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Psychotic disorders

Sunday, April 3, 2005

S-11. Symposium: Neurobiological and neurocognitive findings in persons at risk for psychosis

Chairperson(s): Stephan Ruhrmann (Cologne, Germany), Jarmo Hietala (Turku, Finland)
14.15 - 15.45, Holiday Inn - Room 1

S-11-01

MRI findings in persons at risk for psychosis

S. Ruhrmann, R. Tepest, P. Falkai, F. Schultze-Lutter, J. Klosterkötter, K. Vogeley, a. t. EPOS Group.. *Depart. of Psychiatry & Psycho, Cologne, Germany*

Objective: Structural and functional brain imaging in the pre-psychotic phase is of major interest as potentially confounding factors like neuroleptic treatment, psychosis-related interactions between environment and function or effects of the psychosis itself can be better controlled. In addition, long-term studies should allow a better understanding of the processes leading to frank psychosis and may also help to improve the capability of early detection of persons at-risk. Recent functional MRI studies using different cognitive tasks point to a mainly pre-frontal hypo-activation in this group. Structural findings (Pantelis et al. 2003) indicated that persons with an imminent risk for psychosis exhibit morphological deficits already in the prodromal state, increasing with transition to psychosis, a finding which seems to support a neurodegenerative model of psychosis. However, studies reporting abnormalities of pre-frontal gyrification in schizophrenia (Vogeley et al., 2000, 2001) indicate that early neurodevelopmental disturbances may also be involved.

Methods: Gyrification index (Zilles et al. 1988) was determined in 3D high resolution sMRI scans of three groups: persons at-risk according to the criteria of the European Prediction of Psychosis Study (EPOS), schizophrenia patients and healthy controls.

Results: Schizophrenia patients as well as persons at-risk for psychosis showed significant larger gyrification indices in the pre-frontal region.

Conclusion: As cortical gyrencephalic structure develops during maturation and is almost completed around birth, results support the meaning of neurodevelopmental aberrations for the brain pathology underlying psychosis. The pre-frontal localisation is in line with findings in schizophrenia and seems also to fit to the functional deficits described above for persons at-risk for psychosis.

S-11-02

P. M. Dingemans, D. Linszen, M. Birchwood. *Department of Psychiatry, Univ, Amsterdam, Netherlands*

Schizophrenia is the most incapacitating disorder among young people worldwide. Their first psychotic episode usually continues throughout life with varying symptoms tending to severity and high morbidity and mortality. Arsenault et al. (2004) reviewed five recent studies examining cannabis as a causal risk factor for psychotic disorders. They found an overall twofold increase in the relative risk of schizophrenia and a raise of the incidence of schizophrenia of 8%. The relationship between cannabis use and personality pathology has also been studied and it was found that a subgroup of cannabis using patients with schizophrenia and pre-existent triats of anti-social personality disorder run an excessive higher risk for relapse (Dingemans et al.1997, 19; Mueser et al, 1999) In the EPOS study cannabis use and personality pathology are risk factors that will examined as separate and combined predictors for psychopathology and transition into psychosis. We will present results of these analyses.

S-11-03

ERP findings and antisaccades in the initial prodromal state

A. Brockhaus-Dumke, F. Schultze-Lutter, R. Pukrop, J. Klosterkötter, S. Ruhrmann. *University of Cologne Psychiatry and Psychotherapy, Köln, Germany*

Objective: Within a multidimensional approach to the early recognition of psychosis event-related potentials (ERP) and the antisaccade task are tools to investigate disturbances of information processing for their qualification as a neurobiological at-risk indicator of psychosis.

Methods: P50 and N100 derived sensory gating indices, mismatch negativity (MMN) and P300 were elicited to evaluate different aspects of the auditory information processing. Antisaccades reflecting frontal processes were evaluated using the electrooculography (EOG). Fifty-eight patients at risk, 39 patients with schizophrenia free of neuroleptic medication and 46 healthy controls were investigated.

Results: Patients at risk show gradually reduced amplitudes of the auditory ERPs (P50, N100, MMN and P300) and significantly reduced correct antisaccades as compared to controls. Patients with schizophrenia had significantly reduced amplitudes of the auditory ERPs (P50, N100, MMN and P300), deficits in the P50- and N100-

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derived sensory gating parameters and significantly reduced correct antisaccades as compared to controls.

Conclusion: Functional deficits mediated by the frontal lobe as reflected by the antisaccade task are present already in the initial prodromal state of schizophrenia, whereas disturbances of the auditory information processing seem to be present to a minor degree in patients at risk to develop a psychosis.

S-11-04

Biology of psychosis vulnerability - positron emission tomography studies in first-degree relatives of patients with schizophrenia

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

Objective: Previous positron emission tomography (PET) imaging studies have convincingly documented a dysregulation of striatal dopamine neurotransmission in neuroleptic-naïve patients with schizophrenia. In addition, early studies with PET and [carbonyl]-11C-WAY100635 suggest altered serotonin 5-HT-1A receptor density in medial temporal cortex and prefrontal cortex in unmedicated patients with schizophrenia.

Methods: There is a good consensus from family, adoption and twin studies that genetic factors play a major role in the vulnerability for schizophrenia. Thus, we explored whether the striatal dopamine dysregulation and 5-HT-1A receptor alterations are shared by first-degree relatives of schizophrenic patients We studied two independent samples of non-psychotic first-degree relatives (FDR) of schizophrenic patients and control subjects with PET and [18F]DOPA as well as [carbonyl]-11C-WAY100635.

Results: Striatal and in particular caudate dopamine dysregulation was seen also in FDRs (increased dopamine synthesis). In addition, preliminary analysis on the 5-HT-1A receptor data suggests an increased hippocampal 5-HT-1A receptor density in FDRs of patients with schizophrenia. More detailed analysis on the relationship of these changes and clinical parameters is underway.

Conclusion: These studies suggest that altered dopamine and serotonin transmission in the brain associates also to psychosis vulnerability. The results may be useful in early detection/ intervention strategies.

S-11-05

MR-spectroscopy in prodromal and first-episode tients with schizophrenia

G. Juckel. *Campus Charite Mitte, Berlin, Germany*

Objective: The interplay of neuronal circuits between cortical and subcortical brain structures as well as within these regions are deeply disturbed in patients with schizophrenia. A valid marker for neuronal integrity is N-acetylaspartate (NAA) which can be measured by proton magnetic resonance (MR) spectroscopy in humans. Patients with schizophrenia are chararcterized by reduced NAA in schizophrenia-relevant regions as hippocampus, thalamus or prefrontal cortex. Our study assumed that patients in the at risk mental state, i.e. the so-called prodromal state of schizophrenia, exhibit first signs of impaired neuronal integrity as measured as reduced NAA in left hippocampus, anterior cingulate cortex and medial prefontal cortex

Methods: In order, to explore a possible continuum of NAA changes from the prodromal phase to the first episde of schizophrenic psychosis, we studied 13 patients in early and late prodromal state of beginning psychosis (in part patients of the European Prediction of Psychosis Study, EPOS), 10 first-episode patients with schizophrenia and 21 healthy controls matched by age and gender. MR spectroscopy (1.5 Tesla, Siemens Magneton Symphony) was performed by using by single voxel technique. NAA was calculated as NAA/creatines rations in the spectrograms.

Results: First trend analyses of the data revealed reduced NAA in hippocampus of schizophrenic patients with first episode. NAA in the hippocampus of prodromal patients was, however, similar and that in the anterior cingulate cortex and in the medial prefrontal cortex was enhanced, both compared to healthy controls.

Conclusion: These tentative results are in line with the findings of the only published study to this issue up to now (Wood et al. 2003, Schizophr Bull 29: 831-43) which reports also no difference concerning NAA in hippocampus, but elevated NAA levels in the dorsolateral prefrontal cortex of prodromal patients. It can be speculated whether increased NAA in prefrontal areas of prodromal patients are a correlate of a compensating reaction to the beginning disease process.

Sunday, April 3, 2005

S-08. Symposium: The impact of genetics on schizophrenia: First schizophrenia genes

Chairperson(s): Dan Rujescu (Munich, Germany), Wolfgang Maier (Bonn, Germany)
14.15 - 15.45, Gasteig - Black Box

S-08-01

Functional candidate genes in schizophrenia: Findings from animal models

D. Rujescu, A. Bender, M. Keck, A. M. Hartmann, F. Ohl, H. Raeder, I. Giegling, J. Genius, R. Greene, H.-J. Möller, H. Grunze. *University of Munich Dept. of Psychiatry, Munich, Germany*

The psychotomimetic effects of noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonists such as PCP and ketamine in healthy humans and their ability to exacerbate several psychotic symptoms in schizophrenic patients have promoted a view of schizophrenia as being related to an altered glutamatergic neurotransmission. This prompted us and others to develop animal models for schizophrenia. Attempts to mimic these effects in rats has lead to the recognition of parallels between schizophrenia and molecular, cellular, functional and behavioral abnormalities in these animal models. In our model, chronic, low-dose treatment with the NMDA receptor antagonist MK801 alters the expression of NMDA receptor subunits in a pattern similar to schizophrenia on the molecular level. On a cellular level, the number of parvalbumin- but not calretinin-positive interneurons was selectively decreased, a finding which parallels observations in post mortem brain from schizophrenic patients. On a functional level, recurrent inhibition of pyramidal cells was altered, as postulated from the histological findings. Finally, on a behavioral level, these animals showed cognitive deficits like disturbed working memory, which again parallels findings in schizophrenia. Thus, our pharmacologic model of NMDA receptor hypofunction has a significant potential as an animal model of psychosis-related phenotypes and as a tool in the identification of candidate genes for this disorder. We used a

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