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Beyond Consent in Research

Revisiting Vulnerability in Deep Brain Stimulation for Psychiatric Disorders

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Abstract: Vulnerability is an important criterion to assess the ethical justification of the inclusion of participants in research trials. Currently, vulnerability is often understood as an attribute inherent to a participant by nature of a diagnosed condition. Accordingly, a common ethical concern relates to the participant's decisionmaking capacity and ability to provide free and informed consent. We propose an expanded view of vulnerability that moves beyond a focus on consent and the intrinsic attributes of participants. We offer specific suggestions for how relational aspects and the dynamic features of vulnerability could be more fully captured in current discussions and research practices.

Keywords: vulnerability; informed consent; research; deep brain stimulation; psychiatry; neuroethics

Introduction

Vulnerability is an important criterion used to assess the ethical inclusion of participants in clinical research trials.[1] Although vulnerability is not well defined, it appears to be most commonly understood in the present research environment as an attribute inherent to a participant by nature of a diagnosed condition.

The potential effectiveness of deep brain stimulation (DBS) for severe treatment-refractory psychiatric conditions (e.g., depression, obsessive compulsive disorder) is a focus of substantial research.[2] A shift in the use of DBS, from use in approved neurological indications to use in investigational trials for patients with psychiatric diagnoses, raises important ethical questions

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for researchers and clinicians alike.[3,4,5,6,7] A common ethical concern in psychiatric research trials is how the participant's disease itself, or present mental state, may impair decisionmaking capacity and the ability to provide free and informed consent to enter the trial. A common question is whether and how patients with psychiatric conditions can ethically be enrolled in more invasive medical trials such as DBS.[8] In the context of DBS research, proposals for special protections for patients with a psychiatric diagnosis are dominated by suggested provisions targeting the informed consent process.[9]

When concerns about vulnerability revolve around the question of whether or not patients with a psychiatric diagnosis are able to provide free and informed consent, these concerns reflect a view of vulnerability fundamentally defined by the participant's decisionmaking capacity.[10] This is an important consideration, but in this article, we propose an expanded view of vulnerability that considers the *shared* contributions of research participants and investigators in the context of research. In fact, concerns that patients with psychiatric disorders, by virtue of having a psychiatric disorder, are intrinsically vulnerable and thus require extensive safeguards—beyond those already required for other types of clinical research—find little support in the current empirical literature.[11,12,13] We propose that sources of vulnerability are rooted in a relational context: for example, both participant and investigator may introduce factors that can disadvantage a participant through the deepening of existing power asymmetries.[14] We suggest that relational aspects and the dynamic features of vulnerability need to be more fully captured in current discussions and research practices. This article offers specific suggestions about how this broader relational notion of vulnerability can be attended to and mitigated in order to reduce parentalism and the use of unfounded assumptions and stereotypes about patients with psychiatric diagnoses. This will lead to better support for research participants and a more inclusive approach to research.

This article is based on an interdisciplinary international workshop examining the relationship between vulnerability and consent in DBS trials for patients with psychiatric diagnoses held at the Institut de recherches cliniques de Montréal and was enriched by the working group through subsequent research and writing. Although we have focused on the example of DBS trials in patients with a psychiatric diagnosis, similar concerns arise throughout clinical research more generally. Research ethics approval was not required for the study. No human volunteers were sought.

Intrinsic versus Relational Concepts of Vulnerability

A set of clinical trials and case reports has demonstrated that some proportion of treatment-refractory patients with obsessive compulsive disorder or major depression may respond or even remit with the stimulation of various brain targets using DBS.[15] Concerns about these patient populations participating in DBS research persist, however, based on the criterion of vulnerability in the following interrelated areas:[16]

- Vulnerability related to the nature of the psychiatric disorder, affecting decisional capacity (the component abilities to understand, appreciate, and reason with relevant information about participation in a specific trial)
- Vulnerability influenced by desperation, distorting the ability to

assess the information provided and potentially increasing willingness to participate
- Vulnerability heightened by the nature of the intervention itself: for example, specific characteristics of invasiveness and risk as well as the medical complexity compared to other treatment approaches for psychiatric disorders

In general, the notion of vulnerability in this literature locates vulnerability within an individual and his or her diagnosis; it is then judged vis-à-vis the potential impact on free and informed consent and decisionmaking.[17,18,19,20,21] Repercussions of this assessment of vulnerability may be the exclusion of the patient with a psychiatric diagnosis from participating in trials, thereby also excluding him or her from the possibility of individual benefit. This notion of vulnerability is essentialist, meaning that it is seen to be inherent to a diagnosis—and is judged based on criteria for informed consent.[22] In this way, it gives individual attributes of the diagnosis and participant precedence as sources of vulnerability and signals that the remediation of vulnerability lies in the informed consent process.

An approach that emphasizes the intrinsic attributes of research participants relative to vulnerability is problematic when it reinforces stigma, produces unfairness, hinders research unnecessarily, ignores systemic problems, and restricts individuals' exercise of autonomy.[23,24] In clinical research, the vulnerability of participants may actually be exacerbated by regulatory guidelines applied in research studies: for example, requiring an a priori (but nonempirically validated) level of understanding in order to give informed consent may paradoxically increase vulnerability by demanding that participants meet an arbitrary performance standard. Similarly, discourse about DBS and about patients with psychiatric diagnoses frequently reproduces this rhetoric of vulnerability (e.g., research trials are described as "last resort" investigational approaches; patients as "desperate").

Importantly, empirical evidence does not clearly support that all of the concerns raised with respect to impaired decisionmaking capacity or informed consent in the context of DBS are warranted[25,26] or are even fundamentally different from similar challenges experienced in other research populations. For example, concerns about therapeutic misconception (misunderstanding the goals of research compared to clinical care and misestimation of potential benefit or risk) may be equally problematic in phase I oncology trials.[27] In a few specific circumstances (e.g., patients suffering from delusions, patients with significant cognitive impairment, as in dementia), impaired decisionmaking may be tightly associated with the patient's condition; these are exceptions, however, and cannot be generalized to develop beliefs or policies that are universally applied to all psychiatric patients.

The desire to identify individuals or specific groups of individuals in need of special protections in research may seem to favor an approach in which attributes of populations are used to categorize those to whom we owe greater protections. A view that only examines individuals as the source of their own vulnerability, however, limits consideration of what is more likely to be true—namely, that the possible causes and impacts of vulnerability are numerous, that vulnerability is generated through a relational asymmetry between participants and investigators, and that both participants and investigators are sources of vulnerability. This also entails moving away from perceptions of the vulnerable

patient or participant to the more comprehensive view of the patient or participant in a context conducive to vulnerability. This approach does not outwardly change the concern that, when vulnerability is present, research participant interests may not be protected. However, it refines our understanding of the sources of potential vulnerability and, with it, the associated ways that we can respond to or mitigate its effects.

We contrast intrinsic versus relational concepts of vulnerability in the following sections.

Intrinsic Vulnerability

Vulnerability as an *intrinsic property* is viewed as a static and intrinsic property of the participant (e.g., by nature of his or her diagnosis) that jeopardizes decisionmaking capacity and the ability to give free and informed consent.

The causes of vulnerability as an intrinsic property are considered to be essentially related to the individual patient or participant.

Remediation of vulnerability as an intrinsic property includes improving the capacity of the participant to consent and the removal of individual attributes creating barriers to consent.

Relational Vulnerability

Vulnerability as a *relational property* is viewed as a contextual and situational property whereby the participant is in an asymmetrical power relationship with the investigator.

The causes of vulnerability as a relational property are both individual (related to the participant) and external (e.g., related to the investigator, potential surrogates, or the study context); they are located in the relationships among participant, investigator, and sociocultural context.

Remediation of vulnerability as a relational property includes augmenting the participant's understanding and decisionmaking literacy, training the team to support the participant, identifying and eliminating investigator-driven biases, and altering the discourse toward a relational understanding of vulnerability.

Attention to the presence of vulnerability helps researchers to highlight important ethical and practical tensions—for example, concerns for protection of participants by ensuring they are capable of consent—while striving to respect autonomy and to provide just access to clinical trials; it also allows them to attend to appropriate development and implementation of research safeguards while not unnecessarily constraining or preventing the ethical and efficient conduct of scientifically valuable research.

Revisiting Vulnerability

We propose moving away from a notion of vulnerability that is limited to the attributes of a patient or participant and toward a relational conception of vulnerability. In so doing, we aim to better capture the relational, dynamic, and graded aspects of vulnerability that have been largely underrecognized. This reformulation recognizes the range of experiences in potential research participants, clarifies ethical tensions that emerge in the narrower approach to vulnerability, and emphasizes strategies to reduce negative ethical consequences.

Principle 1: Vulnerability Is Situated in a Relational Context

We suggest adopting a relational understanding of vulnerability for the purposes of evaluating whether, and to what degree, research participant protections are necessary. For example, in

DBS trials for patients with a psychiatric diagnosis, intrinsic and extrinsic sources of vulnerability contribute to a relational asymmetry between participants and investigators.

Rationale. Conceptions of vulnerability and its mitigation may be overly focused on the intrinsic attributes of a participant or a patient group. A by-product of the reduction to individual or group attributes is that patient groups can be further stigmatized by the application of general labels.[28] Requiring special safeguards (such as a more extensive or burdensome consent process) that are not required for other fully capable research participants enrolling in nonpsychiatric research demonstrates a lack of respect for participants who retain full decisionmaking capacity. Moreover, this may discourage investigators from being thoughtful about their own active role in exacerbating the prejudicial effects of relational asymmetry (e.g., exposing participants to suboptimal study designs) and about the need to discriminate between individuals or patient groups in terms of the actual vulnerability experienced. Importantly, the intrinsic view may also strengthen an exceptionalist stance toward patients with psychiatric diagnoses who are considering enrollment in DBS trials. They could be *assumed* to possess attributes (e.g., desperation) that make them more vulnerable than other similar patient groups (e.g., patients with epilepsy enrolling in DBS trials).

Positive impact of the principle. This principle can help researchers develop an understanding that relational asymmetry can be diminished or exacerbated by attention to attributes, beliefs, assumptions, and presuppositions made by investigators, research teams, and the system of research oversight.

Principle 2: Vulnerability Is a Dynamic Construct

We suggest embracing views of vulnerability, psychiatric diagnoses, and brain modulation that reflect their dynamic nature.

Rationale. Vulnerability is too often evoked to describe a static state without acknowledgment that relational asymmetry can be amplified or reduced through both individual and contextual factors throughout the course of a study. Static conceptions may also reinforce false views of the nature of psychiatric diagnoses as being unchanging and may ignore the basic rationale of brain modulation—the idea that brain processes themselves can be modified over time by interventions (pharmacological, psychotherapeutic, or DBS). The state of potential vulnerability of any participant needs to be attended to even after the consent form has been signed.

Positive impact of the principle. This principle can help researchers acknowledge that a participant can be vulnerable in one set of circumstances or at one point in time but not in other circumstances or at other times, and that vulnerability fluctuates and can be mitigated (e.g., relational asymmetry can be reduced). It may also lead to remediation of vulnerability through the application of temporal strategies such as pauses in study participation, time-outs, or a phased consent process.

Principle 3: Vulnerability Occurs on a Graded Continuum

We suggest recognizing that vulnerability appears in different degrees on a continuum and that all research participants may display some degree of vulnerability. As a concept of degrees, it is therefore neither all-inclusive nor determinative.

Rationale. Vulnerability perceived as an all-or-none intrinsic property may lead investigators to ignore the actual heterogeneity that exists in the diverse sources of vulnerability across individual patients and among different patient groups. As a result, this may reinforce a view of vulnerability as inherent to psychiatric diagnoses in general or to all individuals in certain diagnostic categories.

Positive impact of the principle. This principle can assist researchers in recognizing that treating all patients and all diagnoses the same with regard to their potential vulnerability lacks sensitivity to the heterogeneity of factors leading to relational asymmetry in individuals and in patient groups. Additionally, this principle takes into account the idea that the presence of vulnerability, in and of itself, does not present sufficient reason to assume that participants are unable to protect their own interests when enrolling in DBS trials.

A summary figure of the revised concept of vulnerability can be found on the authors' Web site.[29]

The revised concept of vulnerability extends beyond impaired decision-making and the scope of consent and incorporates three principles. We capture relational, dynamic, and graded aspects of vulnerability by grounding the notion in an understanding of relational asymmetry. This reformulation recognizes important elements in the experiences of participants in these trials and enriches reflection about the sources, dynamism, and ethical significance of the concept of vulnerability. At the same time, the relational view directs our attention to ways that different stakeholders can act to manage or mitigate relational asymmetry in DBS trials for patients with psychiatric diagnoses.

Relational Vulnerability in Action: Suggestions for Stakeholders

Suggested Actions for Clinical DBS Research Teams

- Identify ways to reduce vulnerability and advocate for management of potential sources of vulnerability by the team.
- Collaborate with patient advocacy groups in the development of research trials where this helps to balance their knowledge of research and contributes to a leveling of relational asymmetry.
- Modify the perception of vulnerable patients or participants (intrinsic sources of vulnerability) to the more comprehensive view of patients or participants in a context conducive to vulnerability (acknowledging extrinsic and intrinsic sources of vulnerability).
- Limit the use of specific language that encourages and shapes vulnerability in patients with a psychiatric diagnosis participating in DBS trials (e.g., "desperation" or "last resort option").

Suggested Actions for Research Ethics/ Institutional Review Boards

- Avoid vulnerability as a label for persons and use it instead to label situations in research ethics practices and policies.
- Acknowledge the parentalism of viewing vulnerability as an intrinsic attribute and examine how our current standards, tools, and methods can compound intrinsic vulnerability.
- Encourage researchers to examine contextual or investigator-driven sources of vulnerability in their research studies as well as to give due reflection to their own beliefs

and presuppositions about the vulnerability of psychiatric patients as research participants.
- Evaluate systems for the reassessment of vulnerability at meaningful time points in studies and when the presence of certain specific factors triggers such a reassessment.

Suggested Actions for Ethics Researchers

- Investigate approaches to elucidate the contribution of different sources of vulnerability to the participant's overall ability to protect his or her own interests. Although quantifying such contribution may be difficult or even impossible, qualitative appreciation and application of relational ethics to understanding the ethical impact of different sources of vulnerability are needed.
- Develop ways to measure and assess different sources of vulnerability beyond consent in DBS trials for patients with psychiatric diagnoses.

Other stakeholders to consider include health agencies (e.g., to augment health literacy to tackle vulnerability exacerbated by a misunderstanding of DBS) and media outlets and reporters (e.g., to enhance public understanding of mental illness, and to raise awareness of the current state of DBS research, including the limits of what is known so far).

Conclusions

Vulnerability is an important concept signaling the need for careful ethical reflection in research trials. Current discussions around DBS trials involving patients with psychiatric diagnoses have raised concerns about vulnerability and have identified informed consent as needing further consideration and investigation. This focus on individual attributes and the capacity for consent fails to fully capture the extrinsic factors that influence a participant's vulnerability. We call for an expanded definition and enriched understanding of vulnerability and suggest principles reflecting its relational, dynamic, and graded nature. We must further our understanding of sources of vulnerability and develop and test interventions to mitigate them. Moreover, further work is needed to identify to what extent, when, and to what effect the concept of vulnerability is invoked in general clinical research trials.

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