well as four times post infusion. Data were analysed using multilevel random regression techniques.

Results: During the stress condition, significant increases in plasma HVA and cortisol were found. The increase in plasma HVA level during the stress condition was significantly stronger in patients than in controls, whereas this was not the case in relatives versus controls. The increase in plasma cortisol during the stress condition was significantly less in patients than controls, but no significant difference in the increase of plasma cortisol during stress was found in the comparison between relatives and controls.

Conclusion: Patients with psychosis, but not their non-psychotic first-degree relatives, show an altered neurobiological response to metabolic stress, suggesting that this dysregulation is not a genetically transmitted vulnerability, but an illness-related effect, possibly reflecting acquired sensitisation of catecholamine systems by repeated environmental stressors or repeated stimulation with agonistic drugs.

Sunday, April 3, 2005

SS-02. Section symposium: New developments in functional and structural neuroimaging in schizophrenia

Chairperson(s): Tilo Kircher (Aachen, Germany), Philip McGuire (London, United Kingdom)
08.30 - 10.00, Holiday Inn – Room 1

SS-02-01

Neural networks involved in hallucinations: Integrating structure and function

T. Dierks, D. Hubl, R. Kreis, K. Lövblad, W. Strik. *Bern, Switzerland*

Objective: It has been suggested that alterations in connectivity between frontal and temporal speech-related areas might contribute to pathogenesis of auditory hallucinations and that these circuits are assumed to become dysfunctional during the generation and monitoring of inner speech. Using MR diffusion imaging to assess the directionality of cortical white matter (WM) tracts, we investigated whether previously described abnormal activation patterns observed during auditory hallucinations relate to changes in structural interconnections between frontal and temporal speech-related areas.

Methods: WM directionality (Fractional anisotropy; FA) was assessed in patients prone to auditory hallucinations, in patients without auditory hallucinations, and in healthy control subjects. Structural MR imaging was conducted. A ROI analysis was computed based on an ANOVA for FA maps restricted to WM. Additionally, descriptive voxel-based t tests between the groups were computed

Results: Patients with hallucinations demonstrated significantly higher WM directionality in the lateral parts of the temporoparietal section of the arcuate fasciculus and in the anterior corpus callosum compared with control subjects and nonhallucinating patients. Comparing hallucinating patients with nonhallucinating patients we found significant differences most pronounced in left hemispheric fiber bundles, including the cingulate bundle.

Conclusion: Our findings suggest that during inner speech, the alterations of white matter fiber tracts in patients with frequent hallucinations lead to abnormal coactivation in regions related to the acoustical processing of external stimuli. This abnormal activation may account for the patients' inability to distinguish self-generated thoughts from external stimulation.

SS-02-02

Brain folding in schizophrenia

J. L. Martinot, A. Cachia, T. Kircher. *Orsay, France*

Objective: The most striking, yet poorly understood gross morphological features of the human cerebral cortex are the diverse and complex arrangements of its foldings: the sulci and gyri. Cortical folds are formed during fetal age and childhood (Chi et al. 1977). It has been suggested that abnormal maturation could be a risk factor for schizophrenia (Lewis and Lewitt 2001). Precise evaluations of the folding patterns could then provide cues of the neurodevelopmental aspects related to the pathology (LeProvost et al. 2003).

Methods: We apply new brain morphometry tools providing automatically 3D sulci shape descriptors (surface and depth) from MRI data (Mangin et al. 2004; Cachia et al. 2003). This methods avoids the bias inherent to the image analysis procedures using spatial normalisation. MRI datasets from 30 patients with schizophrenia are compared with 30 controls matched for gender, age, and handedness. MRI were acquired on 1.5 T imagers with sequences providing high contrast between gray and white matters. Sulci were automatically segmented from MR images using Brainvisa software (*http://brainvisa.info*). The heteromodal cortex was investigated, as impaired maturation was hypothesised in these cortical regions in schizophrenia. The Superior Temporal, Frontal and Cingulate sulci (main folds and branches) were automatically delineated, labelled and measured.

Results: Preliminary results from a subset of subjects indicate differences in sulci morphology and asymetry between groups. They are being validated on the whole samples.

Conclusion: Results will be presented during the symposium. Applied on all brain folds, this automatic procedure might highlight regions with developmental variations.

SS-02-03

Auditory hallucinations and the brain in schizophrenia

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

Objectives: Auditory verbal hallucinations are a key feature of schizophrenia. Neuroimaging provides a way of investigating the mechanisms that underlie them in vivo.

Methods: Functional neuroimaging studies have measured regional brain activity while subjects were actually experiencing hallucinations and contrasted this with activity when hallucinations were absent. Another strategy has been to examine cognitive processes that are putatively defective in patients who are prone to hallucinations, and compare the neural correlates of these processes with those in patients who do not experience hallucinations. These functional imaging studies have been complemented by investigations using structural imaging which have examined the grey and white matter correlates of hallucinations.

Results: Overall, functional neuroimaging studies studies suggest that auditory verbal hallucinations involve brain areas that

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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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