degenerative processes. These processes, once turned on, are not disease-specific but part of a final common deleterious pathway characterized by disturbed neurotrophic/neuroprotective capacity. Neuroprotective therapy in these diseases should reduce degeneration and enhance regeneration. As an example, erythropoietin (EPO) is a candidate compound for neuroprotection in neuropsychiatric disorders. We have prepared the ground for its application in a first neuroprotective add-on strategy in schizophrenia, aiming at improvement of cognitive function as well as prevention/slowing of degeneration.

Methods: Methods and Results: Using rodent studies, immunohistochemical analysis of human post mortem brain tissue and nuclear imaging technology in man, we demonstrate that: (1) peripherally applied recombinant human (rh) EPO efficiently penetrates into the brain, (2) rhEPO is enriched intracranially in healthy men and more distinctly in schizophrenic patients, (3) EPO receptors are densely expressed in hippocampus and cortex of schizophrenic patients but less in healthy controls, (4) rhEPO attenuates haloperidol-induced neuronal death in vitro, and (4) peripherally administered rhEPO enhances cognitive functioning in mice in the context of an aversion task involving cortical and subcortical pathways believed to be affected in schizophrenia. These observations, together with the known safety of EPO, render it an interesting compound for neuroprotective add-on strategies in schizophrenia and other human diseases characterized by a progressive decline in cognitive performance. A multicenter proof-of principle trial on "EPO in chronic schizophrenia" will be unblinded in April 2005.

S-65-03

Gene expression profiling: Disease-specific or common patterns?

P. Falkai. *Dept. of Psychiatry Saarland University, Homburg, Germany*

Objective: Recently risk genes for schizophrenia like dysbindin and neuregulin and for bipolar disorders like G 72 were described. Interestingly G 72 seems to be involved into the pathophysiology of schizophrenia and bipolar disorder as well. Gene expression studies give important information of the specific distribution of these risk genes in the pathophysiologically relevant brain structures in the mentioned disorders.

Methods: Using Medline and PubMed with the keywords "affective disorders, psychotic and gene expression" 197 references were found. Based on the abstracts 16 articles were identified dealing with the outlined topic. There are only a few studies where post-mortem tissue from patients with bipolar disorders and schizophrenia in comparison to control subjects were researched at the same time. Therefore the results from different papers are summarized and used for a comparison of gene expression profiles between the two disorders.

Results: Interestingly neuregulin shows a specific distribution in the frontal cortex in schizophrenia depending on the specific isoform. Dysbindin was found to be reduced in the glutamatergic terminals of the hippocampal formation in schizophrenia. These and other results are discussed in view of the pathophysiology of schizophrenia.

S-65-04

Are antipsychotics effective in schizophrenia and affective disorders?

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

New generation antipsychotics have been evaluated against a host of psychiatric disorders and syndromes beyond those of the schizophrenia spectrum. With regard to affective disorders they have been studied in acute bipolar mania, bipolar depression as well as in long-term recurrence prophylaxis. Some evidence is also available concerning treatment refractory depression. Within the schizophrenia spectrum, these agents, next to demonstrating antipsychotic efficacy, also appear to have advantages over traditional neuroleptics in treating concomitant depressive symptoms, especially during the actue phases of the illness. Aripiprazole, olanzapine, quetiapine, risperidone and ziprasidone have demonstrated good antimanic effects either as monotherapy or in combination with mood stabilizers. Recurrence prevention trials are still scarce but at least olanzapine has been shown to prevent both manic and depressive episodes. Clozapine has been suggested to be helpful in treatment resistant bipolar patients and very recent results point to antidepressant effects of quetiapine. A combination of fluoxetine and olanzapine has helped patients with treatment refractory depression. All in all, the evidence is most convincing for antipsychotic and antimanic properties of second generation medications. Whether or not these drugs also have true antidepressant effects, both during acute and maintenance treatment remains to be seen.

S-65-05

Synthesis of part I and part II

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

Wednesday, April 6, 2005

S-69. Symposium: Imaging genomics in psychiatric research

Chairperson(s): Eva Meisenzahl (München, Germany), Colm McDonald (London, United Kingdom)
08.30 - 10.00, Holiday Inn - Room 1

S-69-01

A brain bank for the identification of genes affecting brain structure

E. Meisenzahl. *Psychiatrische Klinik der Ludw, München, Germany*

S-69-02

Genes which influence the structure of the normal brain

I. Giegling, D. Rujescu, A. Kirner, T. Frodl, G. Schmitt, S. Ufer, G. Leinsinger, U. Hegerl, K. Hahn, H.-J. Möller, E. Meisenzahl. *University of Munich Dept. of Psychiatry, Munich, Germany*

Despite the considerable interindividual variation in the size of the human brain, the etiology of less extreme differences is largely unknown. Twin studies point towards a substantial heritability of differences in brain size, and more detailed analyses indicates that strong genetic influences contribute to the variability of each brain structure studied up to now. Recently it was shown that the estimated heritability is 81% for intracranial volume, 79% for the midline cross-sectional area of the corpus callosum, and 79% for lateral ventricle size. Interestingly, the manner in which the brain responds to the environment with advancing age is also genetically determined to a large degree, as demonstrated for the enlargement of the lateral ventricles. Despite the major genetic contribution to

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the variability of brain morphology there is, as yet, only few data available on candidate chromosomal regions or genetic variations which might contribute to these individual variations in humans. Brain development depends on a complex and tightly regulated sequence of events which are highly organized in terms of time and space. Genetic variations that affect the ability of neural cells to proceed through these precisely defined steps of neurodevelopment may cause developmental delays, which are often accompanied by early death of the affected neurons. Thus, genes which are known to participate in neurodevelopment and/or neurodegeneration seem to be appropriate candidate genes. We will report on first common genetic polymorphisms which may influence individual differences of brain volume in healthy volunteers. These, however, being novel findings should warrant further investigation. Nevertheless, our results will hopefully stimulate further studies in this emerging field.

S-69-03

The brain structural phenotypes of schizophrenia and bipolar disorder

C. McDonald. *Institute of Psychiatry Psychological Medicine, London, United Kingdom*

Sunday, April 3, 2005

SS-01. Section symposium: Genes for schizophrenia: Susceptibility to what? part I: Insights from gene-environment interactions

Chairperson(s): Machteld C. Marcelis (Maastricht, Netherlands), Robin Murray (London, United Kingdom)
08.30 - 10.00, Gasteig - Philharmonie

SS-01-01

The impact of childhood trauma on co-morbid symptoms in first episode psychosis

M. Birchwood. *Early Intervention Service, Un, Birmingham, United Kingdom*

Objective: To evaluate the impact of childhood trauma as a risk factor for the development of co-morbid disorders in individuals with first episode psychosis. Background evidence is accruing that levels of trauma and abuse are high in clinical populations but the effect of different types of abuse on co-morbid symptoms of psychosis remains unclear.

Methods: Clients of a first episode early intervention service (n=26) were compared with a non-clinical sample (n=54) employing the Childhood Trauma Questionnaire (CTQ); Dissasociative Experiences Scale (DES) and Hammarberg Scale for PTSD. Samples did not differ in age or gender.

Results: Significant differences were found between the samples for levels of emotional neglect ($p<0.001$) physical abuse ($p>0.02$) sexual abuse ($p<0.04$) and PTSD (p,0.02) with significant correlations between dissociation and childhood trauma sub-scales. Further analysis revealed patterns of substance use and positive symptoms associated with trauma sub-scales in the clinical sample.

Conclusion: A consideration of the role of early trauma on the development of co-morbid symptoms including PTSD and dissociative disorders may have implications for assessment and intervention approaches for individuals with psychosis.

SS-01-02

R. Murray. *Institute of Psychiatry, London, United Kingdom*

SS-01-03

Genes that make you feel blue in the flow of daily life: A momentary assessment study of gene-stress interaction

N. Jacobs. *Maastricht University, Maastricht, Netherlands*

Objective: Individual differences in stress-reactivity constitute a crucially important mechanism of risk for depression. As stress is better conceptualized as the continuous occurrence of minor daily hassles, this study focused on emotional reactivity to stress in the flow of daily life and examined to what degree individual differences in emotional reactivity could be explained by genetic and/or environmental factors.

Methods: 275 female twin pairs (170 monozygotic and 105 dizygotic) participated in this Experience Sampling study (ESM). ESM is a validated structured diary technique assessing stressors and mood in daily life. Individual emotional stress-reactivity was conceptualised as changes in negative affect in relation to minor daily life stressors. Structural equation modelling was used to fit univariate models. The best fitting model was chosen, based on likelihood and parsimony. In addition, saliva samples were collected for determination of functional polymorphims (such as 5-HTTLPR).

Results: Genetic factors (explaining 55 to 68% of individual differences) and individual-specific environmental factors (explaining 32 to 45% of individual differences) influenced daily life stress-reactivity. The best fitting model also incorporated negative sibling interaction.

Conclusion: The demonstration of a genetic influence on the dynamic relationship between minor stress and affective response in the flow of daily life sheds light on the gene-environment interactions that drive the risk to develop stress related disorders such as depression. Differences in stress-reactivity between children in the same family may result in part from compensatory sibling interactions. In addition, the role of functional polymorphisms, such as 5-HTTLPR, in moderating the individual response to minor daily life stress will be discussed.

SS-01-04

Abnormal response to metabolic stress in schizophrenia: Marker of vulnerability or acquired sensitisation?

M. C. Marcelis, E. Cavalier, J. Gielen, P. Delespaul, J. van Os. *Dept. of Psychiatry Maastricht University, Maastricht, Netherlands*

Objective: Previous work suggests that individuals with schizophrenia display an altered HVA-response to metabolic stress. The present study replicated and extended this paradigm, including individuals with elevated genetic risk for schizophrenia.

Methods: Patients with psychosis (n=50), non-psychotic first-degree relatives of patients with psychosis (n=51) and controls without psychosis (n=50) underwent, in randomised order, double-blind administration of placebo and the glucose analog 2-deoxy-D-glucose (2DG), which induces a mild, transient clinical state of glucoprivation. Plasma HVA and cortisol were assessed twice before the start of the 2DG/placebo infusion (baseline values), as

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