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

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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

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