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Neuroethics in Neuroscience Series
Deep Brain Stimulation: The Convergence of Medicine, Science, Engineering and Ethics

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Introduction

In 2010, Dr. Helen S. Mayberg of Emory University gave a talk before a large audience at the Society for Neuroscience Annual Meeting in San Diego. The title of the talk was “Tuning Depression Circuits”; the subject was Deep Brain Stimulation, or DBS, a technology which she and her colleagues had been testing on patients who had severe depression. Dr. Mayberg showed a video of one such patient, a woman, sitting and facing the camera while being asked questions. Her depression was obvious in her face and manner. She had been living with the condition for some time, and medication was not helpful. Then, the doctors activated the DBS device that had been surgically inserted into her subcallosal cingulated white matter, a structure of her brain that had been identified as part of an emotion modulation circuit. The audience watched as a change came over this woman. Her face brightened. Her posture lifted. Her speech became more animated. She recognized people in the room that she hadn’t noticed before. This woman had changed. She seemed, and was, happy [1].

This woman is one of thousands of patients who have or will receive a DBS implant. The list of disorders that have been targeted by DBS procedures in the last twenty years reads like the table of contents of a Neurology or Psychiatry textbook: depression, Parkinson ’s disease , Huntington’s disease, obsessive-compulsive disorder, Tourette’s syndrome, epilepsy, obesity and chronic eating disorders, cluster headaches, Alzheimer’s disease, traumatic brain injury, even alcohol and tobacco addiction. Most of the patients treated are not responsive to medication or other therapies, and have no other alternatives aside from brain surgery. For them, DBS represents hope where there used to be little or none.

From the perspective of neuroethics—the study of the ethical repercussions of advances in neuroscience—significant concerns arise from the use of DBS that extend beyond the normal realm of medical ethics. For these concerns to be effectively addressed, they must be understood by the three groups of people that drive DBS development: the neuroscientists who identify potential targets in the brain, the biomedical engineers who develop the devices, and the medical practitioners who implement the technology in patients, in addition to the patients and their families. In the next sections, I explain the basics of DBS, the neuroethical concerns with the technology, and the fundamental questions that must be addressed and reviewed as DBS becomes a widely accepted form of treatment.

What is Deep Brain Stimulation?

The idea of using electricity to interact with the brain has been around for over two centuries, but only recently has that idea been made practical through the development of a family of technologies referred to, interchangeably, as neural interfaces, brain-machine interfaces or neural prosthetics. Neural interfaces include cochlear and retinal implants, brain-motor interfaces for robotic prosthetics, and nerve stimulators. Taken together, they may seem to have a kind of miraculous quality as they may make the "blind see, the deaf hear, and the lame walk".

A DBS device is the simplest iteration of a neural interface, both in design and application. At its most basic, a DBS device is essentially a long wire connected to a battery pack. It is often referred to as a "pacemaker for the brain". When a DBS device is implanted, the probe tip is lowered into a specific region of the brain through a small hole in the skull using a stereotactic frame, targeting a region previously identified with detailed brain imaging. After the procedure is completed, the output of the device can be modified or shut off, or the device can be completely removed if necessary. The battery pack is inserted under the skin so that no part of the device is externally visible. The effects of the device are what are most evident to observers of the implanted patient.

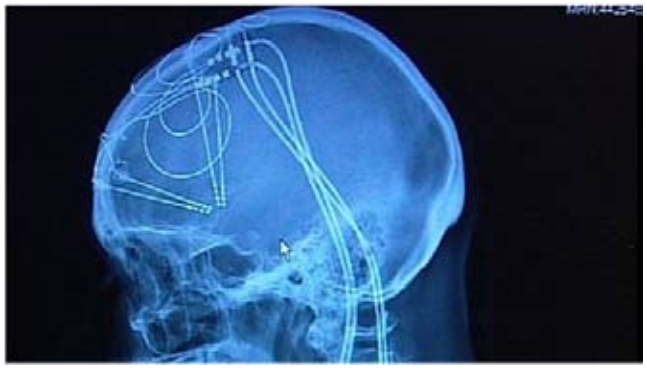

Fig. 1. X-ray showing DBS electrodes implanted in a patient to treat depression.
www.bbc.co.uk/news/health-12274271

The key to understanding how DBS works, and the key to understanding the ethical implications that emerge from it, is to think about the brain in terms of circuits and networks. Every part of the brain is connected to others in functional circuits, and if one part is damaged or altered, many circuits can be affected. DBS seeks to restore normality and balance to those circuits. For example, DBS in Parkinson's patients seeks to compensate for the loss of the substantia nigra—a cell group involved in multiple regulatory circuits and which has died off in those patients— by stimulating other parts of the affected circuits to compensate for the lost neurons [2]. DBS is not a cure; it is a patch. Therefore, an accurate understanding of the schematic of the brain, revealed by neuroscience, is critical to the effective application of DBS, and any potential side effects of the procedure depend on how other circuits are corrected or altered.

Neuroethics of DBS

The ethics of DBS use are, in many ways, similar to the ethics of other medical treatments. Modern medical practitioners have a very good handle on the ethics of working with surgical candidates, having benefited from many years of success and tragedy on this front. Doctors understand the need to evaluate candidates both physically and psychologically, with adequate attention given to ensure that patients have a rational understanding of the procedure, the mode of action, the possibility that results may not be optimal, and the potential side effects (none of which are trivial issues in neurology or psychiatry patients)[2,3,4,5]. Today's patients generally understand and accept that an alteration of the brain can affect behavior and personality, and have seen examples in which problems with the brain have been corrected successfully through artificial means. Therefore, society as a whole is prepared for the rise of DBS as a common treatment.

However, there are aspects of DBS technology that pose entirely unique ethical challenges. There is a fundamental and significant difference between altering the brain with a drug and altering the brain with an implanted device. From a purely practical standpoint, DBS can do what a drug may be designed to do, but through much more direct, precise and immediately regulatable means—all good attributes for a medical treatment. But those attributes, observed from another perspective, have deep ethical implications. DBS technology represents the capacity to "tinker" with the brain, not just affect it. Recall that DBS is successful because it targets circuits, based on a known schematic map of its connections. That is the same language used for fixing a machine. The effects of a DBS device can be turned on or off instantly, "with the flick of a switch". These points lead to a central and potentially unsettling question: if a simple electronic device can interact so seamlessly with the deep circuits of the brain, what does that make a person?

DBS implants can have real impacts on the self-image of patients, not just from the physical presence of a foreign device, but from the effects. DBS can quickly correct a disorder that has been present for years, causing one set of effects on a patient's psychology and social status. At the same time, there may also be side effects that influence a patient's mood and personality, sometimes challenging a patient's sense of individuality and personhood [2,3,4,5].

Several cases highlight the neuroethical concerns of current DBS applications. Consider the case of the depressed woman mentioned earlier. In Dr. Mayberg's presentation, she noted that her depressed patients had to learn to be sad again, for when they felt sad they worried that their device was not working, that they would sink back into depression. There is the elderly Dutch man, whose DBS implant released him from a paralyzing Parkinsonian tremor but induced in him an uncontrollable mania, forcing him to choose between being bedridden or institutionalized [6]. There is the obese man whose memory actually improved after receiving DBS to help control his cravings [7]. There are the cases when DBS works, and then, after several years, gradually loses its effectiveness, the last resort of an individual finally failing. These cases and others demand serious reflection about the benefits, risks, and ethical application of DBS.

As mentioned, DBS is the simplest iteration of a neural interface. The implication for the future is that DBS can only become more elaborate, more integrated, more capable of not just stimulating the brain, but interacting with it. Far more elaborate neural interfaces are used routinely in animal research, so the sophistication of DBS devices for humans could increase in leaps, and quickly, thereby increasing in their potential medical applications and in their overall power to affect the brain in complex ways. Added to these is the rise of trans-magnetic stimulation (TMS), a non-invasive, transient method of altering deep brain circuits, which potentially provides the temporary benefit of a DBS device without the commitment of implantation. As the capacity of DBS technology increases, the ethics of DBS become more similar to those of genetic engineering, as both represent the power to change fundamental biology with intricate precision. The difference is, DBS is much easier to do in people.

Abuse of such power is easily imagined. Could DBS be used to target circuits for non-medical reasons? Could there be something akin to "cosmetic" or "recreational" DBS? Could it be used on enemy combatants? It should be clear that all of these concepts have already been preemptively considered ethically wrong and, in many cases, illegal in some countries. Brain surgery can't legally be done on well people, and invasion of the mind easily falls under the classification of torture. However, the advance of technology, and the

will of individuals, can operate independently of accepted ethical codes. What eventually happens as DBS evolves can only be speculated, but it should be anticipated that the neuroethical issues of current DBS applications will be different to those of the future.

Conclusions

The preface of the book "Toward Replacement Parts for the Brain," published in 2005 but emergent from a scientific meeting held in 1999, stated that the inspiration for the meeting was "…a growing realization among neuroscientists, engineers, and medical researchers that our society was on the threshold of a new era in the field of neural prosthetics [8]." That era is now well underway. In the coming years, it is likely that the number of people with successful DBS implants will increase significantly. For many, DBS is not just the best chance at recovery, but the only option left. Its neuroethical concerns should not preclude its development, refinement and use except on an individual case basis.

As mentioned, the three groups that are driving the development of DBS technology are neuroscientists, biomedical engineers and medical practitioners. Ideally, all three should be responsible for ensuring that DBS technology is used and developed in an ethical manner. Of course, only those in the hospitals with the patients— the doctors, the hospital administrators, the medical ethicists— bear the responsibility of educating patients and evaluating DBS candidacy and success. But the larger neuroethical dialog of which DBS discussions are a part, the global conversation about the relationships between neurons, the brain, the mind, the person, even the soul, is a conversation in which all three groups should finds ways to participate. The future of DBS, and all technologies that interact with the brain for medical reasons, is an optimistic one if approached responsibly and ethically by all involved.

Biography

This article was prepared on behalf of the International Neuroethics Society as part of a special series on Neuroethics (J. Illes, Series Editor). David Sloan is a post-doctoral fellow at the West Virginia University Sensory Neuroscience Research Center. He received his doctorate in neuroscience at the University of Virginia. His research focus is sensory systems and in vivo electrophysiology.

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Please join us at the Annual Meeting of the International Neuroethics Society, October 11-12, 2012 in New Orleans. www.neuroethicssociety.org

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Editor's Column

The article in this issue (#75) of the *Carrier* begins a new and very significant series. The Ethics in Neuroscience series will be presented as a recurring feature of the *Carrier* for the foreseeable future, along with the Reviews in Neuroscience and other articles. The issue of ethics in neuroscience is of growing importance as we move further and further toward understanding how the nervous system produces our humanness and consciousness. Not only the practicing neuroscientist but importantly, our students, as well as the public in general, must begin to deal with the very challenging issues that are becoming more evident with new understandings of human behavior and brain function. David Kopf Instruments, since 2005, has sponsored the David Kopf Lecture on Neuroethics at the Society for Neuroscience annual meeting. This lecture series has been one of the most popular lectures of the meeting. The speakers have given informative and provocative lectures on various areas of neuroethics, raising questions about how the information being learned in the study of the nervous system may affect the future of mankind. This is truly one of the most pressing and underappreciated issues facing the neuroscience community.

In 2006, the Neuroethics Society was founded and in 2011, it was renamed the International Neuroethics Society (INS). This organization has as its mission "…to promote the development and responsible application of neuroscience through interdisciplinary and international research, education, outreach and public engagement for the benefit of people of all nations, ethnicities, and cultures." (from the ISN website, neuroethicssociety.org). The society actively promotes greater understanding of the ethical issues raised by neuroscience research and application, and dialog on how to meet these issues. If you are not already a member of the ISN, please consider becoming one. Members of the society will author the articles for the *Carrier* series.

In the present article, David Sloan, Ph.D. examines issues raised by deep brain stimulation in humans. It is surprising that this seemingly simple and often very beneficial procedure can have profound ethical questions attached to it. The article is thought provoking and a bit disturbing. However, such issues must be brought to the fore and opened for frank and wide discussion. If such a discussion is not held, the consequences for the future could be dire. Please keep looking for more of these articles in future issues of the *Carrier*.

Society for Neuroscience

It is almost time for the annual Society for Neuroscience meeting. It will be in New Orleans, for the first time since Katrina devastated the city in 2005. It will be great to get back to this great city and its varied sites and sounds. The Neuroethics Lecture speaker this year will be Barbara Sahakian, Ph.D. from the University of Cambridge and will be given on Monday, Oct. 15 from 10:00-11:10 am. Her lecture is titled: The Impact of Neuroscience on Society–The Neuroethics of 'Smart Drugs'. David Kopf Instruments Company is once again proud to sponsor this important lecture. Please plan to attend.

While you are at the meeting, come to the Kopf booth to say hi to the company representatives and see the largest and most varied display of the highest quality stereotaxic and related instruments in the world. Kopf has been developing these instruments for over 50 years (since 1956) and the quality is simply unmatched.

While writing this column, I am in our second home, a condo in Dublin, Ohio. We have been visiting grandchildren here and at

our older son's home just north of Detroit for about two months. Incidentally, we are visiting with their parents, too. Great fun! We are closely watching what will become hurricane Isaac that is forming in the Caribbean Sea and is predicted to move over Cuba and then to eastern Florida by early next week. We hope it does not do too much damage. By the time this is published, we will know what happened.

If you want to write an article for the *Carrier*, please see the Instructions for Authors that are available by request to kopfinsturements.com or by emailing me at drmike@earthlink.net. I would very much like to hear from you.

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