psychosis susceptibility genes are identified over the next few years, this will have a major impact on our understanding of disease pathophysiology and nosology. This presentation will give an overview of the current state of knowledge and the directions in which the field is moving.

S-30-05

Anomalous asymmetry as the key to the pathophysiology of schizophrenia and bipolar disorder

T. Crow. *POWIC - Dept. of Psychiatry University of Oxford, Oxford, United Kingdom*

Monday, April 4, 2005

S-37. Symposium: Pharmacogenetics of antipsychotic treatment: Predicting clinical efficacy and side effects

Chairperson(s): Dan Rujescu (Munich, Germany), Robert Kerwin (London, United Kingdom)
16.15 - 17.45, Gasteig - Black Box

S-37-01

Effects of polymorphisms in the cytochrome p450 system on response to antipsychotics

J. Brockmöller. *Abteilung Klinische Pharmakolo, Göttingen, Germany*

S-37-02

Towards pharmacogenomics: A large scale association study on response to haloperidol

D. Rujescu, I. Giegling, M. Schafer, N. Dahmen, T. Sander, A. Szegedi, M. R. Toliat, B. Bondy, A. M. Hartmann, H. H. Stassen, H. J. Möller. *University of Munich Dept. of Psychiatry, Munich, Germany*

Haloperidol is highly efficient in the treatment of acute psychosis, especially when severe symptoms predominate. This study investigates the association of response to short-term haloperidol treatment with 120 microsatellites and 200 SNPs in various candidate genes selected based on their role in neurotransmission. One hundred patients with acute psychosis (schizophrenia, schizoaffective, brief psychotic, and substance-induced psychotic disorder) were treated with haloperidol for up to 28 days. Diagnosis was established by applying the SCID I and II interview. Patients were assessed at baseline and on days 3, 7, 14, 21and 28. Improvement and response were measured by using the Positive and Negative Syndrome Scale. Haloperidol plasma levels were also obtained. We will present, for the first time, data on this ongoing large-scale association study on response to haloperidol. Genotyping of further 400 SNPs is under way.

S-37-03

Genetic predictors of response to clozapine and other atypical antipsychotics: Current status and implications of pharmacogenomics

M. J. Arranz, R. Kerwin. *Institute of Psychiatry Clinical Neuropharmacology, London, United Kingdom*

Psychopharmacogenetic research, focusing on evidence selected candidate genes, has identified several contributors to antipsychotic variability. Metabolic enzymes participating in drug bio-transformation were identified as important contributors to response variability as early as the 1950s. Polymorphisms of functional significance have been described in several cytochrome P450 enzymes (Nebert, 2000) and their contribution to antipsychotic biotransformation and treatment related side-effects has been proved (Scordo et al., 2002). Additionally, genetic variants of neurotransmitter receptors and transporters have also been associated with treatment and variability. In particular, dopaminergic, serotonergic and adrenergic gene alterations may contribute to clinical outcome. Current pharmacogenetic investigations include the combination of genetic information for the selection of the most beneficial treatment according to the individual's pharmacogenetic profile. Pharmacogenomic research, using high-throughput techniques, is aiming at better understanding the mechanism of action of psychotropic drugs. Several strategies have been developed using human or animal brains and DNA micro-array technologies for this purpose. Although still at early stages, multi-gene micro-array analyses of brains from drug-treated animals can provide information on the systems altered by antipsychotic treatment and improving our knowledge on drug mechanisms of action. By comparing results from similar studies in human brains, novel targets for antipsychotic activity can be discerned. Pharmacogenomic research will produce a wealth of information during the next decade that hopefully will serve to develop improved and safer psychotropic drugs.

S-37-04

Genetic markers and mechanisms of antipsychotic drug-induced weight gain

G. Reynolds. *Queen's University Belfast Dept. of Neuroscience, Belfast, United Kingdom*

Objective: Weight gain is increasingly recognised as a major problem in treatment with antipsychotic drugs, with effects on both treatment adherence and long-term morbidity. The substantial differences between individuals in the occurrence of this side effect suggests the importance of genetic factors.

Methods: We have undertaken association studies of common promoter region polymorphisms in two candidate genes, the 5-HT2C receptor and leptin, both of which are implicated in the control of feeding and body weight. These studies have been undertaken in first-episode drug-naive psychotic subjects from Chinese Han and Spanish Caucasian populations.

Results: We have reported that the -759C/T polymorphism of the 5-HT2C receptor gene strongly influences short-term treatment-induced weight gain in previously untreated Chinese patients receiving antipsychotic medication. This was also seen in a series of Spanish first-episode patients, in which the genetic effect was sustained over 9 months. In both series, we have found association of antipsychotic drug-induced weight gain with a functional polymorphism of the leptin gene, an effect that appears to be greater in the longer term. Along with initial BMI, these two pharmacogenetic factors account for 30% of the variance in drug-induced weight gain. Studies in the Spanish series demonstrate that leptin levels before treatment were strongly associated with 5-HT2C receptor genotype.

Conclusion: In addition to providing an indication of the common mechanism, effects on leptin secretion, of two genetic polymorphisms controlling drug-induced weight gain, these findings demonstrate the predictive value of pharmacogenetics in determining liability to a major side effect and indicate the potential of genetic testing in informing prescribing decisions and health and lifestyle advice for the patient and doctor.

Monday, April 4, 2005

S-39. Symposium: Early recognition of psychoses

Chairperson(s): Joachim Klosterkötter (Köln, Germany), Patrick McGorry (Victoria, Australia)
16.15 - 17.45, Holiday Inn - Room 1

S-39-01

W. Maier. *Department of Psychiatry, Univ, Bonn, Germany*

S-39-02

The development of schizophrenia and depression from onset until remission of the first psychotic episode

H. Häfner. *Central Institute of Mental Health, Mannheim, Germany*

Objective: Depression is the most frequent comorbidity diagnosis in schizophrenia (40 to 80% in psychosis, 10 to 30% in interval). We studied the question, relevant to early recognition and early intervention, when and how schizophrenia and depression become distinguishable in the early course until remission of the first episode

Methods: We studied a representative sample of 130 first admissions for schizophrenia, 130 age- and sex-matched first admissions for MDD – moderate to severe unipolar depression (ICD-10: F32.10, 32.11, 32.2, 32.30, 32.31) – and 130 equally matched population controls retrospectively until onset using the IRAOS, SANS and DAS and prospectively at first admission and 6-month follow-up using the PSE.

Results: As 81% of schizophrenia patients and 79% of depression patients were drug-naive, comparisons of fairly "natural" symptoms were possible. Early illness course lasted for 5.4 years in schizophrenia and 7.2 years in depression. Risk of attempted suicide was significantly increased in depression – less so in schizophrenia – before first admission. The most frequent first symptoms in both disorders were depressive in type, closely followed by single negative symptoms and indicators of functional impairment. These symptoms constitute a prodromal core syndrome, which, showing a high degree of stability, attained maximum prevalence with the accumulating positive symptoms of beginning psychosis. The syndrome remitted simultaneously with positive symptoms. Several of the prodromal symptoms of both disorders were early and highly significantly separable from health.

Conclusion: Substantial, significant differences between schizophrenia and depression did not emerge until psychotic symptoms appeared. Implications for early recognition and early intervention will be discussed.

S-39-03

P. McGorry. *Department of Psychiatry, Univ, Victoria, Australia*

S-39-04

Neuroimaging in the at risk mental state

P. McGuire. *Institute of Psychiatry, King', London, United Kingdom*

Objective: Relatively little is known about brain structure and function in people with prodromal symptoms

Methods: Subjects meeting PACE criteria for the At Risk Mental State were studied using a 1.5T MRI camera. Diffusion weighted, volumetric and functional MRI data were acquired. Images were processed using X-BAMM. Data were also collected in controls and from patients with first episode psychosis.

Results: Overall, subjects with an At Risk Mental State showed qualitatively similar differences relative to controls as patients with first episode psychosis, but the severity of these differences was less marked

Conclusion: The structure and function of the brain is altered in people with prodromal symptoms.

S-39-05

Early recognition and indicated prevention

J. Klosterkötter, S. Ruhrmann, A. Bechdolf, M. Wagner, W. Maier. *Department of Psychiatry University of Cologne, Köln, Germany*

Objective: This paper presents an outline on the actual results of studies on early recognition and prevention. Accordingly, within a year, the rate of transition into first psychotic episodes using the current prodromal criteria amounts to approx. 37%. Apparently, psychological and pharmacological early interventions seem to decrease the rate and to improve prodromal symptoms and global functioning.

Methods: The presentation of current results will focus on the two multi-centre intervention studies within the German Research Network on Schizophrenia. For the early prodromal phase a psychological treatment program was developed. The late prodromal phase, defined by transient or attenuated psychotic symptoms, is treated with amisulpride in comparison to a psychologically advanced clinical management.

Results: According to first preliminary results a decrease of prodromal symptoms, an improvement of global functioning and a reduction of transitions to psychotic first episodes can be achieved by both, psychological as well as pharmacological early interventions.

Conclusion: First results of the intervention studies in the German Research Network Schizophrenia as well as the international standard of knowledge support the applicability of "indicated prevention".

Tuesday, April 5, 2005

S-43. Symposium: German schizophrenia research network: Results from clinical follow-up and intervention studies