontal lobes but did not significantly sample the orbitofrontal cortex, insula, anterior cingulate, or subgenual cingulate. Although his seizures were initially presumed to have a left temporal origin, the seizure onset was reported to involve a more diffuse, rapidly spreading bitemporal pattern originating from the left hemisphere, suggesting the potential involvement of a broader epilepsy network. After a thorough discussion with the patient regarding available treatment options, including resective surgery and neuromodulation, the decision was made to proceed with bilateral ANT-DBS. The surgery was performed without complications, and the postoperative course was uneventful. Over the next 5 years, the patient experienced a notable reduction in seizure frequency, although a significant seizure burden persisted (1–2 seizures per day). In addition, the patient reported progressive memory decline, which increasingly interfered with his professional responsibilities as an engineer.

Given the continued seizure burden and cognitive concerns, the patient was referred to our epilepsy center for further evaluation. After a comprehensive phase I workup, it was hypothesized that the patient's seizure onset zone might not have been fully delineated during the previous depth electrode assessment. A more comprehensive evaluation using SEEG was recommended to characterize the seizure network better and potentially identify regions amenable to additional surgical intervention. Notably, the patient did not wish to have his existing DBS device removed or altered, as it had demonstrated some benefit. A multidisciplinary team meeting was held to discuss the potential for SEEG electrode implantation in the context of the patient's preexisting DBS system. The hypotheses for the repeat SEEG electrode implantation included involvement of the anterior cingulate cortex (Brodmann areas 24, 25, and 32), orbitofrontal cortex (Brodmann area 11/12), lateral frontal lobe, and anterior insula, as well as traditional mesial temporal targets.

Surgical Planning

Preoperative planning was conducted using contrast-enhanced brain MRI and preoperative CT angiography (CTA) with thin-slice imaging to assess anatomical structures and guide electrode placement. A 0.6-mm thin-cut CTA system was used. For MRI, a 1.5T, horizontal field, closed-bore system with a spatial field gradient ≤ 30 T/m and a gradient slew rate ≤ 200 T/m/sec per axis was used. The studies were performed on a Siemens Aera 1.5 running XA30 software, and magnetization-prepared rapid acquisition gradient echo (MPRAGE) precontrast, T2 space, and MPRAGE postcontrast sequences with a total run time less than 25 minutes with a transmit/receive head coil for additional signal quality were obtained. Electrode trajectories were meticulously planned with the proprietary ROSA software (Zimmer Biomet), and orthogonal configurations were selected to minimize potential interference with the implanted device components, including the leads and associated wiring. Special attention was given to the windowing of the CTA images to ensure accurate visualization and prevent electrode placement from transgressing the location of the implanted generator or its associated wiring. Thin-cut CTA allowed for excellent visualization of all the DBS components, including tunneled wires and burr hole covers, allowing us to plan electrodes around these structures.

We typically attempt to use orthogonal implantations for most of our electrodes to maximize the number of cortical regions sampled, as well as to create a 3D grid of seizure propagation. Orthogonal implantations lent themselves reasonably well toward placement around the DBS electrodes, as the DBS electrodes tend to be implanted on the vertex of the skull and are tunneled posteriorly. Conversely, anterior insular electrodes, which we typically place from a cranial trajectory near Kocher's point, presented a technical challenge. In our case, we sampled the anterior insula from an orthogonal trajectory starting in the lateral temporal lobe and projecting through the sylvian fissure, requiring care to avoid damaging the significant vasculature in this region using techniques that have been well documented in previous literature.[8,9] Posterior parietal or temporo-occipital electrodes also provided a technical challenge due to the location of tunneled DBS wires in this region, and SEEG electrode angles, trajectories, and entry points had to be modified accordingly.[4]

Careful consideration was given to maintaining an appropriate distance between the electrode bolts and the existing DBS components to minimize the risk of infection. A total of 15 SEEG electrodes were planned for placement, targeting the bilateral insular cortex, amygdalohippocampal regions, orbitofrontal cortex, and other cortical areas of interest. Additionally, the placement of the Leksell stereotactic frame was precisely planned to avoid overlap between the DBS system's tunneled leads and the intended trajectories of the SEEG electrodes.

Procedural Technique

The patient was brought to the operating room and placed under general anesthesia via endotracheal intubation. Prior to surgery, the

DBS system (Abbott) was turned off. The Leksell stereotactic headframe was securely applied using skull bolts, with special attention paid to prevent damage to or interference with the existing DBS hardware. The ROSA robotic system was then connected to the headframe, and intraoperative stereotactic neuronavigation was set up using laser facial registration. Perioperative antibiotics were administered, and the patient was prepared and draped in a sterile manner using a betadine solution.

The SEEG electrodes (Adtech) were carefully placed into the brain for long-term monitoring, utilizing the ROSA robotic system, stereotactic neuronavigation, high-speed drill (Stryker), and fixation bolts. No incisions were made with a knife, and the drill was used to pierce the skin directly, prior to drilling the burr hole. We attempted to open the dura without electrocautery using a semiblunt probe if it was not already opened by the drill after breaching the inner table of the skull. Bolts were inserted into the skull and electrodes were passed to their preplanned targets using normal techniques. Electrode impedances were checked to ensure proper placement. A total of 15 electrodes were successfully implanted. Intraoperative fluoroscopy was used to confirm the correct positioning of the electrodes (Fig. 1). Once the electrode placement was verified, the electrodes were wrapped in a sterile fashion and securely tethered to the patient's head once again, avoiding any damage to the DBS system (Figs. 2 and 3). Following the procedure, the patient was removed from the frame, extubated without incident, and transferred to the epilepsy monitoring unit (EMU). Postoperative CT demonstrated no evidence of hemorrhage and accurate placement of all the electrodes to their appropriate targets.

Outcomes

The patient was monitored in the EMU for 7 days, and ASMs were slowly weaned off and stopped. The patient had 7 of his typical seizures during the EMU stay. Additionally, SEEG monitoring was performed with DBS "on" and "off" for nonoverlapping 24-hour periods without changes to ASMs to assess potential changes in the epileptogenic network with the ANT-DBS. This methodology generated a significant volume of data, which will be further analyzed to assess changes in the epileptogenic network and the patient's response to DBS in real time. Future studies will focus on integrating these findings to understand better the impact of DBS on seizure dynamics during ongoing monitoring with SEEG.

The 7 electroclinical seizures captured during the EMU stay localized to the orbitofrontal region and subgenual cingulate (Fig. 4). The seizures were recorded while the DBS was both "on" and "off." Given the more localized epileptogenic zone identified through this repeat evaluation, a targeted ablative or resective surgical treatment can now be offered to the patient that can help reduce his seizure burden. The literature on the use of laser interstitial thermal therapy or RNS in patients with a preexisting DBS device placement remains limited, warranting further exploration in future clinical studies.

Informed Consent

The necessary informed consent was obtained in this study.

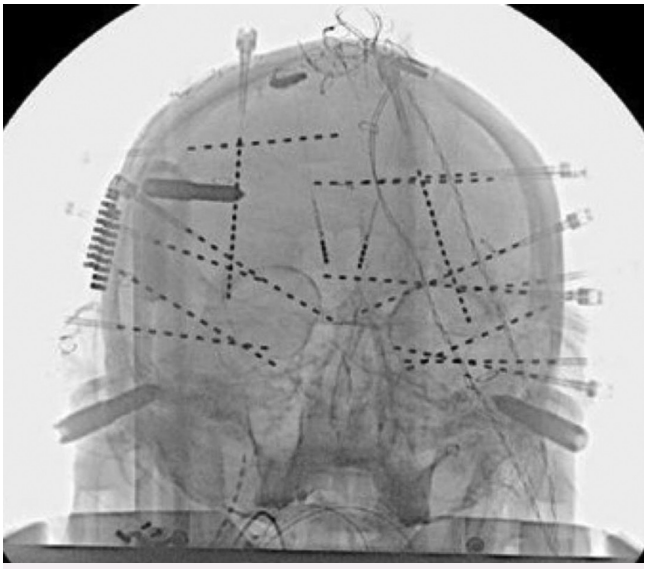

FIG. 1. Intraoperative fluoroscopy image showing SEEG leads targeting bilateral insular, cortical, and orbitofrontal cortex as well as visualized bilateral centromedian thalamic DBS leads.

FIG. 2. Lateral and anterior-posterior radiographs of the skull and cervical spine of the patient, demonstrating the DBS leads with tunneled leads along the right scalp and neck.

FIG. 3. Left: Intraoperative photograph showing the patient in the Leksell frame with marked entry sites for the DBS electrodes (noted with a crescent mark and an "x" over the center of the anchoring site). The *dashed line* represents the tunneled track of the DBS leads, notable anterior to the posterior Leksell pin site. The ROSA laser can be visualized as the *red dot* adjacent to the right-sided DBS anchoring location. **Right:** Intraoperative photograph showing the SEEG leads with the patient's scalp prepared with betadine and draped in a sterile manner.

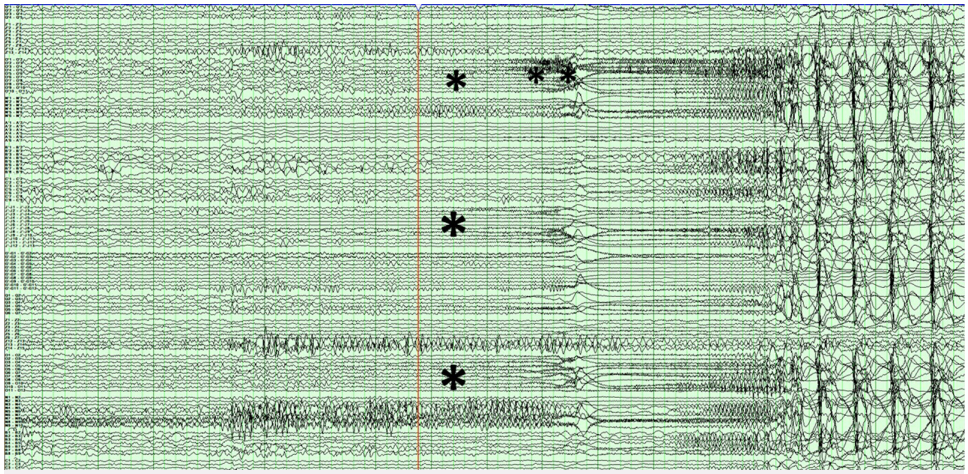

FIG. 4. Stereo-electroencephalogram of a typical seizure. There is an emergence of a fast discharge in the bilateral gyrus recti, medial and lateral orbital frontal regions, pars orbitalis, and subgenual cingulate (marked with *single asterisks*). Five seconds later, the fast discharge is seen in multiple electrodes, with the best evolution in the left gyrus rectus, medial and lateral orbital frontal cortex, and pars orbitalis (marked with a *double asterisk*).

Discussion

Observations

On reviewing the previous invasive implantation, it was determined that certain key areas of interest, including the orbitofrontal cortex, cingulate cortex, insula, and likely the mesial frontal regions, were inadequately sampled. Subsequent analysis of the intracranial electroencephalography recordings revealed that the repeat invasive evaluation with SEEG captured robust seizure onsets in the regions that had not been targeted during the first depth electrode implantation. The neurophysiological data obtained from the repeat evaluation indicated that the epileptogenic zone was more focal than diffuse as was postulated from the first depth electrode evaluation.

There is a palliative nature of most neuromodulation devices for epilepsy; as such, patients might continue to undergo these repeated procedures for adequate seizure control, and there can be a growing need for protocols for repeated SEEG in patients with DBS or even RNS device implantation. Furthermore, to further titrate settings, there could be a role for SEEG evaluation around a DBS device that is functioning but not optimized. Alternatively, it could be difficult to interpret what changes might be generalizable to a patient's seizure frequency and electrical activity outside the short confines of the SEEG monitoring phase. Changes in interictal signaling might be fraught with issues and might require further innovation, in terms of mapping changes in epilepsy networks, in the short term.

While we expected the risk profile for SEEG electrode implantation to be low, the risk profile for placement of SEEG leads around the DBS device included damage to the physical hardware, interference with signaling, infection, and hematoma formation.[4,10,11] There was also a risk of damage to the tunneled leads and to the generator itself. However, there were no significant complications with our patient, and the DBS was interrogated pre- and postoperatively to ensure nominal functioning. The patient had an Abbott DBS device implanted, with specific DBS settings configured for intermittent delivery: 1 second "on" followed by 5 seconds "off," with a ramp time of 8 seconds. The parameters for each lead were as follows: lead 1 (left ANT) was set to an amplitude of 5.35 mA, pulse width of 90 μsec, and frequency of 144 Hz; and lead 2 (right ANT) was set to an amplitude of 5.25 mA, pulse width of 90 μsec, and frequency of 144 Hz. Clinical follow-up indicated a reduction in seizure frequency and improvement in recovery time following this adjustment.

Preoperative imaging, including MRI of the brain with and without contrast, was not significantly impacted by the presence of the DBS system. The DBS leads induced only minimal artifact on the imaging, allowing for clear visualization of the targeted brain regions.

Lessons

SEEG in the setting of preexisting DBS demonstrated safety and efficacy. Adequate EMU monitoring was completed, and characterization as well as localization of the epileptogenic zone was obtained. The DBS continued to be functional after the evaluation, and no complications were encountered. The information gained from the SEEG evaluation allowed for further treatment options for the patient.

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Disclosures

Dr. Grover reported stock ownership in Synpase Symphony, Inc. and Precision Neuroscopics, Inc.; and grants from Precision Neuroscopics, Inc. outside the submitted work.

Author Contributions

Conception and design: Whiting, Jaffee, Kramer, Kite. Acquisition of data: Whiting, Jaffee, Valeriano, Arora. Analysis and interpretation of data: Whiting, Jaffee, Arora, Grover. Drafting the article: Whiting, Jaffee, Kramer, Merkley, Kite, Arora. Critically revising the article: Whiting, Jaffee, Gupta, Kramer, Kusyk, Merkley. Reviewed submitted version of manuscript: Whiting, Jaffee, Gupta, Kramer, Kusyk, Merkley, Kite, Arora. Approved the final version of the manuscript on behalf of all authors: Whiting. Statistical analysis: Jaffee. Administrative/technical/material support: Jaffee. Study supervision: Whiting.

Correspondence

Alexander C. Whiting: Allegheny Health Network, Pittsburgh, PA. alexander.whiting@ahn.org.