



Deep Brain Stimulation: Paradoxes and a Plea

Judy Illes

To cite this article: Judy Illes (2012) Deep Brain Stimulation: Paradoxes and a Plea, AJOB Neuroscience, 3:1, 65-70, DOI: [10.1080/21507740.2011.635629](https://doi.org/10.1080/21507740.2011.635629)

To link to this article: <http://dx.doi.org/10.1080/21507740.2011.635629>



Published online: 05 Jan 2012.



Submit your article to this journal [↗](#)



Article views: 144



View related articles [↗](#)

Article

Deep Brain Stimulation: Paradoxes and a Plea

Judy Illes, University of British Columbia

Deep brain stimulation (DBS) represents a promising new frontier in medicine and neuroscience for managing disorders of mental health that represent an enormous burden of disease on our societies. The caution and significant restraint of leaders in the evolution of DBS today stand in sharp and refreshing contrast to previous episodes in history. In embracing the anticipatory and pragmatic problem-solving approach of neuroethics to clinical neuroscience, four significant paradoxes for DBS today come to the fore: caution and innovation, capacity and allocation of resources, notions of wellness and disease, and the high-stakes/high-benefit imperative of communicating about science. Tackling these paradoxes is the focus of this article.

Keywords: deep brain stimulation, neuroscience, neurotechnology

As Joseph J. Fins (2011) wrote in the recent *Oxford Handbook of Neuroethics* (Illes and Sahakian 2011), “If there is a unifying theme to neuroethics, . . . it is the predominance of technology. Neuroethics is both made necessary by technology and utterly dependent upon it. Without resort to hyperbole, it could be asserted that neuroethics is essentially an ethics of technology.”

Deep brain stimulation (DBS) is a case study for Fins’s assertion. DBS represents a promising new frontier in medicine and neuroscience, an invasive, high-maintenance, last-resort strategy for managing disorders of mental health, such as major depression and obsessive compulsive disorder that represent an enormous burden of disease on our societies (Menken et al. 2000).

Psychosurgery is one of the comeback kids in the history of medicine. This history is marked by countless good intentions but marred by sometimes reckless applications and unexpected effects of new ideas, with significant adverse consequences for recipients who were often both vulnerable and ill-informed about the risks of the treatments they agreed to undergo. The early days of x-ray use, when the harmful effects of radiation were unknown and the opportunities to obtain an image of the body were readily available at cocktails parties, Boys Clubs, and shopping locations such as Bloomingdales, is an example from this vast history (Kevles 1997). The widespread dissemination of prefrontal leucotomies offered from hotel rooms by Walter Freeman represents another dark stain, highlighting the danger of institutional practices that allow an individual practitioner’s belief in benefit to trump reasoned and objective assessment of outcome (Horne 2009).

The caution and significant restraint of leaders in the evolution of DBS today stand in sharp and refreshing contrast to such episodes (Rabins 2009; Schlaepfer et al. 2010). They model neuroethics alive: a commitment to getting it right, ethically, medically, and socially. Not unexpectedly, the entrepreneurial community is less patient: Some among it have already moved beyond the point of exploration and on to billboards for advertisement. With the history for psychosurgery behind it and in this modern climate of direct-to-consumer sales of health products for either the curious or the unwell, the imperative exists for the development and dissemination of well-defined goals and a transparent ethical framework that are jointly articulated by the scientific and ethics communities. “To safeguard . . . this hopeful development” of DBS (T. Schlaepfer, in Expert Workshop 2011), recommendations for regulations must be pragmatic, flexible, and responsive to the fast-moving science, reasonable to the commercial sector, and relevant to the international community across which research, clinical trials, and ultimately translation will take place.

Although neuroethics vigorously espouses anticipatory and proactive thinking for problem solving in clinical neuroscience (Racine 2010), its approach to guiding, regulating, and holding to account DBS research will be best served by emphasizing both the need to reiteratively examine the possible ways in which we could be repeating (even if in a more benign form) the mistakes of the past rather than simply disavowing a horrifying past, and applying those to the future. In doing so, significant paradoxes come to the fore. Their resolution will be the key to solutions. Here are a few:

This article is based on the author’s summary comment at the Expert Workshop “Deep Brain Stimulation in Psychiatry,” in Bonn, Germany, January 20–21, 2011. Many thanks to Dr. Louise Whiteley for valuable insights on this article and to Ania Mizgalewicz for editorial assistance. The author’s work related to this material is supported by the Canada Research Chairs Program, CIHR/INMHA number CNE 85117, and by NIH/NIMH R01MH84282-06.

Address correspondence to Judy Illes, Ph.D., National Core for Neuroethics, Division of Neurology, Department of Medicine, The University of British Columbia, 2211 Wesbrook Mall, Koerner S124, Vancouver, BC V6T 2B5, Canada. E-mail: jilles@ubc.mail.ca

CAUTION AND INNOVATION

There are few who do not shudder when reminded of the runaway application of psychosurgery in the 1920s, the use of thorazine in the early 1950s (Kirkby 2005), and of proposals in the 1960s to use psychosurgery to manage social unrest (Illes and Bird 2006; Valenstein 1986). It is important to remember, however, that leucotomy was first introduced by António Egas Moniz (1874–1955), a Portuguese neurologist, as “‘a great and desperate’ attempt to find effective treatment for severe forms of mental illness for which there was at the time no effective treatment at all” (Abimbola 2006). In 1963, José Manuel Rodríguez Delgado, a Spanish neurophysiologist, implanted stimoceivers in the brains of fighting bulls. Standing in the ring with one bull at a time, Delgado would halt the charge of a bull with the press of a button via external stimulation of the caudate nucleus (Fins 2003; Horgan 2005)—a further dramatic demonstration of the desire and potential to manipulate behavior and modulate the mind through direct intervention in the brain.

This is the stage on which DBS must perform and against which, for medical efficacy and social and ethical evaluation, its performance will be measured. The cautions provided by these high-profile examples are profound, yet beyond them are the thousands of other experiments with animal models and human subjects that have yielded fundamental insights into brain–behavior relationships in addiction, learning, and memory and species-appropriate forms of executive function (Gazzaniga 2004). Over time, and while much work remains to be done, the collective knowledge afforded by such studies has advanced the management of and mitigated suffering from many diseases of the central nervous system. In work by Mayberg and colleagues (Mayberg 2009; Mayberg et al. 2005), results are providing strong evidence for the promise of DBS at area 25 of the subgenual cingulate region for mood and anxiety disorders. Lozano and his colleagues (Laxton et al. 2010) have early data hinting at positive effects for Alzheimer’s disease with stimulation of the fornix. So, while some commentators may lean to the side of caution and recoil at the idea that psychosurgery may one day be reintroduced into clinical practice, the alternative is to use that caution for the benefit of the innovation. Rather than fear the future of neurosurgical interventions, we can harness the existence of cautions to be a positive force, and one we can direct: one that promotes a self-regenerating process and where each step along the innovation pathway presents a benchmark against which progress and failure of effectiveness, of reasonableness, and of ethical acceptability are measured continuously.

A FERRARI FOR THE MOST DISABLED?

Candidates for DBS are a special class of patients. To qualify for trials, they must suffer from a condition that is refractory to all other interventions (Kennedy et al. 2011; Lozano et al. 2008; Rabins et al. 2009). Except for those who are at risk of suicide and excluded from eligibility, the highest benefitters are also those who represent the highest scientific risk for

research. In prospective recipients, accordingly, this entails a paradox. The research places the demands of hardware upkeep and compliance with ongoing mental health support on individuals who have exhibited variable and sometimes limited ability over time to manage even the simplest aspects of daily life. Will newly found mental wellness be naturally accompanied by the motivation needed to uphold the requirements of ongoing maintenance that accompany this therapy? Whether or not this is the case, will patients be permitted to ease into this new mental status or take a break from the stimulation to regroup and recalibrate? How will implanted devices be managed longitudinally as these patients age mentally and physically?

Entangled with this paradox are particularly complex issues surrounding informed consent. Requirements for disclosures are well trodden: They need to include the potential consequences of DBS, information about participation in other research, warnings about interactions with other treatments, and specific language about discontinuation of treatment, all while avoiding exculpatory language (Mathews et al. 2010; Rabins et al. 2009). Discussions surrounding the topic of who has the capacity to consent to DBS have entailed questions about the individual assessment of adults, the appropriateness of enrolling children, and recommendations versus requirements for third-party involvement in decision making (Lipsman and Lozano, in Expert Workshop 2011). Still, neurons are not people, and synapses are not interconnected lives. The fact that DBS may effectively alleviate underlying symptoms of disease but not provide a cure is difficult to explain in the often mechanistic process of consent. Moreover, this distinction may also be less meaningful, if not merely a nuance, for refractory patients who are often desperate for relief.

There is also a well-known inverse relationship between the length of protocol descriptions, disclosures for transparency and risk management, and the effectiveness of information uptake in the consent process (Sachs et al. 2003). As measured by recall error, for example, a longer process of consent does not equate with more understanding. The combination of technical complexity and high levels of patient vulnerability, which characterizes informed consent for DBS procedures, is a force that taxes both givers and receivers of information and makes communication about risks and benefits, warnings and hopes, and research and therapy highly problematic. If, as Morse suggests (in Expert Workshop 2011), the already cumbersome processes of consent for DBS are still inadequate and necessitate a new form of hyperdisclosure, then new mechanisms or vehicles are needed too. Staged consent may be one solution, as others have demonstrated with populations such as cancer patients and children (Angiolillo et al. 2004; Edner et al. 2007; Lavori et al. 1999; Wade et al. 2009). Perhaps multimedia, video-based information, or messaging using social media to support an ongoing and interactive consent process, will provide other viable options. None of these strategies will displace conventional person-to-person contact and follow-up, but they might help to mitigate complacency or pessimism about the potential for betterment

that can accompany the chronic disorders of mental health at the focus of DBS (Dunn, in Expert Workshop 2011). As is already being explored more generally in health care delivery, similar innovations may also provide effective support for inter-session cognitive-behavioral therapy, provide reminders of appointments, and ensure battery (fuel in the tank) and other hardware checks.

BETTER TODAY, BETTER TOMORROW?

In the midst of an economic downturn, with all its associated challenges for maintaining employment and quality of life, and in the context of rampant stigma and discrimination against those who suffer from mental illness (Angermeyer et al. 2004), getting well, or getting even better, is not a linear process. Wellness is a dynamic of physical and mental well-being, and the extent to which the environment is supportive and welcoming will be a significant factor in determining where along the continuum of possible outcomes a person treated with DBS falls. While quantitative metrics such as Hamilton Depression Scores (Hamilton 1960) may signal improvement in mood and cognition, the subjective experience of an individual with a diagnosis of depression may be discordant with such measures. Composite evaluation strategies that account for the broader psychosocial context of recipients are therefore vital. Kubu and colleagues (in Expert Workshop 2011) are well on the way to delivering these, highlighting a metric of evaluation that takes into account not only the experiences and perception of the person treated, but also the views and expectations of the people in the patient's world—the network of families and providers along the full corridor of health care. The wheels of change may be turning for an individual patient in the ongoing DBS journey, and a closed loop of broad-based and well-coordinated interventions is needed to ensure that the wheels all turn over the long term in the same direction.

COMMUNICATING WITH THE PUBLIC: HIGH RISK, HIGH REWARD

Communicating about research with the public is an ethical duty, especially for investigators who are supported by public funds, and can be considered a neuroethics one in the context of neuroscience (Racine et al. 2010). Tensions between hype and hope in media reporting may seem like an old hat for neuroscience, but their presence in the context of psychosurgery, whether for treating pathology or surrounding the neurofantasy of creating supercognitive humans, is far from trivial.

On the one hand, there is good news. During the last 30 years, successful strategies to improve communications building on trust and reciprocal engagement between scientists and journalists have been implemented. From one study involving more than 1300 researchers across five countries, Peters and colleagues (2005) reported a high rate of interaction between biomedical scientists and the media, and high satisfaction ratings of these interactions. On the other hand, neuroscientists still report that they experience

frustration with the press, with sound bites and headlines, and with alterations being made to text that has been previously fact-checked.

In a small survey study of our own of a convenience sample of 600 neuroscientists, whose work spans the academic and scientific range of the professional community (Robillard and Illes 2011), 34% of those who responded ($n = 73$) reported that advances in brain research are poorly (29%) or very poorly (5%) communicated. One respondent commented: "Research tends to be oversimplified and sensationalized, . . . but 'real' science probably doesn't sell." Moreover, 44% of those who responded ($n = 73$) indicated that their efforts to communicate about their research to the public were not valued by their institution. The rewards of public visibility may be personally gratifying and professionally beneficial when successful, but it is not the case that no press is bad press: When information disseminated is erroneous or misleading, few institutional protections exist. In parallel, journalists often are frustrated by scientists' reluctance to speak candidly about their findings and their lack of skill in doing so. In 2009, colleagues and I who gathered at a workshop on this subject in Banff, Alberta, proposed greater cooperation between academia and media through a shift that might move players outside their comfort zones and away from easy assumptions about scientists and journalists. Our work led to an explicit encouragement of high-quality interactive and communication products, identification of neuroscience communication specialists, and the creation of a roadmap to new empirical research on neuroscience communication (Illes et al. 2010). For DBS specifically, Bell et al. (2009) have appropriately argued for a specific focus on the impact that media has on patient knowledge and goals and patient-physician relationships, and for public engagement to improve public understanding. It is also especially important to address challenges of communication in the social media environment that has opened the world up to volumes of uncurated information available at unprecedented speed.

EPILOGUE

Much has been written about research ethics in DBS by practitioner and allied health care communities looking reflectively, the outside community peering in, and through the partnership of both. In addition to the largely unresolved issues I have touched upon in this article from this literature, there is general consensus that DBS research should be performed only at centers with specific expertise, and by multidisciplinary teams working together closely. As Hariz and colleagues (2010) suggest, gone by is the era of DBS done by the solo practitioner. There have also been calls for a centralized archive of procedures and outcomes, akin to calls and the creation in some cases for archives or banked genetic data, neuroimaging scans, and even incidental findings. The realization of both would further allow DBS research today to stand apart from its historical roots where protection of humans was not achieved. Existing guidelines for research and translational partnerships between

members of the academy and industry are not sufficient for this new application, where such relationships are not just necessary, they are inevitable; they must not, however, place the collection of valuable data or patient safeguards in jeopardy (Fins and Schiff 2010; Fins et al. 2011).

Where less discussion exists is in the area surrounding administrative load and other barriers to research associated with institutional compliance to ethics procedures. Tairyan and colleagues (2010) and Racine and colleagues (2011) have shown that this is a particularly acute problem for investigators whose work, such as for DBS, relies on neuroimaging. While recommendations for remedies such as the development and dissemination of best practices and standardized ethics review for neuroimaging are ongoing (Kehagia et al. 2011), they still need to be implemented, tested, and refined based on rigorous measures of outcome.

Other areas prime for further exploration are the extension of the knowledge and capabilities afforded by DBS to new targets and indications, new developments in DBS and associated technologies, and longitudinal effects and acceptance of DBS interventions. Similarly, the interaction of DBS treatment with the question of how biological models of mental illness interact with stigma (Borgelt et al. 2010), coercive uses or uses in the criminal system in possible analogy to ethics discussion around chemical castration (Scott and Holmberg 2003), unintended effects (depression improved/pedophilia unleashed?), and frank advertising and consumerism are areas wide open for discovery. The latter, for example, may promote autonomy and a sense of empowerment, but is laden with challenges seen in other areas where access to medical technology has been advanced in the open marketplace. There is no shortage of bold messages about saving life “before it is too late” that prey on fear and the most vulnerable (Illes et al. 2004).

The meeting around which this special section of *AJOB Neuroscience* is constructed was held in Bonn, Germany, the home of Ludwig van Beethoven. His music fell between an era of Classicism, characterized by order and hierarchy, and Romanticism, characterized by innovation and expression. This is an intermediate-period description that fits nicely to the current state of DBS. The new science is exquisite, methodical, and careful. It has provided a strong footing for the coming generation that is rich with enthusiasm, creativity, and promise. With it, we need to heed the lessons of the past and harness what we have learned to move ahead. We need to develop measurement and assessment tools where they are currently missing, harmonize them for cross-national collaborations, and gain traction on the concept of benefit from different cultural perspectives. To do this, we also need to seek guidelines that are relevant to countries whose human ethics processes differ and embark on partnerships with them. Perhaps we need to even consider going wireless.

Let’s not get waylaid by rhetoric or foolish traps that would move our attentions to the cosmetic creation of the hyper-intelligent or age-resistant human. In weighing the

state of the art today in research with risk and benefit, DBS to reverse or mitigate depression, OCD, or movement disorders such as Parkinson’s, a “yes”; addiction or the progression of Alzheimer’s Disease, perhaps yes, eventually (Carter and Hall 2011); DBS to prolong life to the age of Methuselah (Illes 2007), no. Consider the short time in 1904 when researchers in California and New York toyed with the idea of using x-rays for the improvement of the skin color of African Americans. They combined x-ray treatment with radium to “turn the complexion of the blackest man to a beautiful, soft, creamy white color” (Di Santis 1991, as cited in Kevles 1997). This is one episode in medicine best left to the history books, and one to keep us focused on disease and not distracted by manufactured problems derived from social constructs.

There is plenty of work to be done with DBS to reduce human suffering, and to ensure that the positive benefits for mental health endure in the harsh and cynical Western societies that appear, at least to some extent, to be able to afford it. In the *Oxford Handbook of Neuroethics*, Fins (2011) concludes with reference to C. P. Snow’s prescient comment: “Technology, remember, is a queer thing; it brings you great gifts with one hand, and it stabs you in the back with the other” (Lewis 1971). In considering the future of DBS, let’s remember that the villains of the past are not straw men of today—we are fully accountable for the steps we take. Let’s keep our eyes open and focused on the technological gifts that might one day bring real relief to the sufferers.

REFERENCES

- Abimbola, S. 2006. The white cut: Egas Moniz, lobotomy, and the Nobel prize. *BMJ Archives* 14: 1–44.
- Ambert, A. 2009. Divorce: Facts, causes and consequences. *Contemporary Family Trends* 3: 1–39.
- Angermeyer, M. C., M. Beck, S. Dietrich, and A. Holzinger. 2004. The stigma of mental illness: Patients’ anticipations and experiences. *International Journal of Social Psychiatry* 50: 153–162.
- Angiolillo, A. L., C. Simon, E. Kodish, et al. 2004. Staged informed consent for a randomized clinical trial in childhood leukemia: Impact on the consent process. *Pediatric Blood Cancer* 42: 433–437.
- Barfield, R. C., and C. Church. 2005. Informed consent in pediatric clinical trials. *Current Opinion in Pediatrics* 17(1): 20–24.
- Bell, E., G. Mathieu, and E. Racine. 2009. Preparing the ethical future of deep brain stimulation. *Surgical Neurology* 72(6): 577–856.
- Borgelt, E., D. Buchman, and J. Illes. 2010. “This is why you’ve been suffering”: Reflections of providers on neuroimaging in mental health care. *Journal of Bioethical Inquiry*. doi: 10.1007/s11673-010-9271-1: 1–15.
- Carter, A., and W. Hall. 2011. Proposals to trial deep brain stimulation to treat addiction are premature. *Addiction* 106(2): 235–237.
- DiSantis, D. J. 1991. Wrong turn on radiology’s road of progress. *Radiographics* 11: 1121–1138.

- Edner, M., A. Yamokoski, P. Wittman, and E. Kodish. 2007. Improving informed consent: Suggestions from parents. *Pediatrics* 119(4): e849–e859.
- Expert Workshop, “*Deep Brain Stimulation in Psychiatry.*” 2011. Bonn, Germany, January 20–21.
- Fins, J. J. 2003. From psychosurgery to neuromodulation and palliation: History’s lessons for ethical conduct and regulation of neuropsychiatric research. *Neurosurgery Clinics of North America* 14(2): 303–319.
- Fins, J. J. 2011. Neuroethics and the lure of technology. In *The Oxford handbook of neuroethics*, ed. J. Illes and B. J. Sahakian, 895–907. Oxford, UK: Oxford University Press.
- Fins, J. J., and N. D. Schiff. 2010. Conflicts of interest in deep brain stimulation research and the ethics of transparency. *Journal of Clinical Ethics* 21(2): 125–132.
- Fins, J. J., H. S. Mayberg, B. Nuttin, et al. 2011. Misuse of the FDA’s humanitarian device exemption in deep brain stimulation for obsessive-compulsive disorder. *Health Affairs* 30(2): 302–311.
- Gazzaniga, M. 2004. *The cognitive neurosciences* 3, 3rd ed. Cambridge, MA: MIT Press.
- Hamilton, M. 1960. A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry* 23: 56–62.
- Hariz, M. I., P. Blomstedt, and L. Zrinzo. 2010. Deep brain stimulation between 1947 and 1987: The untold story. *Neurosurgical Focus* 29(2): e1.
- Horgan, J. 2005. The forgotten era of brain chips. *Scientific American* 293(4): 66–73.
- Horne, J. 2009. Frontal assault. *Biologist* 4: 221–224.
- Illes, J. 2007. Blurring our edges: A review of books by J. Harris and A. De Grey. *Nature* 450: 351.
- Illes, J., and S. J. Bird. 2006. Neuroethics: A modern context for ethics in neuroscience. *Trends in Neurosciences* 29(9): 511–517.
- Illes, J., and B. K. Sahakian. 2011. *The Oxford handbook of neuroethics*. Oxford: Oxford University Press.
- Illes, J., D. Kann, K. Karetsky, et al. 2004. Advertising, patient decision-making, and self-referral for computed tomographic and magnetic resonance imaging. *Archives of Internal Medicine* 164(22): 2406–2408.
- Illes, J., M. A. Moser, J. B. McCormick, et al. 2010. Neurotalk: Improving the communication of neuroscience research. *Nature Reviews Neuroscience* 11(1): 61–69.
- Kehagia, A. A., K. Tairyan, C. A. Federico, G. H. Glover, and J. Illes. 2011. More education, less administration: Reflections of neuroimagers’ attitudes to ethics through the qualitative looking glass. *Journal of Science and Engineering Ethics*. doi: 10.1007/s11948-011-9282-2.
- Kennedy, S. H., P. Giacobbe, S. J. Rizvi, et al. 2011. Deep brain stimulation for treatment-resistant depression: Follow-up after 3 to 6 years. *American Journal of Psychiatry*. 168: 455–456. doi: 10.1176/appi.ajp.2010.10081187.
- Kevles, B. H. 1997. *Naked to the bone*. New Brunswick, NJ: Rutgers University Press.
- Kirkby, K. C. 2005. Social context and health consequences of the antipsychotics introduction. *Annals of Clinical Psychology* 17(3): 141–146.
- Lavori, P., J. Sugarman, M. Hays, and J. Feussner. 1999. Improving informed consent in clinical trials: A duty to experiment. *Controlled Clinical Trials* 20(2): 187–193.
- Laxton, A. W., D. F. Tang-Wai, M. P. McAndrews, et al. 2010. A phase I trial of deep brain stimulation of memory circuits in Alzheimer’s disease. *Annals of Neurology* 68(4): 521–534.
- Lewis, A. 1971. Dear Scoop Jackson. X-ray to turn black men white. From: *New York American*. December 28, 1903. Available at: <http://select.nytimes.com/mem/archive/pdf?res=F30A11F73454127B93C7A81788D85F458785F9>
- Mathews, D. J. H., P. V. Rabins, and B. D. Greenberg. 2011. DBS for treatment-resistant neuropsychiatric disorders. In *The Oxford handbook of neuroethics*, ed. J. Illes and B. J. Sahakian, 441–454. Oxford, UK: Oxford University Press.
- Mayberg H. S. 2009. Targeted electrode-based modulation of neural circuits for depression. *Journal of Clinical Investigation* 119(4): 717–725.
- Mayberg, H. S., A. M. Lozano, V. Voon, et al. 2005. Deep brain stimulation for treatment-resistant depression. *Neuron* 45(5): 651–660.
- Menken, M., T. L. Munsat, and J. F. Toole. 2000. The global burden of disease study: Implications for neurology. *Archives of Neurology* 57(3): 418–420.
- Peters, H. P., D. Brossard, S. de Cheveigné, et al. 2008. Science communication. Interactions with the mass media. *Science* 321(5886): 204–205.
- Rabins, P., B. Appleby, J. Brandt, et al. 2009. Scientific and ethical issues related to deep brain stimulation for disorders of mood, behavior, and thought. *Archives of General Psychiatry* 66(9): 931–937.
- Racine, E. 2010. *Pragmatic neuroethics: Improving treatment and understanding of the mind-brain*. Cambridge, MA: MIT Press.
- Racine, E., S. Waldman, J. Rosenberg, and J. Illes. 2010. Contemporary neuroscience in the media. *Social Science & Medicine* 71: 723–733.
- Racine, E., G. Northoff, R. Menon, J. Kimmelman, and J. Illes. 2011. A Canadian perspective on ethics review and neuroimaging: Tensions and solutions. *Canadian Journal of Neuroscience* 38(4): 572–579.
- Robillard, J. M. and J. Illes. 2011. Lost in translation: Neuroscience and the public. *Nature Reviews Neuroscience*. 12: 118. doi: 10.1038/nrn2773-c2.
- Sachs, G. A., G. Hougham, J. Sugarman, et al. 2003. Conducting empirical research on informed consent: Challenges and questions. *IRB: Ethics and Human Research* 25(5): S4–S10.
- Schlaepfer, T. E., S. H. Lisanby, and S. Pallanti. 2010. Separating hope from hype: Some ethical implications of the development of deep brain stimulation in psychiatric research and treatment. *CNS Spectrums* 15: 285–287.
- Scott, C. L., and T. Holmberg. 2003. Castration of sex offenders: Prisoners’ rights versus public safety. *Journal of American Academic Psychiatry Law* 31(4): 510–513.

Tairyan, K., C. Federico, A. Tabet, G. Glover, and J. Illes. 2010. Reducing barriers to ethics in neuroscience. *Frontiers in Human Neuroscience* 4(167): 1–5.

Valenstein, E. S. 1986. *Great and desperate cures: The rise and decline of psychosurgery and other radical treatments for mental illness*. New York: Basic Books.

Wade, J., J. Donovan, J. A. Lane, D. Neal, and F. Hamdy. 2009. It's not just what you say, it's how you say it: Opening the 'black box' of informed consent appointments in randomized controlled trials. *Social Science and Medicine* 68: 2018–2028.