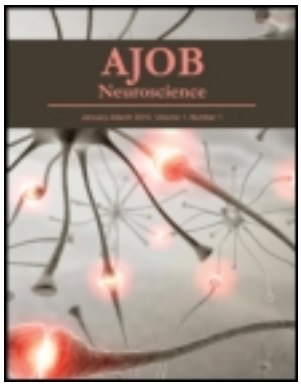

AJOB Neuroscience
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/uabn20

Research Consent for Deep Brain Stimulation in Treatment-Resistant Depression: Balancing Risk With Patient Expectations

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Published online: 13 Jan 2011.

To cite this article: Nir Lipsman , Mary Pat McAndrews , Andres M. Lozano & Mark Bernstein (2011) Research Consent for Deep Brain Stimulation in Treatment-Resistant Depression: Balancing Risk With Patient Expectations, AJOB Neuroscience, 2:1, 39-41

To link to this article: http://dx.doi.org/10.1080/21507740.2010.537295

currently emphasized for psychiatric DBS (Schlaepfer and Fins 2010), should be extended to rare and/or particularly complex neurological disorders as well, as the same core arguments apply. Thus, a skeptical deconstruction of prima facie concerns on psychiatric patients might help not only to de-stigmatize these patients, but also to sensitize our perspective on neurologic DBS and the ethical shortcomings in this field. ■

REFERENCES

Clausen, J. 2010. Ethical brain stimulation—Neuroethics of deep brain stimulation in research and clinical practice. *European Journal of Neuroscience* 32: 1152–1162.

Dunn, L. B., P. E. Holtzheimer, J. G. Hoop, H. S. Mayberg, L. Roberts, and P. S. Appelbaum. 2011. Ethical issues in deep brain stimulation research for treatment-resistant depression: Focus on risk and consent. *AJOB Neuroscience* 2(1): 29–36.

Glannon, W. 2009. Stimulating brains, altering minds. *Journal of Medical Ethics* 35: 289–292.

Kamm, C., W. Fogel, T. Wachter, et al. 2008. Novel ATP1A3 mutation in a sporadic RDP patient with minimal benefit from deep brain stimulation. *Neurology* 70: 1501–1503.

Kubu, C. S., and P. J. Ford. 2007. Ethics in the clinical application of neural implants. *Cambridge Quarterly of Healthcare Ethics* 16: 317–321.

Okun, M. S., and K. D. Foote. 2004. A mnemonic for Parkinson disease patients considering DBS: A tool to improve perceived outcome of surgery. *Neurologist* 10: 290.

Oyama, G., H. H. Fernandez, K. D. Foote, et al. 2010. Differential response of dystonia and parkinsonism following globus pallidus internus deep brain stimulation in X-linked dystonia-parkinsonism (Lubag). *Stereotactic and Functional Neurosurgery* 88: 329–333.

Racine, E., S. Waldman, N. Palmour, D. Risse, and J. Illes. 2007. "Currents of hope": Neurostimulation techniques in U.S. and U.K. print media. *Cambridge Quarterly of Healthcare Ethics* 16: 312–316.

Schlaepfer, T. E., and J. J. Fins. 2010. Deep brain stimulation and the neuroethics of responsible publishing: When one is not enough. *Journal of the American Medical Association* 303: 775–776.

Synofzik, M., and T. E. Schlaepfer. 2008. Stimulating personality: Ethical criteria for deep brain stimulation in psychiatric patients and for enhancement purposes. *Biotechnology Journal* 3: 1511–1520.

Synofzik, M., and T. E. Schlaepfer. 2010. Neuromodulation—ECT, rTMS, DBS. In *Ethics in psychiatry. European contributions*, ed. H. Helmchen and N. Sartorius, 299–320. Heidelberg: Springer.

Research Consent for Deep Brain Stimulation in Treatment-Resistant Depression: Balancing Risk With Patient Expectations

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The timely article by Dunn and colleaegues (2011) raises several pertinent issues relevant to all health care teams treating and studying patients with resistant psychiatric disease. Importantly, the article places a strong emphasis, even in its title, on deep brain stimulation (DBS) *research* rather than *therapy*, an issue clouded in other treatments of this topic. It is sometimes the case that commentaries and articles, in both the academic literature and popular press, that deal with ethical issues in psychiatric surgery conflate the potential of the technology with its current use as an almost exclusive experimental research tool, aside from a few highly studied established indications. Such a conflation

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certainly poses risks to the informed consent process, as discussed here, and may be due to high-profile coverage of early-phase surgical trials.

For several reasons, therapeutic misconception is particularly potent in research surrounding psychiatric surgery. First, psychiatric patients are more diverse, heterogeneous, and vulnerable than other neurosurgical patients, such as those with brain tumors or aneurysms. This variability requires a more dynamic approach to discussion surrounding research, as DBS is not yet a routine component of psychiatric care. As a result, risk evaluation will differ in these patients and will be colored by the nuances and idiosyncrasies of the psychiatric disease in question. For example, engaging in a hobby for a depressed patient, and touching a doorknob by a patient with obsessive–compulsive disorder, are activities that don't have the same salience as they do in psychiatrically healthy populations. As such, consenting to surgery may, in some ways, provoke less anxiety and concern than other activities. By sheer fact that inclusion criteria necessitate a failure of all accepted therapies, an emphasis should be made that surgery, such as DBS, is not an extension of the treatment regime, but rather an experimental procedure. Although refractoriness is certainly a criterion for other surgical trials for novel indications, such as DBS for epilepsy, surgery for psychiatric conditions is not a routine part of psychiatric care. Indeed, although DBS is minimally invasive neurosurgery, it is the most maximally invasive psychiatric treatment available. The seeming success of DBS for psychiatric indications in other early-phase trials, and the resultant enthusiasm for the procedure, may also drive the therapeutic misconception in DBS research. Although DBS has been in use in the movement disorder literature for more than 25 years, there has been only a recent surge in research surrounding DBS for psychiatric conditions. It is therefore important to emphasize to potentially eligible research subjects that the novelty surrounding DBS is not necessarily driven by the device itself, but by the indication for which it is being used.

Dunn and colleagues (2011) rightly allude to the idea of desperation in treatment-resistant depression patients, which is a concept that is impossible to operationalize, but not necessarily beyond empirical study. The question becomes whether patients who have exhausted all treatment options should be excluded from a study merely because they "desperately" want to be better. The answer is a clear "no," as long as patients and their caregivers understand the differing objectives of research and treatment. This understanding should be the focus of empirical research, not necessarily the operationalization or definition of "desperation."

As a first step in psychiatric surgery research, the establishment of patient competence is of paramount importance. The point by Dunn and colleagues (2011) that patients with resistant depression are not ipso facto incompetent is key and cannot be overemphasized. Indeed, depression is a thoroughly ego-dystonic condition, which in its most severe and melancholic form can be as dangerous to one's well-being and health as coronary artery disease or malignancy. Psychiatrists are trained to routinely assess competence in the face of, sometimes involuntary, medical and psychiatric care, and the evaluation of competence prior to consent to experimental surgery should be approached in the same way, with similar methodology. It is possible, however, that the inclusion of a multidisciplinary team that is involved in the care of the patient can further confound the therapy–research distinction. It has been our practice, therefore, prior to enrollment in DBS for psychiatry clinical trials, to refer eligible patients to a third-party psychiatrist, not involved in the study, to comprehensively evaluate the patient and thereby reinforce the experimental nature of the study. This accomplishes two goals: (i) It provides redundancy in diagnosis confirmation, and (ii) it suggests to the patients that there are enough unknown questions regarding surgery that additional confirmation regarding their eligibility is required. The purpose of the clinical trial is thus made clearer, facilitating an additional level of understanding for the eligible subjects, that their participation and consent are for research, not treatment.

Previous work done by our group has evaluated whether patients enrolled in chemotherapy clinical trials for brain tumors were aware of the therapy–research distinction (Knifed et al. 2008). Several themes emerged in interviews, including a generally clear and accurate understanding of the objectives of the clinical trial, as well as the belief that their *care* would not be compromised by participation. These points, particularly the latter whereby patients acknowledged that the trial was not part of routine care, confirmed to us that patients were aware they were participating in research, and not therapy. A similar approach to obtaining consent can therefore be applied prior to DBS for psychiatry research. The process then becomes an interactive interview that requires the patients to articulate their expectations and understanding of the trial's objectives. Interestingly, our study also found a minimization of risks by patients, demonstrated by a significant lack of relevant trial risk recall on prompting. Such a finding would be interesting to explore in the context of a surgical therapy in psychiatric disease, which is substantially riskier than conventional psychiatric therapy.

Such issues underscore the importance of expectation and goal management in patients undergoing psychiatric surgery research. Patients should be asked to volunteer their expectations, which could then be addressed by the research team, should these be factually incorrect and/or display a lack of recognition of probabilities given known information. Caregivers and family members as well should be involved in the process, thereby highlighting the importance of their expectations and goals as well. Psychiatric conditions affect families as well as patients, and it is clear that forces external to the patient can have a substantial impact on the trial and its outcomes. Informed consent, the discussion of risks, and the management of expectations and goals are all dynamic processes that should be repeated, the latter

in particular, throughout the trial and at every follow-up after surgery.

We have previously attempted to establish the minimum criteria that psychiatric neurosurgery clinical trials need to satisfy prior to their publication and dissemination (Lipsman, Bernstein, and Lozano 2010). Among them was a clear and transparent discussion of the risks of the trial as well as the patients' and caregivers' expectations and goals. DBS research continues globally, with several centers involved in randomized double-blind trials for psychiatric indications. As both academic and public attention is focused on neuromodulation in psychiatry, due attention needs to be paid to patient management and expecations. This will become even more important in the future, as neurosurgical procedures become safer, with the therapeutic dosage amenable to adjustment, and as their consequences become more and more reversible, as is the intention for DBS therapy, and as the risk/benefit assessment of DBS moves asymptotically toward that of medications.

The necessary involvement of a multidisciplinary research team will address the competency issue surrounding the *ability* to give consent. In addition, a dynamic, interview-type, consent process is needed to ensure that patients understand the objectives of a clinical trial in general, and of the trial in question specifically. Standard informed consent comprehension measures and questionnaires exist, but these may not be suitable for surgical interventions in a psychologically vulnerable and "desperate" population. These issues can, and should, be developed both conceptually and empirically, as it is clear that unrealistic goals and expectations could lead to misleading trial results as well as unhappy, and increasingly desperate, patients. ■

REFERENCES

Dunn, L. B., P. E. Holtzheimer, J. G. Hoop, H. S. Mayberg, L. Roberts, and P. S. Appelbaum. 2011. Ethical issues in deep brain stimulation research for treatment-resistant depression: Focus on risk and consent. *AJOB Neuroscience* 2(1): 29–36.

Knifed, E., N. Lipsman, W. Mason, and M. Bernstein. 2008. Patients' perception of the informed consent process for neurooncology clinical trials. *Neuro Oncology* 10(3): 348–385.

Lipsman, N., M. Bernstein, and A. M. Lozano. 2010. Criteria for the ethical conduct of psychiatric neurosurgery clinical trials. *Neurosurgery Focus* 29(2): E9.

They Might Retain Capacities to Consent But Do They Even Care?

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Dunn and colleagues (2011) present a balanced article, which makes the following important points about the use of deep brain stimulation (DBS) in the case of treatment-resistant major depression (TRD). They claim that the belief that depressed patients have diminished decision-making capacity due to having a mental illness is not well founded; in fact, most depressed patients retain adequate decision-making capacity. They compared desperation in TRD with other threatening illnesses, to arrive at the conclusion that it is not necessary to have special safeguards to insure an adequate informed consent process. They also argue that ethical issues about informed consent are not different from other higher risk studies or to other "equally distressing, disabling, treatment-refractory conditions" (Dunn et al. 2011). Dunn and colleagues conclude by suggesting that more empirical evidence is needed in order to assess the ethical issues of DBS for TRD patients. They recommend a broader research agenda involving additional measures to assess decision-making capacity in TRD patients.

Let us start with the issue of diminished decision-making capacity. Dunn and colleagues conclude that "depressed patients in general do not prima facie have significantly impaired decision-making capacity" (Dunn et al. 2011). However, this conclusion seems to be the payoff from reducing decision-making capacities to a certain set of intellectual and rational abilities. One consistent conceptual difficulty in this area is to define *decision-making capacities*, a task that Dunn and colleagues seem to equate with the legally relevant intellectual capacities and abilities to consent, such as an ability to state a choice, understand relevant information, appreciate the nature of one's own situation, and evaluate information (Appelbaum and Grisso 2004). In the case of TRD patients' assessment of decision-making capacity, it might be useful to reconsider the weight given

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