

# Toward a neurobiologically informed psychiatry

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## Abstract

Schizophrenia is a severe and, at the same time fascinating disorder. It is traditionally defined as a «dissociation» of higher brain functions, which implies a modular organization of the brain up to its highest levels of organization. This short review shows how the study of the disorder is still flawed by fundamentally different definitions of the disorder, and that a consistent naturalistic approach may help to revise the vocabulary of psychiatric disorders, opening the way towards a neurobiologically informed psychiatry. Empirical studies and clinical importance supporting this novel approach are summarized.

## Keywords

Neuroscience, Phenomenology, Schizophrenia,

Psychiatry is traditionally placed at the ridge between humanities and natural sciences. This position is in principle very attractive. It should allow studying all the different dimensions of human experience and behavior, which can be understood at the same time as expressions of the living organism, and its metaphysical reality. However, the contribution of psychiatry to a comprehensive view of body and soul (or brain and mind) is notably disappointing. Since the important contributions of late 19th-century neuroanatomy, the different streams of research, applying either humanistic or naturalistic research methods, appeared to be fundamentally antagonistic. Each claimed to own the proper and exclusive method to understand mental phenomena and human behavior. A recent culmination of this apparently never-ending controversy was reached with the public discussion about the existence of a free will in humans.<sup>1</sup>

Recent progress in functional brain imaging has created hope to overcome this conjectural logjam: Studies were published showing links between brain activation patterns and mental phenomena like romantic love,<sup>2</sup> religious faith,<sup>3</sup> shame or guilt.<sup>4</sup> Although such apparent conciliations between natural science and humanities were appealing at first glance, the fundamental constraint remains unresolved: the correlational nature of the psychological constructs with the biological measures. In fact, a consistent naturalistic approach requires testable, mechanistic hypotheses to link brain activity to behavior.

Schizophrenia is a severe mental disorder and, at the same time, a fascinating model to study the relationship between brain activity and essential capacities of the human mind like logical thinking, action planning, and complex emotional interactions. The classical concept of “dissociation” of such brain functions is embedded in the name schizophrenia that was created more than a century ago.<sup>5</sup> It implicitly assumes underlying brain structures with functional segregation—in modern words, a modular organization of the brain up to its highest hierarchies. This model of specialized parallel information processing, however, is in clear contrast to a holistic model implicitly applied in many neuropsychological studies, where pooled information is assumed to be exchanged without anatomical restrictions or priorities between all brain regions and through all levels of organization.<sup>6,7</sup>

The study of schizophrenia may help to resolve the described problem of psychiatric research. The long-term project of our group Systems Neuroscience of Psychosis (SyNoPsis; [www.synopsis.net](http://www.synopsis.net)) aims at mapping psychotic symptoms on brain systems. In this framework, it was

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necessary to create a methodologically consistent basis for both the clinical features and the underlying brain activity. Revising the clinical vocabulary based on our current knowledge about the structural and functional constraints of higher order brain systems, a novel semiotics of psychotic disorders was developed and validated.<sup>8</sup> It was specifically designed to disentangle the clinical manifestations of schizophrenia in behavioral domains that match the functions of three well-defined and functionally segregated, cortico-basal brain systems that are pivotal for human communication. These are, namely, the limbic, the associative and the motor loops including their sensorimotor cortico-cortical connections. In the framework of SyNoPsis, a series of brain imaging and clinical studies have supported the link of specific symptom patterns with functionally interpretable aberrations in the respective brain systems.

In particular, language-related psychotic symptoms, such as the subjective phenomenon of auditory verbal hallucinations and formal thought disorders, were linked to dysfunctions of the auditory and language system that overlaps with the associative loop,<sup>9–14</sup> limbic aberrations were found in patients with specific emotional dysregulations in terms of paranoid experiences of threat or power,<sup>15,16</sup> and motor disorders with components of the motor loop and the executive system<sup>17,18</sup> with immediate clinical importance.<sup>19,20</sup> Recently, even the arcane clinical syndrome of catatonia was related to a hyperactivity of the supplementary motor area, indicating an excess of inhibitory control on motor behavior.<sup>21</sup>

The results of these and other empirical studies support the hypothesis that the proposed three-dimensional symptom structure, segregated in the affective, language, and motor domain, can be specifically mapped on structural and functional abnormalities of the respective brain systems. Proof of concept comes from noninvasive brain stimulation.<sup>22,23</sup> Further, the pathophysiological hypotheses derived from this systems-oriented approach have helped to develop and improve treatment strategies.<sup>24</sup> In clinical practice, the novel approach of a neurobiologically informed psychopathology allows to focus and confine the deficits of the individual patient and thus to shift the attention from the symptoms to the intact communication resources. This is extraordinarily valuable for the clinical management of complex mental disorders. We have studied and observed important advantages of this approach for personalized treatment and clinical management based on clearly defined, easily teachable clinical parameters.<sup>25</sup> Clinical experience further showed that the fundamental revision of our vocabulary for mental suffering based on its natural basis provides arguments and empathy that match the personal perception of our patients and can thus help to strengthen the therapeutic alliance and to develop powerful de-escalation strategies.

Further studies based on neurobiologically informed psychopathology will help to better understand the

differential pathogenesis of subsyndromes within the identified domains. This is promising to give new momentum to focused and hypothesis-driven treatment research on biologically more homogeneous patient groups. Similar strategies may also be applied to other major psychiatric disorders, with evident contribution of specialized brain functions.

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