

Oral presentation

## Endophenotypes of psychosis

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from International Society on Brain and Behaviour: 3rd International Congress on Brain and Behaviour  
Thessaloniki, Greece. 28 November – 2 December 2007

Published: 17 April 2008

*Annals of General Psychiatry* 2008, **7**(Suppl 1):S55 doi:10.1186/1744-859X-7-S1-S55

This abstract is available from: <http://www.annals-general-psychiatry.com/content/7/S1/S55>

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There is growing appreciation that the major psychiatric disorders may be composed of sub-syndromes that can be characterized by specific pathophysiological markers. For example, schizophrenia can be deconstructed into several separable sub-syndromes - i.e., psychosis, negative symptoms, and mood instability. Notably, some or all of these sub-syndromes may develop in patients with other major psychiatric disorders, such as bipolar disorder. Each of the sub-syndromes of schizophrenia may be traced to disturbances in specific neurobiological systems. In recent studies of patients with schizophrenia and their non-psychotic siblings, we have identified specific abnormalities in the structure of the thalamus that are attributable to genetic factors, and correlated these abnormalities with losses of gray matter in particular regions of the cerebral cortex. In turn, we have shown that abnormal thalamic structure can underlie defective thalamo-cortical activation. Finally, we have associated abnormal activation of thalamo-cortical pathways with poor performance on tests of working memory and, in turn, with greater severity of negative symptoms. Thus, one can make the inference that negative symptoms in patients with schizophrenia can be traced to a series of disease-related structure-function relationships. Similar relationships may underlie psychosis and mood instability in both schizophrenia and bipolar disorder. Elucidation of these relationships may challenge our current psychiatric nosology, but may be helpful in our attempts to develop novel pharmacological treatments.