are normally responsible for the generation and perception of verbal material. Patients who are prone to hallucinations show functional changes in the lateral temporal, parahippocampal and cerebellar cortices. There are some structural imaging data that suggest that hallucinations are associated with changes in the volume and connections of these areas, but these findings have not been consistently replicated.

Conclusions: The existing neuroimaging data are consistent with cognitive models that propose that auditory verbal hallucinations represent inner speech which has been misidentified as alien.

SS-02-04

Neural correlates of thought and language processes

T. Kircher. *Klinik für Psychiatrie u. Psychotherapie, RWTH, Aachen, Germany*

Objective: Alterations in thought and language are core symptoms of schizophrenia. Studies with structural and functional imaging (fMRI) as well as magneto/electroencephalography (EEG, MEG) on language in schizohrenia will be selectively described. A model will be presented, where brain structure, function, receptorchemistry, cognitive deficits and psychopathology of language related phenomena are integrated. A diffuse brain trauma (genetic, viral) during fetal neurodevelopment results in pathological cell migration, mediated through Relin, within the superior temporal gyrus. Consequently, alterations of the glutamate receptor system and decreased mismatch negativity have been described in schizophrenia. These structural and biochemical changes result in a dysruption of the normal cerebral language lateralisation during childhood. As a result, the mental lexicon, normally in the left superior temporal gyrus, is reversed in adult schizophrenic patients. The production of thought disordered speech is in part due to a decreased activation of the Wernicke Area and the recruitment of the right mental lexicon with its diffuse semantic fields.

Sunday, April 3, 2005

SS-05. Section symposium: Genes for schizophrenia: Susceptibility to what? part II: Insights from neuroimaging

Chairperson(s): Stephen Lawrie (Edinburgh, United Kingdom), Wolfgang Fleischhacker (Innsbruck, Austria)
16.15 - 17.45, Gasteig - Philharmonie

SS-05-01

A. Hofer. *Innsbruck University, Innsbruck, Austria*

SS-05-02

Neuroimaging in people vulnerable to psychosis

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

While genetic factors are clearly important in determining the risk of psychosis, many of those at high risk have no family history of psychosis and in these individuals environmental factors appear to be more relevant. Subjects with prodromal symptoms (meeting PACE criteria) were recruited locally and studied using a 1.5T MRI camera. Most came from ethnic minority groups and had no family history of psychosis. MRI, DTI and functional MRI data were acquired from subjects with prodromal symptoms, healthy volunteers and patients with first episode psychosis. Images were processed using non parametric methods. Compared to controls, subjects with prodromal symptoms showed qualitatively similar differences to those seen in patients with first episode psychosis. However the severity of these differences was less marked in the at risk subjects. Changes in the structure and function of the brain are evident in people with prodromal symptoms and these may be particularly related to environmental risk factors for psychosis.

SS-05-03

R. Kahn. *University Medical Center, GA Utrecht, Netherlands*

SS-05-04

Brain dopamine d1 receptors in monozygotic and dizygotic twin pairs discordant for schizophrenia

J. Hietala. *Turku University & Turku PET C, Turku, Finland*

Objective: Schizophrenia has a heritability of about 80% but the detailed molecular genetic basis of the disorder has remained elusive. We hypothetized that altered dopamine transmission is related to psychosis susceptibility and started a series of neuroimaging studies on the dopamine system in monozygotic and dizygotic twin pairs discordant for schizophrenia.

Methods: We have previously shown that caudate dopamine D2 receptor upregulation is related to genetic risk for schizophrenia using this twin design. Higher dopamine D2 receptor density in caudate was also associated with poorer performance on cognitive tasks involving cortico-striatal pathways (Hirvonen et al, Arch Gen Psychiatry, in press.We now report D1 receptor binding results on the same twin sample.D1 receptor density in the brain was measured with [11C]SCH 23390 and 3D PET.

Results: High D1 receptor density in heteromodal association cortex (angular and supramarginal gyri), superior temporal gyrus and medial prefrontal cortex was associated with increased genetic risk for schizophrenia (unaffected MZ> unaffected DZ>control twins). High D1 receptor binding was also associated with impaired neurocognitive performance.

Conclusion: Our findings suggest that cortical dopamine dysregulation is associated to psychosis vulnerability. The results provide also theoretical rationales for early pharmacological intervention strategies in high risk prodromal subjects.

SS-05-05

What is genetically mediated in subjects at high genetic risk?

S. Lawrie. *Division of Psychiatry University of Edinburgh, Edinburgh, United Kingdom*

Objective: We have found several clinical, cognitive and imaging measures which differ between subjects at high genetic risk of schizophrenia and healthy controls, but these presumably reflect both genetic effects and gene-environment interactions.

Methods: We have examined which of these variables are associated with two specific measures of genetic liability to schizophrenia – a quantitative measure developed by Pak Sham and

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a simple categorical measure according to the presence of affected first degree relatives or not.

Results: Statistically significant associations include performance on three cognitive tests (Rivermead story delayed recall, VF animals, Hayling A); the volumes of the pre-frontal lobes and thalamus; and fronto-frontal functional disconnectivity on fMRI across distinct sentence completion, encoding and retrieval cognitive tasks. Notable non-significant associations include psychotic symptoms, the volumes of the medial temporal lobes; obstetric complications, minor physical anomalies and neurological soft signs. None of the apparently genetically mediated measures were however predictive of psychosis within the high risk cohort.

Conclusion: Overall, the results suggest that some abnormalities of brain structure and function in high risk subjects are genetically mediated, but that others may only become apparent around the time of psychosis onset for as yet unclear reasons.

Monday, April 4, 2005

SS-08. Section symposium: Schizophrenia - Nature and narratives

Chairperson(s): Michael Musalek (Wien, Austria), Christoph Mundt (Germany)
08.30 - 10.00, Holiday Inn - Room 1

SS-08-01

Self and identity in schizophrenia

G. Stanghellini. *Florence, Italy*

SS-08-02

Change of schizophrenic syndromes?

C. Mundt. *Germany*

SS-08-03

Present status of cycloid psychoses

I. Brockington. *Lower Brockington Farm, Hereforshire, United Kingdom*

SS-08-04

Schizophrenia - what for?

M. Musalek. *Anton Proksch Institut, Wien, Austria*

Since the first description of dementia praecox by Emil Kraepelin and the early works on the group of schizophrenias by Eugen Bleuler many definitions of schizophrenic psychoses have been proposed by different schools leading to a Babel in today's diagnostics. The provisional end of the diagnostic dilemma represents the diagnostic criteria of the ICD-10. for schizophrenia in which divergent symptom clusters as delusions, hallucinations, thought disorders, emotional deviations, and social problems or handicaps are included. As schizophrenia is one of the most stigmatizing diagnosis in psychiatry, we thoroughly have to put the question: do we need this diagnostic category any longer. Main goals of diagnostics are the validity of diagnostic criteria with respect to selection of treatment procedures, prognosis making, improvement of communication, topographical aspects, dangerousness, economical and/or political dimensions. As it could be shown in recent analyses the today's most commonly used diagnostic criteria for schizophrenia do not fulfill these main demands. Therefore the diagnostic label of schizophrenia should be abandoned and replaced by diagnostic procedures or models with higher validity concerning the mentioned main goals of diagnostics. A way-out of the today's frustrating diagnostic situation could be a change of paradigms from categorical to dimensional diagnostics. In contrast to categorical diagnostics, e.g. DSM-IV or ICD-10, dimensional diagnostics are phenomenon-, pathogenesis- and process-oriented. Providing a more valid basis for treatment planning and prognosis making dimensional diagnostics represent suitable alternatives to classical diagnostic procedures.

Monday, April 4, 2005

SS-09. Section symposium: Antipsychotics: Effectiveness beyond mere symptom control in schizophrenia patients

Chairperson(s): Manfred Ackenheil (München, Germany), Wolfgang Fleischhacker (Innsbruck, Austria)
14.15 - 15.45, Gasteig - Philharmonie

SS-09-01

Evaluating antipsychotics: Methodological challenges

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

A broad range of study designs are employed to evaluate the pharmacotherapy in psychiatry. These range from small exploratory open studies via the gold standard of the randomized placebo-controlled clinical trial to large pragmatic naturalistic studies. Outcome criteria have traditionally focused on improvement of psychopathological symptoms and on the assessment of safety and tolerability issues. More recently additional outcomes, previously considered as "soft criteria", such as quality of life and social adjustment have gained importance. Various rating scales and assessment instruments are available to reliably quantify changes in the parameters described above. Ideally, the evaluation of psychiatric treatments should be based on studies of different design and scope to minimize the risk of misinterpretation. For instance, while any open clinical trial is subject to an observer bias, RCT's have been shown to lead to a selection bias, that may hamper the generalizability of the results obtained. An earlier use of non-inferiority trials, which have so far been used exclusively in post registration studies is also encouraged. As the focus of safety/tolerability assessment has shifted from a strong emphasis on extrapyramidal motor dysfunctions to non-motor adverse events such as metabolic and sexual dysfunctions, cardiac safety and others, clinical trials designs need to account for this by including more specific side effect rating scales and laboratory tests. In addition, subjective tolerability and compliance need to be assessed with more vigor. In conclusion, a modern evaluation of pharmacotherapy must go beyond traditional measures of psychopathological symptoms and include real life outcomes such as quality of life, psychosocial

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