S35-02 - **PHARMACOGENETIC STUDIES OF TREATMENT RESPONSE IN FIRST-EPISODE PSYCHOSIS**

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Introduction: Antipsychotic drugs are limited in their efficacy by the relatively poor response of negative and cognitive symptoms of schizophrenia as well as by the substantial variability in response between patients. Although there is a substantial number of pharmacogenetic studies of antipsychotic drug response, relatively few have studied response in first-episode patients. Still fewer have separated effects on positive and negative symptoms, despite the established differences in response to drug treatment between these syndromes.

Objectives: To identify genetic polymorphisms contributing to individual variability in the response of different symptoms to antipsychotic drug treatment of first-episode psychosis.

Methods: Functional polymorphisms in several candidate genes implicated in antipsychotic drug mechanisms have been investigated in first-episode psychosis patients and assessed for their association with response of different symptom subgroups.

Results: We have identified the importance of a common functional polymorphism in the 5-HT1A receptor gene on response of negative and depressive symptoms in initially drug-naive psychotic patients; a longer term (one year) study of first-episode subjects demonstrated an association of the 5-HT transporter gene on negative symptom outcome. Despite the discrepancy between these and other reports, most findings are consistent with the conclusion that dopamine D2 and D3 receptor polymorphisms appear to relate to positive symptom response, while negative symptom improvement relates to polymorphisms of genes influencing 5-HT neurotransmission.

Conclusions: Identifying the genetic factors influencing initial symptom response to antipsychotic drugs may provide both an understanding of the underlying neurotransmitter mechanisms and an indication of the clinical utility of genetic testing.

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