Objective: Eye movement disturbances occurring during fixation and smooth pursuit task have been suggested as endophenotypic marker for genetic studies of schizophrenia. The aim of this study was to find a possible relationship of these disturbances with polymorphism of selected genes of dopaminergic system, using candidate gene approach, in schizophrenic patients.

Methods: Eye movement disturbances during fixation and smooth pursuit task were measured by infrared reflectometry system. Genotyping of Ser9Gly polymorphism of dopamine receptor D3 (DRD3) gene, Val158Met polymorphism of gene for catechol-O-methyltransferase (COMT) and SNP polymorphism in the first intron of cytosolic phospholipase A2 (cPLA2) gene were performed.

Results: An association was found between the intensity of abnormal eye tracking and Ser9Gly polymorphism of DRD3 gene: higher intensity of both kinds of disturbances was associated with Ser allele. The study of Val158Met polymorphism of gene for COMT, the enzyme metabolizing dopamine in prefrontal cortex, revealed an association between Met allele and lower intensity of eye movement disturbances in male schizophrenic patients. A connection was found between a greater degree of eye movement abnormalities and A2/A2 genotype of cPLA2, the key enzyme of the phospholipid metabolism, also influencing dopaminergic activity.

Conclusion: The results obtained may show an association between eye movement disturbances and genes of dopaminergic system in schizophrenia. Abnormal eye tracking can be viewed as one pleiotropic manifestation of schizophrenia and association of polymorphism of various genes with eye movement disturbances may be stronger that with the illness itself.

S-55-04

Endophenotypes for molecular genetic studies in schizophrenia

D. Rujescu. *Department of Psychiatry, Ludwig-Maximilians-University, Munich, Germany.*

Clinical classification systems in psychiatric disorders, including schizophrenia, may describe heterogeneous disorders implying that the current clinical psychiatric classification might not be optimal for genetic studies. Therefore, simpler, quantifiable measures of neuropsychiatric functioning may be more useful in gene discovery. This approach helps to circumvent questions about etiological models. The rationale for the use of endophenotypes in gene discovery is that the endophenotypes associated with a psychiatric disorder are more elementary compared to clinical phenotypes. This also implies that the number of genes required to produce variations in these traits may be fewer than those involved in producing a psychiatric diagnostic entity. Endophenotypes are thus likely to bridge the gap between genes and clinical phenotypes.
We describe our strategy which includes a broad range of schizophrenia endophenotypes and present new data.

Tuesday, April 5, 2005

S-51. Symposium: Treatment of first episode schizophrenia

Chairperson(s): Wolfgang Gaebel (Duesseldorf, Germany), Wolfgang Fleischhacker (Innsbruck, Austria)
14.15 - 15.45, Gasteig - Philharmonie

S-51-01

Outcome in first episode patients under naturalistic conditions

R. Bottlender. *Psychiatrische Klinik der Ludw, München, Germany*

Schizophrenia is one of the most serious mental disorders and often affects quite young people. Although more than two third of patients experiencing their first episode of schizophrenia will recover under modern psychopharmacological treatment strategies, most of these patients will experience a further episode during the following few years, and after a longer course of the illness two thirds will sustain lasting impairment. About one third of patients will be so severely impaired that they will be classified as suffering from a residual or deficit type of schizophrenia. On that background it is of major interest to identify prognostic factors that can be modified by therapeutic/preventive interventions. In the past decade, studies of first-episode schizophrenia noted that the periods between the onset of the patients' psychotic symptoms and their first treatment (=duration of untreated psychosis, DUP) are alarmingly long. Moreover these studies indicate that these extended periods of DUP are important because it may be during this period that the chronicity of schizophrenia happens. Further findings concerning these evidences that were obtained by the project April 2, 1 ("basic study") of the German schizophrenia research network are presented. The project April 2, 1 is a prospective multicenter study on the short and mid-term course and outcome of schizophrenic patients under naturalistic treatment conditions. Major aim of the study is a multidimensional description of the acute and 2-years course and outcome in patients with schizophrenia under naturalistic treatment conditions.

S-51-02

Treatment of first episode schizophrenia

W. Gaebel. *Heinrich-Heine University Dues, Duesseldorf, Germany*

Bringing together schizophrenia research projects in Europe has been initiated by the German Research Network on Schizophrenia. While the last cooperating symposia of five mostly transnational and network-based studies at the AEP congress in Geneva 2004 focused on the presentation of transnational and network-based studies dealing with the prevention and treatment of first episodes, this symposium will deal with the further development of new treatment strategies. In particular the implementation of new treatment strategies into routine care facilities will be carried out with special regard to the role of research networks within the process of research transfer.

S-51-03

Side effects and compliance in first episode schizophrenia

W. Fleischhacker. *Psychiatrische Univers.-Klinik Innsbruck, Innsbruck, Austria*

The first episode of schizophrenia is generally the most responsive to treatment. However, although first-episode patients are the most responsive to treatment, they are also among the most susceptible to antipsychotic-induced adverse events, which is known to have profound implications on compliance. The first contact with antipsychotics will shape the future acceptance of drug treatment. Compliance may be jeopardized by attitude issues ("I don't want to take drugs that change my character") and tolerability problems

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("this medication makes me feels stiff, impotent, fat ..."). As a consequence, it is critical that those patients experiencing their first episode of psychosis are treated with an effective drug that produces minimal side effects. Several studies have reported the improved efficacy and tolerability of second generation antipsychotics compared with conventional agents in first-episode patients. Aside from the issue of side effects, one has to be aware of the fact that compliance problems have a multifaceted etiology. It is influenced by factors related to the patients themselves, to their illness, to the treatments employed and to the patients environment, including most importantly, the relationship between the patients and their care team. All of these factors have to be taken into account when trying to tackle compliance problems. Given the tremendous impact of compliance on the outcome of schizophrenia, successful management of compliance problems has highly relevant consequences both for the welfare of our patients and the economics of our healthcare system. Fleischhacker WW, Hofer A, Hummer M (2003) Managing schizophrenia: the compliance challenge. Science Press.

S-51-04

Neuropsychological correlates of prodromal symptoms in first episode schizophrenia

W. Wölwer, W. Gaebel. *H.-H.-Universität / RKD, Düsseldorf, Germany*

The differential impact of the components of the Vulnerability-Stress-Coping (VSC) model of schizophrenia on relapse and the relationship to prodromal symptoms preceding a relapse are unclear yet. As part of an ongoing comprehensive study on acute and long-term treatment strategies in first episode schizophrenia patients within the German Research Network on Schizophrenia (GRNS), the present subproject aims at (1) a longitudinal assessment of neuropsychological vulnerability indicators and (2) an investigation of the relationship of these indicators with prodromal symptoms and relapses. This subproject focuses on the predictive power of neuropsychological impairments for the risk of relapse and on a comparison of risk indicators of the first manifestation with risk indicators of relapses (in cooperation with a parallel project in high risk individuals by Wagner et al). Assessments take place at inclusion into the long-term treatment study (T0), after 1 year of controlled medication and psychological treatment (T1) and after 1 year of discontinued treatment (T2). A total of 140 patients entered the ongoing study until now. First preliminary analyses revealed the expected neuropsychological impairments at T0. These impairments are more pronounced than - but qualitatively comparable to – the impairments found in prodromal subjects before their first episode. Neuropsychological impairments prove to be unrelated to prodromal symptoms allowing to use both in combination to improve the prediction of poor clinical course. From the latter result a further improvement of relapse prediction can be expected by additional inclusion of stress and coping indicators.

Tuesday, April 5, 2005

S-60. Symposium: The European Prediction of Psychosis Study (EPOS) - First follow-up results

Chairperson(s): Joachim Klosterkötter (Köln, Germany), Don Linszen (Amsterdam, Netherlands)
16.15 - 17.45, Holiday Inn - Room 1

S-60-01

Overview on the recruitment, sample characteristics, and distribution of inclusion criteria of the European Prediction of Psychosis Study (EPOS)

J. Klosterkötter, J. Klosterkoetter, M. Birchwood, D. Linszen, R. K. R. Salokangas, S. Ruhrmann, G. Juckel, A. Morrison, S. Lewis, H. Graf von Reventlow. *Department of Psychiatry University of Cologne, Köln, Germany*

Objective: Early detection and indicated early intervention in the initial prodromal phase should considerably improve the course of psychoses. Yet, the current data base is insufficient for a conclusive, evidence-based evaluation of the benefits of such programmes. This report presents an overview on the recruitment and numbers of subjects seen for inclusion, included into the study, the general sample characteristics and distribution of inclusion criteria of EPOS, an European 4-country naturalistic field-study of the initial Prodrome.

Methods: Across six centres (Germany: Cologne, Berlin; Finland: Turku; The Netherlands: Amsterdam; United Kingdom: Birmingham, Manchester), 16 to 35 year old persons attending specialized services or general psychiatric services were examined. Inclusion criteria were the presence of APS, BLIPS, at least 2 of 9 Basic Symptoms (BS), and Familial risk or Schizotypal Personality Disorder plus reduced functioning (FR+RF). In addition, psychopathological, neurocognitive, neurobiological, psychosocial, and service and treatment-related assessments are carried out at baseline, 9- and 18-months follow-up.

Results: Shortly before the end of the inclusion period, more than 1500 persons had been seen for inclusion into EPOS, of whom almost 250 putatively prodromal persons had so far been included. A high percentage had presented themselves with BS and/or APS, a smaller percentage with BLIPS or FR+RF. However, the distribution of inclusion criteria remarkably varied among the different European regions.

Conclusion: These data will give a first sufficient foundation for an evaluation of the applicability and cost-benefit ratio of an integrative European early detection and intervention programme.

S-60-02

D. Linszen. *Academic Medial Centre, Univer, Amsterdam, Netherlands*

S-60-03

Quality of life of patients at risk of psychosis. Results of the EPOS study

R. K. R. Salokangas, R. K. R Salokangas, A.-M. Heinisuo, J. Klosterkötter, S. Ruhrmann, D. Linszen, P. Dingemans, M. Birchwood, P. Patterson. *Department of Psychiatry, Univ, Turku, Finland*

Objective: The main aim of the European Prediction of Psychosis Study is to study a large sample of young patients who are at risk of psychosis and to estimate their conversion rate to

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