

MECHANISMS OF GENE-ENVIRONMENT INTERACTION IN SCHIZOPHRENIA

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Environmental factors and both common and rare genetic variants increasing risk for schizophrenia are being discovered, but the neural mechanisms that mediate their impact are only now coming into focus. We discuss work from a translational genetics approach, with a focus on neuroimaging, delineating mechanisms of genetic risk through interaction of prefrontal cortex with striatum, midbrain and hippocampus. Using social status as an example, we identify dissociable neural responses to perceived social rank using functional magnetic resonance imaging (fMRI) in an interactive, simulated social context. In both stable and unstable social hierarchies, viewing a superior individual differentially engaged perceptual-attentional, saliency, and cognitive systems, notably dorsolateral prefrontal cortex. In the unstable hierarchy setting, additional regions related to emotional processing (amygdala), social cognition (medial prefrontal cortex), and behavioral readiness were recruited. Furthermore, social hierarchical consequences of performance were neurally dissociable and of comparable salience to monetary reward, providing a neural basis for the high motivational value of status. Finally, we discuss GEI impacting on these circuits, with a focus on validating epidemiologically identified GEI on the neural circuit level.