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The ethics of research on deep brain stimulation for depression: decisional capacity and therapeutic misconception

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Abstract

Research on deep brain stimulation (DBS) for treatment-resistant depression appears promising, but concerns have been raised about the decisional capacity of severely depressed patients and their potential misconceptions about the research. We assessed 31 DBS research participants with the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR), a well-validated capacity measure, and with a scale to measure therapeutic misconception, which occurs when subjects do not recognize key differences between treatment and clinical research. Correlations with baseline depressive symptoms were explored. Subjects' performance on the MacCAT-CR was excellent, but therapeutic misconception was still apparent. A trend toward significance was found in the correlation between baseline depression ratings and total therapeutic misconception score. Responses to open-ended prompts revealed both reassuring and concerning statements related to expectations of risk, benefit, and individualization. Even severely depressed patients did not manifest impairments in their capacity to consent to DBS research. Therapeutic misconception, however, remained prevalent.

Keywords

research ethics; deep brain stimulation; decisional capacity; therapeutic misconception

Introduction

Nearly one in six Americans will experience major depression in their lifetimes.¹ Yet, despite 50 years of evolving pharmacologic treatments, up to half of depressed patients fail

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Conflicts of interest

The other authors report no conflicts.

to achieve remission after two adequate antidepressant trials,² and rates of remission decline in subsequent trials.³ Patients with such treatment-resistant depression (TRD) face higher rates of disability,⁴ social impairment,⁵ medical co-morbidity,⁶ and mortality.^{5,7}

Deep brain stimulation (DBS)—an effective intervention for severe treatment-refractory Parkinson's disease, essential tremor, and primary dystonia⁸—has recently emerged as a promising therapy for TRD.^{9–12} DBS involves stereotactic implantation of electrodes to stimulate specific brain regions, powered by a pulse generator implanted along the chest wall. Results from a growing number of small trials suggest DBS can be effective not only in reducing depressive symptoms but in improving physical health and social functioning in patients with TRD.^{9–13}

Given the risks associated with DBS, including hemorrhage and infection, and the limited therapeutic options available to eligible subjects, several ethical issues regarding trial design and protection of human subjects have been raised.^{14–18} These include the worry that TRD may itself impair subjects' capacity to make informed decisions regarding enrollment in DBS research, and concerns that subjects may hold therapeutic misconceptions about participating in DBS research,^{19–21} i.e., by failing to recognize adequately the key differences between treatment and clinical research.²² Additional concerns are that subjects may underestimate the likelihood of risk associated with a DBS trial or have unrealistic expectations of personally benefitting from the study.¹⁸ These concerns are based in part on media portrayals of DBS studies, which tend to exaggerate the therapeutic effects while downplaying risks.^{21,23} Indeed, even when used for standard, approved indications (e.g., movement disorders), physicians have struggled to establish realistic expectations for patients undergoing DBS.²⁴

To date, despite substantial discussion of these ethical issues in the literature, there has been limited empirical investigation. Prior studies on decisional capacity to enroll in clinical research have consistently found that patients with depression have little if any impairment,^{25,26} even when compared with healthy controls.²⁷ In the first empirical examination of these issues in DBS research subjects, we explored risk and benefit perceptions and the presence of therapeutic misconception among depressed patients after an informed consent discussion for participation in trials of DBS for TRD.²⁸ On the whole, these patients offered accurate appraisals of the trials' risks and benefits, were able to distinguish among a variety of procedural risks, and expressed reasonable hopes for personal benefit. However, nearly two-thirds of subjects (64.5%) displayed evidence of therapeutic misconception regarding the DBS trial; that is, they incorrectly answered at least one question related to the study's purpose, likelihood of personal benefit, or individualization of treatment. This finding is consistent with the prevalence of therapeutic misconception identified in a variety of clinical research settings.^{29–33} Thematic analyses suggested that research subjects made their decisions to enroll in the trials based on a number of complex, yet sometimes idiosyncratic considerations.³⁴ There was no clear evidence from either the quantitative or qualitative data to suggest that these depressed subjects lacked adequate capacity to consent to these DBS trials.

In the present analysis of data from this sample of potential participants in DBS research for TRD, we examined consent-related abilities, as measured by a well-validated research capacity assessment tool, including whether performance on this measure was associated with depression severity. We also more closely examined the types of therapeutic misconceptions held by these patients and determined the correlations among therapeutic misconception, depression severity, and estimation of risks associated with the DBS trial. In addition, we conducted an exploratory investigation of subjects' perceptions of risks, benefits, degree of study individualization, and their motivations for participation, based on

responses to open-ended prompts, to identify illustrative themes underlying apparent misconceptions.

Methods

Participants

Participants were recruited from two separate DBS for TRD studies (both of which targeted the subcallosal cingulate gyrus or Cg25) at two urban medical schools. Site A conducted a nonprofit, foundation funded study,¹¹ and Site B was part of an industry-sponsored pivotal trial (from which the data have not yet been published). Key inclusion criteria at Site A were 18–70 years old, a diagnosis of major depressive disorder (MDD) or bipolar II disorder, current major depressive episode of greater than 12 months duration, nonresponse to more than four adequate antidepressant treatments, and either life-time failure of electroconvulsive therapy (ECT) or inability to receive ECT. Key exclusion criteria were clinically significant medical or psychiatric comorbidities, recent substance use disorder, and untenable suicide risk (i.e., active suicidal ideation with plan or intent, or recent suicide attempts). At Site B, key inclusion and exclusion criteria were similar to Site A's, except the age range was limited to 21–70 years old, the diagnosis was restricted to MDD, and nonresponse to a psychotherapy of known efficacy was required.

Individuals who passed an initial screening and who had undergone consent procedures for the DBS study, including a presurgical observation period to ensure that they continued to meet severity criteria based on the Hamilton Depression Rating Scale (HDRS-17),³⁵ were asked to participate in this ancillary study of ethical issues in DBS research. (At Site A, the HDRS-17 score inclusion criterion required an average preoperative score of 20 or greater, averaged over screening and weekly presurgical evaluations, and a final preoperative HDRS-17 score no more than 30% lower than the baseline screening HDRS score. HDRS-17 scores were not inclusion criteria at Site B.) Consent was obtained by a study psychiatrist at Site A and by a research coordinator or study psychiatrist at Site B. The clinical study itself consisted of DBS surgery followed by a sham (stimulation off) control period (Site A: one month of sham; Site B: six months of either sham or stimulation). All subjects received diagnostic and follow-up studies (e.g., MRI and neuropsychological testing), but Site A included several additional research-related procedures (e.g., positron emission tomography (PET), endocrine function testing, and electroencephalography (EEG)).

Our optional, ancillary study was approved by institutional review boards at the participating institutions, and all subjects provided written informed consent.

Measures: decisional capacity

Subjects were assessed with the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR),³⁶ a semistructured, open-ended interview instrument designed to aid in the assessment of capacity to consent to participate in clinical research. The MacCAT-CR was designed for protocol-specific adaptation; therefore, relevant information was selected by PSA, PEH, and LBD based on each site's trial specifics (versions used for this study are available from the corresponding author on request). As specified by the MacCAT-CR, the instrument was administered after a full consent discussion. Disclosures (briefer presentations of information relevant to specific sections of the MacCAT-CR) were read aloud, and a standard set of questions was asked. The MacCAT-CR subscales explored the following:

- Understanding: comprehending study details (e.g., purpose, duration, procedures, risks, and potential benefits—including the possibility of no benefit).
- Appreciation: applying the information to the subject's own situation (e.g., recognizing that personal benefits are not the primary objective of the study, acknowledging the possibility that being in study might not be personally beneficial).
- Reasoning: comparing research participation with other treatment options and describing the potential consequences of participating versus not participating.

Trained research staff administered the MacCAT-CR to study subjects; these interviews were video-taped and subsequently transcribed verbatim. Subjects were permitted up to three trials of the Understanding subscale questions to achieve their best possible score (one more than recommended in the MacCAT-CR manual³⁶) and one trial each of the Appreciation and Reasoning subscales. Although the MacCAT-CR also assesses subjects' abilities to evidence a choice, all subjects in this study were able to indicate their choice and so those data are not reported here. At Site A, the study psychiatrist (PEH) administered the MacCAT-CR. At Site B, a trained staff member administered the MacCAT-CR.

Measures: therapeutic misconception

Based on prior work by Appelbaum, Lidz, and others on therapeutic misconception,^{32,37,38} eight true/false statements were used to evaluate beliefs regarding the likelihood of personal benefit from the study, the individualization of treatment, and the purpose of the study. Each item was scored 0 (correct) or 1 (incorrect), with higher scores indicating a greater degree of therapeutic misconception. Eight additional questions examined perceptions about overall study risks, potential for personal benefit, and altruistic motivations, all scored on 5-point Likert-type scales (because certain study procedures—endocrine testing, PET, and EEG—were only conducted at Site A, the number of subjects differs for some of the risk ratings). In addition, responses to open-ended items were elicited at baseline and six months regarding subjects' perceptions of risks, benefits, and altruistic motivations (data from the six-month follow-up were incomplete and hence are not reported here). The statistical results of this portion of the study are described in more detail elsewhere.²⁸ In the present report, we tested for associations between therapeutic misconception scores and baseline clinical variables, and we further explored open-ended items to identify common themes.

Measures: perceptions of risks

Nine further questions examined perceptions about specific study and procedural risks, each scored on a 4-point ordinal scale: minimal risk or less (risks involved in everyday activities), minor increase over minimal risk, moderate risk, or high risk.

Data analysis

Descriptive statistics were used to characterize responses. Pearson correlations were used to describe relationships between variables. Three investigators (CEF, LBD, PSA) reviewed responses to the open-ended prompts to identify common themes. As these items were designed to stimulate ideas for further research rather than to describe exhaustively the subjects' perceptions and beliefs, we did not try to quantify the number of instances in which each theme was expressed. Therefore, these data provide a snap-shot, rather than an in-depth portrayal, of some of the thoughts of these participants as they were considering enrollment.

Results

Thirty-one participants from both sites reached the consent process for the DBS trials. At Site A, 24 individuals passed the initial screening and reached the consent process; of these, three did not complete the full set of questionnaires, leaving 21 subjects with usable data. At Site B, 10 participants reached the consent process for the DBS study, but one did not complete the full set of questionnaires, leaving nine individuals with usable MacCAT-CR data. Not all subjects were administered every MacCAT-CR item, leading to variable total responses to subscale items.

Demographic and clinical characteristics of participants are presented in Table 1. Participants ranged from 27 to 63 years old (mean 43.3, $SD = 9.1$), the majority (60.7%) were women, and 42.9% reported never having been married. The sample had an average of 16.7 ($SD = 3.0$) years of schooling; 89.3% of participants had at least some college education. Site differences were observed in participants' marital status (chi-square = 9.78, $P = 0.04$). Clinically, participants reported a mean of 6.4 depressive episodes, with a mean age of first-episode onset of 21 years. The mean HDRS-17 score was 23 ($SD = 3.5$, range: 17–30).

Research consent capacity

Figure 1 presents data from the MacCAT-CR assessment. The vast majority of subjects performed very well on the measures of all three abilities related to capacity to decide. On the final trial of the Understanding scale, 18 of 28 subjects scored perfectly, and out of a possible range of 0–38, all but one subject scored 33 or greater. On the Appreciation scale, all but two subjects scored perfectly, and on the Reasoning scale, all but four subjects scored perfectly. No subject scored lower than 4 (out of 6) on the Appreciation scale or 6 (out of 8) on the Reasoning scale. Regarding the individual items asked as part of these subscales, only two items had more than two subjects who did not achieve a perfect score: *purpose of special procedures* (missed by 5) and *major risks* (missed by 7).

Correlations with depression scores

Correlations with baseline depression scores are presented in Table 2. A trend toward significance was found in the negative correlation (Pearson's $r = -0.322$, $P = 0.082$) between baseline HDRS-17 scores and the overall measure of therapeutic misconception. No significant correlations were found between baseline depression scores and individual therapeutic misconception items; that is, items regarding the purpose of the study, the potential for personal benefit, the individualization of treatment, or altruistic motivations. In contrast, subjects' ratings of the risk of two of the procedures (MRI and EEG) were significantly negatively correlated with baseline depression ratings ($r = -0.376$, $P < 0.05$ and $r = -0.570$, $P < 0.05$, respectively). The absence of substantial variation in MacCAT-CR scores precludes meaningful exploration of their relationship with depressive symptoms.

Common themes and illustrative statements

As an exploratory aim in this study, we augmented the rating-scale items with open-ended questions designed to elicit subjects' perceptions of study purpose, risks, benefits, as well as to explore their motivations for participation. Table 3 displays examples of identified themes.

Discussion

This study examined the capacity of severely depressed outpatients to consent to DBS research, evaluated the associations between depression severity and therapeutic

misconception, and investigated misconceptions regarding this novel treatment modality. Even in a highly selected TRD sample, subjects showed very good performance across all domains of decisional capacity. On a scale measuring therapeutic misconception, however, some subjects tended to view the study's purpose as directed specifically at helping the subjects involved, rather than exploring the efficacy of an experimental intervention; to underrate the risks of the neurosurgical intervention; and to overrate the likelihood of personal benefit and degree of individualization of their care in the study. Therapeutic misconception scores suggested that subjects who were more depressed might have had fewer misconceptions about the nature of the research study, a potential relationship warranting further exploration in larger and more heterogeneous samples.

Concerns about the capacity of depressed patients to consent to research are not new.²⁰ Repeatedly, though, studies have failed to find substantial impairments in the decisional capacity of people with psychiatric disorders to consent to research,^{25,39} including studies that evaluated severely depressed inpatients and those requiring electroconvulsive therapy.^{26,27} Although the MacCAT-CR is individualized for each investigation, which limits the validity of quantitative comparisons across studies, it is notable that participants in this study, representing a sub-set of extremely depressed individuals, performed extraordinarily well on all MacCAT-CR capacity measures. Indeed, most subjects achieved perfect or near-perfect scores. In part, this may be due to the intensity and quality of the informational process to which prospective DBS subjects were exposed. It bears noting, however, that seven subjects did not score perfectly on the "major risks" item of the understanding subscale, suggesting that this section could benefit from greater emphasis during consent discussions. That said, taken together, these findings suggest that the persistence and prevalence of concerns about the capacity of depressed patients to consent to research may be disproportionate to the real risks, as long as adequate safeguards and sufficient information are present. Given the consistency of these findings, the research community should consider whether most individuals with psychiatric disorders are actually as vulnerable to decisional impairments as they are commonly portrayed,²⁰ or if such concerns might instead be a reflection of the widespread stigma and prejudice against psychiatric disorders.

This study further demonstrates that, when asked to elaborate on rating-scale responses regarding study purpose, risks, and benefits, participants generally evidenced a grasp of the purpose of the study as testing a new therapeutic modality for its safety and efficacy; that there were risks to surgery, particularly brain surgery; and that personal benefit was not guaranteed. There were clearly varying levels of sophistication in these responses from this highly selected group of participants who may not be representative of the level of research sophistication of most depressed individuals.

Participants expressed an interesting range of responses when asked to reflect on their ratings of their level of altruism. Some clearly endorsed the desire to help themselves first, with altruism being only a secondary consideration. Others more directly stated that they wanted other people not to suffer as they had, or that they wanted to contribute or give meaning to their suffering. These sorts of responses do not seem distinctly different from those seen in patients with other serious illnesses—for example, advanced cancer patients who volunteer for early-phase clinical trials.³⁰

Nevertheless, this study also reinforces the message that even decisionally capable subjects may have problematic—even mistaken—beliefs about clinical research. The degree of therapeutic misconception found in these subjects (64.5%) is comparable with findings from similar studies conducted in psychiatric and nonpsychiatric populations, suggesting that this population is not uniquely susceptible to therapeutic misconception.^{32,33,37,38} As noted

elsewhere, educational approaches focused on the differences between research and treatment—including the use of educators not directly involved in the study—may help subjects avoid therapeutic misconception and better understand the nature of the clinical trial in which they are enrolled.³⁷ However, social forces relevant to DBS may present additional challenges. The extensive media coverage of DBS for TRD, ranging from unrealistic expectations about the brain's newfound “happy switch”⁴⁰ to alarmism about “psychosurgery redux,”⁴¹ highlights the ways in which distorted views of the procedure may enter the public imagination. Extra vigilance and effort on the part of the scientific community to promote public understanding are thus required to combat broader misunderstandings about this novel intervention, as well as to foster better understanding of the purpose and limitations of clinical research. The fact that subjects in this study exhibited very good performance on measures of decisional capacity but still showed evidence of common misconceptions indicates that refinements and elaborations of the consent process alone may not be sufficient to remedy these misunderstandings and counteract the forces that operate at broader levels to drive overall public understanding.

It is interesting that there was a trend toward a negative correlation between baseline depression ratings and total therapeutic misconception score, i.e., subjects who were more depressed demonstrated fewer misconceptions about the nature of the research study. They also showed lower levels of concern about the low-risk aspects of the study (MRI scans and neuropsychological testing). These findings might be a reflection of *depressive realism*,⁴² the idea that depressed individuals make more accurate judgments than their nondepressed counterparts. On the other hand, more recent studies of this phenomenon have called the idea of depressive realism into question, suggesting that clinically depressed individuals make negatively distorted judgments.⁴³ Particularly given the limitations of this study noted subsequently, further work on this question is warranted.

Among this study's limitations is that this sample comprised a small, prescreened, well-educated subset of subjects with TRD. Subjects also had to be highly motivated to participate in the study's demanding procedures—in some cases, they would have to move to a new city to participate. Moreover, our subjects' desire to be in a study of DBS for TRD may have influenced their responses, i.e., they may have been concerned that admitting to the “wrong” motivations would compromise their ability to remain in the study (although we found multiple instances of subjects providing frank assessments of their motivations and desperation). In addition, the validity of our findings may be limited by the absence of validated measures for several of the concepts that we sought to assess, including *desperation* and *altruism*. Similarly, the scale used to measure therapeutic misconception, although theoretically grounded and based on those used in previous studies, had not been validated. Finally, there was no control group, making it difficult to know the extent to which other variables may have accounted for our findings.

Further studies are needed to examine decisional capacity and therapeutic misconception across a broader sample of participants with TRD. There is also a need for further methodological refinement and validation of tools to assess influences on decision making. It might be most useful to compare TRD subjects with those with other serious illnesses considering early phase or invasive research in an effort to identify which, if any, of the phenomena we explored are specific to DBS for TRD research. This is particularly important at a time when multiple brain-based interventions—for example, gene therapy trials that include sham surgery—are being mounted for a variety of neurological and neurodegenerative disorders.

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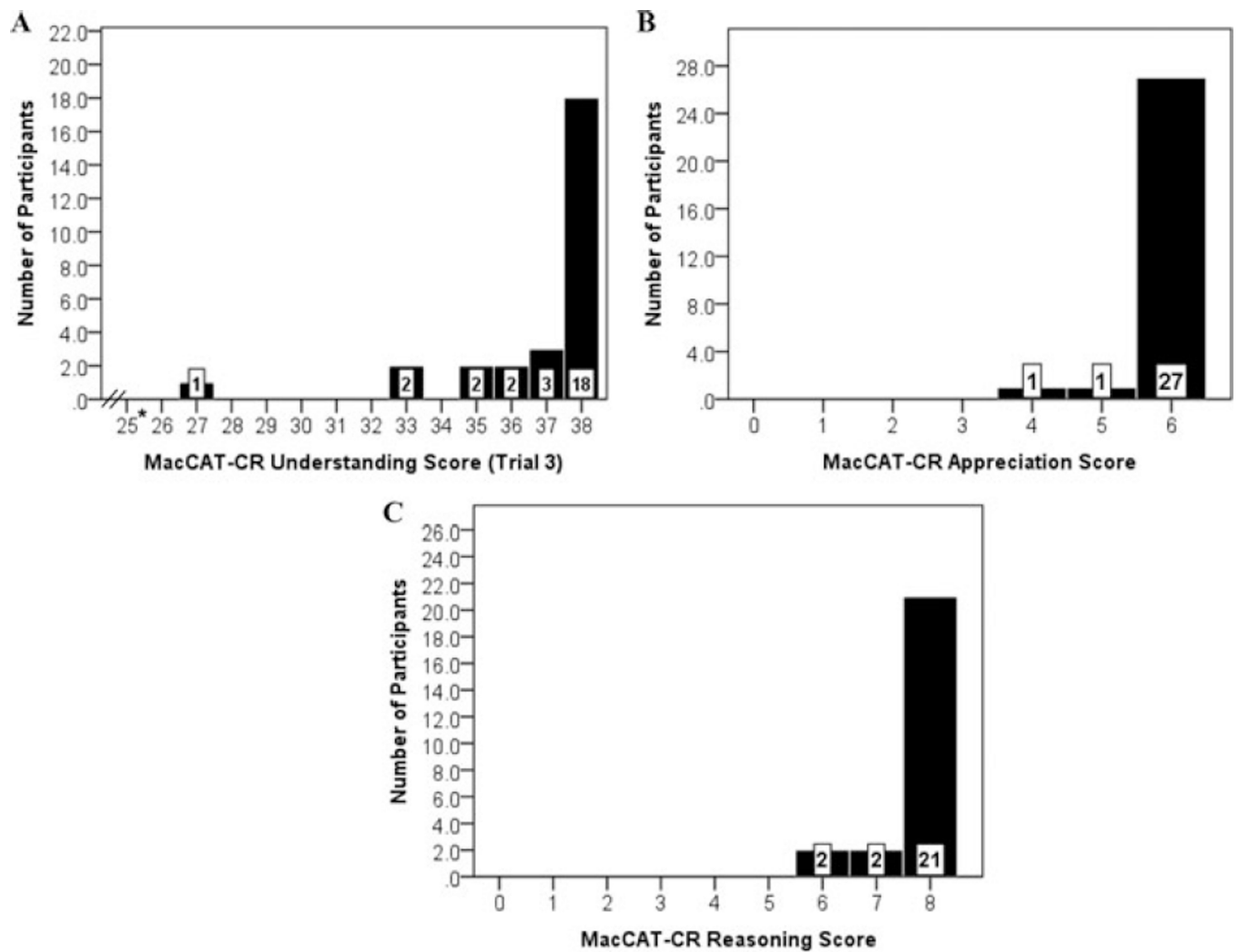
H. Mayberg consults and receives licensing fees for intellectual property related to deep brain stimulation for depression from St. Jude Medical, Inc. P. Holtzheimer serves as a consultant for St. Jude Medical, Inc. In this role he assists in the design and conduct of their clinical trials in depression. S. Lisanby has received research grants on DBS to her institution (Columbia and Duke University) from ANS/St. Jude Medical, Inc. S. Lisanby has received research grants to her institution on technologies not related to the topic of this manuscript from Brains way and Neosync. She has received equipment support to her institution on technologies not related to the topic of this manuscript from Magstim and Magventures.

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* The x-axis of panel A starts at 25 because no subject scored lower than 27.

Figure 1.
MacCAT-CR scores.

Table 1Demographic and clinical characteristics of participants ($N = 31$)

Characteristic	Site A ($N = 21$) Mean (SD)	Site B ($N = 10$) Mean (SD)
Age	42.7 (9.6)	44.4 (8.0)
Years of education	16.8 (3.4)	16.6 (1.5)
Age of depression onset	21.0 (10.5)	20.1 (4.0)
Number of depressive episodes	7.11 (9.0)	4.3 (3.2)
Number of hospitalizations	4.9 (5.3)	1.3 (0.5)
Number of suicide attempts	1.68 (2.9)	1.29 (2.2)
HDRS-17 baseline score	24.0 (3.4)	20.3 (2.3)
Number of hypomanic episodes	4.53 (11.6)	N/A
	$N(\%)$	$N(\%)$
Gender (% female)	13 (61.9%)	4 (57.1%)
% never married *	8 (38.1%)	4 (57.1%)
% at least some college education	18 (85.7%)	7 (100%)
% family history of bipolar disorder	42.1%	N/A

* Chi-square = 9.78, $P = 0.04$.

Table 2

Correlations of therapeutic misconception scale and risk ratings with baseline HDRS-17 scores

Scale	Correlation (Pearson's <i>r</i>)	<i>N</i>
<i>Therapeutic misconception total score</i>	−0.322 [*]	30
<i>Risk ratings</i>		
MRI	−0.376 ^{**}	29
Neuropsychological testing	−0.273	29
Implantation surgery	−0.194	29
Endocrine testing [^]	−0.014	20
PET scan [^]	−0.369	20
EEG [^]	−0.570 ^{**}	20

^{*}
 $P = 0.082$.

^{**}
 $P < 0.05$.

[^]
 These procedures were only conducted at Site A.

Table 3

Examples of responses to open-ended items

Question domain (<i>Prompt</i>)	Examples of responses (Site A or B subject)
Purpose of study (<i>"What would you say is the main purpose of this research project? That is, why are the researchers doing it?"</i>)	<p>Safety/efficacy/mechanism investigation</p> <ul style="list-style-type: none"> - "To test the safety, efficacy, and mechanism of action of DBS" (A) - "Study [the] efficacy and safety for TRD" (A) - "Find out if [the] device works or not, safe or not" (A) - "To test the implant's efficacy" (A) - "To investigate the efficacy of DBS of Cg25 in severe TRD and improve understanding of neural networks, depression, etc." (A) - "To learn more about whether DBS is an effective treatment for depression, and if so, to investigate the mechanism by which DBS affects depression" (B) - "To determine [the] safety and effectiveness of DBS" (B) - "DBS has not been FDA approved. . .still [a] study question on why/how DBS works for depression" (B) <p>Possible misunderstanding of purpose of investigating DBS as depression "cure"</p> <ul style="list-style-type: none"> - "To find out if DBS is a cure for depression" (A)
Benefits (<i>"How likely do you think it is that you personally will benefit from being in this study? Please explain your rating."</i>)	<p>Pessimistic about personal benefit due to prior experience</p> <ul style="list-style-type: none"> - "I am skeptical about positive impact because of [my] poor responses to other treatments, including meds, therapy, ECT, and other adjunctive treatments" (A) <p>Realistic estimation of uncertainty of personal benefit</p> <ul style="list-style-type: none"> - "It's in the middle—not for sure" (A) - "Nothing to inform decision except very limited study" (A) - "The device is a great unknown" (A) - "There does not exist enough data to make any meaningful estimation of the benefits I may experience" (B) <p>Quantified chances</p> <ul style="list-style-type: none"> - "50–75% prior results" (A) - "I feel there is a 40–50% chance of improvement" (B) <p>Hesitant to be hopeful</p> <ul style="list-style-type: none"> - "Don't want to be completely hopeless. Don't want to be overly hopeful" (A) - "I'm neutral—but I'm also not getting my hopes up that I will be 'cured'" (A) <p>Hopeful/optimistic</p> <ul style="list-style-type: none"> - "I'm optimistic due to previous studies" (A) - "I'm very hopeful this study will help lift my depression" (A) <p>Misestimation/overestimation of potential personal benefit</p> <ul style="list-style-type: none"> - "I've been told that they have had good results so far so I have reason to believe I will benefit as well" (B)
Risks (<i>"How risky do you believe this study is to you, personally? Please explain your rating."</i>)	<p>Awareness of risks; realistic estimates of risks/unknowns; acceptable level of risk for potential benefit</p> <ul style="list-style-type: none"> - "Surgery is a possible risk" (A) - "The unknown of the long-term effects—could backfire" (A)

Question domain (<i>Prompt</i>)	Examples of responses (Site A or B subject)
Altruism (<i>"To what degree was the desire to help others in the future a motivation for your participating in this study?"</i>)	- "Brain surgery—[it's] realistic to believe in at least moderate risk" (A)
	- "It's risky and invasive—but I'm okay with the risks associated" (A)
	- "Some risk but acceptable amount" (A)
	- "I see a lot of complications regarding DBS on the consent form" (B)
	- "Many risks in pamphlet" (B)
	- "There are risks during brain surgery" (B)
	- "There are guidelines and boundaries, but can still be considered experimental, which carries many risks" (B)
	Risks in context of prior data/other surgeries/neurosurgery/ experience of surgeons
	- "They've done this in Parkinson's disease and I don't think there have been a lot of problems" (A)
	- "I'm hoping and according to data that it will go smoothly" (A)
	- "I understand there are risks involved with brain surgery and any surgery for that matter but that these risks are fairly low" (A)
	- "Given what I have been told and read it is relatively less risky than other neurosurgery but it is still brain surgery and that feels scary to me." (A)
	- "I've been told the surgeons here have performed the procedure hundreds of times with very few people having side effects" (B)
	Risks in relation to living with depression/risk of suicide
	- "Worst thing is more impairment, more depression" (A)
	- "Alternative (suicide) is a bigger risk" (B)
	Possible underestimation or discounting of personal risk
	- "I am healthy & do fine with surgery" (A)
	- "Optimism. Serious effects. Some chance. . .not worried about it" (A)
	- "Only know what I've read and what people tell me. I don't think I personally have any particular risk" (A)
	Overestimation of personal risk
	- "I feel I have 'bad luck' period" (A)
Kinship	- "I'm concerned for my kids" (A)
	- "I don't want my (child) and others to have the frustration I have experienced" (A)
	Helping prevent suffering of others/feeling that one is contributing/ bringing meaning to one's suffering
	- "I don't want anyone to suffer as long as I have" (A)
	- "Very, very willing to help find cure for this illness" (A)
	- "Like to help prevent others from suffering" (A)
	- "My lifelong struggle with depression will not have been my pain only" (A)
	- "Participating. . .helps me feel like I'm contributing something in this world" (B)
	General statements about helping others or advancing depression treatment

Question domain (<i>Prompt</i>)	Examples of responses (Site A or B subject)
	<ul style="list-style-type: none"> - “If it doesn’t help me, maybe it will help others and future developments in treating TRD” (A) - “I believe that even if I am not helped by the study it may provide valuable information in future advances in TRD and DBS” (A) <p>Explicit statements of personal concern being primary, and altruism secondary</p> <ul style="list-style-type: none"> - “I will be glad if my participation helps others but I have chosen to participate purely for selfish reasons (i.e., hoping it helps me)” (A) - “I would certainly like to help the future sufferers of depression—but my first priority has to be myself” (B) - “I am desperate at the moment, that is my concern. Helping others is secondary. I’m not proud of this, but it is true” (B)