and delineated distinct biological characteristics of this group of psychoses.

In a twin-study, a very similar concordance rate between monozygotic and dizygotic pairs of probands with cycloid psychoses was found, suggesting a lack of hereditary influence according to the rule of Galton. On the other hand, in mothers of patients with cycloid psychoses infectious diseases in the first trimester of gestation occured significantly more frequently than in patients with other psychoses. These infections were correlated with further obstetric complications and an early onset of the disorder. In agreement with these findings, patients with cycloid psychoses showed an increased rate of non-specific CCT-abnormalities of the brain which most likely resulted from pre- or perinatal brain damage. Neurophysiological investigations also provided specific findings. Studies of event-related potentials revealed characteristic features of amplitude and topography of the P300 in cycloid psychoses which were distinguishable from P300-alterations in schizophrenic psychoses and other psychiatric disorders. Moreover, cortical blood flow during acute phases proved to be significantly elevated in patients with cycloid psychoses, but showed no persistent abnormalities after clinical remission, especially no hypofrontality.

Altogether, these findings point to the fact that somatic influences may play an important role in the aetiology of cycloid psychoses and suggest that cycloid psychoses represent a nosologically independent entity which should be separated from affective and schizophrenic psychoses and is not identical with schizoaffective psychoses.

S70-4

ELECTROPHYSIOLOGICAL EVIDENCE FOR SUBGROUPING OF SCHIZOPHRENIA

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The current international diagnostic systems are developed based on a mixture of rationales including clinical utility and reliability of the diagnostic assessment. Monopolization of this method for the evolution of the psychiatric classification which follows practical clinical goals or even the simplicity of the diagnostic criteria instead of hypothetic ethiopathogenetical mechanisms is suspected to lead to a scientific impasse due to categories representing an amalgam of different natural disease entities. Leonhard's classification is based on clinical cross-sectional and longitudinal observations, ordered according to possible pathophysiological mechanisms, and allows to formulate testable hypothesis. In a series of studies based on 20-channel recordings of cognitive event-related potentials (ERPs), the neurophysiological differences between psychotic subgroups in Leonhard's classification and in the categories of the DSM and ICD were investigated. The P300 component of the ERPs differed between cycloid psychoses and systematic/unsystematic schizophrenia, and between these groups and manic disorders. While topographical alterations indicated deficits of left temporal lobe function in schizophrenia (Strik et al, Psychiat Res: Neuroimaging, 55: 153–166; 1993), increased P300 amplitudes were found in cycloid psychosis as a sign of a generalized increase of arousal (Strik et al, Acta Psychiat Scand, 94: 471–476; 1996). These differences were blurred with loss of statistical significance when the international diagnostic standard categories were applied. In manic patients, on the other hand, no amplitude differences compared to controls, and a topographical difference possibly indicating reduced frontal lobe control were found. The results revealed different neurophysiological mechanisms at the basis of the investigated subgroups and, thus, support the existence of different natural disease entities beyond the classical dichotomy of psychoses.

S70-5

MATERNAL GESTATIONAL INFECTIONS IN THE ETIOLOGY OF SCHIZOPHRENIC PSYCHOSES

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The contemporary neurodevelopmental hypothesis of schizophrenia and affective psychosis has emerged from pathobiological findings of early brain lesions and malformations of fetal brain development. In chronic schizophrenia we found that not the frequency, but the monthly distribution of maternal gestational infections was significantly different compared to controls. Twenty per cent of the mothers of schizophrenics recalled a manifest infection during pregnancy. The incidence of maternal gestational infections was significantly increased in the second trimester, especially during the fifth month of gestation. Respiratory infectious disesases (i.e. influenza and febrile cold) were frequent and accounted for 56% of all infections and of 64% of mid-pregnancy infections. Infections during mid-pregnancy were significantly associated with Leonhard's systematic schizophrenias with low familial aggregation of psychosis and a chronic non-remitting course with severe psychopathology. Furthermore, prenatal infections were significantly associated with the occurrence of further OCs, which are thought to constitute a significant risk factor for the development of schizophrenic psychosis. In our recent study, the cycloid psychoses with low heritability and good long-term prognosis were found to be significantly associated with first trimester respiratory infections (i.e. influenza, febrile cold). Acute respiratory infections explained 56% of all infections and all first trimester infections in cycloid psychosis. Furthermore, maternal infections seem to cause an early onset in cycloids. In manic-depression we failed to identify such associations to maternal gestational infections or other obstetric complications. These findings are suggestive that exogenously induced disturbances of fetal brain maturation during the first trimester of gestation are involved in the etiology of cycloid psychosis and those during the second trimester in systematic schizophrenias.

S71. Genetic epidemiology of mental illness

Chairs: P Munk-Jørgensen (DK), H Ewald (DK)

S71-1

ALZHEIMER'S DISEASE, GENETIC AND ENVIRONMENTAL FACTORS

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Several genetic and environmental factors have been implicated in Alzheimer's disease (AD). In recent years, considerable progress has been made in unraveling the genetic etiology. Three genes have been identified that are predominantly implicated in autosomal dominant forms of early-onset AD, the β-amyloid precursor protein gene and two homologous genes presenilin 1 and 2. Further, the apolipoprotein E gene (APOE) has been shown to be an important genetic risk factor for early- and late-onset AD. Although it is

https://doi.org/10.1016/S0924-9338(99)80307-1 Published online by Cambridge University Press

clear that other yet unknown loci must be involved in AD, findings of studies aiming to identify new (candidate) genes have been controversial. Putative environmental risk factors for AD are alcohol, smoking, head injury and several disorders including vascular disease and depression. Anti-inflammatory drugs and estrogen replacement therapy have been reported to have a protective effect on AD. There is some evidence for synergistic effects between environmental and genetic factors, in particular the APOE gene. The APOE genotype may modify the risk of AD associated with head trauma and several vascular factors, i.e., atherosclerosis, serum cholesterol and estrogen replacement therapy. However, studies of environmental factors have generally been small and of low validity. Large scale, long term follow-up studies, ongoing at present, may clarify the role of environmental factors in AD and their interaction with genetic factors.

S71-2
GENETIC AND ENVIRONMENTAL FACTORS IN SCHIZOPHRENIA

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The accumulated results of family, twin and adoption studies leave little doubt that genetic factors have a substantial role in the aetiology of schizophrenia. However, the discordance rate of just over 50% in identical twins indicates that genetic factors (at least of the straightforward mendelian type) are not sufficient to cause the disorder. It can be estimated from quantitative genetic analyses that about 20% of the variation in liability to schizophrenia is accounted for by non-genetic factors and that these are entirely non-familial, that is, they do not include environmental factors shared within families. A number of putative environmental factors have been identified such as birth injury and maternal infection but these are likely to have small effects. It is possible that "environmental" factors also include stochastic epi-genetic phenomena that cannot be detected using standard epidemiological approaches.

S71-3
STATUS OF THE SEARCH FOR GENES INVOLVED IN BIPOLAR AFFECTIVE DISORDER

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The search for genes involved in bipolar affective disorder is difficult as the mode of inheritance is unknown and very likely involves different combinations of genes with major, moderate and minor effects acting in concert. The relative lack of pathophysiological knowledge makes the perhaps 30,000 genes of relevance for the function of the brain potential candidates. The search is made even more complex as there is no universally recognised biological abnormality which helps to separate affecteds from unaffecteds, to identify homogenous subgroups or to identify gene carriers.

Different methods aiming at localising the disease loci by identifying a shared chromosomal segment inherited from a common ancestor have resulted in suggestion of loci on a number of chromosomes of which at least chromosomes 4p16, 18q23 and Xq26 are very promising.

In parallel investigation of the minority of neurogenes that are presently known have lead to identification of interesting DNA sequence variation in a number of genes including the serotonin transporter gene.

Though primarily disease susceptiblity genes have been sought for genes influencing several important features such as severity, course, treatment response, side effects, abuse and personality characteristics of importance for compliance to treatment is beginning to receive attention.

When the relevant DNA sequence variation have been found it will be possible to determine the neurobiological and clinical significance of the gene. This will be hopefully allow faster diagnoses, prediction of course, severity, treatment response and side effects aided by DNA knowledge in the individual patient and the development of new and powerfull forms of treatment.

TC72. ICD-10 advanced training seminar IV

Chairs: A Bertelsen (DK), J van Drimmelen (WHO, CH)

DEB74. Physician-assisted suicide

Chairs: P Cosyns (B), M Kelleher (IRL)

Eli Lilly & Co.

Lilly-SAT1. Zyprexa™: Redefining the management of schizophrenia

Chair: J Gerlach (DK)

Lilly-SAT1-1
MANAGEMENT OF FIRST-EPISODE PATIENTS

René S. Kahn. *Department of Psychiatry, University Hospital, Utrecht, The Netherlands*

Patients with recent-onset schizophrenia – that is, patients who recently experienced their first psychosis – are a very important group, both in clinical management and from a research point of view. It appears that these patients are different in some respect from patients who have been ill for several years. In the first place, these patients show a better treatment response. Second, this patient group is exquisitively sensitive to the side effects of the typical antipsychotics. Therefore, newer medications, such as the atypical antipsychotics, may be particularly indicated in this patient group.

From the research point of view, first-episode schizophrenic patients are very important because it is during this period that most of the deterioration in functioning becomes evident. Therefore, studying these patients with regard to their course of illness, treatment interventions, and neurobiological changes may be fruitful in elucidating the pathogenesis of the disease.

Indeed, several studies have suggested that schizophrenic symptoms appear many years before the onset of first psychotic symptoms. Early intervention may therefore be indicated, although difficult to establish, since the first presenting symptoms are nonspecific. Early treatment is important because treatment response is more favorable, and biological changes (such as increasing

https://doi.org/10.1016/S0924-9338(99)80307-1 Published online by Cambridge University Press