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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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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