

A systems approach to schizophrenia

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A main unanswered question in current psychiatry concerns diagnosis of mental illness. Diagnoses are currently based upon observed behavior rather than the etiology of the respective condition [1], as the etiology is most often unknown [2]. This applies in particular to schizophrenia: a currently incurable, very severe, relatively common mental condition. Its symptoms are as complex and widespread as to possibly represent more than one disease in its own right. It structurally and functionally affects various cortical and subcortical regions involved in cognitive, emotional and motivational aspects of behavior, but its cause remains unknown and its treatment elusive.

Dopamine and serotonin abnormalities in schizophrenia constitute today the most established and popular etiological hypothesis (which forms the bases for development of newer antipsychotics). However, schizophrenia has many neurobiological features suggesting an underlying dysregulation of emotional arousal, including limbic, endocrine and autonomic abnormalities. It is possible that the neurotransmitter disfunction may be induced by hyperarousal, making it a consequence of dysregulation, rather than its cause.

We elaborate a theoretical paradigm that could account for the complexity of the disease. Our mathematical model builds upon recent hypotheses that the etiology of schizophrenia is based on neural vulnerability [3] [4] and limbic dysregulation [5] [6]. The theory attributes the mental disorder to a hereditary predisposition that reduces the individual's psychological threshold towards stimuli, to the point where even minor daily stresses will directly trigger psychotic experiences.

The model represents a simplified mathematical view on the evolution of the limbic system under perturbation. Interpretation of the dependence of parameters of the system's dynamics offers an analytical explanation for the "normality/disease" dichotomy. The concept of "bifurcation" could be the key to understanding the threshold between these two states.

Our system models the amygdala – prefrontal interaction as follows (see Figure 1). The linear part accounts for the amygdala responsiveness (and could thus be regarded as a measure of the subject's trait anxiety). The nonlinear part accounts for the endocrine and autonomic modulation of the prefrontal cortex, intermediated by the hippocampus. The nonlinearity is responsible in this set-up for tuning the limbic vulnerability characteristic to schizophrenia. Understanding its effect on the dynamics would be crucial to detecting this vulnerability, as well as to evaluating its strength.

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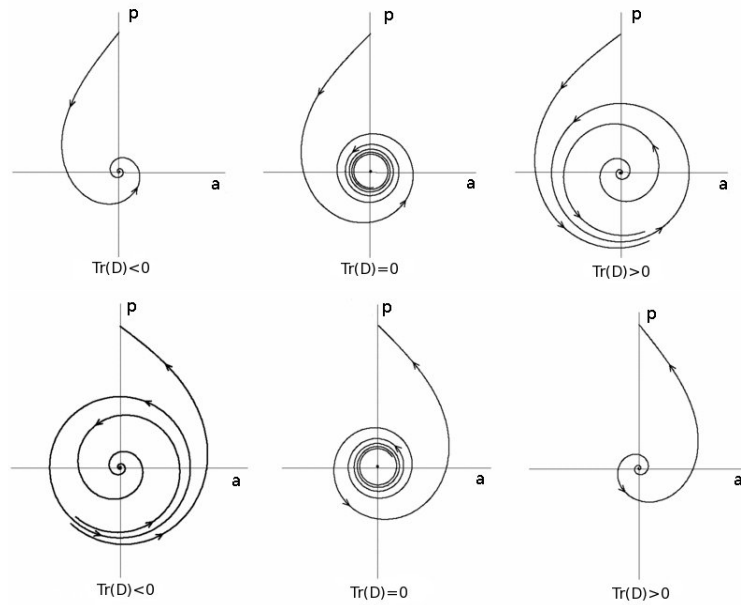


Figure 1: A nonlinear system with negative Lyapunov number $\sigma < 0$ (first row) has a global attractor: a fixed attracting point, for lower amygdala responsiveness and an attracting cycle, for high amygdala responsiveness. In our model, such systems correspond to normal, well-regulated behavior. A system with positive Lyapunov number $\sigma > 0$ (second row) has a locally attracting fixed point for low responsive amygdala and a global repeller otherwise. Such systems correspond to dysregulated, schizophrenic behavior.

References

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