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ETHICS CASE

Applying Guidelines to Individual Patients: Deep Brain Stimulation for Early-Stage Parkinson Disease

Commentary by Bryn Esplin, JD, Andre G. Machado, MD, PhD, Paul J. Ford, PhD, and Kara Beasley, DO, MBe

As 39-year-old Sam Ruffini sat confidently in the clinic chair, his hand tremor would have been noticeable only to a trained expert. The other signs of Parkinson disease, however, were unmistakable, such as the once-spry man's shuffling gait. Mr. Ruffini had come to see Dr. Blue, a neurosurgeon renowned for treatment of functional nervous system disorders.

"I simply don't want to suffer through years of trial and error with medications and their side effects. I'm a young, active guy. I can handle a surgery. If this can be improved with a one-time procedure, even if it's brain surgery, I'd rather do that now and not wait until I've suffered through years of disability."

Dr. Blue faced a dilemma. In previous years, he would have politely dismissed Mr. Ruffini and referred him back to the neurology department, since deep brain stimulation (DBS) surgery for Parkinson was still a measure of last resort for patients whose conditions had become refractory to best medical therapy. Mr. Ruffini had responded fairly well to levodopa and other standard medications for Parkinson, and he continued to function in his job as an investment banker. Although he complained about fatigue and other side effects of the medications, these did not seem to be disabling.

On the other hand, Dr. Blue had recently read about a clinical trial showing good results for patients who received DBS in the early stages of their disease, before their level of disability had progressed to the point of being "medically refractory." He wondered if this foretold a new paradigm in thinking about proactive surgical interventions for neural disorders, including not only Parkinson but also essential tremor, depression, chronic pain, and others. In some cases, the stipulation that a patient's condition be "medically refractory" prior to contemplation of surgery seemed to be a holdover from the era when that procedure was experimental and particularly risky. Dr. Blue's rate of serious complications with DBS had become so low (less than 5 percent) that, depending on the patient's preferences, he believed it could be a viable alternative to medical therapy even when the latter hadn't failed.

When he met with the interdisciplinary DBS committee that week, Dr. Blue floated the idea of doing DBS for Mr. Ruffini. This idea was met with acrimonious objections from the neurologists and psychiatrists in the room. Based on the standard

of care, they argued, Mr. Ruffini should be treated with medications, which were noninvasive and well understood, and must exhaust all reasonable nonsurgical therapies prior to being offered an invasive brain surgery.

Commentary 1

by Bryn Esplin, JD, Andre G. Machado, MD, PhD, and Paul J. Ford, PhD

Proper selection of patients who will reliably benefit from treatment is critical to the successful outcome of deep brain stimulation (DBS). The ethical duties of the clinicians in this case involve careful balancing of a variety of interests of the patient, society, and their own practices. They need to create fair systems based on the best available research that allow individualized decisions for each patient and assess the likelihood of harm and benefit. In doing so, each clinician should be cognizant of whether decisional elements are merely a matter of tradition, rely on outmoded data, or are based on unwarranted assumptions.

In the current case, the surgeon needs to evaluate carefully which model of the patient-physician relationship is appropriate to apply, based on the facts' relationship to the models. In particular, the surgeon must consider the role of informational vulnerability, paternalism, and an obligation to improve practice for all patients. This is no doubt a complex task because how various subjective values are balanced could lead to different conclusions. Acceptable solutions must be based on a clear ethical justification according to the values at stake.

The proper selection of a model for physician-patient relationship provides structure, security, and transparency to the relationship through designated roles and mutual obligations. A classic 1992 article by Ezekiel A. Emanuel and Linda L. Emanuel highlights four distinct models of relationships physicians may adopt, two of which, the interpretive and paternal models, are relevant here [1].

In the interpretive model, the physician aims to elucidate the patient's values and assists him or her in choosing the available medical treatment that best preserves those values. By the surgeon's account, Mr. Ruffini's hand tremor is "mild," his shuffling gait is becoming more pronounced—a marked change from his once-spry self—and he complains of fatigue and other side effects of medications that "did not seem to be disabling." But the patient's illness experience is also crucial. What may be described as a "mild" hand tremor by a physician may have a severe impact on a patient's everyday life. Categorizing things like disability as mild, moderate, or severe may yield more disagreement and confusion than clarity; quality-of-life assessments are value-based and vary from patient to patient. A patient's perception of disability is critical to evaluating whether his or her expectations about potential benefits correspond to realistic outcomes of the procedure.

The interpretive model anticipates that a patient's values may not be known or fixed, and so the physician helps the patient articulate goals, aspirations, and commitments and provides clear guidance about which treatment plan best balances these values [1]. This model allows the patient to come to know more clearly his own identity and

how various treatment options may bear upon that identity, a proposition particularly important when treating a neural disorder that, by its very nature, transforms and may largely dictate the lived experience of the body.

For example, Mr. Ruffini, valuing his active lifestyle, may be feeling anxious that his PD will slowly rob him of agency, and thus intervening before he has “suffer[ed] through years of trial-and-error with medications and their side effects” is reasonable. Additionally, Mr. Ruffini states, “If this can be improved with a one-time procedure, even if it’s brain surgery, I’d rather do it now and not wait until I’ve suffered through years of disability.”

However, it is vital to be aware that the procedures of implanting and stimulating the electrodes are brain-invasive and entail significant risks. Although the paternalistic model has fallen out of favor as a default standard model, there are instances where elements of it should still be employed. This model calls for the physician to act in the patient’s best interest based on what he or she knows of the patient. In particular, when clinicians encounter a patient with significant vulnerabilities, they incur a greater obligation to protect that patient’s interest. Besides a patient’s usual medical vulnerability, Mr. Ruffini’s lack of understanding of DBS constitutes an informational vulnerability [2]. First, Mr. Ruffini believes that DBS is a one-time procedure. However, once implanted, the system may become infected, parts may wear through the skin, and the lead or lead/extension connector may move [3]. Additionally, systems require battery changes throughout the life of the technologies and need ongoing monitoring and programming. A DBS procedure is not like a traditional ablative procedure in which a lesion is made and then the intervention is complete.

Informed consent in this case involves more than understanding the expected good and bad short-term outcomes; it involves understanding the ongoing burdens of the technology. Mr. Ruffini’s informational vulnerability results not only from a lack of specialized knowledge but also from misinformation. Patients often come to DBS with an informational vulnerability, having received misleading information or skewed portrayals of outcomes from the media and other forms of public discourse that occur outside the clinical encounter. Studies have pointed to overwhelmingly positive reporting of neuromodulation, heralding the arrival of the future and prominently featuring “miracle stories” [4]. Reports tend to showcase only the spectacular while obscuring the spectrum of all possible outcomes. Patients’ susceptibility to this type of informational vulnerability may justify or, perhaps, obligate the team to respond more paternalistically and protectively. Physicians seeking to protect patients must do their best to overcome patient misunderstandings caused by inaccurate or sensationalized accounts from the media or other discourses and must be careful to address assumptions that may not be correct—particularly that “less invasive” always means “less harm.”

In this particular case, though, the team members’ attempt to prioritize protection over self-determination may not be ethically justified, because the criterion they are

relying on to determine harm may not make sense. The traditional proposition that the least invasive intervention is always preferable can serve the purpose of limiting harm associated with overambitious goals. However, this obvious-sounding proposition is dubious in this instance. The faulty premise here is equating “more invasive than medications” with “more dangerous in the long term than medications.” Medications to treat PD are associated with not only fatigue but also a variety of neuropsychiatric symptoms, including depression, apathy, anxiety, obsessive behaviors, impulse-control disorders, hallucinations, and delusions that are difficult to treat, cause great disability, and can distress both patient and family [5]. Social and physical harms associated with uncontrolled side effects of medications that will ultimately fail to manage PD symptoms create a new dynamic.

While the long-term efficacy and safety of DBS implemented early in the course of the disease is uncertain [6], DBS can result in significant improvement in many of the motor symptoms while also decreasing the need for PD medications and improving overall quality of life [3]. An emphasis on long-term benefit might indeed lead to a preference for DBS in this case.

Ultimately, it is the patient’s assessment of risks and benefits that should guide deliberation. A recent article evaluating EARLYSTIM has argued that the appropriate time for surgery is when the needs and expected benefits outweigh the risks for a patient who has received objective and comprehensive information about individualized risks and benefits of the DBS [7]. In the current case, the goals that Mr. Ruffini wants to accomplish are not disclosed, but the metric still needs to be about the likelihood of achieving those goals with DBS. Whether using a paternalistic or interpretive model, the calculus should not be about a simplistic change in physical symptoms, but rather the functional impact the changes may make for the patient.

Despite cognizable risks, patients may remain steadfast in their desire to move forward with treatment. Even when patients aggressively advocate for procedures, there are limits on patient-centered care, including internal and professional limits, such as the institution’s standard of care provision. While these limits are important safeguards, their appropriateness should be reassessed if there is proof of advances in treatment. The interdisciplinary DBS committee needs to give clear reasons why this specific patient should not receive DBS at this time. If the patient’s centrally important goals could be reached and due diligence has been undertaken to offset vulnerability and collaborate on proper consent, there is ample justification for this team to offer DBS—provided it carefully monitors and collects information in a systematic manner for this patient.

Offering DBS to Mr. Ruffini could be undertaken based on several different models, all of which should reinforce that the surgeon’s obligations to provide high-quality care to all his patients remain the same. If the team decides to pursue DBS for Mr. Ruffini, there are two main options for offering it. First, the patient could be offered the procedure as “off-label” use. In this instance, Dr. Blue still has an obligation to

collect information to ensure best outcomes for this patient and for his future practice. Dr. Blue could either review the case series in the future or contribute to a national registry. However, the amount of data would be modest, and many people could be put at risk before an unknown negative consequence became apparent.

The other option is to offer DBS only as part of a well-controlled research study. Although this option increases burdens for the patient and the clinicians, it is least likely to cause harm to future patients and protects this patient through the careful oversight afforded research participants. Offering this procedure as part of a research protocol would be the ideal, but many practicalities of our current medical system pose barriers to doing so [8]. Moreover, by the time a research study was funded and approved by the regulatory bodies, Mr. Ruffini's condition could have already advanced to a severity level that he is attempting to avoid through early DBS, which, worse yet, could make him a "standard" DBS candidate and preclude his inclusion in the study. Too little information is provided in the current case to give a definitive opinion as to whether it is obligatory to offer DBS, but the option of offering the procedure to Mr. Ruffini is ethically supportable if proper safeguards are put into place and robust outcomes information is collected.

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Disclosure

AGM may in future receive distributions for intellectual property from Cardionomics, ATI, and Enspire (all Cleveland Clinic spin-off companies).

Commentary 2

by Kara Beasley, DO, MBe

The ethical issues and treatment options that must be considered in this case can be framed by considering the interests of the involved stakeholders and what they might, potentially, have to lose. This technique was developed by Paul Ford and has shown itself extremely valuable in teaching ethical analysis to students and residents.

The Stakeholders

The clinical team. Evaluation of patients for DBS ideally occurs through a process employing a multidisciplinary team that includes neurosurgeons, neurologists, neuropsychologists, and psychiatrists. As Paul Ford and Cynthia Kubu argue, “an ongoing multidisciplinary conversation around patient selection and care provides an important avenue for establishing good practice” [1]. The first group of stakeholders we will consider are the members of the interdisciplinary team. With the exception of Dr. Blue, they are conservative in nature and have strictly applied the criterion of “medication-refractory” disease. They are not without good reasons.

Firstly, there is sound clinical reasoning for their position. Clinicians traditionally consider the ideal DBS patient to be one in whom there is a 30 percent reduction in the United Parkinson's Disease (UPDRS) rating scale motor subsection in response to levodopa, motor fluctuations, or troubling side effects caused by medication and no significant cognitive impairment. The rationale behind the typical protocol, in which DBS is offered four to five years after onset of symptoms, is that waiting helps ensure that patients truly have idiopathic Parkinson disease (PD), rather than

Parkinsonism associated with other disease entities that could be negatively affected by DBS. While DBS is not a cure, there is evidence to indicate that DBS remains effective for the motor symptoms of PD despite clinical progression [2].

Furthermore, the team's interest in professionalism and high-quality care could also call for caution. There are strong arguments for judicious use of new technology; examples of indiscriminate use of procedures such as frontal lobotomy have colored the history of elective intracranial surgery for decades. Furthermore, invasive procedures should be offered based upon high-quality evidence, which in this case is lackluster. While there are studies that indicate that DBS is safer when used earlier in the disease [3, 4], the most compelling study only includes 30 patients.

Society and medicine. A second group of stakeholders might also have reasons for concern about offering DBS to Mr. Ruffini—society and the profession of medicine. Should Mr. Ruffini have a poor outcome, it might cost the public a great deal economically in terms of care for his complications. Poor outcomes in early uses could also hamper further adoption of the technology and hence access to DBS.

The patient. Mr. Ruffini, of course, is the other important stakeholder in this situation. His request is not unreasonable. Evidence indicates that, with the subthalamic nucleus target (STN), patients can typically reduce their medication burden by 50 percent. In their multicenter randomized trial of DBS versus best medical therapy, Weaver et al. concluded that “deep brain stimulation was more effective than best medical therapy in alleviating disability in patients with moderate to severe PD with motor complications responsive to levodopa and no significant cognitive impairment” [5]. Thus the treatment Mr. Ruffini seeks is effective for his condition and within therapeutic goals. He is a well-educated and highly functional patient who is informed about the risks, benefits, and alternatives of the procedure as well as the conventional indications. He is aware of the low complication rate of his selected surgeon, Dr. Blue, and he would elect to move forward if offered surgery.

To consider Mr. Ruffini's interests in this situation is to consider the fact that Mr. Ruffini is the only person who can truly determine what facets of his disease and his treatment negatively affect his quality of life and whether other possibilities, like medication trials, would be overly burdensome to him. An overly paternalistic decision would obviously conflict with his self-determination and right to direct his course of care in an informed fashion. The team may correctly argue that he does not meet the established criteria and does not have the right to demand a therapy that, in their expertise, they have deemed inappropriate at this time. But such a decision, while consistent with the medical and surgical guidelines routinely practiced, could have the consequence of leaving Mr. Ruffini feeling that he had no voice in the decision making about his care.

Furthermore—perhaps most importantly—the team is making evaluations and decisions based upon outdated data and in their recommendation should take into consideration the evidence regarding earlier implantation. Two studies—Charles et

al. [3] and Schuepbach et al. [4]—have provided evidence that DBS is safe for much earlier use than has been typical. In the Charles et al. study, 30 patients were randomized to optimal drug therapy (ODT) or ODT plus DBS three years earlier than is conventionally accepted. The authors concluded that DBS is “well tolerated in early PD” [3], and a larger multicenter trial has been approved. The Schuepbach et al. study randomized 251 patients with PD and early motor complications to best medical therapy or DBS plus best medical therapy. Overall, in a two-year period, the DBS plus medication group had a 26 percent improvement in quality of life and improved mobility, suggesting that “instead of waiting for patients to have very marked fluctuations, peaks and very deep valleys, [we can] move in when the peaks and valleys are not that steep” [4].

Four Possible Solutions

There are four possible solutions to this dilemma. The first would be to honor the decision of the multidisciplinary team and deny Mr. Ruffini access to DBS until he has “exhausted all reasonable medical options.” Should he choose to pursue DBS in the immediate future, he would need to do so with a different group. The second option would be for Dr. Blue to move forward with surgery based upon his medical judgment, despite the recommendations of the rest of the team. The third is for the team to agree that, while surgery will not be offered at this time, they will reevaluate the evidence and revisit the option of surgery for Mr. Ruffini in three to six months. Finally, the team could agree to consider the patient’s treatment wishes in light of the medical and scientific evidence and move forward with implantation so long as true informed consent is obtained.

Analysis of the Solutions

The first solution—to deny surgery based on the multidisciplinary team evaluation—errs on the side of paternalism and disenfranchises the patient. Each patient has a unique set of symptoms, goals for treatment, and family and social support structure. Patients should be considered holistically and not simply subjected to an impersonal checklist. Furthermore, new evidence supporting earlier utilization has emerged, calling into question the rationale behind the standard. The criterion of “medical-refractory” candidacy could allow Mr. Ruffini’s PD to jeopardize his perceived quality of life and create despair in an otherwise active and empowered patient. These consequences of withholding DBS far outweigh the risks involved in offering it.

On the other hand, it would not be advisable for Dr. Blue to disregard the recommendations of the team. This would force other team members to provide treatment they were not in agreement with; the neurologist in particular would have to oversee medication management and programming of the device. Such an action could erode future cooperation and professional trust. Strife in the team could limit access to care for other future patients, as team members may be unwilling or unable to continue a professional partnership that would benefit them.

The third solution holds some merit. It gives the team further time for discussion and review of the literature while leaving a window open for implantation in the not-so-distant future. It would ensure, and show, that the patient's unique situation and personal autonomy are being respected without jettisoning standards of care. If the team is unwilling to move forward with the fourth and most ideal solution in this case, then consideration in the immediate future is a concession with minimal downside.

The most ethically justifiable option would be for the team to step away from strict adherence to the "medically refractory" criterion and consider the specific and individual case before them. Not every patient should be offered the surgery this early on, but the aforementioned attributes—the surgeon's low complication rate, the new data supporting earlier utilization of the procedure, the patient's understanding of the risks and benefits and his strong preference to intervene before his condition progresses—make a strong argument for reconsideration and recommendation to offer him surgery in this particular set of circumstances. At the end of the day, patients are people with individual circumstances, goals, and values. They should be treated as such rather than forced to conform to a predetermined set of criteria. Furthermore, as scientific evidence develops, those forming standards and guidelines should stay current and flexible, altering their criteria and evaluations as appropriate.

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Disclosure

Kara Beasley is a consultant for Functional Neuromodulation Ltd. and Medtronic.

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