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PEER REVIEWED SUBMISSION

Ethical Issues in Psychiatric Applications of Deep Brain Stimulation: Learning from Canadian Healthcare Providers

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ABSTRACT

Objective and Methods: The potential ethics issues for Objective and Methods: The potential ethics issues for the investigational use of deep brain stimulation (DBS) in psychiatric conditions have been the subject of discussion in neurosurgery and bioethics. We examined the perspectives of healthcare providers (HCPs) working in DBS teams on ethical and social issues for the use of DBS in psychiatric disorders.

Results and Discussion: We identified some shared ethics concerns (e.g., informed consent, selection of research subjects) between Canadian HCPs in our study and the international literature. We also identified new ethical considerations (e.g., the psychosocial context of psychiatric illness, and resource allocation challenges) important to providers in the Canadian context but barely captured in current guidance.

Conclusions: Promising demonstrations about the potential therapeutic efficacy of DBS for refractory psychiatric patients should be matched with a flexible and dynamic ethics process which takes into account a range of experiences and perspectives from stakeholders, and promotes ethically responsive practices to an evolving field of interdisciplinary clinical practice.

Key words: *Deep brain stimulation, psychiatric disorders, ethics, resource allocation, stigma.*

INTRODUCTION

Over time, proposed uses of deep brain stimulation (DBS) have changed and approved indications have evolved as evidence of efficacy and safety has accrued (Benabid, 2007). Today, DBS is approved and used primarily to treat and control severe motor symptoms in disorders such as Parkinson's disease, where it has been shown to improve both motor symptoms and overall quality of life for patients (Weaver et al, 2009; Williams et al, 2010). More recently, promising results from small research trials (Nuttin et al, 2003; Mayberg et al, 2005; Schlaepfer & Lieb, 2005; Greenberg et al, 2006; Lozano et al, 2008; Nuttin et al, 2008; Malone et al, 2009) (for a review see Lakhan & Callaway, 2010), have prompted further examination of the effectiveness of DBS in treating carefully selected refractory psychiatric patients, suffering from depression or obsessive compulsive disorder. In some cases this has resulted in the application of DBS for "humanitarian use" (FDA, 2009).

Accompanying the investigational use of DBS for psychiatric disorders has been a swift attention to ethical concerns by scholars

in the fields of bioethics, psychiatry, and neurosurgery. A number of specific issues have been discussed in the literature including the potential impacts of DBS on narrative identity (Schechtman, 2010) and personality (Synofzik & Schlaepfer, 2008), the decision-making capacity of refractory psychiatric patients (Glannon, 2008) and the necessary conditions for informed consent (Glannon, 2010; Dunn et al, 2011) as well as on the risks of selective publication of individual applications of DBS (Schlaepfer & Fins, 2010). There has also been more general guidance specifying criteria for carrying out ethically sound psychiatric DBS trials (Synofzik & Schlaepfer, 2008; Kuhn et al, 2009; Lipsman et al, 2010;

Malone, 2010; Carter et al, 2011; Hall & Carter, 2011) and some consensus statements developed by experts about the significance and handling of current and future potential ethics issues (Nuttin et al, 2003; Rabins et al, 2009).

Even in the standard practice of DBS in movement disorders, Canadian healthcare providers (HCPs) have brought forward some unique perspectives about ethical and social challenges in the field (Bell et al, 2010). At the same time, Canadian researchers have contributed to international discourses (Glannon, 2008; Bell et al, 2009; Glannon, 2010; Lipsman et al, 2010), and generated recent guidance regarding ethical issues in psychiatric trials of DBS (Lipsman et al, 2010), even leading a survey study of North American functional neurosurgeons on the topic (Lipsman et al, 2011). However, no made for Canada tailored guidance in this area exists, although academic centres in Canada are involved in emerging psychiatric trials for DBS, and at times are at the forefront of investigating novel applications of DBS.

Our qualitative study of HCP perspectives in Canada on ethical and social issues in the use of DBS in psychiatric disorders examined Canadian perspectives and how they may reflect similar or different concerns in comparison to international perspectives and the literature on the topic of ethics in psychiatric DBS. We consider this an important bridge to understanding how DBS HCPs themselves, across different disciplines (nursing, neuropsychology, neurosurgery, neurology), define and tackle ethical questions in the practice of psychiatric trials of DBS.

METHODS

An invitation to participate in the study was sent (by email) to HCPs in active DBS centers in Canada. Only centers which were identified as being active in performing DBS, and who were engaged in or had some exposure to the use of DBS for psychiatric disorders were included. We identified participants with the help of local investigators affiliated with DBS programs in Canada and through web searches for neurostimulation programs in Canada. Unfortunately, because participants were invited to participate often based on their identification by local investigators, this open recruitment strategy did not enable us to determine how many potentially appropriate candidates were not invited to participate or how many candidates were approached about the study by local investigators and declined participation.

HCPs in the study completed a semi-structured interview with a member of the research team. The general aim of the interview was to characterize HCP perspectives on a range of ethical and social issues in functional neurosurgery using neurostimulation, including the use of DBS for psychiatric disorders. Topics included informed consent for DBS in psychiatric patients, patient selection in psychiatric trials, resource allocation and the management of patients, and the potential use of DBS for mood or cognitive enhancement purposes.

The audio recorded interviews were first transcribed verbatim and then analyzed based on a conventional thematic qualitative content analysis approach (Hsieh & Shannon, 2005). A coding guide was elaborated to support the content analysis in which common issues from the interviews were grouped together. The coding guide was developed based on several rounds of

test coding to ensure validity and consistency. Final coding involved achieving consensus between the primary and secondary coder, and included arbitration by a third coder in difficult cases.

Research ethics approvals were obtained prior to the beginning of this study for each targeted site, and informed consent was received from all HCPs prior to participation. The identity of participants was protected by an alpha-numeric code system where the letter identifies the site they belong to and the number indicates the order in which they were recruited at each site (i.e., A1, B2). When reporting qualitative content we use the annotation of "…" to indicate that we have removed a portion of a sentence. Small edits to quotes were made to improve readability.

RESULTS

We report results from five Canadian sites and 20 HCPs from a variety of specialties, including neurology (N=4), neurosurgery (N=4), psychiatry (N=2), nursing (N=2), occupational therapy (N=1), neuropsychology (N=5) and clinical neurosciences and neurophysiology (N=2). We acknowledge that the results of this study represent the perspectives of a small number of participants and HCPs in the field of DBS. Because our study was designed to collect perspectives related to the investigational uses of DBS, our recruitment was limited to major academic centers and recruitment was therefore centered across 6 sites covering 6 provinces in Canada. Although the sample size is small and this limits the representativeness of the perspectives reported in the study there are a limited number of DBS programs in Canada involved in these experimental uses. Moreover, many programs are composed of small

numbers of specialized members and some HCPs are not solely affiliated with neurostimulation programs (i.e., nurses and neuropsychologists). Nevertheless, our data assembles the perspectives and experiences of HCPs on ethical challenges in emerging psychiatric indications of DBS, such as depression and OCD. We report these perspectives under the topics of (1) designing and funding research trials; (2) enrollment and selection of research subjects; (3) informed consent; (4) safety and efficacy of DBS; (5) understanding the relationship between DBS and a biological basis for mental illness; (6) long term management of patients; (7) resource allocation; (8) contextual features of mental illness; and (9) mood and cognitive enhancement. Other non-overlapping

results of this study have been published elsewhere (Bell et al., 2009; Bell et al., 2011).

Designing and funding research trials

HCPs discussed issues related to the design and funding of research trials in psychiatric indications of DBS. Several ethically-salient obligations were judged to be present in the conduct of research (Table 1). Advocating for double-blind trials initiated on the basis of pre-clinical and clinical theoretical work to inform stimulation targets, HCPs stressed that one of the key goals of trials should be to clarify the potential role of placebos in patient response and to identify factors and characteristics which delineate patients who do and do not respond to DBS. One of the key challenges in fulfilling these ethically salient obligations was that public funding of the research was either impractical (too costly to fund) or unavailable. As a result, HCPs reported having to partner with industry in order to fund DBS trials, although they acknowledged that, in this scenario, there are often disparities between the overall goals of research; for industry this goal may be profit, and for researchers it may be producing valuable knowledge.

Table 1: Ethically salient issues in designing and funding research trials in emerging psychiatric indications of DBS

Study design
Generating research studies based on sound and explicit theoretical foundations.
Designing rigorous double-blind trials to ON and OFF stimulation.
Designing trials to identify the absence or presence of a placebo effect.
Gathering evidence to identify characteristics predictive of patient response.
Research Funding
Working with industry to ensure funding of trials.
Acknowledging and mitigating potential conflicts of interest in industry funded trials.
Advocating public funding bodies to increase funding for trials.

Enrollment and selection of research subjects

HCPs emphasized the importance of enrolling and selecting appropriate research subjects for participation in psychiatric trials. Confidence about the accuracy of diagnosis and the history of patients' illnesses was judged essential. HCPs diverged in the way they described the severity of patient's illness and how this impacted eligibility for DBS surgery. Some described appropriate psychiatric DBS research participants as being at a stage of last resort (e.g., "it's the last resort" (A3)). Interestingly, the same HCP also mentioned how some severe patients may also have demonstrated suicidal ideation ("It's not mild depression, it's not even moderate, it is suicidal ideation" (A3)). HCPs commonly spoke about the refractoriness of the psychiatric

condition as an inclusion criterion for participation in trials. However, definitions of "refractory illness" varied between HCPs (e.g., "all therapies", "several therapies", "a minimum of 5 treatments", "adequate trials including pharmacotherapy, psychotherapy and ECT", the illness being "absolutely not reversible"). A few HCPs spoke about the very poor quality of life of research participants, "patients are very sick – those are debilitating disorders and the quality of life of these patients is severely compromised" (B3). A final observation was how slow the process can be to recruit and enroll appropriate research subjects to DBS trials. One HCP stated that in a three year span, they only recalled seeing one participant registered in a DBS trial for OCD.

Informed consent

There was strong agreement on the need for a thorough informed consent process in psychiatric DBS trials. The influence of desperation in these patients, the resulting potential vulnerability, difficulty setting realistic expectations and the impacts of these were widely discussed. Some suggested that the information load was greater in research applications of DBS because these patients may not be as familiar with the intervention as patients with other indications for DBS. For example, "most patients with Parkinson's disease have already heard about these devices and know somebody else through their Parkinson's society or some other means… ." (B2)

HCPs also identified the important role that (1) psychiatrists and (2) REBs play in the informed consent process. Psychiatrists were seen as having a unique expertise important to

understanding and evaluating capacity in psychiatric illness. They were mentioned as important allies to engage in the informed consent process. REBs were also occasionally recognized as being involved in the informed consent process. In one psychiatric DBS research study, an independent ethicist from the local REB, in addition to the research team itself, gathered informed consent prior to subject enrollment.

Efficacy and safety of DBS in psychiatric disorders

There was a tacit agreement by HCPs for the importance of undertaking more research for the use of DBS in psychiatric disorders such as depression and no strong opposition to research was voiced. Although HCPs alluded to potential physical or psychosocial risks when explaining why more research was needed, they did not discuss specifically how they carry out a risk assessment or how they determine a favorable risk-benefit ratio.

Understanding the relationship between DBS and a biological basis for mental illness

HCPs identified how the investigation of DBS in psychiatric disorders impacts more generally understandings about a biological basis of mental illness (Table 2). On the one hand, HCPs discussed how DBS could decrease stigma associated with psychiatric disorders in patients who have undergone the intervention, the basis of which may be a confirmation that their illness is biological in

nature. On the other hand, a few HCPs alluded to a connection between how we understand the basis of mental illness and how we come to accept that DBS may constitute a valid therapy for some patients. Their comments suggest that recognition of the neurocircuitry of psychiatric disorders is coherent with the rationale for and mechanism of action of DBS.

TABLE 2: UNDERSTANDING DBS AND ITS RELATIONSHIP TO A BIOLOGICAL BASIS OF MENTAL ILLNESS

A. Impact of DBS on perception of psychiatric disorders and patients
Normalization of psychiatric disorders: … "oh my god, maybe this person really did have a brain illness which the doctors are actually trying to treat". So it may normalize the illness to some extent and allow it, for it to be more accepted in society. (A5)
Destigmatization of psychiatric disorders: … I think an interesting thing now I've realized is that people see this as a de-stigmatising intervention… . People actually see the surgical treatment of depression as somehow, almost legitimatizing the brain malfunction of depression. (B1)
B. Impact of our understanding of the biological basis of psychiatric disorders on the acceptance of DBS
General acceptance of the neurocircuitry of psychiatric disorders: … the era of functional neuroimaging, the notion of circuits of emotion, has been reasonably well dealt with in the media, and so people actually see, they can understand this in a way that 20 years ago we would have been more likely to have thought that depression was a disease of the mind, and not the brain. (B1) … if we were to divide the psychiatric disorders into two wide groups: The diseases that I think are organic diseases of the nervous system – I think that schizophrenia is a disease of the brain, I think that there is something wrong with the circuitry; I think certain kinds of depression relate to brain circuitry disorders. … The circuitry disorders, what I would consider structural diseases of the brain, I think that probably we are going to find roles for neurostimulation. (C2)
Greater acceptance of biological interventions: Whereas 15 or 20 years ago somebody would have said: "Charlie, are you crazy? You are letting somebody shove bioelectricity inside your brain?" I think that that is much less likely to be a problem today. (B2)
Overly enthusiastic acceptance of the biological model of psychiatric disorders: I felt the media in the 30 seconds … would like to portray "we found the spot, you stimulate it and life is beautiful". (B1)

TABLE 3: FUTURE CONSIDERATIONS ABOUT THE LONG TERM MANAGEMENT OF PSYCHIATRIC PATIENTS WITH DBS IMPLANTS

Are subjects able to monitor device function and detect device failure (i.e., battery replacement when needed)?
Should subjects be allowed to control their devices?
What are the new issues patients may confront with regards to health and function with DBS implant (and at a younger age)?
What will be the standard of care for patients outside of the protocol and how will care be provided over the long term (and in long term studies)?

Long term management of patients

Some issues reported by HCPs captured the prospect of ethics challenges emerging with the long term care of psychiatric patients with DBS. Although these were not always explicitly identified as ethical concerns in our conversations, we have highlighted examples from our interviews which capture the breadth and scope of the issues with respect to long term management of these patients (Table 3). On all but one occasion (with regards to the patient's ability to monitor device failure) each issue was only referenced by a single HCP.

Resource allocation

HCPs elaborated on potential challenges in resource allocation with expanded roles for DBS in psychiatric conditions. HCPs insisted that cost should be examined alongside effectiveness, taking into account the wider economic and social burdens of severe mental illness, both at an individual and at a societal level. One provider emphasized the need to be able to justify increased resources for DBS over ablative lesion therapy (sometimes applied in cases of refractory depression, Andrade et al, 2010), suggesting the need for a better characterization of the costs and efficacy between these two interventions.

> "…we know that obsessive compulsive disorder, for example, we are probably better off treating these with stimulators rather than lesions. And yet the lesions will go on for far longer, just because um, we are not anxious to treat many patients with stimulators. So in my case I have hadto make an ethical decision, where I do not treat patients with lesions because I would essentially be treating them with lesions just because there is no budget for stimulators." (A1)

HCPs also thought that the healthcare system was ill-equipped to contend with heightened demand if DBS was approved for psychiatric conditions and expressed concern about a lack of functional neurosurgical expertise not corrected for by current training and fellowship programs in Canada.

Contextual features of mental illness

HCPs acknowledged that the challenges of extending DBS to psychiatric conditions interact with social, cultural and environmental factors in mental health and mental healthcare. This context is important to understand the existing and future challenges for DBS in mental health. Factors identified by HCPs

as shaping this context were impaired social function in some severe psychiatric patients (e.g., alienated family and friends, "not functioning in life") and a lack of a general social support system. In fact, one HCP acknowledged that in psychiatric DBS trials they had been involved in, very few patients had any "significant family support" (A1). Other factors were more systemic problems in access to care in the mental health system (in the community and for acute care) and the underfunding of mental healthcare and psychiatric research.

> "… schizophrenia for example probably accounts for the largest number of days of inpatient bed stays of any illness. It affects one percent of the population at a young age and often chronically and they are unproductive for the rest of their
> lives. Yet it probably receives much less funding than many diseases that are much rarer and the reason for that simply probably because there is a lot of stigma associated with psychiatric research, not just psychiatric research but psychiatric diseases in general." (A5)

Many HCPs discussed the barriers that psychiatric patients experience having suffered disability in social or occupational function at key times in their lives. Illness may have prohibited some patients from achieving educational or occupational goals, and/or some patients may have been on disability for a large portion of their prime earning years. As a result, patients may have a long list of social rehabilitation needs and may require sustained support to overcome obstacles which can exist even after the psychiatric symptoms of their disorder are improved.

Enhancement

Prompted about the issue of mood and cognitive enhancement with DBS, HCPs were divided about whether healthy individuals would ever seek out DBS in this context. However, HCPs drew on four different ethical arguments to explain why this would be inappropriate (Table 4).

DISCUSSION

Our paper reports a multi-site study of Canadian HCPs working in the field of DBS and involved or exposed to the experimental use of DBS in psychiatry. The data demonstrate that providers are attuned to certain ethical concerns in the research and practice of DBS for psychiatric disorders. HCPs reflected on the need for scientifically rigorous research trials and the need for transparency with regards to conflicts of interest, and discussed other issues such as ensuring appropriate patient selection, understanding the role of desperation and refractoriness in gathering voluntary informed consent. Sometimes providers emphasized the role of psychiatrists and REBs in obtaining consent. However, the ultimate acceptance of research and

care using DBS in psychiatric disorders was recognized to play out in a more general way with regards to an understanding of a biological basis of mental illness. Moreover, it was recognized that DBS will be impacted by obstacles related to resource allocation in the Canadian context and that psychiatric patients may experience challenges related to long term management with DBS. The presence of a constellation of factors related to psychiatric illness, such as a lack of social support and access to care in the mental health system, is presumed to impact the overall endeavor of developing DBS research and care for patients with psychiatric illness. These perspectives gathered from HCPs therefore bring valuable concerns to the forefront in the existing ethics discussion on the future uses of DBS. Our data bring added context to Canadian psychiatric DBS and are unique in helping to bridge perspectives from academic experts in DBS and ethics to HCPs in the field. Therefore, this creates an opportunity to discuss ethical issues that are important to Canadian HCPs in the area of DBS and psychiatry, as well as to examine how these concerns can be addressed by international discussions and guidance. Comparing our data to existing guidance reveals three situations meriting further attention: 1) cases where ethical concerns of HCPs mirrored ethics challenges explicitly addressed by current international guidance; (2) cases where HCPs raised vague ethical concerns mapping onto ethical areas which also lack detailed guidance in the literature; and (3) cases where HCPs identified ethical problems for which very limited or no guidance at all is available.

Table 4: Ethical arguments challenging the appropriateness of DBS for human enhancement

Resource Allocation	Lack of evidence
"… we have so much difficulty providing access to people who really need it, I don't think that we would even for the next 50 years certainly in the current context be applying this to healthy people. Eventually, just as there will be potentially medications that will allow for enhancement of attention or memory or awake states, you know." (A1)	"Umm basically at this point the literature is varied and sparse so umm you know you're, you would be making decisions, clinical decisions almost on case studies in terms of DBS to improve mood and cognition in otherwise healthy individuals and obviously that's very far off from an evidence-based medicine approach." (D3)
Regulation	**Risk and safety**
"Somebody can't just come off the street, shake a little bit at the neurosurgeon and be plopped into the O.R. the next day. … Certainly in Canada, and the U.S. too, given the regulatory environment, it would be impossible, in my view, to have Joe Sheploclinak set up his freestanding DBS clinic … you have to have this done by somebody who is a regulated member of the health care profession, they're not all of a sudden overturn[ing] their standards of practice in order to make a few more bucks."(B2)	"I mean there are still certain risks associated with these types of procedures. Theoretically it's possible, I'll tell you at this point everything is a risk benefit ratio. … Where I could see it being used for example, would be for transcranial magnetic stimulation where the risks are particularly low. So then you look at the equation uh and the risk benefit doesn't look so bad." (A5)

TABLE 5: TOPICS DRAWN FROM INTERVIEWS WITH HEALTHCARE PROVIDERS RELATED TO THE LONG TERM MANAGEMENT OF PSYCHIATRIC DBS PATIENTS AND A REVIEW OF THE RELATED LITERATURE AND GUIDANCE.

Are subjects able to monitor device function and detect device failure (i.e., battery replacement when needed)?
Background and perspectives from the literature: • Psychiatric patients implanted with DBS require battery replacement of the pulse generator every approximately 10-18 months (Malone, 2010). • Concerns expressed in regards to psychiatric indications include sudden symptom reoccurrence with battery depletion, and or worsening of psychiatric symptoms, including depression because of device failure (Synofzik & Schlaepfer, 2008). • One common management issue in DBS identified as "hardware malfunction" (Okun et al, 2008). Prevalence of hardware-related complications ranges from 2.7%-50% (Deuschl et al, 2006). • Some movement disorders patients experience sudden recurrence of symptoms when battery of the pulse generator reaches the end-of-life (Okun et al, 2008) . • Device malfunction may be linked to behaviors (i.e., exposure to elements which cause the device to turn off). Okun et al. (2008) suggest having subjects keep track of their daily activities with diaries to trace unpredictable device failures unrelated to battery depletion.
Should subjects be allowed to control their devices?
Background and perspectives from the literature: • No current data demonstrating the benefits or risks of self-control of DBS implant in psychiatric patients (Rabins et al, 2009). • No recommendation reached by a 2-day consensus conference on this topic. Although, agreement by participants that more research on this is needed, and information related to permissions regarding subject control should be found in informed consent documents (Rabins et al, 2009). • In movement disorders it has been suggested that some patient control of stimulation parameters can enhance symptom control. In addition, having patients turn off their stimulator at night will decrease battery depletion (Deuschl et al, 2006). • It is recommended that movement disorder patients are instructed on how to check the status of the stimulator, and suggested that only highly cooperative patients and or caregivers who have a clear understanding of the clinical effects of changing stimulation parameters are offered device controllers to manipulate actual device stimulation settings (pre-set) (Deuschl et al, 2006). • Some movement disorder patients select stimulation parameters in order to facilitate how they want to feel in certain situations (Synofzik & Schlaepfer, 2008).
What are the new issues patients may confront with regards to health and function with DBS implant (and at a younger age)?
Background and perspectives from the literature: • Recommendation that informed consent in psychiatric clinical trials should include a discussion of long term results of participation including: potential limits because of DBS device to participate in future research, to undergo some therapies and or some tests (Rabins et al, 2009). • There are no data suggesting that DBS patients are limited with regards to professional or recreational opportunities although patients should be advised to avoid sports and activities, for instance contact sports, which may cause damage to the device (Deuschl et al, 2006).
What will be the standard of care for patients outside of the protocol and how will care be provided over the long term (and in long term studies)?
Background and perspectives from the literature: • "When study protocols include a long follow up phase… it is debatable if subjects continue to be a research subject with same rights to device withdrawal and device maintenance as a subject in the active phase" (Rabins et al, 2009). • It has been suggested that a solution for covering long term care and device maintenance (or removal) costs, would be to require stakeholders (including device companies and institutions, but not patients) to support these costs through a general fund or insurance policy (Rabins et al, 2009). • Kuhn et al. (2009) have suggested that multidisciplinary long term follow up should include evaluations from psychosocial, ethical and legal perspectives (Kuhn et al, 2009). • "Patients with severe, chronic, and highly resistant psychiatric illness typically require multiple treatment modalities to support their daily struggles and process of recovery" (Greenberg et al, 2008). It is suggested that psychiatric patients with DBS are given frequent care and long term care to manage and monitor clinical response and changes in overall functioning (Greenberg et al, 2008). • Informed consent in clinical trials should address the issues of how continued support will be accessed after the trial is finished, under what circumstances the device may be removed (Rabins et al, 2009) as well as how the team will deal with long term "informed revocation of consent" and or trial drop-out (Ford, 2007). • In movement disorders, considerations of the potential for dementia, has led to discussion surrounding the possible role of advance directives to guide decision-making with regards to repair or replacement of implanted device over the long term (Farris & Gianola, 2009).

Observations aligning with ethical issues represented in international guidance on DBS for psychiatric disorders

HCPs in our study did not refer to any specific piece of ethics guidance regarding DBS in psychiatric disorders. Nonetheless, some of the issues raised and recommendations made by providers are in line with current international ethics guidance. For instance, the ethical imperatives of careful patient selection, informed consent, transparency in funding, and ethics board oversight are all supported by the guidance that already exists (Nuttin et al, 2003; Rabins et al, 2009; Lipsman et al, 2010; Malone, 2010). There is some variation between our data and the guidance in specific aspects underlying these general concepts. For example, HCPs in our study stressed the influence of desperation and expectation on voluntary informed consent, which has been discussed before (Rabins et al, 2009; Lipsman et al, 2010) but commented less on the issue of ensuring decision-making capacity in psychiatric patients, something that also appears in consensus statements (Nuttin et al, 2003; Rabins et al, 2009). Similarly, although HCPs in our study discussed how mitigating and acknowledging conflicts of interest in obtaining funding from industry were important, the formal guidance on this topic is much more explicit and detailed, stating that "investigators must disclose potential conflicts of interest to … ethics committees … and to potential enrollees during the informed consent process" (Nuttin et al, 2003).

HCPs in our study identified careful patient selection as a key ethical obligation in the conduct of research trials in psychiatric DBS. Although HCPs used a range of expressions regarding what constitutes a "good" candidate, issues such as diagnosis, severity of illness and treatment

refractoriness were highlighted. This is in line with the guidance that patients should meet defined criteria for severity, diagnosis, disability and treatment refractoriness (Nuttin et al, 2003; Lipsman et al, 2010; Malone, 2010). An additional criterion, which has been suggested in the literature, also mentioned in our study, is that patients should be selected based on a demonstration of the impact of their illness on their quality of life (Kuhn et al, 2009).

There was general agreement between the perspectives brought by HCPs in the Canadian context (in our study) and international perspectives on the appropriateness of the use of DBS for human enhancement purposes. International guidance stipulates that DBS should only be used to "restore normal function" (Nuttin et al, 2003), and not be used to "augment" normal function (Malone, 2010). These data also correspond to results stemming from a qualitative study of Canadian neurosurgeons, which reports that the majority considered surgery to enhance non-pathological personality traits to be unethical (Mendelsohn et al, 2010). The current data demonstrate that Canadian DBS HCPs do not support the use of DBS for enhancement for a variety of ethical reasons including the presence of unknown benefit and overly high risk for healthy individuals. These data are in line with the perspective presented by Synofzik and Schlaepfer (2008) and the results of the prior Canadian study (Mendelsohn et al, 2010). One important point exemplified in the comments made by HCPs in our study was consideration of the differences between public versus privately funded systems. HCPs in our study drew on arguments of resource allocation and regulation in the North American context (and the Canadian context of publically funded healthcare) when discussing reasons why enhancement would be objectionable. These same objections may not apply if systems enable

or encourage the use of DBS in a practice which does not operate following the expectations, values, and goals of a public healthcare system.

In summary, Canadian HCPs identified and recognized the importance of some of the same ethical and social issues that have been highlighted in existing international guidance for DBS in psychiatric disorders. There are strong areas of consensus between Canadian HCPs in our study and the international guidance on ethical aspects of psychiatric DBS trials, demonstrating the presence of shared ethical standards and adding strength to existing guidance.

Ethical concerns discussed in the literature, lacking detailed guidance, and potentially overlooked by HCPs

In our study, complex topics related to the long term management of psychiatric DBS patients were raised in discussion with HCPs. These touched on patients' abilities to control their devices and to monitor device failure and also involved questions related to care in and outside of a trial over the long term (see Table 3). Most of these issues are considered in the literature on DBS at large (Deuschl et al, 2006; Okun et al, 2008) and their importance is better understood by drawing on evidence in movement disorders patients having undergone DBS. Until recently (Rabins et al, 2009) and at the time we were terminating our data gathering for the study, the issue of long term management in psychiatric DBS patients lacked detailed guidance. Although recent consensus statements provide guidance regarding some of the above issues on the long term management for DBS in psychiatric patients (i.e, what should be included in protocols to account for the long term management of patients) in other cases they expose the lack of consensus (i.e., whether or not patients should be allowed to control their device) (Rabins et al, 2009). In Table 5 we have assembled the scholarly literature and existing guidance on DBS in movement disorders and psychiatric disorders which support the ethical importance of the long term management issues raised by HCPs in our study.

Interestingly, while some aspects of the long term management of psychiatric DBS patients were alluded to by HCPs in our study (see Table 3), as a whole the scope and breadth of the ethical implications of these were not discussed. In fact, on all but one occasion (with regards to the patient's ability to monitor device failure) each issue was only referenced by a single HCP. Again, it's important to note that HCPs in our study were interviewed before some of this literature or guidance was published. We can speculate about the reasons there was not wider discussion of these issues; 1) because issues that lack detailed guidance are less familiar to HCPs than issues where detailed guidance has been established and put into practice; 2) because they are ethical issues which are of secondary importance to other ethical imperatives in the conduct of research trials in these patients from the standpoint of HCP and/or guidance; 3) because they may be issues that are thought by clinical teams to be sufficiently managed, but also; 4) because HCPs were not asked to share their perspectives on these topics specifically, or 5) because the long term follow up of patients is not something that all HCPs interviewed would be

involved in or responsible for. This non-exhaustive list of possible explanations highlights the importance of identifying more clearly if there are gaps between guidelines and practice and the reasons underlying such gaps.

New ethical reflections for psychiatric applications of DBS offered by Canadian healthcare providers in the field

On a few occasions, HCPs in our study introduced new ethical reflections in the use of DBS for psychiatric disorders which have not been the topic of broad discussion.

Relationships between DBS, stigma and the biological etiology of mental illness

Cumulatively, HCPs painted a picture that a directional relationship exists where an enriched understanding of the neurocircuitry of mental illness increases the acceptance of DBS as an intervention for psychiatric disorders, and that the use of DBS to treat patients with psychiatric illness reduces the stigma associated with or attached to mental illness. However, the paradigm presented by HCPs in our study is not entirely consistent with previous psychosocial examinations of the relationships between biological explanations of psychiatric disorders, people's treatment preferences, and the stigma that individuals attach to patients with mental illness. In fact some, but not all, studies where the public has been sampled have demonstrated increased attitudes of stigmatization towards individuals with mental illness when there is a greater acceptance of a biological model (Read & Harré, 2001; Walker & Read, 2002; Pescosolido et al, 2010). In addition, others have suggested that while there has been a substantial increase in members of the public who believe that there are biological causes of mental illness, this does not always lead to a greater endorsement of medical therapies such as antidepressants to treat the same disorders (Goldstein & Rosselli, 2003). The inconsistency between what HCPs in our study described as the effects of DBS on stigma, and what has actually been observed in the general public's application of stigma when the biological basis of mental illness is accepted is well described in Pescosolido and colleagues (Pescosolido et al, 2010). In a follow-up sample of the American general public's opinion in 2006, Pescosolido et al. found that 1) more individuals than in 1996 endorsed the biological model of mental illness, 2) that endorsing a biological model led to a greater support for medical care for mental illness, 3) that endorsing a biological model did not decrease the stigma placed on individuals with

depression and 4) that in some cases endorsing a biological model increased the stigma placed on individuals with psychiatric conditions (Pescosolido et al, 2010). They concluded that anti-stigma campaigns and policy aimed at emphasizing the biological basis, and specifically the neuroscientific basis of mental illness are "at best ineffective and at worst potentially stigmatizing" (Pescosolido et al, 2010). In the case of DBS, a better understanding of how DBS affects previous stigma placed on patients at an individual level (i.e., disadvantaged occupational opportunities, housing options, and relationships with others) would clarify whether the intervention is, as some HCPs in our study expressed, positively impacting DBS patients' own experiences of stigma.

The impacts of stigma at an individual (i.e., reduced social support) and societal level (i.e., reduced funding for mental health and access to mental health care) were described by HCPs in our study who highlighted the context within which trials of DBS in psychiatric disorders take place. They were sensitive to the fact that mental health patients are faced with enormous social disadvantages and they highlighted why these issues need to be better explored in the future. One issue that falls under this area, a general lack of social support for psychiatric patients, has been alluded to briefly in the guidance. Kuhn and colleagues (2009) propose the inclusion of a "near-by person" to ensure the ethical protection, care and monitoring of the psychiatric patient undergoing DBS.

Shortage of skilled personnel in functional neurosurgery

A second issue brought up by HCPs in our study was the shortage of neurosurgical expertise in the area of DBS, which was surmised to be ill-prepared for a potential expanded role for DBS in treating psychiatric illness. This reflected specific concerns in the Canadian context with regards to the number of stereotactic and functional neurosurgeons employed and being trained across the country. This finding is important in a context where there is a demonstrated surplus of residents being trained in the specialty of neurosurgery in Canada, compared to the number of positions available (or currently occupied) (Woodrow et al, 2006). At the same time, Toyota (2006) makes a case for increased neurosurgical positions across Canada. From our data, we can see that HCPs in the field understand the complex challenges that could be faced if emerging applications of DBS are not matched by specialty training and supported by increased positions in stereotactic and functional neurosurgery. We believe that our study is the first reporting this issue in the field of DBS and it should be better examined in order to allow Canadian provinces, institutions, and policy makers to carry out strategic planning for the future.

LIMITATIONS

There are some limitations inherent to the methodology of our study. First, although we have sampled across healthcare teams working in DBS across Canada, it is possible that these results do not generalize to all providers or to groups outside this context. Second, the results we present in this study no not necessarily represent general and extensive views of HCPs on these topics, but rather the issues communicated by HCPs. The latter may represent salient issues

and spontaneous viewpoints that are influenced by any number of factors, including media coverage and/or recent events. In addition, the absence of directive language or specific recommendations from HCPs in the study may stem from the fact that they were not tasked to generate specific recommendations in the interview. For this reason as well, the full scope of the match between HCP perspectives and the international guidance would benefit from being explored in a more focused study.

CONCLUSIONS

The perspectives of Canadian HCPs on ethical and social challenges for psychiatric applications of DBS sometimes reflected aspects of the Canadian context (e.g., resource allocation), and at

other times raised new or infrequently discussed concerns in the literature (e.g., social aspects of mental illness). Other issues of ethical concern expressed by HCPs corresponded to those previously identified in the literature and also to guidance regarding psychiatric DBS trials (e.g., patient selection, informed consent, research ethics oversight). This overlap may reflect the appropriateness and relevance of the existing guidance. However, it was unclear if HCPs, themselves, were familiar with the existing international guidance, and the question is open regarding the actual penetrance of the ethics guidance in DBS healthcare teams. We have seen that the ethics guidance itself in this field is evolving, tackling a broader range of issues (e.g., long term management), but this makes it even more important that healthcare teams be aware of the ethics guidance and with respect to their practice. For this reason, we advocate for a dynamic ethics process including: the development of evidence in ethics to support best practices; increased training in ethics and research ethics for practitioners; a bridging of practice guidelines and the hospital reality (including the integration of healthcare teams in ethics reflection and process); and an evaluation of current ethics practices followed by their endorsement or modification. Promising demonstrations about the potential therapeutic efficacy of DBS for refractory psychiatric patients should be matched with a flexible and dynamic ethics process which takes into account a range of experiences and perspectives from stakeholders, and promotes ethically responsive practices to an evolving field of interdisciplinary clinical practice.

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Funding and support:

Canadian Institutes of Health Research, NNF 80045, States of Mind: Emerging Issues in Neuroethics (ER), New Investigator Award (ER), Canadian Institutes of Health Research Operating Grant MOP 97982, and Social Sciences and Humanities Research Council of Canada (EB).

Acknowledgements:
The authors would also like to thank Lila Karpowicz and Daniele Pistelli for assistance with transcription and Bruce Maxwell for assistance with data analysis.

Competing interests: *None*

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Published: *February 27, 2012*