

# ***SFB 35 Colloquia in Membrane Transport***

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### **"Neurogenetic mechanisms and distributed neural processing in schizophrenia"**

Disturbed connectivity has been hypothesized to be central for the pathogenesis of schizo-phrenia since Wernicke. Neuroimaging has confirmed and specified this hypothesis by dem-onstrating aspects of decreased, but also increased connectivity, with a focus on prefrontal cortex, the extended limbic system, and the connections between the two. A dysregulation of prefrontal control, impacting on dopaminergic neurotransmission and salience attribution, may be a final common pathway to psychosis, leading to positive symptoms of stimulation of pre-frontal cortex, and abnormal connectivity between prefrontal cortex and hippocampus has been found to be a regionally specific abnormality in schizophrenia. New methods to quantify the entire connectome, derived from graph theory, have extended these regional findings by showing a generalized abnormality in the hierarchical wiring of neocortex and limbic system in schizophrenia. Since the disease is highly heritable, the study of the neural effects of genetic variants implicated in risk for schizophrenia offers a research strategy to dissect the neuroge-netic risk architecture of the disorder leading to, and potentially preceding, first episode psy-chosis. In this talk we review results from the study of risk genes related to dopaminergic stimulation (COMT, RGS4), canonical (DARPP-32) and non-canonical, beta-arrestin mediated signal transduction (AKT1), as well as results from the study of newly discovered variants ge-nome-wide significantly associated with risk for schizophrenia (ZNF804A, CACNA1C) identify-ing systems of disturbed connectivity mediating genetic risk for the disease.