Special Section: Technology and the Body:
Linking Life and Technology

Ethics in the Clinical Application of Neural Implants

CYNTHIA S. KUBU and PAUL J. FORD

Once a neural implant has shown some efficacy during initial research trials, it begins to enter the world of clinical application. This culminates when the implant becomes approved for a particular indication. However, the ethical challenges continue as the technology is adopted as a standard of practice. Patient eligibility criteria, as documented by inclusion and exclusion criteria with any new treatment, are not always clearly quantified and defined. These vagaries can result in considerable debate regarding who should or should not proceed with surgery. There is often considerable room for clinical judgment that can result in extension of the treatment to a wider range of patients. The ethical questions that arise in clinical decisionmaking differ significantly from those inherent in engineering design and research development.

Most often neural implants fall under the purview of functional neurosurgeons. Functional neurosurgery is designed to ameliorate disease symptoms and is typically an elective surgery in which the patient chooses to undergo surgery to improve quality of life. Most often the target for functional neurosurgeons is the brain. Thus, the potential risks associated with the procedure can include changes in features that may be considered essential parts of a person's identity (i.e., cognition, mood, and personality). Although one could argue that any major physical change can result in phenomenological changes to the self, there is widely held belief that altering the brain has the potential to engender these changes in a very fundamental, physically intimate way.

Patients who are candidates for neural implants are typically patients with severe disease who often have other medical and/or psychiatric comorbidities. The complexity of the patient's medical condition(s), coupled with the potential that the innovative treatment may alter essential aspects of a person's identity, support a multidisciplinary team approach in the identification of appropriate surgical candidates. Such a multidisciplinary team approach helps ensure the careful application of new and emerging neural implants.[1] These committees are useful in establishing good practices and evaluating complex cases. Depending on the disorder under treatment, the committee membership is often comprised of neurosurgeons, neurologists, neurophysiologists, neuropsychologists, psychiatrists, bioethicists, and allied health (nursing, physician assistants) professionals. Although patients and families are stakeholders, they generally do not take part in multidisciplinary team meetings. Each team member brings to the table his or her unique perspective and biases based on area of expertise. The belief is that through open, respectful dialogue among all

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members of the team, patient care is enhanced and attention is directed to all relevant aspects of the patient's care. This can be particularly important when the clinical care is innovative and/or involves new technology.

Deep Brain Stimulation for Parkinson's Disease as a Paradigm

We have chosen to focus our discussion regarding the ethics involved in the clinical application of neural implants by structuring the remainder of our discussion around a specific therapy. Deep brain stimulation (DBS) for Parkinson's disease (PD) provides a paradigm for thinking about other emerging neural interfaces. This is an FDA-approved brain implant applied to a population with a neurodegenerative disorder.

To fully appreciate the challenges in applying DBS to the treatment of patients with PD, it is important to understand a little about the disorder and DBS. PD is a movement disorder characterized by the cardinal motor symptoms of tremor, rigidity, bradykinesia, and postural instability. In addition to the motor symptoms, there are a variety of neurobehavioral symptoms that can accompany the disease. PD is one of the prototypical subcortical dementias. Although not all patients with PD will manifest dementia, most will demonstrate some cognitive deficits that can range from mild to severe. In addition, PD and/or Parkinsonian medications are associated with a variety of other neuropsychiatric symptoms, including depression, apathy, anxiety, obsessive behaviors, impulse dyscontrol (gambling, hypersexuality), hallucinations, and delusions.[2] These neurobehavioral symptoms can be very distressing for the patient and family and difficult to treat.

DBS involves the surgical placement of an electrode into deep brain structures. The electrode is connected, via a wire, to a pulse generator (similar to a cardiac pacemaker), that is placed in the chest. The pulse generator is activated by a magnet, and various stimulation parameters can be adjusted to titrate the level of stimulation. DBS applied to specific deep brain nuclei results in significant improvement in many of the motor symptoms associated with PD.[3] Furthermore, DBS in the subthalamic nuclei can result in decreased need for PD medications, thereby resulting in fewer medication side effects. However, DBS is not a cure for PD. In well-selected patients with PD, the cognitive risks associated with surgery are relatively mild. The neuropsychiatric risks are less well known, but generally viewed to be minimal in those same well-selected patients.[4] The clinical challenge arises in determining which patients are appropriate candidates for surgery, particularly from a neurobehavioral perspective. This challenge is even more apparent in those cases in which some cognitive or neuropsychiatric concerns are apparent, yet they do not clearly meet the generally accepted exclusion criteria for surgery, for example, evidence of some cognitive decline yet not frankly demented. Some of these challenges are illustrated in the following case vignette.

The Case

A 59-year-old, married gentleman with PD (details have been altered to protect confidentiality) presented for comprehensive, multidisciplinary preoperative DBS evaluation. He was evaluated by the neurologist, neurosurgeon, and

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neuropsychologist before being presented to the multidisciplinary team. Both the neurology and neurosurgical evaluations indicated that the patient was a very good candidate from a motor perspective and there were no apparent medical contraindications. Formal neuropsychological assessment revealed a pattern of cognitive decline characteristic of Parkinson's disease, but no evidence of frank dementia. His family described a recent history of poor judgment (e.g., attempting to walk without proper support, trying to climb ladders) and disinhibition (gambling, hypersexuality). The disinhibition was viewed to most likely reflect medication side effects and it was possible that the cognitive effects might reflect medication burden as well. The team was concerned that given the evidence of cognitive decline, a neurosurgical procedure might increase the likelihood of further decline. The team was also concerned about the history of poor judgment and the potential for increased physical harm to a patient with poor judgment who now had significantly increased mobility due to a successful surgery. Finally, the DBS electrode is placed in motor circuits in the brain that are adjacent to known neuropsychiatric circuits. Consequently, it is theoretically possible that surgery and/or stimulation could result in neuropsychiatric side effects. The team was worried that these potential risks might be heightened in a patient who had already demonstrated some neuropsychiatric symptoms. The available literature provides no clear guidance regarding potential cognitive or neuropsychiatric risk following DBS in these borderline cases. Considerable discussion ensued during the team meeting regarding the possible justification for offering or withholding surgery in this patient.

The team valued "benefiting" and "doing no harm" with regard to this patient. The balance between a high probability of improved motor function versus the potential risk to cognition and behavior following surgery became a point of great discussion. This was further complicated by a question of an obligation to use this as an opportunity to increase knowledge regarding neurobehavioral outcome in similar "borderline" patients versus the team's obligation to protect the patient against a questionable increased risk. This latter point illustrates the tension between innovative clinical care and standard clinical care.

The team expressed concern regarding the value of respect for autonomy by suggesting that the patient and those closest to him define what constituted a benefit worth undergoing the potential risk. The value of respect for autonomy was also applied to the team members by acknowledging that the team members are also autonomous, moral agents. The team members expressed the belief that the professional obligation to protect patients supersedes a patient's desire for a therapy that the team views to be largely unsafe.

Finally, the team raised concerns about "justice" related to access to the potential therapy. Should our limited knowledge regarding neurobehavioral risks justify denying a patient a treatment with well-established efficacy? Justice requires similar decision algorithm for all similar patients. However, the question remains as to which factors are morally relevant for similarity, that is, good family support, ability to pay, access to good medical treatment, safe environment, and so on. How much responsibility rests with the team to make wise decisions regarding surgical candidacy such that a potentially viable treatment option continues to be available to many patients? It would be unjust

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to wrongly keep a patient from a beneficial therapy, but what are the potential costs to society and future patients if the therapy is indiscriminately applied and patients have poor outcomes? A series of poor neurobehavioral outcomes could result in fewer people seeking a highly effective and generally safe treatment.

In the end, the patient underwent a neuropsychological reevaluation following reduction of medications. Although the disinhibition improved, his poor judgment and cognitive issues were still apparent. The patient did not meet criteria for dementia and there were no other absolute contraindications to surgery. The available published data indicated that it was very likely that the patient's motor symptoms would significantly improve following surgery. The decision to offer surgery to the patient was made based on evidence of a strong family support system that could care for the patient if further cognitive decline occurred and realistic patient and family goals for surgery. The team believed the patient would be safe and closely supervised and that the risks were still within accepted standards of practice.

Over time, the clinical decisionmaking surrounding similar borderline patients has evolved in our team as a result of explicit discussion regarding balancing the values articulated above. Many similar borderline patients may now go on to have a unilateral surgery, rather than placement of bilateral DBS electrodes. This practice reduces surgical risk (which presumably reduces potential neurobehavioral risk) and provides substantial motor benefit (although possibly not to the same level as bilateral electrode placement). Furthermore, outcome data are prospectively collected on these patients so that the team can formally evaluate treatment decisions and outcomes. In many senses, good clinical care occurs through a dynamic, recursive process reflecting on clinical experiences with challenging cases that lead to innovations. This innovation can include formal research and informal off-label application.

Conclusions

Although there are no easy algorithms to decide neuroethical clinical questions for all patients who are candidates for neural implants, best clinical practice dictates an explicit consideration of ethical issues. Given the complexities of clinical use as well as the propensity to expand the application of devices, multidisciplinary teams are essential in the consideration of patients for whom candidacy is unclear. Consultation with colleagues is particularly important when treatment involves innovative practice. Careful attention to justice and the limits of individual patient decisionmaking should be taken into account. These elements are particularly important in the context of neural implants given the potential of the technology to intimately affect not only the patient's quality of life but essential aspects of the person's identity. All of these questions and considerations should be fed back through the research process as the technologies are revised. Further, centers need to be transparent about the limits of the technology as well as the limits of what is known regarding existing patient candidacy criteria.

Notes

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4. See note 2, Voon et al. 2006.

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