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Top-down modulation, emotion, and hallucination

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Abstract: We argue that the pivotal role assigned by Northoff to the principle of top-down modulation in catatonia might successfully be applied to other symptoms of schizophrenia, for example, hallucinations. Second, we propose that Northoff’s account would benefit from a more comprehensive analysis of the cognitive level of explanation. Finally, contrary to Northoff, we hypothesize that “top-down modulation” might play as important a role as “horizontal modulation” in affective-behavioral alterations.

In a thought-provoking tour de force, incorporating notions from psychoanalysis, neuropsychology, and pharmacology, but firmly grounded in neuroscience, Northoff’s target article attempts to provide an integral account of catatonia. More specifically, alterations in interactions between prefrontal cortex and parietal and subcortical areas are implicated in the neural basis of catatonia. Consistent with this hypothesis, fMRI evidence reported by Northoff and associates points to an important role for top-down modulation in catatonia. Crucially, this is not observed in the motor disorders associated with Parkinson’s disease, which lends the model considerable specificity. Top-down modulation is defined as “a modulation of subcortical structures by cortical areas as reflected, for example, in the modulation of caudate and other basal ganglia by lateral orbitofrontal cortex” (target article, sect. 5.1). We will adhere to this definition, and use the term accordingly, although it should be noted that “top-down processing” in the cognitive experimental literature refers to the modulation of modality-specific perceptual processing by higher-order processing (e.g., initiated in prefrontal areas) (Kosslyn 1994). We propose that the notion of top-down modulation might not only have explanatory power for neuropsychiatric symptoms such as catatonia, but also for other symptoms such as hallucinations.

Recent theoretical accounts of hallucination have implied that alterations in information processing in which the system assigns a decisive priority to top-down factors in determining the final percept, at the expense of bottom-up information, might contribute to the genesis of hallucinations (Behrendt 1998; Grossberg 2000). With regard to the visual system, evidence from functional neuroimaging indicates that attentional modulation does not only influence processing in sensory areas, but may also affect subcortical processing, that is, activation of the lateral geniculate nucleus (O’Connor et al. 2002). A study of top-down modulation in the auditory modality also observed activation of the thalamus (Frith & Friston 1996). Considering that activation of subcortical structures has been consistently observed in neuroimaging studies of auditory hallucination (Shergill et al. 2000), we hypothesize that altered activation of frontal and subcortical (thalamic) areas might lead to activation of the temporal auditory association cortex, giving rise to the phenomenal experience of hallucination.

In the “levels of explanation” approach to the study of schizophrenia (Mortimer & McKenna 1994), it is assumed that the cognitive level is intermediate between symptoms and neuropathology, and that a detailed cognitive analysis of specific information processing abilities in patients might enable one to connect neu-

rosience with phenomenology. As an example, a recent cognitive neuropsychological case-study of a continuously hallucinating patient contrasted performance of this patient with that of nonhallucinating control patients on a number of cognitive tasks targeted at measuring visual and auditory mental imagery and perception (Aleman et al. 2002). Evidence was found for an increased role of auditory imagery over perception in information processing for the hallucinating patient, as compared to the control patients. Such findings can fuel further neuroimaging research into the neural underpinnings of putative cognitive mechanisms underlying a particular symptom, which in turn will provide data that constrains the psychological models. We would be keen to learn more about this cognitive level in catatonia.

Finally, contrary to Northoff, we hypothesize that “top-down modulation” might play as important a role as “horizontal modulation” in affective-behavioral alterations. Notably, a recent study reported that, contrary to the prevailing view, all brain regions, including the amygdala, responding differentially to emotional faces, did so only when sufficient attentional resources were available to process the faces (Pessoa et al. 2002). The authors concluded that, similar to the processing of other stimulus categories, the processing of facial emotional expression is under top-down control. Given the evidence of alterations in orbitofrontal cortex activation associated with emotional processing in catatonia, and the fact that the orbitofrontal cortex is intimately connected to the amygdala, the hypothesis of altered top-down modulation of the amygdala gains plausibility. We concur, therefore, with Northoff’s assertion that more data are needed concerning the function of the amygdala in catatonia, specifically in relation to the medial orbitofrontal cortex (target article, sect. 4.3.1). Research aimed at elucidating the role of top-down modulation in different neuropsychiatric conditions will undoubtedly further our understanding of these conditions and, ultimately, yield new avenues for treatment.

Nonconscious processing, anterior cingulate, and catatonia

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Abstract: A composite cognitive model of a neuropsychiatric condition should integrate clinical symptoms with the impairments of cognitive information processing. A model of catatonia, for example, should emphasize deficits of nonconscious information processing that impair a patient’s ability to use implicit motor feedback for execution and termination of a voluntary motor activity.

Our understanding of the pathophysiology of neuropsychiatric disorders is limited by the lack of composite cognitive models that could integrate clinical symptoms with the impairments of cognitive information processing. The models that are based only on clinical symptoms imply that the disorders manifesting similar cognitive deficits have similar neural deficits. This implication, obviously, is misleading because it ignores the fact that a cognitive function involves a number of processing steps, and that each step is mediated by distinct cortical areas. Impairment at any of these areas could theoretically cause similar overt cognitive deficits. Therefore, the strategy that is most likely to provide deeper understanding of the nature of a neuropsychiatric condition involves delineation of underlying deficits of cognitive information processing.

An increasing amount of evidence suggests that impairments in the processing of nonconsciously acquired and stored (implicit) information profoundly affect overt cognitive processes (for discussion see Badgaiyan 2000a and b; Schacter & Badgaiyan 2001). In fact, findings from our recent experiments have indicated that

efficient execution of a conscious (explicit) action depends heavily on the efficiency of implicit processing (Badgaiyan 2000b; Badgaiyan & Posner 1997; Badgaiyan 1999). These observations have suggested that prior to the initiation of a conscious action, relevant information is implicitly retrieved, and that this information plays a critical role in the formulation and execution of a conscious action (Badgaiyan 2000 a and b). It is therefore evident that our ability to perform a conscious action is limited if implicit information is either unavailable or is somehow altered. Catatonia is an example of such a limitation. In this condition, nonconscious information regarding the body position and motor activity is either altered or is unavailable to conscious awareness (motor anosognosia). This limits the ability of a patient to formulate and execute a conscious action, resulting in premature termination of the action, and the consequent “catatonic posture.” Thus, even though the deficit in catatonia appears overtly to be an impairment of conscious action, the underlying cause may be the alteration of nonconscious information processing, which results in inappropriate motor action.

Cognitively, motor actions are described either as “willed” or “automatic” actions (Norman and Shallice 1986). While willed actions are voluntary, automatic actions are thought to be carried out nonconsciously. Norman and Shallice (1986) suggested that willed actions are performed by voluntary selection of one or another available alternatives of activity (schema), and that when the activity requires a complex action, selection and coordination between different actions is facilitated by a supervisory system. The automatic action, according to this model, is carried out by a “contention-scheduling” mechanism, which selects an action by lateral inhibition of competing action sequences. Northoff’s hypothesis (Northoff 2003) supports the concept of lateral inhibition by arguing that the catatonic motor impairments are due to altered “horizontal processing.”

Norman and Shallice’s (1986) model assumes that nonconscious actions are not complex, and therefore do not require a supervisory system (Badgaiyan 2000a). Because the supervisory function is carried out by a central executive system, by inference, nonconscious actions should not engage this system. Neuroimaging studies (Berns, Cohen & Mintun 1997; Badgaiyan & Posner 1998), however, have shown that the anterior cingulate, which is a part of the central executive (Badgaiyan 2000a), is involved in a variety of nonconscious actions, including response selection and error monitoring. These findings support the author’s earlier suggestion that nonconscious actions are also regulated by the supervisory function of the central executive system (for discussion see Badgaiyan 2000a).

It is possible that a disruption of this supervisory function at the anterior cingulate is responsible for the catatonic symptoms. Studies suggest that reciprocally connected (Devinsky 1997) discrete regions of the cingulate support either cognitive, affective, or motor function (Badgaiyan & Posner 1998; Bush, Lun & Posner 2000). Because catatonic episodes are often triggered by emotional stimuli, it appears that due to the activation of the affective part of the cingulate, its motor part is excessively inhibited, resulting in the arrest of a motor activity. Further, since the cingulate is involved in the response selection process (Berns et al. 1997; MacDonald et al. 2000; Pardo et al. 1990; Berns et al. 1997) an inhibition of its motor function may interrupt an ongoing motor activity. Excessive inhibition of the motor part in catatonia could possibly be a result of failure, or alteration, of the supervisory regulation. Northoff’s hypothesis (Northoff 2003) suggests that the reciprocal inhibition of groups of cingulate neurons explains some of the behavioral symptoms of catatonia. This suggestion supports the idea that a failed supervisory system could be one of the underlying deficits in catatonia. Such a failure would explain both the behavioral and the motor symptoms of catatonia.

As argued in the beginning, a cognitive model of a neuropsychiatric disorder should ideally emphasize impairments of cognitive information processing and not the symptoms, because symptom-based models can be misleading. For example, catatonia and

an injured peripheral nerve could overtly present with a similar symptom (lack of motor activity), despite the fact that the neural bases of impairments in the two conditions are entirely different. This underscores one of the problems with Northoff’s hypothesis (Northoff 2003). The idea of drawing parallels between catatonia and the akinesia of Parkinson’s disease (PD) indicates the hypothesis’ emphasis on the symptom, rather than on cognitive information processing. Even though both conditions clinically present as a paucity of motor activity, the deficits in these conditions are a result of entirely different neurocognitive impairments. In catatonia, the deficit is mainly cognitive, whereas it is primarily motor in Parkinsonian akinesia. The fact that motor cognition is severely impaired in catatonia, but remains relatively intact in PD, suggests that altered implicit information processing is a characteristic of catatonia, but not of Parkinsonian akinesia.

Because of their distinct cognitive identities, drawing parallels between these two conditions can be misleading. The hypothesis, however, acknowledges that the altered nonconscious processing may be responsible for the overt motor deficits of catatonia. This makes it an interesting and promising hypothesis that could be a good starting point for the formulation of a composite cognitive model of catatonia.

Catatonia isn’t ready for a unified theory

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Abstract: Northoff’s target article presents a unifying theory of the pathophysiology of catatonia, as compared to Parkinson’s disease. We address two arguments in particular that do not appear justified by available evidence: (1) The physiological basis of catatonia is the breakdown of right hemisphere prefrontal-parietal cortical connectivity, and (2) Dysfunction in this system results in specific deficits in termination of action.

In the target article, Northoff proposes that the distinction between cortico-cortical modulation (“horizontal”) and cortical-subcortical modulation (“vertical”) may serve to clarify the heretofore hazy separation between “neurologic” and “psychiatric” disorders. Unfortunately, the argument is made in the context of a novel and, we believe, untenable unified theory of catatonia. Northoff’s theory of catatonia holds that right parietal dysfunction is critical to the pathology, and that catatonia can be functionally characterized as a deficit specifically in the termination of action. It is to these claims that we direct our comments.

The multiple and varied etiologies of catatonia pose a challenge for any attempt to relate it to a particular underlying pathology. Catatonic symptoms may arise from various psychiatric conditions (schizophrenia, major depression, bipolar disorder), or any number of neurologic and medical etiologies, including epilepsy, posterior fossa atrophy, and Wernicke’s encephalopathy (e.g., Realmuto & August 1991). Lesions of diverse etiology, including the frontal lobe, limbic system, diencephalon, and basal ganglia have also been reported to produce catatonia (Saver et al. 1993). Rosebush et al. (1990), on whose study Northoff et al. (1999a) base several of their diagnostic criteria for catatonia, reported that 10 out of 15 catatonic patients had “evidence of pre-existing CNS vulnerability for their catatonia” (p. 358), including hydrocephalus, lacunar infarction, and generalized cerebral atrophy. Further, in this study CNS abnormality was evident in 8 of 12 responders to lorazepam, suggesting that the effects of lorazepam may be highly nonspecific, and that distinctions between “psychogenic” and “nonpsychogenic” catatonia may not be functionally meaningful. The fact that these “organic” catatonic syndromes may account for a significant proportion of catatonic cases – and that very few result from specific deficits in the circuitry that Northoff proposes to be dysfunctional in catatonia – appears to pose a significant problem for the theory.