

DBS for Depression? Lessons From Patients' Beliefs for Research, Treatment, and Noninvasive Brain Modulation

Citation for published version (APA):

Horstkötter, D., & Linden, D. (2018). DBS for Depression? Lessons From Patients' Beliefs for Research, Treatment, and Noninvasive Brain Modulation. *AJOB Neuroscience*, 9(4), 232-234. <https://doi.org/10.1080/21507740.2018.1553903>

Document status and date:

Published: 01/01/2018

DOI:

[10.1080/21507740.2018.1553903](https://doi.org/10.1080/21507740.2018.1553903)

Document Version:

Publisher's PDF, also known as Version of record

Document license:

Taverne

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

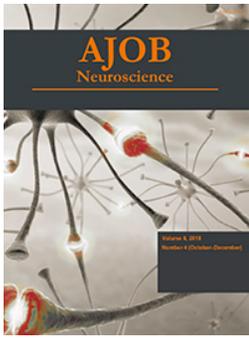
www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.



DBS for Depression? Lessons From Patients' Beliefs for Research, Treatment, and Noninvasive Brain Modulation

Dorothee Horstkötter & David E. J. Linden

To cite this article: Dorothee Horstkötter & David E. J. Linden (2018) DBS for Depression? Lessons From Patients' Beliefs for Research, Treatment, and Noninvasive Brain Modulation, AJOB Neuroscience, 9:4, 232-234, DOI: [10.1080/21507740.2018.1553903](https://doi.org/10.1080/21507740.2018.1553903)

To link to this article: <https://doi.org/10.1080/21507740.2018.1553903>



Published online: 25 Feb 2019.



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



View Crossmark data [↗](#)

Finally, we agree with the authors that vulnerability remains a main ethical concern. In their discussion, the authors talked about relational vulnerability, but do not address how that relates to the way that they present the information they gave participants about DBS. They also interpret the participants' desire to consult with other providers, conduct research on the Internet, and involve trusted family members in the decisions as a form of responding to relational vulnerability. However, relational vulnerability deals with a broader view on the power asymmetry between an investigator and a patient, as well as the epistemic gaps patients have regarding these procedures. Thus, participants are vulnerable to how others in society (such as the media and the Internet) may portray these procedures in ways that do not help inform in a meaningful way the participants' decisions, or in a way that truly addresses those relational vulnerabilities. Yet patients are also vulnerable to how clinicians and researchers approach the topic, and as such the imbalance of power makes issues of decision-making capacity a key area to continue exploring. ■

REFERENCES

- Appelbaum, P. S., C. W. Lidz, and T. Grisso. 2004. Therapeutic misconception in clinical research: Frequency and risk factors. *IRB* 26(2): 1–8.
- Cabrera, L. Y., R. McKenize, M. Brandt, and R. Bluhm. 2018. Comparison of philosophical concerns between professionals and the lay public regarding two psychiatric treatments. *AJOB Empirical Bioethics* 9(4): 252–266.
- Klein, E., S. Goering, J. Gagne, C. V. Shea, R. Franklin, S. Zorowitz, D. D. Dougherty, and A. Widge. 2016. Brain-computer interface-based control of closed loop brain stimulation: Attitudes and ethical considerations. *Brain-Computer Interfaces* 3(3): 140–148.
- Lawrence, R. E., C. R. Kaufmann, R. B. DeSilva, and P. Appelbaum. 2019. Patients' beliefs about deep brain stimulation for treatment-resistant depression. *American Journal of Bioethics, Neuroscience* 9(4): 210–218.
- Leykin, Y., P. P. Christopher, P. E. Holtzheimer, P. Appelbaum, H. S. Mayberg, S. H. Lisanby, and L. B. Dunn. 2011. Participants' perceptions of deep brain stimulation research for Treatment-Resistant depression: Risks, benefits, and therapeutic misconception. *AJOB Primary Research* 2(4): 33–41.
- Ovadia, D. 2015. Deep brain stimulation in the media: Over-optimistic portrayals call for a new strategy involving journalists and scientists in ethical debates. *Frontiers in Integrative Neuroscience* 5: 16–21.
- Racine, E., S. Waldman, N. Palmour, D. Risse, and J. Illes. 2007. Currents of hope": Neurostimulation techniques in U.S. and U.K. print media. *Cambridge Quarterly of Healthcare Ethics* 16(3): 312–316.
- Schlaepfer, T. E., S. H. Lisanby, and S. Pallanti. 2010. Separating hope from hype: Some ethical implications of the development of deep brain stimulation in psychiatric research and treatment. *CNS Spectrums* 15(5): 285–287.

DBS for Depression? Lessons From Patients' Beliefs for Research, Treatment, and Noninvasive Brain Modulation

Dorothee Horstkötter, Maastricht University

David E. J. Linden, Maastricht University

Lawrence and colleagues (Lawrence et al. 2019) present a valuable set of interviews about deep brain stimulation (DBS) with treatment-refractory depression (TRD) patients. Their focus on patients outside an actual DBS setting allows for proactive ethical reflection, informed by the views of respondents who represent the majority of today's TRD patients. Thereby, the study adds a perspective that has been largely neglected in current empirical neuroethics. Still, we have a twofold concern

with their approach and their interpretation of the data.

First, Lawrence et al. fail to differentiate between a—realistic—research context and a—currently hypothetical—treatment context. However, the fears, hopes, and expectations of patients, and also any reasons underlying these beliefs, are likely to differ significantly between these two settings.

Second, the authors introduce DBS to their interview partners in a rather isolated way, to be provided

Address correspondence to Dorothee Horstkötter, PhD, Department of Health, Ethics and Society, School of Mental Health and Neuroscience, Maastricht University, Postbox 616, 6200 MD Maastricht, The Netherlands. E-mail: d.horstkoetter@maastrichtuniversity.nl

independent of any alternative or complementary procedures. However, in any realistic clinical setting (including that of clinical trials), DBS would be combined with other treatment modalities, such as psychotherapy or psychopharmacology, and its take-up has to be judged against other neuromodulation techniques.

Still, the material presented is worthwhile, because it can teach a series of lessons also for the implications of potential noninvasive forms of neuromodulation in TRD and other psychiatric diseases, facilitating ethical thought in these neighboring areas.

DBS IN RESEARCH OR IN TREATMENT

DBS is an established treatment modality for several serious movement disorders, and it is under investigation for a series of psychiatric conditions covering not only depression, but also obsessive-compulsive disorder, anorexia nervosa and other eating disorders, Tourette syndrome, Alzheimer's disease, and several addictions (Linden 2014). By a first approach, DBS research is required, just like all other research with human participants, to live up to internationally acknowledged standards and guidelines of research ethics, like the Helsinki Declaration, and to corresponding national laws. However, DBS research, particularly for new indications, is facing a set of additional challenges not easily covered by these common rules. It often takes place in the context of "experimental treatment" offered as last resort on an individual basis, and uncertainty about possible outcomes is rather high while the candidates who have to consider this treatment option are in great despair (Nuffield Council on Bioethics 2013). To a certain extent, Lawrence and colleagues' interview partners reflect these concerns when they are rather reluctant to have a DBS device implanted, showing concerns about the invasiveness, novelty, and limited efficacy of the procedure, or even being outright against being implanted or being "experimented on" (214). At the other end of the spectrum, some participants are extremely positive, expecting almost miraculous cure, and consider DBS to be something "very big" (213).

However, the context in which both these fears and these hopes do apply remains unclear. In our opinion, this context is very important, not just for clinical judgments but also for ethical considerations. If a treatment is supported by strong evidence as to its likely efficacy, patients may still refuse it, for example, because of an exaggerated fear of a less likely (e.g., anesthesia) or minor risk; if a treatment is entirely experimental and only supported by anecdotal evidence, patients may still select it, driven by despair and hope (Johansson et al. 2013). The ethical challenges in these two scenarios will be both difficult and different. For example, for an established treatment with good evidence, even an invasive one, proxy consent for patients who do not have the capacity to think through the risks and benefits of treatment

might be justifiable (Glannon 2008), but this would not apply for experimental treatments. Conversely, in a research context, exaggerated hopes of desperate patients might be a reason to exclude them because of their therapeutic misconception and the immorality of exploiting vulnerable patients. Mixing up situations of treatment and research runs the danger of eliciting views that are either exaggerations or understatements (Horstkötter and de Wert *under review*).

DBS IN ISOLATION OR IN CONTEXT

A number of neuromodulation treatment modalities for depression and other psychiatric conditions are currently under investigation. Apart from DBS, these include the noninvasive brain stimulation techniques, transcranial magnetic stimulation (TMS) and transcranial electric stimulation, and to an increasing extent also self-regulation training with neurofeedback (NF), based on electroencephalography (EEG) or functional magnetic resonance imaging (fMRI) (Mehler et al. 2018). Another related technique is lesion surgery for psychiatric indications, mainly using cingulotomy or anterior capsulotomy (Subramanian et al. 2017). All these techniques aim to alleviate the symptoms of severe depression, or their respective target disease, in a more or less direct way by modulating underlying neural networks. However, they are hardly provided, or investigated, in isolation from more conservative therapeutic approaches covering cognitive-behavior therapy, psychopharmacological drugs, or even electroconvulsive therapy (ECT). Lawrence and colleagues, however, seem to disregard this point. They not only present DBS in a rather isolated manner; they even ask their participants to make a choice between preferences for different treatment modalities. By contrast, combining treatment modalities is the more likely and more feasible scenario in the potential introduction of neuromodulation for depression and other psychiatric conditions. Participants in the current study appear highly anxious that DBS might take away their current therapies and even cut off their way back to these modalities in case DBS turns out ineffective or even worsens their symptoms. Obviously, it is a problem to withhold effective treatments from patients in research settings; however, in the likely case that neuromodulation, if effective at all, will add to rather than fully replace ongoing treatments, this concern might be much less prominent. At the same time, however, researchers should take this message very seriously, and scientific curiosity in upcoming neuromodulation should pay proper attention to the views and experiences of the patients in, with, and for whom these techniques are developed. Their trust is crucial if new means of therapeutic neuromodulation are to be developed.

LESSONS TO BE LEARNED FOR NONINVASIVE NEUROMODULATION

Against this background, Lawrence and colleagues' qualitative study remains very worthwhile because it gives voice to a group of patients whose views are rarely documented and can also inform research agendas in neighboring areas of neuromodulation. Some complications and concerns, like those linked to invasive surgery, indeed appear unique for DBS (and lesion surgery) contexts, whereas other topics, like concerns about efficacy, adverse outcomes, issues related to diminished agency or transformed identity, and those linked to decision-making capacity are likely to arise also in the context of non-invasive brain stimulation and neurofeedback. It would have been interesting to find out more about patients' views about multifaceted treatment approaches where neuromodulation is embedded in contexts of behavioral and/or cognitive approaches. Concerns about efficacy are, almost by definition, always present in the context of clinical research, and particularly in clinical settings in which experimental treatment is provided.

With regard to DBS, invasiveness also appears as a prominent point of concern. People fear the surgery and dislike the idea that something gets implanted in their bodies or brains. Intuitively, this might give rise to a preference for noninvasive means of neuromodulation, like TMS and NF. However, without proper research into the perception of invasiveness and the exact reasons for any dislike, we cannot confirm this intuition. Neuromodulation by definition invades the functioning of people's neural networks, and if applied in psychiatric contexts, it is meant to invade a person's psychological functioning. This raises the questions of how patients perceive different forms of invasiveness (surgical and psychological or social) and which features (e.g., one-time versus long-term, reversible versus irreversible, visible from the outside versus invisible) trigger any preferences or aversions, and why.

Agency and changes of identity have frequently been discussed in current neuroethical literature on DBS. However, to date it remains unclear whether critical arguments developed in the context of Parkinson's disease (Glannon 2009) also apply in psychiatric contexts where changes to a person's identity might become the intended aim rather than an undesirable side effect. Moreover, the concept of psychiatric DBS has been criticized because patients undergo any changes in a passive way, rather than being actively engaged in their own healing process (Focquaert and Schermer 2015). This raises the question of how patients experience their participation in neuromodulation more generally. Does making a decision in favor of TMS and visiting the researcher or physician count as active engagement? Do patients undergoing neurofeedback experience their participation indeed as being actively self-regulated, as is currently assumed in the literature? From the perspective of agency and identity, would this render neurofeedback

more ethically justified than any competitors that aim to change the brain even more directly? Alternatively, might patients also feel passively regulated even during neurofeedback, for example, by their clinician's instructions and expectations or the mechanism of the EEG or fMRI apparatus? (cf. Horstkötter 2015, 2017). Ethical add-on studies or substudies that accompany research in neuromodulation in psychiatry should put these questions high on the agenda, expanding on the research presented by Lawrence and colleagues. ■

REFERENCES

- Focquaert, F., and M. Schermer. 2015. Moral enhancement: Do means matter morally? *Neuroethics* 8(2): 139–151. doi: [10.1007/s12152-015-9230-y](https://doi.org/10.1007/s12152-015-9230-y).
- Glannon, W. 2008. Deep-Brain stimulation for depression. *HEC Forum* 20(4): 325–335. doi: [10.1007/s10730-008-9084-3](https://doi.org/10.1007/s10730-008-9084-3).
- Glannon, W. 2009. Stimulating brains, altering minds. *Journal of Medical Ethics* 35(5): 289–292. doi: [10.1136/jme.2008.027789](https://doi.org/10.1136/jme.2008.027789).
- Horstkötter, D. 2015. Self-control and normativity: Theories in social psychology revisited. *Theory and Psychology* 25(1): 25–44.
- Horstkötter, D. 2017. Raising self-controlled children. A philosophical analysis of neuroscience and social psychology perspectives. In *Parental responsibility in the context of neuroscience and genetics*, eds. K. Hens, D. Cutas, and D. Horstkötter, 73–90. Berlin: Springer.
- Horstkötter, D., and G. de Wert. (under review). Deep brain stimulation; ethical considerations. In *Managing deep brain stimulation – An interdisciplinary approach*, eds. Y. Temel, S. Chabardes, R. M. A. de Bie, J. Volkmann, and A. F. G. Leentjens. Springer.
- Johansson, V., M. Garwicz, M. Kanje, H. Röcklinsberg, J. Schouenborg, A. Tingström, and U. Görman. 2013. Beyond blind optimism and unfounded fears: Deep brain stimulation for treatment resistant depression. *Neuroethics* 6(3): 457–471. doi: [10.1007/s12152-011-9112-x](https://doi.org/10.1007/s12152-011-9112-x).
- Lawrence, R. E., C. R. Kaufmann, R. B. DeSilva, and P. Appelbaum. 2019. Patients' beliefs about deep brain stimulation for treatment-resistant depression. *American Journal of Bioethics, Neuroscience* 9(4): 210–218.
- Linden, D. E. J. 2014. *Brain control, Developments in therapy and implications for society*. London, UK: Palgrave Macmillan.
- Mehler, D. M. A., M. O. Sokunbi, I. Habes, et al. 2018. Targeting the affective brain—a randomized controlled trial of real-time fMRI neurofeedback in patients with depression. *Neuropsychopharmacology* 43: 2578–2585. doi: [10.1038/s41386-018-0126-5](https://doi.org/10.1038/s41386-018-0126-5)
- Nuffield Council on Bioethics. 2013. *Novel neurotechnologies: Intervening in the brain*. London: Nuffield Council on Bioethics.
- Subramanian, L., T. Bracht, P. Jenkins, et al. 2017. Clinical improvements following bilateral anterior capsulotomy in treatment-resistant depression. *Psychological Medicine* 47(6): 1097–1106. doi: [10.1017/S0033291716003159](https://doi.org/10.1017/S0033291716003159).