SS-15-02

V. Kumari. *Institute of Psychiatry, London, United Kingdom*

SS-15-03

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

SS-15-04

T. Sharma. *Clinical Neuroscience Research, Dartford, United Kingdom*

Monday, April 4, 2005

W-09. Workshop: Schizophrenia, thalamus and the cortex: Molecular and functional neuroimaging studies

Chairperson(s): Peter Danos (Giessen, Germany), Mirjam Talvik (Stockholm, Sweden)
14.15 - 15.45, Holiday Inn - Room 4

M. Talvik. *Karolinska Hospital, Stockholm, Sweden*
V. Kumari. *Institute of Psychiatry, London, United Kingdom*
R. Schloesser. *University of Jena, Jena, Germany*
P. Delamillieure. *CNRS, University of Caen et Pa, Caen, France*
M. Kromkamp. *University Medical Center of U, Utrecht, Netherlands*

Dr Talvik's (Karolinska Hospital, Stockholm, Sweden) PET examinations of drug-naive patients with schizophrenia indicate a lower dopamine D2 receptor binding in the right thalamus as compared to control subjects. This preliminary result has recently been confirmed by two other PET groups. Taken together this new in vivo data adds to results from studies using different methods that all indicate an aberrant thalamic dopamine system in schizophrenia. Dr. Kumari's (Institute of Psychiatry, London, UK) presentation will focus on the role of thalamus as a 'sensory filter' and on schizophrenia as a 'disorder of deficient sensory gating' as assessed with prepulse inhibition of the startle response. Prepulse inhibition provides a cross-species neuropsychological model of sensorimotor gating, serving to prevent the interruption of ongoing perceptual and early sensory analysis. There is reliable evidence for deficient prepulse inhibition in schizophrenia patients and recent neuroimaging evidence demonstrates that thalamic abnormalities play a critical role in this aspect of schizophrenia. Dr. Schloesser (University of Jena, FR Germany) will highlight the connectivity between thalamic and cortical areas during working memory performance in schizophrenic patients and healthy subjects using functional MRI and structural equation modeling. Dr. Delamillieure (University of Caen and Paris V, France) will focus on the results of proton magnetic resonance spectroscopy of the thalamus in schizophrenia. The purpose of these studies is to show the utility of this technique in the understanding of the pathophysiology of schizophrenia. Dr. Kromkamp's (University of Utrecht, Netherlands) studies suggest a shared vulnerability to develop psychosis in thalamic circuits in schizophrenia and bipolar disorder. Homeobox genes involved in development and differentiation of the brain could play an important role in these disorders.

Sunday, April 3, 2005

C-03. Educational course: How to develop a programme against stigma and discrimination because of schizophrenia

Course director(s): Norman Sartorius (Genf, Switzerland)
08.30 - 12.00, Hilton - Salon Studer

The descriptions of the work needed to develop a programme in a setting will serve to illustrate various ways of starting programmes, overcoming obstacles, building teams and evaluating the results of the work done. The course will be interactive, allowing participants who have an interest in starting programmes to obtain advice and guidance from the faculty. Materials that have been developed during the WPA Global Programme Against Stigma and Discrimination because of Schizophrenia will be made available to the participants.

Tuesday, April 5, 2005

C-12. Educational course: Cognitive dysfuction in schizophrenia - Brief clinical assessments and treatment strategies

Course director(s): Tonmoy Sharma (Dartford, United Kingdom), Veena Kumari (London, United Kingdom)
08.30 - 12.00, Hilton - Salon Bialas

Schizophrenia, the most severe form of psychopathology, affects about 1% in the general population. Cognitive impairment is a central feature of this illness and causes poor functional outcome, including deficits in social, occupational, and self-care activities. The cost borne by the society in terms of social welfare administration and criminal justice, the time spent by unpaid caregivers, and the great loss of productivity due to the illness itself, are perhaps greater than the direct costs, such as, hospitalization. Functional deficits in schizophrenia are most strongly predicted by the current severity of cognitive impairment, followed by the severity of negative symptoms. Severity of positive symptoms is not strongly associated with the level of functional impairments, even in those with very poor outcome schizophrenia. There is thus an urgent need to find strategies for improving cognitive functioning in schizophrenia. Whilst atypical antipsychotics have been found to have greater effects on cognitive and negative symptoms than conventional antipsychotics, patients with schizophrenia still have lingering deficits. The proposed course will concentrate on the recent advances of the techniques that enable us to characterize cognitive deficits in schizophrenia clinically and possible methods both psychological and pharmacological in its treatment.

Wednesday, April 6, 2005

C-19. Educational course: Delusions - diagnosis and treatment

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Course director(s): Michael Musalek (Wien, Austria)
08.30 - 12.00, Hilton - Salon Bialas

Concluding the literature on definition, pathogenesis, nosological position and treatment of delusions we are confronted with a wide range of opinions. In the first part of the course the various definitory approaches and their value in clinical practice will be discussed. The main focus of second part of the course is dedicated to the manifold results concerning the pathogenesis of delusions, which showed that delusions are caused by complex interactions of various mental, physical and social factors. The choice of a particular delusional theme is determined by gender, age, civil status, social isolation, and special experiences ("key experiences") whereas the incorrigible conviction is based on cognitive disorders and/or emotional derailments and reinforced by social factors. But delusions cannot be longer reduced to psychopathological manifestations once established and therefore persisting. The delusional conviction is a dynamic process which only persists if disorder maintaining factors become active. These disorder maintaining factors are not necessarily corresponding with the delusion's predisposing an triggering factors. In the third part classificatory problems will be raised. Assumptions concerning nosology and classification o delusions have ranged from an independent nosological entity to the attribution to a certain mental disorder, to multicategorical classification models. Previous polydiagnostic studies indicate that delusional disorders are neither a nosological entity nor due to one particular disorder (e.g. schizophrenia) but represent nosologically non-specific syndromes which may occur superimoposed on all psychiatric disorders. Most of the so-called primary delusions (or delusional disorders in a narrower sense – delusions not due to another psychiatric disorder) have to be considered as diagnostic artefacts caused by the use of diagnostic criteria in particular classification systems. The final part of the course will focus on differentialdiagnostics and differentialtherapeutics. As delusions represent nosological non-specific syndromes with a multifactorical pathogenesis modern integrative treatment approaches (including psychopharmacological, psychotherapeutic and socio-therapeutic methods) have to be based on a multidimensional differentialdiagnosis of all the predisposing, triggering, and disorder maintaining factors. In this context the disorder maintaining factors provide the basis for effective, pathogenesis-oriented treatment of the actual symptomatology, whereas the predisposing and triggering factiors prtovide informations for plannimng prophylactic long-term treatment.

Tuesday, April 5, 2005

O-07. Oral presentation: Psychotic disorders I

Chairperson(s): Philip McGuire (London, United Kingdom), Georg Winterer (Mainz, Germany)
08.30 - 10.00, Holiday Inn - Room 7

O-07-01

Intracellular events preceding excitotoxic neurodegeneration - Implications for schizophrenia as a disorder of glutamate neurotransmission

J. Genius, D. Rujescu, H.-J. Möller. *University of Munich Dpt. of Psychiatry, München, Germany*

Objective: Accumulating data indicate that a disrupted neurotransmission might constitute the pathogenetic substrate of schizophrenia. In animal experiments we could demonstrate that mild alterations of glutamate metabolism play a central role, however the exact cellular mechanisms are elusive. To overcome the complexity of whole-animal experiments we established a cell-culture model to further investigate glutamatergic excitotoxicity.

Methods: Hippocampal neurons were isolated from rat embryos and kept in serum-free culture. PC-12. cells were used to obtain different stages of differentiation by NGF-supplementation. superoxide-generation was determined by lucigenin-chemiluminescence. Intracellular calcium was monitored by FURA-2/AM imaging. Glutamate levels were determined enzymatically determined. LDH-efflux, alamar-blue reduction, trypan-blue exclusion and morphological parameters were used to assess viability. Caspase-3 served as an indicator for apoptosis.

Results: NMDA-induced cell death was mainly necrotic and could be enhanced by MK-801. Real-time monitoring of the events following a NMDA-challenge revealed a rapid rise of intracellular Ca++, which triggers excessive and persistent O2.--generation. Oxidative stress itself elicited a glutamate spillover into the extracellular space. We sought to identify the main source of excitoxicity-induced superoxide-generation. -Mitochondria seem to play a minor role, while a NAD(P)H-oxidase with properties different from the phagocytic isoform represents an attractive candidate.

Conclusion: Conventional models of the excitotoxic cascade as a linear sequence of events should be reconsidered. We deliver evidence for a positive feed-back loop between oxidative stress and glutamatergic hyperstimulation which may be responsible for the dramatic effects of even mild oxidative stress. We further suggest to consider non-mitochondrial intracellular sources as the main effectors of excitotoxicity and possible therapeutic targets.

O-07-02

The impact of neurotransmitters on adult neural stem cells derived from mouse hippocampus

J. Benninghoff, A. Gritti, H.-J. Möller, D. Rujescu, A. Vescovi. *Dept. of Psychiatry LMU University of Munich, München, Germany*

Based on general consensus, schizophrenia is based on an imbalance of different neurotransmitter subsystems causing complex neuroplastic changes. To study the impact of different neurotransmitters such as serotonin, dopamine, norepinephrine, glutamate, and GABA on neurogenesis, we established primary cultures from adult mouse hippocampi. In our in-vitro model, we cultured the neurospheres in serum-free medium containg b-FGF and EGF as growth factors. These stem/progenitor cells gave rise to differentiated neural cells such as astrocytes, oligodendrocytes and neurons. In-vitro we were able to show that these cells express key proteins of their protein synthesis, e.g. tryptophan hydroxylase (TPH). In addition, we screened for receptors and transporter molecules by RT-PCR, which revealed 5-HT1A and 5-HT2C, DRD2 and NMDA receptor subtypes and dopamine and norepinephrine transporter. Next, we looked into the chemoattraction and found a strong chemoattraction by 5-HT versus dopamine in our in-vitro model. Taken together, our results make a case for the neurotransmitter driven influence on the cumbersome process of neurogenesis. Basic research may help us in the future to elucidate this process and looking for corresponding findings in

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