**Objectives:** A common functional polymorphism G1947A of the catechol-O-methyltransferase (COMT) enzyme has gained interest in schizophrenia research because of its critically involvement in dopamine catabolism and frontal lobe function. An assumed mechanism of dopamine is the reduction of noise in prefrontal neural networks during information processing. The hypothesis was tested whether a variation of the COMT genotype is associated with prefrontal noise, which is in part reflected by the frontal P300-amplitude.

**Methods:** The P300-component (auditory oddball) was recorded in 100 schizophrenic patients and 240 healthy controls. Three single nucleotide polymorphisms of the COMT gene were investigated.

**Results and Conclusion:** We observed a significant effect of G1947A COMT genotype on frontal P300-amplitude. Lower frontal P300-amplitudes occurred in homozygous carriers of the Met allele in schizophrenic patients. This suggests that the amount of noise in prefrontal neural networks during information processing might be in part under genetic control, which is mediated by dopamine. Moreover, new results concerning theta and delta activity, which are important oscillatory components of the P300 amplitude, will be presented.

## S-46-05

Abnormalities of auditory information processing in patients at risk for psychosis

A. Brockhaus-Dumke, F. Schultze-Lutter, R. Pukrop, I. Tendolkar, J. Klosterkötter, S. Ruhrmann. *University of Cologne Psychiatry and Psychotherapy, Köln, Germany*

**Objective:** As part of a multidimensional approach to the early recognition of psychosis, sensory gating indices, mismatch negativity (MMN) and P300 reflecting different aspects of auditory information processing were investigated for their qualification as a neurobiological at-risk indicator of psychosis.

**Methods:** P50 and N100 gating (double click paradigm), MMN (3-tone oddball paradigm, duration and frequency deviants) and the P300 (2-tone oddball paradigm) were examined in 66 patients at risk, 37 patients with schizophrenia free of neuroleptic treatment, and 44 controls. The prodromal state was defined by a high-risk cluster of basic symptoms obtained from the data of the Cologne Early Recognition Study (Klosterkötter et al. 2001).

**Results:** Sensory gating resulted in P50 ($p < .05$) and N100 amplitudes ($p < .01$) and the N100 gating score ($p < .003$) were significantly reduced in patients with schizophrenia. Similarly, MMN amplitudes ($p < .05$), P300 amplitudes ($p < .001$) and P300 latencies ($p < .001$) showed a significant amplitude reduction res. latency prolongation in patients with schizophrenia. The ERP parameters of patients at risk lay in between controls and patients with schizophrenia.

**Conclusion:** Our results show deficits in auditory information processing in patients with schizophrenia – extended to a sample of neuroleptic-free patients. The sample of patients at risk is heterogeneous as regards the outcome 'first-episode psychosis' and time until transition (50% risk to develop a psychosis within 2 years after assessment). In patients at risk, early stages of information processing (P50) seem to be affected to a minor degree compared to later stages reflecting automatic processes such as stimulus evaluation (N100) and comparison with a memory trace (MMN) as well as higher cognitive processes (P300).

**Tuesday, April 5, 2005**

# S-55. Symposium: Endophenotypes for molecular genetic studies in schizophrenia

*Chairperson(s):* Dan Rujescu (Munich, Germany), Florence Thibaut (Rouen, France)
14.15 - 15.45, Holiday Inn - Room 1

## S-55-01

Theory and practice in quantitative genectics: The use of endophenotypes in detecting QTLs for schizophrenia

D. Posthuma. *Department of Biological Psych, Amsterdam, Netherlands*

## S-55-02

Genetic variations underlying electrophysiological endophenotypes in schizophrenia

F. Thibaut. *INSERM EMI 9906, IRFMP, Facult, Rouen, France*

**Objective:** Twin and adoption studies, as well as familial clustering, have supported a genetic aetiology for schizophrenia. A model involving numerous interactive genes with minor effects interacting with environmental factors is hypothesized. The complexities of the genetics of schizophrenia and the lack of precise phenotype definition have made classical genetic studies quite unproductive.

**Methods:** Alternative genetic strategies have been used such as the endophenotype strategy. As suggested by previous studies, abnormal sensory gating, measured by the P50 paradigm, could be an endophenotype predisposing to schizophrenia. In addition, we have measured simultaneously three electrophysiological paradigms in schizophrenic patients, non schizophrenic first-degree relatives and normal controls: P50 inhibition, antisaccade paradigm and smooth pursuit. We have evaluated the concordance rates among these 3 markers.

**Results:** We have shown a significant association between the presence of at least one -2 bp deletion located within exon 6 of the alpha7-like nicotinic receptor subunit gene and the P50 sensory gating deficit in the general population. We have also reported a significant association between the promoter -194C polymorphism of the nicotinic alpha7 receptor (CHRNA7) gene and a normal P50 sensory gating. The concordance rates among the three electrophysiological markers will be reported.

**Conclusion:** A recent study has reported polymorphisms located in the core promoter region of the CHRNA7 gene as risk factors for the sensory gating deficit. This -194C allele polymorphism is probably in linkage disequilibrium with other causal variations for the P50 sensory gating deficit. The three different paradigms measure different aspects of central inhibition.

## S-55-03

Genetic analyses using eye movement disturbances as endophenotypic marker in schizophrenia

F. Rybakowski, A. Borkowska, P. Czerski, J. Hauser. *Poznan University of Med. Sci. Psychiatry, Poznan, Poland*

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**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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