S28-01 - **PHARMACOGENETICS OF THE METABOLIC CONSEQUENCES OF ANTIPSYCHOTIC DRUG TREATMENT**

G. Reynolds

Dept of Psychiatry, Queen's University Belfast, Belfast, UK

Introduction: Several antipsychotic drugs cause profound weight gain which can lead to further morbidity as indicated by the development of metabolic syndrome. These metabolic consequences of antipsychotic drug treatment show substantial variability between individuals, due in part to genetic factors.

Objectives: To identify genetic polymorphisms contributing to individual variability in the metabolic consequences of antipsychotic drug treatment.

Methods: Common functional polymorphisms in several candidate genes implicated in the control of body weight have been investigated for association with weight gain in subjects initiating antipsychotic drug treatment, and with metabolic pathology in chronic schizophrenia.

Results: In two studies of initially drug-free patients, we reported a strong association with antipsychotic-induced weight gain of a promoter region polymorphism of the 5-HT2C receptor, which is known to influence gene expression. The gene for leptin, a hormone controlling food intake, also has a functional promoter polymorphism which is associated with antipsychotic-induced weight gain, particularly in the longer term. Both polymorphisms are associated with circulating concentrations of leptin. Findings in chronically-treated patients have revealed association of the leptin gene polymorphism with the incidence of metabolic syndrome, while we find the obesity-related FTO gene is associated with measures of obesity in these subjects, and also interacts with the 5-HT2C gene in influencing weight gain in drug-naive subjects.

Conclusions: Identifying common genetic factors associated drug-induced weight gain and its metabolic consequences may provide clues as to the underlying mechanisms as well as providing opportunities for personalized medicine in the predictive assessment of metabolic risk.

https://doi.org/10.1016/S0924-9338(10)70061-4 Published online by Cambridge University Press