Region-Based Approach versus Mechanism-Based Approach to the Brain

Commentary by Georg Northoff (Ottawa)

In "Neuropathologies of the Self: A General Theory," Todd Feinberg discusses the neurological basis of various defense mechanisms and postulates a hierarchy of them. He thereby presupposes the concept of localization in the brain. In my commentary, I discuss the concept of localization in both its empirical and conceptual aspects and contrast it with an alternative approach, a more holistic one to the function of the brain. This pertains to the question of how information is coded in the brain which in turn is central for the kind of neural structure and organization the brain itself employs in its own processing of stimuli and their related information.

Keywords: defense mechanisms, localization, hierarchy, neural coding, neural structure and organisation

In his fascinating Target Article, Todd Feinberg investigated a series of patients with brain lesions with regard to changes in their self—neuropathologies of the self, as he calls them. He assumes that different neuropathologies of the self such as delusional anosognosia, asomatognosia, delusional misidentification, etc. have a profound relationship with the thought and defense style of the normal child. He argues that immature and early defense mechanisms such as denial, splitting, projection, and wishful fantasy are as crucial in the adult's neuropathologies of the self as they are in the normal development of the child's self.

Neuroanatomically, he observes the occurrence of these early defense mechanisms especially in patients with right frontal cortical lesions. He therefore concludes that proper function of the right hemisphere, especially in the frontal cortex, may be crucial in overcoming immature early defenses since, if it is lesioned, it seems to trigger the recurrence of them in adulthood. Feinberg therefore assumes that there must be "a left-brain to right-brain defensive shift" between the ages of 3 and 8 years—a developmental shift away from immature defense functions and fantasies toward more mature defenses and the inhibition of fantasies, with the latter being mediated by the maturation of the right hemisphere.

Lesion of the right hemisphere lets the left hemisphere, which is associated strongly with verbal functions, take over. The fact that early immature verbal defenses such as projection, splitting, verbal denial, and fantasy are still functioning in the case of right hemispheric damage lets one assume their left hemispheric mediation, while the occurrence of more mature defense mechanisms such as isolation, reaction formation, rationalization, etc. seem to be tied to proper right hemispheric functioning.

A recent brain imaging study that investigated the relationship of early and late defense mechanisms with the glucose metabolization rate in different regions confirms the left–right hemispheric difference (see Reznikova et al., 2004). Investigating patients with multiple sclerosis, they observed that almost all defense mechanisms were negatively related to the glucose metabolization rate, especially in the limbic, frontal, and temporal cortical regions. Moreover, they observed that immature defenses such as denial, projection, and regression were associated with left hemispheric glucose metabolization, whereas all other defenses—that is, more mature ones (intellectualization, reaction formation, compensation, repression)—correlated, rather, with right hemispheric metabolization.

Among the various regions in the brain, the right hemispheric ventromedial prefrontal cortex/orbitofrontal cortex seems to be of special relevance. Solms (1999) and others (e.g., Solms & Turnbull, 2002; Solms, Turnbull, Kaplan-Solms, & Miller, 1998) also pursue a region-based approach to the brain. Solms (1999), for instance, investigated psychoanalytically four patients with lesions in predominantly the right ventromedial prefrontal cortex. He reports that these patients show almost complete loss of their internal monitoring and control over their mental states, with subsequent regression onto a bodily level. Based on these findings, he assumes the ventromedial prefrontal cortex to be crucially involved in inhibiting psychological primary processes and binding drive energy. The ventromedial prefrontal cortex may consequently be crucial in constituting secondary processes while at the same time inhibiting primary processes.

Based on these and other empirical findings, Schore (2003) assumes the right ventromedial prefrontal cortex/orbitofrontal cortex to be crucial in constituting

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socioemotional functions. The right ventromedial prefrontal cortex/orbitofrontal cortex receives afferent connections from all sensory regions, from the reward network including the ventral striatum and the ventral tegmental area, and from the emotion network and the limbic system including the amygdala. According to Shore, this connectivity pattern makes the right ventromedial prefrontal cortex/orbitofrontal cortex ideally suited for representing self- and object-images. The convergence of connections from the other systems allows the right ventromedial prefrontal cortex/orbitofrontal cortex to control them and, as Schore says (2003), to gate them (see also the Target Article). This may then result in selecting certain inputs while inhibiting others, which would be well compatible with Solms's assumption of this region being involved in inhibiting primary processes and constituting secondary processes.

Based on the lesion approaches, Feinberg presupposes what I call a "localization-based approach to the brain." A localization-based approach to the brain assumes that specific regions or network the brain are related to specific psychological functions and ultimately also to specific defense mechanisms. The focus is consequently on inferring from the lesions and their predominant defense mechanisms the specificity of that particular region for that particular defense mechanisms.

Such a localization-based approach must be contrasted with what I call a "mechanism- and coding-based approach" to the brain. Rather than associating specific defense mechanisms with specific brain regions and localizations, I assume corresponding neuronal mechanisms and neural coding that may operate across various regions, if not across the whole brain.[1]

The wider and more inclusive concept of relation entails that my concept of the relational self is no longer based on contents at all, be they bodily, social, or narrative. This allows me to pursue a form- and organization-based concept of self that determines the self by a specific form or organization rather than by specific contents. Most importantly, the shift from content to form allows me to search for corresponding neuronal mechanisms that organize and structure neural activity independent of specific contents and their possible neural correlates. Hence, my shift from a localization-based approach to a mechanisms-based approach.

The focus on neural mechanisms and coding rather than regions and localization also entails that my approach does not start with the distinct regions and localization in the brain. Instead, my emphasis on the brain's neural code and general processing mechanisms such as self-related processing (Northoff & Panksepp, 2008) must be assumed to be presupposed by the regional differentiation, and hence the localization-based approach to the brain. Therefore, I speculatively hypothesize that the neuronal mechanisms and neural coding discussed here are essential in constituting and constructing the regional differentiation with different localization within the brain. This, though, needs to be specified and empirically supported by more concrete data in the future.

If I consider specific regions, I do so only within the context of networks, as, for instance, of midline regions that form a large part of the default-mode network, the brain's apparent resting-state network. For instance, Alstott, Breakspear, Hagman, Cammoun, and Sporns (2009) did make a first step in this direction when they investigated the impact of regional lesions on the brain's neural network; however, they did not specify the exact functional mechanism that guides and lead the impact of a single region's lesion on the rest of the brain's neural network. The transition from regions to networks raises the question of how these networks are constituted and constructed and, more specifically, how the different regions within the networks are integrated to form such networks. I assume here that specific mechanisms are at work—so-called principles of neuronal integration—that allow the coordination and integration of the brain's neuronal activities across its different regions and networks (see Northoff, 2008). Most importantly, I hypothesize that specific defense mechanisms may correspond to specific principles of neuronal integration (for details, see Northoff & Boeker, 2006).

What exactly do I mean by the concept of neuronal integration? Neuronal integration describes the coordination and adjustment of neuronal activity across multiple brain regions. The interaction between distant and remote brain areas is considered necessary for a complex function such as emotion or cognition to occur (Friston, 2003; Price & Friston, 2002). Neuronal integration, focusing on the interaction between two or more brain regions, must be distinguished from neuronal segregation (Friston, 2003; Price & Friston,

[1] Another difference concerns the concept of self. Feinberg assumes a multilayered concept of self when he distinguishes between a bodily, a relational, and a narrative self. The bodily self is the self that is based on our body, the relational self is the one emerging in the interaction with others, and the narrative self is the one that develops and narrates its own history over time. This differs from the concept of self presupposed in my accounts (Northoff & Panksepp, 2008). When I speak of the self as relational, I do not restrict the concept of relation to a particular relation, the social relation to others, as Feinberg does. Instead, I presuppose the concept of relational in a wider sense than Feinberg, including any kind of relation in it, such as one's relation to one's own body mirroring—what Feinberg calls the bodily self—and one's relation to oneself, as in Feinberg's narrative self.

2002). In the latter, a particular cognitive or emotional function or processing capacity is ascribed to neural activity in a single area that is both necessary and sufficient; one can subsequently speak of neuronal specialization and localization. We assume, however, that defense mechanisms such as complex emotional–cognitive interactions cannot be localized in specialized or segregated brain regions. Instead, we assume that defense mechanisms require interaction between different brain regions and, thus, neuronal integration.

For neuronal integration to be possible, distant and remote brain regions have to be linked together, which is provided by connectivity. Connectivity describes the relation between neural activity in different brain areas. There is anatomical connectivity, for which we will use the term *connections* in order to clearly distinguish it from functional connectivity. In addition, Friston and Price (2001) distinguish between functional and effective connectivity: Functional connectivity describes the "correlation between remote neurophysiological events," which might be due to either direct interaction between the events or other factors mediating both events. A correlation can either indicate a direct influence of one brain area on another or their indirect linkage via other factors. In the first case, the correlation is due to the interaction itself, whereas, in the second, the correlation might be due to other, rather indirect factors such as, for example, stimuli based on common inputs.

In contrast, effective connectivity describes the direct interaction between brain areas: it "refers explicitly to the (direct) influence that one neural system exerts over another, either at a synaptic or population level" (Friston & Price, 2001). Here, effective connectivity is considered on the population level because this corresponds best to the level of different brain regions investigated here. For example, the prefrontal cortex might modulate its effective connectivity with subcortical regions, thereby influencing specific functions such as interoceptive processing.

Based on connectivity, neural activity between distant and remote brain regions has to be adjusted, coordinated, and harmonized. Coordination and adjustment of neural activity might not be arbitrary but might be guided by certain principles of neuronal integration (Northoff et al., 2004). These principles describe functional mechanisms according to which the neural activity between remote and distant brain regions is organized and coordinated. I would point out here top-down modulation as an example that may correspond to the defense mechanisms of somatization; there are also other mechanisms of neuronal integration such as reciprocal modulation, modulation by functional unity, and modulation by reversal (Northoff, 2008). Each of these mechanism is supposed to constitute one particular defense mechanism (for details see Northoff & Boeker, 2006).

Taken together, I propose a mechanism-based approach to the brain that focuses on neural coding such as difference-based coding, processual mechanisms such as self-related processing, and principles of neuronal integration rather than on specific brain regions as in a region-based approach. I hypothesize that such a mechanism-based approach to the brain is necessary to fully understand the constitution and construction of defense mechanisms in general and of early and immature ones in particular. The mechanisms-based approach to the brain sketched here only seems to be contradictory to the localization-based approach presupposed by Feinberg. This is so since one may consider both approaches to be complementary rather than contradictory, which, though, would need to be elaborated further in the future.

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Teaching a Neuropsychiatry of Meaning

Commentary by David M. Roane (New York)

Todd Feinberg's Target Article, "Neuropathologies of the Self: A General Theory," offers a way to integrate top-down and bottom-up theories of pathological behavior. Feinberg uses the methodology of both behavioral neurology and psychoanalysis to create a unique synthesis that is greater than the sum of its parts. This approach allows for a discussion of meaning in the clinical investigation of neuropsychiatric disorders. Feinberg's work has broad implications for clinical educators who are charged with the responsibility of helping their students to integrate all the complex aspects of psychopathology. Possible applications for the use of this model in contemporary psychiatric training are considered.

Keywords: neuropsychiatry, meaning of delusions, psychiatric education

The Target Article for this issue of *Neuropsychoanalysis*, "Neuropathologies of the Self: A General Theory," uses the traditions of behavioral neurology and psychoanalysis to move beyond the limitations of both disciplines. Todd Feinberg establishes a model that avoids the polarizing arguments between top-down and bottom-up explanations for behavioral phenomena and creates a new synthesis. For this commentator, a psychiatric educator, Feinberg's article directs us to incorporate a neuropsychiatry of meaning as we educate new clinicians and neuroscientists.

There are several features of Feinberg's thinking worth emphasizing. He begins his account of brain-injured patients, with self-disturbance, using a standard Jacksonian method that explains clinical pathology as a combination of negative and positive factors. He makes an important leap by identifying what he calls "self-related deficits" as a *negative* factor clearly linked to neuropathology. This concept of self-related deficits provides a clear context for the discussion of the critical role of *positive* factors such as psychological defense. Feinberg shows that the former helps make way for the latter by enabling primitive defenses to prevail in frankly delusional cases. In bridging the neurologically produced ego-boundary disturbance with the motivated and adaptive defenses, he has found a unique escape from the dichotomous thinking that has consistently undermined real understanding of neuropsychiatric phenomena.

This feat yields a further benefit. It enables the reader to distinguish, with regard to the symptoms described in these complicated case studies, two concepts that Freud never fully separated: cause and meaning (Gabbard, 2007). While Feinberg's patients implicitly verbalize how they "feel" about their disability, their motivation to deny or otherwise cope with these deficits cannot be viewed as the singular cause of their delusional presentations. Rather, the meaning of the deficit, for the patient, is just one factor in the production of the delusion. The true cause, as elucidated by Feinberg, is best considered to be multidetermined by various precipitating factors. This interplay of hierarchically arranged contributors (see Table 3 in the Target Article) differs from Freudian overdeterminism in two ways. First, the various factors are highly diverse, ranging from cognitive and perceptual deficits to self-related deficits to

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