

A mathematical model of schizophrenic cognition

Schizophrenia is a chronic illness that affects the cognitive, emotional and motivational aspects of behavior. It manifests as a heterogeneous set of symptoms including hallucinations, delusional beliefs, thought disorder and emotional disturbances.

Current schizophrenia research proposes various causes for the illness. I adopted a hypothesis proposed by Dr. Lilianne Mujica-Parodi, head of the Laboratory for the Study of Emotion and Cognition (LSEC) at Stony Brook University: symptoms associated with schizophrenia may constitute an end-stage of a cyclic neurodegenerative process, in which limbic dysregulation (caused by compromised inhibition of the amygdala) leads to hyper-arousal, hypercortisolemia, neurotoxicity and further degeneration of the inhibitory limbic areas, and thus to further limbic dysregulation. The unique quantitative research of the LSEC employs control theory, looking simultaneously at the evolution of a whole set of variables over time.

My research with the LSEC is focused on the limbic subsystem. It aims to detect the point where homeostasis falters by perturbing the system and then making a series of measurements along the feedback loops that regulate the excitatory and inhibitory limbic components. The study employed a battery of fMRI techniques applied on 65 controls and 11 patients diagnosed with DSM-IV schizophrenia. All subjects were scanned on a 1.5T Philips MRI and 165 data-point time-series were acquired for six amygdalean, prefrontal and hippocampal regions of interest. During these scans, subjects viewed block presentations of Pictures of Facial Affect (PFA) depicting angry, happy, neutral and fearful emotions.

For each individual, I calculated the values of the cross-correlations for each pair of time-series and performed a between-groups one-way ANOVA. While controls showed overall closely correlated excitatory (amygdala) and inhibitory (prefrontal cortex, hippocampus) activation, evidence for well-balanced negative feed-back, the same task in schizophrenia patients showed amazingly significant dysregulation. The ongoing dynamical systems analysis is expected to emphasize and refine these differences. Looking at the dynamics in phase-space of brain activation levels, the controls appear to be structurally stable systems, while the patients are highly unstable and exhibit pronounced sensitive dependence on initial conditions.

Limbic imbalance is likely to result in wild swings between excitatory and inhibitory components of the system as the body attempts (with difficulty) to reinstate homeostasis. A hyper-reactive amygdala could explain the paranoia, suspiciousness, and agitation endemic to schizophrenia, and also many of its cognitive abnormalities. Under the limbic dysregulation hypothesis, increased dopamine levels are a consequence, not the cause, as implied by most current studies, of the underlying mechanism responsible for schizophrenia.