functional genomic approach for the identification of hippocampal candidate genes for psychosis-related traits and identified several differentially expressed genes and pathways. These are under investigation in ongoing genetic analyses.

S-08-02

Genetic association studies in schizophrenia

M. Gennarelli. *Genetic Unit, IRCCS Centro S., Brescia, Italy*

Objective: Although schizophrenia is a genetic disorder with estimates of risk heritability of around 80%, the identification of susceptibility genes, which act in concert with epigenetic processes and environmental factors, remains an uphill struggle. Genetic association studies have focused initially on the neurochemical theories of schizophrenia detecting, as putative functional candidates, dopamine and serotonin system-linked genes. The feasible association with DRD3 and 5-HT2A receptor genes implies most likely an involvement of other neurotransmitter pathways. A role of glutamatergic signalling in the pathogenesis of schizophrenia has been suggested by the recent identification of five susceptibility genes (NRG1, DTNBP1, COMT, RGS4, G72), alltogether implicated in interlinked processes at glutamate synapses. These promising results come from positional approach and animal models data confirmed with the genetic association studies. Thus, these studies are useful to confirm the role of "candidate" genes based on map or pre-clinical findings but represent the more direct method to test other "candidate" aetiopathological hypotheses. Additional susceptibility genes are emerged from this approach, such as those linked to brain development (BDNF, GDNF, GSK-3β) and to cytokine network (IL-1, TNFa, IL-10). It was only to be expected, these association studies are characterised by a constellation of replica and nonreplica of data because they suffer of some notorious limitations. New methodological strategies are in progress to overcome these limitations improving the reliability of these studies.

S-08-03

Linkage studies in schizophrenia: New findings promise new insights

M. Owen. *Dept. of Psychological Medicin, Cardiff, United Kingdom*

Objective: Genetic epidemiological studies suggest that individual variation in susceptibility to schizophrenia is substantially genetic. However, like other common disorders, the mode of transmission is complex and probably reflects oligogenic inheritance against a polygenic background.

Methods: Genomic approaches to schizophrenia are becoming increasingly feasible as data from the genome project accumulate and technology improves. Attempts to identify genes for schizophrenia have been based on several approaches; systematic linkage studies, association studies and studies of chromosomal abnormalities associated with the disorder.

Results: As larger samples have been studied, a number of relatively convincing linkages have been reported. Moreover analysis of these chromosomal regions has revealed evidence in favour of several positional candidate genes. This evidence now strongly implicates DTNBP1 and NRG1 as susceptibility genes for schizophrenia, while the data for DAO, DAOA, DISC1 and RGS4 are promising. However, there are reasons to remain cautious pending the results of further genetic and biological studies.

Conclusion: The positive findings potentially converge upon abnormalities in glutamatergic neurotransmission in schizophrenia, for which evidence from a number of other sources has already been adduced. However, there are other possible explanations and more work is needed to elucidate pathogenic mechanisms.

S-08-04

The impact of first schizophrenia genes: Focus on dysbindin

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

The first disposition genes for schizophrenia were identified and replicated in 2002 and 2003: for dysbindin, for neuregulin1, and for G72/G30. These major break-through became possible after genome-wide linkage analyses delineated candidate regions (among them intervals on chromosome 6p, 13q, 8p) which were likely to cover disposition genes. Linkage disequilibrium mapping in these regions was able to identify these three genes. Further candidate regions affirmed in recent metaanalyses, are under intensive study in order to identify additional disposition genes. Although disposition genes are identified, the search for pathogenic mutants is more difficult than expected. Up to now, only associations between haplotypes in these genes and the disorder are replicated, but the pathogenic mutant is not identified for any disposition gene. Yet, genotype-phenotype relationships can also be explored for at-risk haplotypes in disposition genes. We report the first associations between at-risk haplotypes of the dysbindin gene (DTNBP1) and brain structure and function in schizophrenia.

Sunday, April 3, 2005

S-17. Symposium: Recent directions in cognitive and experimental research on delusions

Chairperson(s): Frank Laroi (Liege, Belgium), Steffen Moritz (Hamburg, Germany)
16.15 - 17.45, Holiday Inn - Room 1

S-17-01

Experimental psychology of delusions

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

Objective: The present study investigated whether a failure of self-monitoring contributes to core syndromes of schizophrenia.

Methods: Three groups of patients with a DSM IV diagnosis of schizophrenia (n = 27; with either prominent paranoid hallucinatory or disorganization syndrome, or without these symptoms) and a matched healthy control group (n = 23) were drawing circles on a writing pad connected to a PC monitor. Subjects were instructed to continuously monitor the relationship between their hand movements and their visual consequences. They were asked to detect gain changes in the mapping. Self-monitoring ability and the ability to automatically correct movements were assessed.

Results: Patients with either paranoid-hallucinatory syndrome or formal thought disorder were selectively impaired in their ability to detect a mismatch between a self-generated movement and its

https://doi.org/10.1016/S0924-9338(05)80020-3 Published online by Cambridge University Press

consequences, but not impaired in their ability to automatically compensate for the gain change.

Conclusion: These results support the claim that a failure of self-monitoring may underlie the core symptoms of schizophrenia.

S-17-02

The effects of angry and happy expressions on recognition memory for unfamiliar faces in delusion-prone subjects

F. Laroi, A. D'Argembeau, M. Van Der Linden, C. Bertoni. *University of Liege Cognitive Psychopathology Unit, Liege, Belgium*

Objective: Numerous studies suggest a cognitive bias for threat-related material in delusional ideation. However, few studies have examined this bias using a memory task. We investigated the influence of delusion-proneness on identity and expression memory for angry and happy faces.

Methods: Participants high and low in delusion-proneness were presented with happy and angry faces and were later asked to recognize the same faces displaying a neutral expression. They also had to remember what the initial expressions of the faces had been. Remember/know/guess judgments were asked for both identity and expression memory.

Results: Results showed that delusion-prone subjects better recognized the identity of angry faces compared to non-delusional subjects. Also, this difference between the two groups was mainly due to a greater number of Remember responses in delusion-prone subjects.

Conclusion: These findings extend previous studies by showing that delusions are associated with a memory bias for threat-related stimuli.

S-17-03

Knowledge corruption in paranoid schizophrenia

S. Moritz. *UKE Hamburg, Hamburg, Germany*

Objective: A number of recent memory studies have demonstrated that schizophrenia patients display knowledge corruption, that is, they hold false information with strong conviction. This metamemory abnormality is thought to stem from poor memory accuracy (increased errors) in conjunction with a decreased ability to discriminate correct and incorrect judgments in terms of confidence (i.e., enhanced confidence in errors and decreased confidence in correct responses in comparison to controls). Knowledge corruption is theorized as a potential risk factor for the emergence of fixed, false beliefs (i.e. delusions).

Methods: Two studies will be presented. Thirty-one schizophrenic patients were compared to 62 healthy and 48 psychiatric controls (OCD and PTSD patients) on a source-memory task that assesses both memory accuracy and response confidence. In a second study, 41 first-episode patients were compared to 21 healthy controls on a variant of the same task.

Results: In the first study, schizophrenic patients displayed significantly more knowledge corruption than healthy controls and PTSD as well as OCD patients. In agreement with prior results, schizophrenic patients were over-confident in errors while being at the same time under-confident for correct responses. The second study suggests that a meta-memory deficit can be found in both chronic and first-episode schizophrenic/ schizophreniform patients.

Conclusion: The implications of knowledge corruption on schizophrenic symptomatology are outlined. Candidate cognitive processes subserving knowledge corruption, especially a liberal acceptance bias, will be discussed.

S-17-04

Theoretical and clinical implications of an attribution model of paranoia

P. Kinderman. *University of Liverpool, Liverpool, United Kingdom*

Objective: Attributional theory has been one of the most influential frameworks in clinical psychology. In particular, individuals with persecutory delusions have been hypothesised to demonstrate a particular attributional style that is suggested to protect them from real or delusional threats to their self-esteem. It has further been proposed that this attributional bias could maintain persecutory delusions and is a possible area of therapeutic intervention. More recent research has explored the relationship between 'jumping to conclusions' (Garety & Freeman, 1999) and causal attributions was investigated in persecutory delusions.

Methods: Individuals with persecutory delusions were compared with matched depressed psychiatric and non-psychiatric comparison groups using a modified inductive reasoning task (John & Dodgson, 1994) on which participants requested information before making attributions for common social events.

Results: This presentation will summarize the research literature on attributional abnormalities in paranoia.

Conclusion: Clinical data on the effectiveness of therapeutic approaches based on such attributional models will be presented.

S-17-05

Testing a cognitive model of persecutory delusions using virtual reality

D. Freeman. *Institute of Psychiatry, London, United Kingdom*

Objective: The presenter and colleagues have recently detailed a cognitive model of persecutory delusions (Freeman et al, 2002; Freeman & Garety, 2004). Factors outlined in the model were used to predict the occurrence of persecutory ideation in a controlled neutral virtual reality environment.

Methods: The results of 2 studies will be described. In both studies non-clinical individuals, after completing a range of psychological assessments, entered a VR library scene in which there were 5 characters. After spending time in the environment, participants then completed a measure of persecutory ideation about the computer characters.

Results: In both studies a proportion of participants experienced persecutory ideation. Providing evidence of the validity of the experimental method, persecutory ideation was predicted by higher trait paranoia. The psychological variables from the cognitive model that predicted persecutory ideation were anxiety, interpersonal sensitivity, and hallucinatory predisposition. Further, hallucinatory predisposition distinguished the prediction of paranoid thoughts from social anxiety in virtual reality.

Conclusion: Virtual reality provides a new experimental means of investigating paranoia. Key factors from the cognitive model predicted persecutory ideation: non-clinical paranoid thoughts were most closely associated with anxiety and anomalous

https://doi.org/10.1016/S0924-9338(05)80020-3 Published online by Cambridge University Press

experiences. Reasoning biases may particularly contribute to the development of clinical phenomena.

Monday, April 4, 2005

S-22. Symposium: Brain morphology in schizophrenia: New findings and perspectives

Chairperson(s): Ralf Schloesser (Jena, Germany), Tim Crow (Oxford, United Kingdom)
08.30 - 10.00, Gasteig - Carl-Orff Hall

S-22-01

Schizophrenia as a misconnexion syndrome

T. Crow. *POWIC - Dept. of Psychiatry University of Oxford, Oxford, United Kingdom*

S-22-02

Focal white matter density changes in schizophrenia

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

Objective: Gray matter changes have been demonstrated in several regions in schizophrenia. Particularly, the frontal and temporal cortices and amygdala-hippocampal region have been found decreased in volume and density in magnetic resonance imaging (MRI) studies. These abnormalities may reflect an aberrant neuronal network in schizophrenia, suggesting that white matter fibers connecting these regions may also be affected. However, it is unclear if particular white matter areas are (progressively) affected in schizophrenia and if these are related to the gray matter changes.

Methods: Focal white matter changes in schizophrenia were studied in whole brain magnetic resonance images acquired from 159 patients with schizophrenia or schizophreniform disorder and 158 healthy comparison subjects using voxel-based morphometry. White matter density changes in the patients with schizophrenia were correlated to gray matter density changes and to illness severity.

Results: In the patients with schizophrenia, significant decreases in white matter density were found in the genu and truncus of the corpus callosum in the left and right hemisphere, in the right anterior internal capsule and in the right anterior commissure. No interactions between diagnosis and age were found. Increased illness severity was correlated with low density of the corpus callosum and anterior commissure. Decreased corpus callosum density correlated with decreased density of thalamus, lateral inferior frontal and insular gray matter in patients and controls and with decreased density of medial orbitofrontal and superior temporal gyri in patients. Decreased internal capsule and anterior commissure density correlated with increased caudate, and globus pallidus density in patients and controls.

Conclusion: These findings suggest aberrant inter-hemispheric connectivity of anterior cortical and sub-cortical brain regions in schizophrenia, reflecting decreased hemispheric specialisation in schizophrenia.

S-22-03

Magnetisation Transfer Ratio (MTR) abnormalities in schizophrenia

M. Bagary, J. Foong, M. Symms, G. Barker, E. Joyce, M. Ron. *Institute of Neurology Dept. of Neuropsychiatry, London, United Kingdom*

Objective: Magnetisation Transfer Ratio (MTR) may be more sensitive than conventional volumetric imaging to structural brain abnormalities in both chronic and first-episode schizophrenia populations. We predicted that MTR abnormalities would be more widespread in chronic schizophrenia.

Methods: We acquired magnetisation transfer images from 29 first-episode schizophrenia patients; 30 matched control subjects; 25 chronic schizophrenia patients and 25 matched control subjects using a 1.5T scanner. Images were processed using voxel-based morphometry (VBM) which allows automated whole brain structural analysis, therefore limiting observer bias and providing significant advantages over conventional labour intensive region of interest studies. SPM99 (Wellcome Department of Cognitive Neurology, London) was used for image processing and statistical analysis. Group comparisons of regional differences in MTR were made.

Results: Group comparisons revealed more widespread MTR abnormalities in chronic schizophrenia, particularly in the left prefrontal cortex and parieto-occipital cortex bilaterally.

Conclusion: Based on this cross-sectional analysis of first-episode and chronic schizophrenia populations, MTR abnormalities are more diffuse in chronic schizophrenia. This may reflect study population heterogeneity; medication effects or alternatively that MTR abnormalities may be progressive, at least in some patients. Longitudinal studies are required to confirm these findings.

S-22-04

Novel morphomtric approaches in schizophrenia: Methods and applications

C. Gaser. *FSU Jena Dept. of Psychiatry, Jena, Germany*

In recent years, numerous automated methods to assess brain structure without labour-intense and error-prone manual tracings have been developed. Most of these methods take advantage of image registration algorithms and allow voxel-wise analysis without the need of a priori definition of regions of interests. The most widely used method is voxel-based morphometry (VBM) which relies on segmentation of the brain into different tissue types. Deformation-based morphometry (DBM) on the other hand, uses high-dimensional image registration analyzing deformations needed to warp one brain onto another. Finally, surface-based approaches to determine a 2D gyrification index will be outlined. We will provide a methodological overview about strengths and limitations of these methods and their use in schizophrenia research. The focus of these applications will be: a) cross-sectional analysis in schizophrenia samples analyzing groups differences, effects of single symptoms, and classification into sub-syndromes with anatomical correlates, b) longitudinal studies tracking changes associated with disease progression, and c) assessment of genetic effects comparing structural differences in twins, both in cross-sectional and longitudinal designs.

Monday, April 4, 2005

S-27. Symposium: Catatonia - a neuropsychiatric syndrome across psychiatric diagnoses

https://doi.org/10.1016/S0924-9338(05)80020-3 Published online by Cambridge University Press