SES17. AEP Section "Mental Retardation": Behavioural phenotypes

Chairs: W.M.A. Verhoeven (NL), S. Tuinier (NL)

SES17.01

PSYCHOPATHOLOGICAL PHENOTYPES

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Several syndromes with a specific genetic etiology have been reported to be associated with a more or less typical profile of behavioural abnormalities and meet therefore the definition of a behavioural phenotype. Some syndromes, however, are frequently accompanied by psychiatric symptoms, that should be considered as a psychopathological phenotype.

With respect to psychiatric symptomatology, two syndromes are of special interest, Prader-Willi syndrome (PWS) and Velo-Cardio-Facial Syndrome of Shprintzen (VCFS). PWS is after adolescence associated with relapsing psychotic episodes characterized by emotional turmoil, anxiety, confusion, rapid mood swings, hallucinatory experiences, paranoid ideation and increase of obsessive rituals as well as subacute onset, short duration and full recovery upon treatment with mood stabilizing agents. The psychopathological phenotype of VCFS comprises thoughts of reference, paranoid ideation, anxieties, emotional and affective instability, hallucinatory experiences and psychomotor agitation.

Thus, both syndromes are associated with a relapsing psychotic condition with a variable expression, emanating in the context of a known genetic disorder and probably anteceded by a specific psychological and behavioural profile. Although PWS psychoses meet the criteria for cycloid psychosis, it is advocated to advance the PWS-psychiatric syndrome and the VCFS-psychiatric syndrome as separate diagnostic entities

(1) Verhoeven, W.M.A., Tuinier, S., Curfs, L.M.G. (2000). Prader-Willi psychiatric syndrome and Velo-Cardio-Facial Syndrome. Genetic Counseling, in press.

SES17.02

BEHAVIOURAL PHENOTYPES IN DIFFERENT FORMS OF X-LINKED MENTAL RETARDATION

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X-linked mental retardation (XLMR) is the most frequent genetic cause of mental retardation with an incidence of 1 in 1.000 life births. After the clinical delineation of the fragile X syndrome and the discovery of the Fragile X mental retardation gene (FMR-1), the scientific interest in XLMR has increased significantly in the last 10 years. This has resulted in the clinical delineation and molecular characterization of more than 200 other X-linked mental retardation conditions.

In a minority of these, the mental retardation is associated with distinct clinical signs and these XLMR forms are designated as MRXS (syndromic forms of XLMR). In the majority of these conditions, clinical findings are non-specific (MRX - non-specific forms of XLMR).

In young fragile X children the recognition of their distinct behavioural phenotype is an important part in the clinical diagnosis.

At the present time, it becomes evident that also in MRXS (ATRX syndrome - Coffin-Lowry syndrome - MASA syndrome - XLMR with Marfanoid habitus) the behavioural phenotype may be distinct, and associated with specific neurological symptoms (e.g. dystonia, dysarthria).

We present also data on the new MRX genes and the cognitive and behavioural findings in affected individuals.

SES17.03

BEHAVIOURAL PHENOTYPES IN CLINICAL PRACTICE

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Behavioural phenotypes are recognizable characteristic patterns of behaviour associated with genetically determined disorders. Great advances have been made in our understanding of these underlying cognitive and behavioural profiles of a number of different syndromes. This presention will provide an overview of review findings on the topic of behavioural phenotypes and addresses distinctive behaviour characteristics for the demarcation of some of the genetically determined syndromes associated with mental retardation.

SES17.04

THE BEHAVIOURAL PHENOTYPES OF GENETIC SYNDROMES

A.J. Holland

No abstract was available at the time of printing.

S42. Prediction of course and outcome in psychiatry

Chairs: C. Höschl (CZ), W. Gaebel (D)

S42.01

PRODROMAL SYMPTOMS IN SCHIZOPHRENIA: STATE OF THE ART

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The vulnerability-stress-coping-model is the most influential heuristic concept in understanding the course of schizophrenia, whose prodromal status still offers unsolved conceptual and methodological issues. Improved knowledge about the prodromal phase could provide a better understanding of the developing psychopathology and psychophysiology of schizophrenia and could also be of predictive value in order to attune therapeutic actions to the illness course more precisely. To shed more light on the characteristics of prodromal states, data of a German multicenter study on intermittent vs maintenance neuroleptic long-term treatment in schizophrenia (ANI-study) were reanalysed with respect to prevalence and profile, nature, time course and predictive value of

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prodromal symptoms in impending relapse. Results demonstrate that prodromes are a category of symptoms on their own, but do share variance with other symptom domains. Treatment side-effects, psychotic symptoms, dysphoric mood, and social dysfunction are all associated with prodromal states – the direction of this association, however, is still to be clarified. Prodromal symptoms are also related to the neuroleptic treatment strategy and its relapse preventive efficacy – findings that underscore neuroleptic maintenance medication in preventing both overt and subtreshold psychotic morbidity in schizophrenia.

S42.02

STRUCTURAL BRAIN ABNORMALITIES IN SCHIZOPHRENIA IN RELATION TO OUTCOME

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(a) Background: Schizophrenia is a chronic and prevalent psychiatric disorder with a highly variable outcome. Although numerous studies suggest the presence of structural brain abnormalities in schizophrenia, only ventricular enlargement has been related to outcome. This study was designed to investigate the relationship between outcome and structural brain abnormalities in schizophrenia.

(b) Method: Brain-scans of 24 patients with an extremely poor outcome, 25 patients with an extremely favorable outcome, and 25 healthy controls were obtained using Magnetic Resonance Imaging (MRI). The regions of interest included intracranial volume, cerebrum, grey-matter and white matter, the cerebellum, the lateral ventricles and the third ventricle. Dosage or type of antipsychotic medication was not different for the two groups.

(c) Results: An overall difference in brain structure was found between the three groups (Wilks, $F = 3.4$, df = 10, $p < 0.1$). Poor-outcome patients displayed a significant grey-matter volume decrease ($t = 3.2$, df = 43, $p < 0.01$) and a significant ventricular enlargement ($t = 3.7$, df = 43, $p < 0.01$) as compared to good-outcome patients and healthy controls. No relationship between volumes of white-matter, third ventricle or cerebellum and outcome was found.

(d) Conclusion: Our findings suggest that outcome in schizophrenia is related to grey-matter volume loss and ventricular enlargement. These findings have important implications for the interpretation of previous reports of grey matter volume loss in schizophrenia.

S42.03

TEST OF SEROTONERGIC ACTIVITY IN THE BRAIN PREDICTS THERAPEUTIC RESPONSE OF PATIENTS WITH SCHIZOPHRENIA

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Recently, the interest in the role of serotonin in pathophysiology of schizophrenia was renewed, partly because many novel antipsychotics are high affinity blockers of 5HT receptors. Neuroendocrinological probes of 5HT neurotrasmission (mCPP, fenfluramine, n) were used to predict different responsivity to classical or new antipsychotics. Our objective was to test the hypothesis that the maximum PRL increase after dex-fenfluramin (dFF) challenge is associated with the change of BPRS total score after 4 weeks of individually adjusted haloperidol treatment. The blood samples of patients were collected after overnight fasting before and after 60 mg of dFF for the period of five hours and prolactin serum conentrations were assessed. In a group of patients with early schizophrenia we found a signficant negative association between pretreatmet prolactin increase and the change of total and some factor scores of BPRS over 4 weeks (Mohr et al, 1998). We also detected a significant difference in weight corrected increase of prolactin between predefined responders and non-responders to treatment. The magnitude of PRL response to dFF after the test was associated with the BPRS item score of "blunted affect" at the beginning of treatment. Also, the patients with high "blunted affect" score had higher PRL response at the end of the treatment. The pretreatment maximum prolactin increase after dFF challenge significantly correlated also with the post-treatment scores of BPRS factor "anergy" ($r = 0.4$, $p < 0.05$). Our results support the idea that patients with schizophrenia, who do not respond to haloperidol, tend to have higher serotonergic responses to neuroendocrine challenge and more negative symptoms before and also after the treatment with haloperidol.

(1) Mohr P, Horáček J, Motlová L, Libiger J, Czobor P: Prolactin response to D-fenfluramine challenge test as a predictor of treatment response to haloperidol in acute schizophrenia. Schizophrenia Research., 30, 91–99, 1998

S42.04

PREDICTING LONG TERM RECOVERY IN SCHIZOPHRENIA: FINDINGS FROM THE INTERNATIONAL STUDY OF SCHIZOPHRENIA

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Over the last 20 years, new epidemiological data have challenged the notion that poor prognosis is 'hard-wired' into the diagnosis of schizophrenia. Study findings are often difficult to interpret however on account of sampling biases and follow-up attrition. In 1978–80, the WHO 'Determinants of Outcome of Severe Mental Disorder' (DOSMeD) project identified first episode cohorts of psychosis across a range of international centres, utilising similar case finding methods. Fifteen years later, nine of these joined 5 other Centres that could identify comparable cohorts, to carry out a follow-up study of schizophrenia and related psychoses – the International Study of Schizophrenia (ISOS). 1171 incident cases in 14 centres were followed using standardised assessments; 50% of those traced were rated as recovered for global symptoms, with absent or mild social disability. Although aggregated data for treated recovery ranked among the highest reported, there was marked heterogeneity across research Centres. Regression models uncovered the primary role of *early pattern of course* in predicting long term outcomes in all Centres, but also revealed independent Centre effects on outcome. These findings underline the 'window of opportunity' for innovative treatment programmes in the early course of schizophrenia, and also illustrate the potential role of socio-cultural factors (embedded in the 'Centre' effects) in the long term patterning of psychotic disorders.

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