Perceptions of Invasiveness: A Moving Target for Neuromodulation

Nir Lipsman, Patrick J. McDonald & Judy Illes

To cite this article: Nir Lipsman, Patrick J. McDonald & Judy Illes (2023) Perceptions of Invasiveness: A Moving Target for Neuromodulation, AJOB Neuroscience, 14:1, 15-17, DOI: 10.1080/21507740.2022.2150709

To link to this article: https://doi.org/10.1080/21507740.2022.2150709

Published online: 16 Dec 2022.
Perceptions of Invasiveness: A Moving Target for Neuromodulation

Nir Lipsman, Patrick J. McDonald, and Judy Illes

Major depression is among the most common, challenging and disabling conditions. It is highly heterogeneous, affects patients throughout the lifespan, and up to one-third of people affected, resistant to guideline concordant care. Neuromodulation or direct-to-brain interventions at various stages of development and investigation are available for patients with treatment refractory depression (TRD). The field of neuromodulation has benefited immensely from an improved understanding of the circuitry of mood disorders, driven by rapid advances in brain imaging, device engineering, and targeted therapeutics. By targeting key nodes in affective circuits, focal interventions such as repetitive transcranial magnetic stimulation (rTMS), deep brain stimulation (DBS), and MR-guided Focused Ultrasound, can reset circuits and influence activity of structures down- and up-stream from targeted regions. By changing the structure and function of these circuits, the hope is to exert bottom-up influence on behavior, and ideally supplement or enhance psychotherapeutic and/or—pharmacologic approaches for refractory conditions (Cole et al. 2022; Silk et al. 2022).

The manuscript by Bluhm et al. (2023) describes a qualitative study on the nature of invasiveness for various interventions in major depressive disorder. This is timely and important work, with a clear objective: to better understand how patients and practitioners view the concept of invasiveness, and to begin to elucidate the factors that underlie these perceptions. Despite the current renaissance of neuromodulation (Cole et al. 2022; Silk et al. 2022), there remain many unanswered questions such as the ones that Bluhm et al. pose. Others include as-yet unclear mechanisms of action, optimal settings and anatomic targets, eligibility criteria for various treatments and trials, and defining successful outcomes, among many others. Further, in our experience as neurosurgeons and neuroethicists, and despite a growing literature supporting psychiatric ethics, ed. J. Z. Sadler, K. W. M. Fulford and C. W. van Staden. Oxford: Oxford University Press.


the use of surgical and non-surgical neuromodulation approaches, the actual number of patients referred for neuromodulation remains quite low. The exact barriers for assessment and treatment are unclear and subjects of ongoing investigation. What is clear, however, is that perceptions of neuromodulation in neuropsychiatry are evolving, and part of this is related both to changing perceptions of their relative invasiveness, and to changing attitudes toward psychiatric surgery.

The question of invasiveness has broad clinical, ethical, legal and even political implications; on the acceptability of an intervention within the medical community and the public more broadly; on the relative role of neuromodulation tools in the treatment algorithm for depression; and has bearing, eventually, on funding decisions for research and treatment. Put simply, how invasive an intervention is perceived will influence its ultimate adoption. The risk is that potentially safe and effective treatments, which are perceived as too invasive may not be used or even investigated.

The authors discover that determining invasiveness in neuromodulation is far from straightforward. While for some interventions, like surgery, the answer is clearer, for others, including ECT and tRMS, and even psychotherapy, opinions vary and ultimately influence their acceptability. Our team of researchers has examined a similar issue in a previously published study examining the readiness of neuromodulation for research and clinical adoption (Coates McCall et al. 2020). We too found divergent opinions, from patients and clinicians, that varied with the nature of the intervention, the disease in question and the pre-clinical evidence supporting clinical translation. In short, experience and values came strongly to bear on personal views, and had a substantial influence on how ready these interventions are to be widely applied. We further discovered that perceptions of invasiveness should be understood in relation to key disease and patient factors which extend beyond the technology, namely to the number, type and effectiveness of available treatments for a given disease. For example, there are no known effective treatments for diseases like amyotrophic lateral sclerosis (ALS) and Alzheimer’s disease (AD) and, in our experience, the dearth of available treatments has influenced patient perspectives on invasiveness of a proposed intervention, particularly in the context of clinical trials (Abrahao et al. 2019; Lipsman et al. 2018).

At the extremes of invasiveness there is general consensus on what is meant by invasive and noninvasive, as the authors allude to in their work. Our experience too suggests that breaking the skin is a rough estimation of this for patients and practitioners in a broad sense. However, it is technologies at the gray zone that will best inform the understanding of this critically important question. Deep brain stimulation, for example, involves an operation, so clearly breaking skin, but does not involve permanent structural changes to the brain; there is no lesion, and stimulation can be stopped and the device removed if needed. How to reconcile then an intervention that involves cranial access but that causes no permanent changes to targeted brain structures in the context of invasiveness?

The reverse is the case with MR-guided focused ultrasound and Gamma Knife Radiosurgery, both established tools for the treatment of pain, tremor, and anxiety disorders (Elias et al. 2016; Kondziolka et al. 2008; Mureb et al. 2020). Here, there is no operation, no penetration of the skin, incisions or cranial openings, but it is nevertheless a permanent, ablative lesion made in key brain structures and pathways driving pathologic symptoms. How to reconcile then an operation that does not involve cranial access, but that nevertheless generates a permanent, irreversible brain lesion? Is this invasive or noninvasive?

To most patients and practitioners, there is little doubt the DBS is an invasive intervention, and that MRgFUS, a lesion notwithstanding, is less so. The invasiveness question likely comes down to one of risk: Are side effects transient or permanent, do they impact quality of life, are the perceived benefits of a given intervention worth taking the actual or theoretical risks? The development of better technology, with improved safety profile, that is more precise and personalized, will likely only make these discussions more complex, and important. The drive to reduce risk, that is the pursuit of noninvasiveness, is what drives most researchers in the field. This is doubtless good for patients. What is critical, however, is that the pursuit of less invasive options does not become a barrier to just access to the full spectrum of neuromodulation, including approaches that entail more risk, and that treatments and recommendations are centered on the urgent need to pursue safe and effective treatments for the most vulnerable patients who are shouldering the burden of these disorders.

FUNDING
The author(s) reported there is no funding associated with the work featured in this article.

REFERENCES
Abrahao, A., Y. Meng, M. Llinas, Y. Huang, C. Hamani, T. Mainprize, I. Aubert, C. Heyn, S. E. Black, and K.
While the various therapeutic neurotechnologies currently in development—TMS, tDCS, and related treatment modalities—have the potential to greatly augment the treatment of a spectrum of diseases and disorders inadequately managed by pharmaceuticals and other currently available interventions, public hesitancy toward the adoption of these treatments remains a major hurdle for their widespread use. This hesitancy is (in part) a symptom of the substantial disconnect between clinicians, researchers, and other experts on one hand and the general public on the other in their respective views on the broader socio-medical implications of these treatments. Issues related to equity of access, acceptable balances between risk and potential benefit, and tolerability of interventions seem to take on drastically different meanings depending on the observer and their position as an expert or, alternatively, as a member of the general public (Antal et al. 2022). While some aspects of the ethics of these technologies have already been extensively discussed in prior bioethical works (Day, Twiddy, and Dubljević 2022; Dubljević 2015), the majority of these examples focus on primarily theoretical concerns pertaining to possible uses of emerging neurotechnologies, rather than more practical, mundane considerations (Voarino, Dubljević, and Racine 2016). While these concerns are valid and worthy of examination—after all, history is replete with