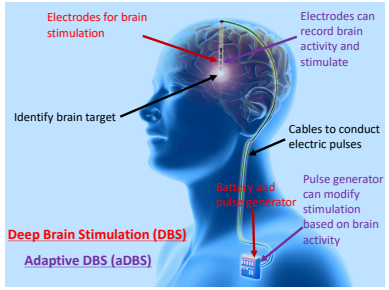
Researcher Perspectives on Ethical Considerations in Adaptive Deep Brain Stimulation Trials

Katrina A. Muñoz M.B.E., Kristin Kostick Ph.D., Clarissa Sanchez M.P.H., Lavina Kalwani, Laura Torgerson M.S., Rebecca Hsu, Demetrio Sierra-Mercado Ph.D., Jill O. Robinson M.A., Simon Outram Ph.D., Barbara Koenig Ph.D., Stacey Pereira Ph.D., Amy McGuire Ph.D., J.D., Peter Zuk Ph.D., Gabriel Lázaro-Muñoz Ph.D., J.D., M.B.E.

Baylor College of Medicine | CENTER FOR MEDICAL ETHICS & HEALTH POLICY | BRAIN INITIATIVE

BACKGROUND

Interest and investment in closed-loop or adaptive deep brain stimulation (aDBS) systems have quickly expanded due to this neurotechnology's potential to more safely and effectively treat refractory movement and psychiatric disorders compared to conventional DBS (1,4). However, the defining features of aDBS that make it promising (i.e., automatically adjust stimulation, store neural data), may exacerbate certain neuroethics concerns (e.g., felt authenticity of affective states, patient privacy) (4). Few studies have examined stakeholder perspectives about ethical issues in aDBS research and other next-generation DBS devices.



METHODS

To help fill this gap, we conducted semi-structured interviews with researchers involved in aDBS trials (n=23) to gain insight into the most pressing ethical questions in aDBS research and any concerns about specific features of aDBS devices, including devices' ability to measure brain activity, automatically adjust stimulation, and store neural data. Thematic content analysis was utilized to identify themes in researcher responses to six different questions (see Table 1).

RESULTS 8 Central Themes in Researcher Responses:

Data Privacy and Security Issues (91%)

"I think the main concerns would be privacy of the data. We stream these data to external computers. Someone's brain data is now [...] it could be considered personal health information, in a way. Eventually, we may be able to decode specific things about that person's identity and personality from their brain data. So, we do have to consider it as personal health information, even if it's de-identified…" (R_011).

Risks and Safety (83%)

"There's the fact that we just don't know that much about DBS and how it works. That's the danger of doing any kind of experiment on humans directly, even though it's pretty well understood, what the random risks are" (R_006).

Informed Consent and Adequate Patient Understanding (74%)

"DBS…seems, to them – because it's so risky, but can have such promise – that it's like a silver bullet, so to speak" (R_005).

Automaticity and Device Programming (65%)

"My concern is that it might stimulate when it's not supposed to, causing [an] unwanted side effect. Or the opposite, if it's not stimulating when it's supposed to causing the patient unnecessary suffering. Those are glitches that, as we develop these techniques, hopefully will not be an issue. But those are concerns that I have from an ethical perspective" (R_020).

Autonomy and Control Over Stimulation (57%)

"I think we need to be careful in affording control of the device to the patient. For any stimulation of the reward system, there's potential for self-abuse. There are restrictions [where] patients can turn the device off or on, but they can't modulate it. That strikes me as a wise precaution" (R_026).

Patient Selection and Candidacy Considerations (39%)

"When you have a population that does not have a sufficient response to pretty much everything [other treatments], and you can have a 60% response rate in that group [to aDBS], good lord, that's incredible. I worry about the side effects of not doing something for those individuals" (R_018).

Post-Trial Access to Care and Device Maintenance (39%)

"I think, honestly, the biggest issue right now is the amount of money that it costs patients to maintain the device, or obtain a replacement after the study is over" (R_004).

Personality and Identity (30%)

"In the study where we're manipulating mood potentially, the goal is to improve mood, which most people would say would be a good thing. But then at some point, do you give somebody a new mood that changes their personality? There are a lot of ethical issues behind potentially manipulating people's mood and personality [be]cause that could be a good thing or a bad thing" (R_010).

Table 1. Percentage (%) of Respondents (n=23) who Discussed Main Ethical Concerns related to aDBS

Questions Explored:	Data Privacy and Security	Risks and Safety	Informed Consent and Patient Understanding	Automaticity and Device Programming	Autonomy and Control	Patient Selection and Candidacy Considerations	Post-Trial Access to Care and Device Maintenance	Personality and Identity
Across Questions	91	83	74	65	57	39	39	30
1) When you think about the current state of aDBS, what do you think are the most pressing ethical issues in **adaptive DBS research**?	17	30	43	0	26	26	26	26
2) From a more personal perspective, what are the biggest ethical challenges that you have had to deal with in your **own adaptive DBS research**?	9	26	52	0	13	17	9	4
3) Compared to conventional DBS, are there ethical issues **unique to adaptive DBS**?	30	65	17	43	26	13	9	0
4) As you know, an important component of adaptive DBS is that it works by **measuring the participant's brain activity.** What, if any, ethical concerns does this raise?	61	17	4	17	0	0	0	4
5) The adaptive DBS system **automatically changes stimulation** based on the participant's brain activity. What, if any, ethical concerns does this raise?	9	30	4	39	35	0	0	4
6) The adaptive DBS system **stores the data it collects** about the participant's brain activity. What, if any ethical concerns does this raise?	78	17	0	4	9	0	4	4

NEXT STEPS

Minimize Cybersecurity Vulnerabilities	Advance Biomarker Validity	Promote the Balance of Device Control	Enhance Patient Knowledge & Ongoing Informed Consent
Ex) Incorporate more security patches and upgrade software systems for both hospital networks and patient devices (6).	Ex) Conduct research on translatability of clinic-derived biomarkers to patient functioning in more naturalistic settings (5).	Ex) Assess individual patient preferences, brain target, and different means of device control (3).	Ex) Identify psychosocial supports (e.g., pre and post op counseling) (2).

CONCLUSION

- Researchers highlighted many pressing concerns. While some were relevant to conventional DBS and aDBS, most were exacerbated by distinct features of aDBS.
- Due to the need to measure and store neural data, aDBS researchers raised concerns about protecting the privacy of neural data and preventing unwanted third-party access to data.
- The automatic nature of stimulation sparked risk and safety concerns about the experimental nature of identifying biomarkers to automatically adjust stimulation outside the clinic as well as concerns about patients' ability to properly consent to continuous alterations in stimulation.

Our findings therefore suggest that the technical features that give aDBS advantages over conventional DBS systems also raise distinct issues.

References

1) Beudel, M., Brown, P. (2016). Adaptive deep brain stimulation in Parkinson's disease. Parkinsonism Relat Disord. 22:S123-S126.
2) Chiong, K., Leonard, F., & Chang, F. (2018). Neurosurgical Patients as Human Research Subjects: Ethical Considerations in Intracranial Electrophysiology Research. *Neurosurgery*, *83*(1), 29–37. de Haan, S., Rietveld, E., Stokhof, M., Denys, D., & Haan, S. (2015). Effects of Deep Brain Stimulation on the Lived Experience of Obsessive-Compulsive Disorder Patients: In-Depth Interviews with 18 Patients: e0135524. *PLoS ONE*, *10*(8), e0135524.
3) Klein, E. (2020). Ethics and the emergence of brain-computer interface medicine. *Handbook of Clinical Neurology*, *168*, 329–339.
4) Provenza, N., Matteson, E., Allawala, A., Barrios-Anderson, A., Sheth, S., Viswanathan, A., et al. (2019). The Case for Adaptive Neuromodulation to Treat Severe Intractable Mental Disorders. *Frontiers in Neuroscience*, *13*, 152.
5) Pugh, J., Pycroft, L., Sandberg, A., Aziz, T., & Savulescu, J. (2018). Brainjacking in deep brain stimulation and autonomy. *Ethics and Information Technology*, *20*(3), 219–232.

Acknowledgments

Research for this article was funded by the BRAIN Initiative-National Institutes of Health (NIH), parent grant R01MH114854 and supplemental grant R01MH114854-01S1 (Lázaro-Muñoz, McGuire, Goodman). The views expressed are those of the authors and do not necessarily reflect views of the NIH, Baylor College of Medicine, Rice University, the University of Puerto Rico, or UC San Francisco.