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Guest Editorial

What Neuroscience and Neurophilosophy Can Tell Us About the Effects of Deep Brain Stimulation on the Self

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The articles by Goering, Klein, Dougherty, and Widge (2017) and Gilbert and colleagues (2017) are impressive examples of how a psychiatric intervention like deep brain stimulation (DBS) touches upon deep neuroscientific and neurophilosophical issues. Briefly, Gilbert and colleagues (2017) investigate subjective experience of the self and report self-estrangement in some DBS patients with Parkinson's disease (PD), while Goering, Klein, Dougherty, and Widge (2017) discuss the feasibility of closed-loop DBS and its potential effects on personal identity and agency. I highlight two areas for discussion: (i) neuroscientific and neurophilosophical determination of self and self-estrangement, and (ii) neuronal mechanisms of closed-loop DBS and their involvement of the self.

DEEP BRAIN STIMULATION—SELF AND SELF-ESTRANGEMENT

What is the self? Gilbert and colleagues (2017) discuss different notions of self as suggested in the context of DBS. These include the definition of self by self-representational capacities, foundational–functional model, narrative or relational self-constitution, enactive affordance-based model, and pattern theory of self (for details see Gilbert et al. 2017). What can neuroscience tell us about the concept of self and what does that imply for DBS?

The self can be investigated in functional brain imaging by applying self-related or personally relevant stimuli like person's the own name and comparing them with non-self-related ones like another person's name (Qin and Northoff 2011). These investigations observed predominant involvement of various cortical midline structures (CMS) as the core default-mode network (DMN) (Raichle et al. 2001) during self-related activity (Northoff et al. 2006; Northoff and Bermpohl 2004). Most surprisingly, CMS activity does not change during self-related activity when compared to the so-called resting-state activity (defined by the absence of specific stimuli or tasks) (Schneider et al. 2008; D'Argembeau et al. 2005; Qin and Northoff 2011); this has been described as "rest–self overlap" (Bai et al. 2015; Northoff 2016).

What does the finding of rest–self overlap imply for the concept of self? The brain's resting state or, more precisely, its spontaneous activity can be characterized by a complex spatiotemporal structure. That spatiotemporal structure is maintained by the functional connectivity between different regions forming different neural networks like the DMN with fluctuations or oscillations in different frequency ranges (from at least 0.001 HZ to at least 240 Hz) (Cabral, Kringelbach, and Deco 2013; Northoff 2014a; 2014b). The exact spatiotemporal dynamics of the spontaneous activity including its relevance for our behavior and its mental features remains unclear, though.

A recent study demonstrated that the spontaneous activity's spatiotemporal structure is directly related to self-consciousness: The higher the power of slower frequencies relative to faster ones in CMS spontaneous activity (as measured with the power spectrum as indexed by the power law exponent/PLE), the higher is the degree of private self-consciousness (Huang et al. 2016). Together with others (Qin and Northoff 2011; Duncan et al. 2015; Bai et al. 2015), these data suggest that the spontaneous activity contains information about the self amounting to what I describe as "rest–self containment" (Northoff 2016). Put more philosophically, "rest–self containment" suggests that the brain's spontaneous activity is intrinsically

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individual and subjective. Since that very same individuality and subjectivity is based on the spatiotemporal features of the spontaneous activity, one may characterize and determine the self in a spatiotemporal way, that is, by its degrees of spatiotemporal extension and continuity.

What does "rest–self containment" imply for the effects of DBS on the self? Based on their own findings, Gilbert and colleagues (2017) suggest that the effects of DBS on self are not exclusively and causally related to the DBS itself. Instead, they observe relationship between the preoperative effects of the disease on self and postoperative self-estrangement. This, as I suggest, may be related to the patients' spontaneous activity and its spatiotemporal features. If their spontaneous activity's spatiotemporal activity in specifically CMS is already affected by the disease itself, patients may be predisposed to subsequent self-estrangement effects by DBS. Specifically, one may hypothesize that the preoperative spontaneous activity's CMS frequency spectrum with the relationship between slower and faster frequencies predicts postoperative DBS effects on self. Clinically, one may therefore want to include the measurement of the power spectrum in the brain's spontaneous activity (as in functional magnetic resonance imaging [fMRI] and electroencephalography [EEG]) in relation to the self (as measured by self-task and/or self-consciousness) in future preoperative diagnostics for risk assessment of DBS-related self-estrangement (Gilbert et al. 2017) or alienation (Goering et al. 2017) effects.

Gilbert and colleagues (2017) are right. There is no principal difference between DBS and other forms of therapy like pharmacotherapy and even psychotherapy. They all must interact and interfere with the spontaneous activity's spatiotemporal structure and thereby, by default, also with the self (as it is contained in the former). That interaction may restore the self (rather than replacing it, as the critics argue). I showed in earlier studies (Northoff 1996; 2001; 2004) that the insertion of fetal cells in brain tissue transplantation in PD did not affect the patients' sense of self and their personal identity. Instead, very much like Gilbert and colleagues (2017) report for DBS, the fetal tissue improved the patients' movements and thereby also restored their original predisease self and personal identity (Northoff 1996; 2001; 2004; Northoff and Wagner 2017).

This is even more remarkable given that fetal cells are much closer to the brain and its cells than the rather foreign electrode as inserted in DBS. However, the material used for intervention does not really matter by itself. Whether it is an electrode, fetal cells, drugs, psychotherapy, or magnetic stimulation—what matters for the self is how that intervention modulates the brain's spontaneous activity and its spatiotemporal structure (as it contains the self). Since the self is often altered by especially psychiatric diseases themselves (Northoff 2014c; 2016), DBS-triggered modulation of its underlying spatiotemporal structure in the brain's spontaneous activity may restore the original predisease self. This is exactly what both I and Gilbert and colleagues (2017) observed in the self of patients with Parkinson's disease undergoing fetal tissue brain transplantation and DBS.

CLOSED-LOOP DBS-NEURONAL MECHANISMS AND THE SELF

Goering, Klein, Dougherty, and Widge (2017) point out the future of closed-loop DBS and how it potentially impacts the self. Roughly, closed-loop DBS registers neural activity and delivers stimulation each time when the neural pattern occurs that is related to the target symptom. While the authors welcome the introduction of closed-loop DBS, they are careful if not skeptical about its potential effects on the self, specifically agency. These effects, say the authors, may be mitigated by the support of family and close ones which lets the authors speak of "relational agency."

What can neuroscience and neurophilosophy contribute to closed-loop DBS? Neuroscientifically, one first and foremost needs to be clear about the neuronal mechanisms underlying specific psychopathological symptoms. Despite all progress, current neuroscience and biological psychiatry have not yet revealed how alterations in neuronal activity transform into psychopathological symptoms. Let me give an example of recent resting-state fMRI studies on bipolar disorder (BD) by our group (Martino et al. 2016; Northoff et al. 2017).

We observed that manic BD patients showed increased neuronal variability in the resting-state somatomotor cortex. Such increase in neural activity changes may be closely related to increased spontaneous initiation in movements with subsequent psychomotor agitation as a hallmark feature of manic BD. The opposite pattern was observed in depressed BD patients, who showed decreased neural variability in the somatomotor cortex. This is very compatible with decreased spontaneous initiation of movement and action resulting in psychomotor retardation in depressed BD and major depressive disorder (MDD) (for the latter see Northoff et al. 2017).

Can the findings in somatomotor neuronal variability explain the symptoms, that is, psychomotor retardation and agitation, in BD? Yes and no. Yes, they do indeed offer an interesting insight in that changes in neuronal variability in somatomotor cortex may be related to psychomotor changes. No, they do not yet show a direct link between neuronal and psychomotor changes.

To close that gap, one would need to demonstrate direct, causal, and temporal correspondence: Each time that the resting-state neural variability surpasses a certain threshold or peak, a novel movement and thus a change in action may be initiated. If the number of times neuronal variability surpasses the threshold is rather low, no movements will be initiated, resulting in psychomotor retardation—this may be the case in BD depression. If, in contrast, neuronal variability rather often surpasses that threshold, too many movements

will be initiated—this results in psychomotor agitation as in manic BD.

This provides the ground for closed-loop DBS. Closed-loop DBS could be used to either excite or suppress neuronal variability. One would then deliver an excitatory DBS stimulus each time the depressed BD patient's somatomotor variability remains below that threshold; this serves to excite and thus initiate movement and action. One would deliver a suppressing DBS pulse in manic BD each time neural variability surpasses that very same threshold; this serves to inhibit the increased movement and action as in psychomotor agitation.

How about the impact of such closed-loop DBS on the self? At first glance, one would suspect that such closed-loop DBS should have no impact on the self since it only modulates somatomotor cortical activity. However, that is to neglect the other half of our findings. In addition to altered somatomotor neural variability, we also observed changes in DMN with the CMS as core (Martino et al. 2016). Specifically, we observed neural variability changes in DMN opposite to the ones in the somatomotor network: Depressed BD showed increased neural variability in DMN, while manic BD featured decreased neural variability in DMN. This suggests a reciprocal balance between DMN and the somatomotor network in neural variability in manic and depressed BD.

What do these findings imply for the potential effects of closed-loop DBS on the self and its agency? First and foremost, one would expect that "normalization" of sensorimotor neuronal variability also rebalances its relationship to DMN/CMS, which, in turn, should also "normalize" the self. We all know it only too well. If we do not move, we easily develop ruminations and get "stuck" in our self. If, in contrast, we move too much and are forced to do multiple actions at the same time (as in "multitasking"), we tend to forget our self. In short, psychomotor behavior and self are closely linked.

How about the effects of sensorimotor closed-loop DBS on the self? "Normalization" of psychomotor behavior in depressed and manic BD should go along with "normalization" of the self; this is possible by either "liberating the self" from its ruminations in depressed BD or "bringing the self back" as in manic BD. Accordingly, closed-loop DBS may restore the "original self" by replacing the "disease self."

Second, Goering, Klein, Dougherty, and Widge (2017) may now be concerned about the effects of such sensorimotor closed-loop DBS on the agency. If movements and actions are either initiated or suppressed by the electrode, one may attribute that to an external agent like the electrode rather than to the person's own self and its brain. That, as I postulate, may be dependent upon the degree to which the effects of closed-loop DBS are integrated within the brain's ongoing spontaneous activity: The better the DBS pulse is adapted to and thus integrated within the spontaneous activity and its contained self, the more the respectively initiated or suppressed movement will be attributed to the self (rather than to the electrode or some external agent).

Therefore, in addition to the family relations (as suggested by Goering, Klein, Dougherty, and Widge [2017]), agency may be determined by the brain's spontaneous activity and its spatiotemporal structure, including its relation to the world, the world–brain relation, as I like to say (Northoff 2016). Briefly, agency is relational in a spatiotemporal sense.

To conclude, I very much welcome the introduction of closed-loop DBS as psychiatrist to provide better and more individually-tailored therapy. In contrast, I remain careful about it as neuroscientist and neurophilosopher. As neuroscientist, I suggest that we first understand the neuronal mechanisms underlying the psychopathological symptoms; this makes closed-loop DBS more specific and, I guess, will most certainly avoid the rather ambiguous results of current DBS. As neurophilosopher I suggest we redefine our notion of self in spatiotemporal terms that cross the boundaries between neuronal and social dimensions and thus between the brain and world. That makes possible a novel view on self, that is, a spatiotemporal view. At the same time, we can then investigate experimentally the self in spatiotemporal terms by its frequencies spanning between brain and world and how they can be rebalanced by closed-loop DBS. ■

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