**Monday, April 4, 2005**

## S-33. Symposium: Molecular foundations of schizophrenic psychoses

*Chairperson(s):* Johannes Thome (Swansea, United Kingdom), Gavin Reynolds (Belfast, United Kingdom)
14.15 - 15.45, Holiday Inn - Room 1

### S-33-01

Genetics of electrophysiological endophenotypes in schizophrenia

G. Juckel. *Campus Charite Mitte, Berlin, Germany*

For many years, changes haven been consistently found in the electrophysiological parameters in schizophrenic patients. The event-related auditory P3000 which is considered as expression of general cognitive processes such as attentionn, and the mismatch negativity (MMN) which is associated with the working memory function, both show amplitudes lower than those found in healthy controls. The so-called loudness dependence of auditory evoked potentials (LDAEP), currently in discussion as an indicator of the central serotonergic function, is lower in schizophrenic patients, which suggests excessive serotonergic activity in these patients. These electrophysiological changes, however, are not found in all patients, a fact which might indicate the existence of biologically homogenous subgroups. In the talk, various studies will be presented which point out that genetic polymorphisms are related to the electrophysiological endophenotypes in schizophrenic patients above mentioned. A close relationship was found on the one hand between the P300 and polymorphisms of COMT and of the D3-receptor and on the other hand between loudness dependence of auditory evoked potentials and the serotonin transporter polymorphism.

### S-33-02

M. Noethen. *Centre for Medical Genetics University of Antwerp, Antwerp, Belgium*

### S-33-03

Neurotransmitter pathology of schizophrenia

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

**Objective:** The role of neurotransmitter systems in schizophrenia is far from fully understood. One can identify three different ways in which neurotransmitters may be involved in the disease; there are those neurotransmitters associated with the neuronal deficits reflecting brain pathology, those demonstrating dysfunction secondary to that neuronal pathology, and those affected by antipsychotic drug treatment. Thus while GABA and glutamate in the first group, dopamine is in the second and third groups.

**Methods:** The neurotransmitters most strongly associated with the neuropathology of schizophrenia are GABA and glutamate. We have investigated these pathologies in human brain tissue collected at post mortem by identifying GABAergic neurons containing calcium binding proteins, by assessing markers for glutamatergic synapses and by determining levels of N-acetylaspartate, a marker for the integrity and viability of neurons.

**Results:** We have identified, in the hippocampus and frontal cortex, specific deficits of a subtype of GABAergic neurons, defined by the presence of parvalbumin, as well as dysfunction of glutamate systems as demonstrated by e.g. losses of N-acetylaspartate and glutamate uptake sites. Whether these abnormalities are present during early development, or appear later as the psychotic symptoms emerge, remains unclear. However it has been hypothesised that GABAergic deficits may occur in a vulnerable period during development and this would subsequently lead to effects on glutamate systems. Some of the findings (e.g. NAA deficits in the cortex, parvalbumin deficits in the hippocampus) can be mimicked in certain animal models of the disease.

**Conclusion:** The involvement of neurotransmitters in many aspects of the pathophysiology and pharmacology of schizophrenia has been a source of confusion, but understanding this involvement is the one way in which we may successfully bridge the substantial gap in understanding how drug action can influence the effects of brain pathology in schizophrenia.

### S-33-04

J. Thome. *School of Medicine, Dept. of Psychiatry, University of Wales, Swansea, United Kingdom*

**Objective:** Traditionally, alterations in neural plasticity have been postulated as important factors involved in the etiopathogenesis of schizophrenic psychoses. Using molecular biological methodologies including genomics, epigenomics and proteomics, it is possible to test such hypotheses and to clarify the role of neural plasticity in schizophrenias. For example, neurotrophic factors and synaptic vesicle proteins represent interesting molecule families which are possibly involved in the pathogenesis of at least some forms of schizophrenia and also regulated by antipsychotic drugs. The phenomenon of neurogenesis represents a further form of neural plasticity with potential relevance for psychotic disorders and their treatment.

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## S-30. Symposium: New challenges to the dichotomy schizophrenia versus affective disorder - Part I

*Chairperson(s):* Heinz Häfner (Mannheim, Germany), Wolfgang Maier (Bonn, Germany)
14.15 - 15.45, Gasteig - Black Box

### S-30-01

Depression as prodrome of schizophrenia

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

**Objective:** Depression is a frequent comorbidity diagnosis and a depression factor the fourth symptom dimension of schizophrenia. Risk factors common to both are genes, pre- and perinatal complications, mild structural brain anomalies and neuroticism, all more pronounced in schizophrenia.

**Methods:** We studied temporal and psychopathological associations between schizophrenia and depression in a representative sample of 130 first admissions for schizophrenia, individually matched by age and sex, 130 first admissions for unipolar depression

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