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Using Neuroscientific and Clinical Context to Assess and Manage Changes in Core Personal Traits Caused by Deep Brain Stimulation

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Recent debate has arisen in the neuroethics literature on the extent to which deep brain stimulation (DBS) may cause changes to core personal traits. This has prompted calls for more empirical data to characterize personality changes across clinical conditions, target brain regions, and stimulation parameters: "when the putative effects of DBS on PIAAAS [personality, identity, agency, authenticity, autonomy, and self] are raised by theoretical neuroethicists, most authors do not distinguish diseases and stimulation parameters ... The presumption here is that all patients suffering from different presenting neurological conditions and stimulated in different brain regions and with differing parameters would react in the exact same way to treatment" (Gilbert et al. 2021). In the target article by Zuk and colleagues, the team interviewed researchers and clinicians about their experiences with changes in personality, mood, and behavior in patients with Parkinson's disease, dystonia, essential tremor, Tourette syndrome, obsessive-compulsive disorder (OCD), and depression treated with DBS (Zuk et al. 2023). In this commentary, we wish to further explore clinical and neuroanatomical complexities that may be obscured when generalizing across such varied conditions, many of which combine elements that have traditionally been categorized as either "neurologic" or "psychiatric."

While Zuk et al. include interviews with researchers in neurology and psychiatry, many of the quoted examples in the manuscript are potentially challenging to interpret without knowledge regarding the expertise of the researcher (i.e., neurology, psychiatry, or both) or the condition and brain region being discussed (Zuk et al. 2023). These clinical details have subtle yet important implications for the neuroethical and personal questions posed by different studies. For example, DBS in the subthalamic nucleus (STN) of the basal ganglia is used to treat both Parkinson's disease and OCD, and acute effects of DBS on mood have been reported in both populations during in clinic programming sessions. In Parkinson's disease, STN DBS can elicit "elevated mood" states characterized by hypomania and irritability, which are considered adverse effects that indicate the need to adjust stimulation parameters (Seritan et al. 2021). The likelihood of cognitive and emotional sequelae of STN DBS is partially mediated by the volume of tissue activated. It is believed to be particularly related to current spread into ventral subregions with strong connectivity to limbic circuits involved in reward, motivation, and emotion (Rossi, Gunduz, and Okun 2015). DBS teams leverage this knowledge of STN neuroanatomy to minimize the likelihood of acute mood effects in Parkinson's disease by adjusting device parameters or even surgically repositioning leads to specifically target motor subregions (e.g. dorsolateral STN) and avoid limbic nodes (e.g. ventromedial STN). However, clinical observations of STN DBS effects on mood in Parkinson's disease were part of the justification for targeting non-motor territories of the STN for DBS in OCD (Chabardès et al. 2013). Therefore, the ventral, limbic subregion of STN is a target in OCD but a territory to be avoided in Parkinson's disease. The contrast between ventral STN being an area to avoid in Parkinson's disease versus a target in OCD demonstrates how similar mood effects

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of DBS delivered within the same limbic circuitry can be considered negative or positive outcomes depending on the condition and treatment goals.

Zuk et al. also emphasize that the general awareness of potential changes in mood and behavior reported by clinicians treating patients with DBS is not well represented in the literature (Zuk et al. 2023). One major reason for this gap is that clinical scales are not well suited to measuring changes in core personal traits, leaving a dearth of accurate measurement tools. We agree with the authors and others that have proposed that one potential solution to this problem is to solicit patient and caregiver goals and experiences. Previous research has found that systematically assessing patient goals in Parkinson's disease reveals important information about symptom severity and improvements following DBS that are not captured by standard clinical research measures (Kubu et al. 2017). This finding indicates that patient and caregiver perspectives may help clinicians, researchers, and ethicists to identify the cognitive, emotional, and social effects of DBS and particularly to understand their impact (i.e., valence and intensity) on quality of life.

Another promising tool for measuring changes in core personal traits is computational modeling of mood and behavior. The field of computational psychiatry aims to develop models of cognitive processes underlying cognitive and emotional symptoms that quantify disease-relevant behaviors to improve understanding, prediction, and treatment of mental illness (Huys, Maia, and Frank 2016). These models can provide an objective complement to subjective reports, which can vary in utility depending on the nature of the changes and the degree of each patient's awareness and insight into those changes. For example, apathy is a presenting symptom in $\sim 20\%$ of patients with Parkinson's disease (Le Heron et al. 2019), and caregivers often initiate clinical care in these cases because the patients are not aware of their condition. Even when patients are aware of their condition, subjective reports are susceptible to recall bias, placebo, and nocebo effects that confound both biomarker development and assessment of potential personality changes. Therefore, the detailed characterizations of cognitive, emotional, and social processes provided by computational models of behavior may help clarify debates over what core personal traits are changed by DBS.

Another important contribution from Zuk et al. is their data highlighting potential alternative explanations for changes in personality, mood, or behavior related to neurosurgery, disease progression, and other treatments such as medications (Zuk et al. 2023). The authors note that the direct effects of DBS may be addressable through changes to stimulation parameters, while indirect effects related to other aspects of the disease or treatment will require more comprehensive solutions. We believe that accurate understanding of the etiology of changes in mood and behavior will be vital not only for ethical analysis but also for clinical management of DBS treatments for neurological and psychiatric disorders. For example, apathy in Parkinson's disease is thought to arise from degeneration of dopaminergic reward circuits, but apathy in depression may be rooted in complex interactions across mental and neurobehavioral phenomena such as unhelpful learned beliefs. Neurophysiological data obtained through such devices (particularly sensing-enabled devices) may help to elucidate such etiologic links. For many target conditions, neurotechnological interventions will likely work best when combined with existing pharmacological and psychosocial therapies.

In conclusion, we argue that any potential effects of DBS on personality, mood, or behavior must be interpreted within the clinical context of the patient's disease, history, stimulation target, medication, and other confounding factors. Patient and caregiver perspectives may help identify these changes and understand how they impact quality of life, but objective measures are needed to circumvent flaws in subjective reports. Computational models of behavior are a promising route for quantifying these patterns and isolating the effects directly related to DBS. It will also be imperative to avoid reductionist views that obfuscate the important role of psychosocial components of cognitive, emotional, and social symptoms and wellbeing, particularly in psychiatric conditions for which symptoms may be both intrinsic to the disease and reactive to the environment. Accounting for these factors when identifying and managing changes in core personal traits in the context of DBS will be critical to avoiding misperceptions about these issues for patients, caregivers, clinicians, researchers, neuroethicists, and the general public.

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Changes in Personality, Mood, and Behavior Following Deep Brain Stimulation: No Progress Without Concepts

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When experts disagree regarding whether a certain effect occurred, or a specific phenomenon was observed, in response to an intervention, the controversy need not stem from differing opinions about whether any change was actually detected; it may equally well arise from divergent *definitions* of the phenomenon in question.

In their target article, Zuk and colleagues examine how deep brain stimulation may impact patients' mood, behavior, and personality on the basis of semistructured interviews with researchers involved in deep brain stimulation (DBS). While there was unanimity in believing that DBS can induce changes in mood and behavior, the interviewees were divided regarding its influence on personality: 57% of the interviewed experts maintained that DBS can be associated with modifications of personality, while 22% denied that such a correlation exists (Zuk et al. 2023). Some reported that they "had cases where someone's personality has been changed by DBS" (Zuk et al. 2023, 292), whereas others insisted that they "really haven't seen any big personality changes" (Zuk et al. 2023, 291). How is this extensive discrepancy to be explained?

Semistructured approaches have the advantage of being able to uncover insights that participants might not be able to share in fully structured interviews.

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