Objective: The clinical efficacy of drugs targeting the central nervous system critically depends on the compounds' ability to pass the blood-brain barrier, which is regulated by active transporter molecules, such as ABCB1 (MDR1, P-glycoprotein (P-gp). One of the reasons for an only partial response or refractoriness is an insufficient intracerebral concentration. We hypothesized that genetic variability in ABCB1 influence the response to drugs with central nervous system (CNS) actions, including the clinical response to antidepressants. We used transgenic mice lacking the two homologues of the human ABCB1 drug transporter gene (abcb1a and abcb1b) to assess whether antidepressants were substrates of P-gp following subchronic administration. We than genotyped 56 single nucleotide polymorphisms (SNPs) in ABCB1 in 286 depressed in patients treated with antidepressants and tested for associations with treatment response. The animal experiments showed that the intracerebral concentrations of some but not all antidepressants were regulated by P-glycoprotein. In the human genetics studies, there was an association of ABCB1 SNPs with remission status after 6 weeks of antidepressant treatment. This association was present in patients treated with antidepressants that are substrates of P-gp, but not in patients treated with antidepressants that are not substrates of P-gp. Our findings indicate that polymorphisms in ABCB1 influence intracerebral concentrations of antidepressants and by that response to treatment. Genotyping ABCB1 polymorphisms may thus help to optimize antidepressant treatment. These implications are likely to extend to other classes of CNS drugs.

S-15-04

Adverse drug reactions: Role of pharmacogenomics

P. Zill. *Psychiatric CLinic, Munich, Germany*

Objective: The inter individual variability of drug response is a major problem in clinical practice and drug development, which can lead to therapeutic failure or adverse effects in patients. There is growing evidence that not only the involvement of pharmacokinetic factors (drug metabolism) might predispose to adverse effects, but also genetic variations in drug targets (pharmacodynamic factors) play an important role. Moreover the existence of comorbid disorders, as for example the metabolic syndrome, characterized by elevated abdominal obesity, triglycerides, blood pressure, fasting glucose, which has been suggested to be associated with depression and schizophrenia is supposed to have an impact on the incidence of side effects after psychopharmacological treatment. rous previous studies could demonstrate an involvement of polymorphisms in drug metabolizing enzymes (e.g. Cyp450 system), as well as in drug target genes and the incidence of adverse effects, but these results remain partially inconclusive.

Results: In own studies with 160 schizophrenic patients and 272 patients with major depression we found that a –579C/T polymorphism in the 5-HT2C gene seems to be involved in weight gain during neuroleptic and antidepressant treatment. The 5HT2C –597 C/T and a ß2-adrenergic receptor polymorphisms (Arg16Gly) might also be involved in glucose metabolism.

Conclusion: These results suggest that symptoms of the metabolic syndrome are among the common side effects, but these findings have to be replicated in further prospective studies. Knowledge from these studies will ultimately lead to the individualization of psychiatric drug treatment, as well as to future treatment strategies. This project is supported by the German Federal Research Ministry within the promotional emphasis "Competence Nets in Medicine"

Monday, April 4, 2005

S-21. Symposium: Anxiety and depression, first results of the DSM-5 steering group

Chairperson(s): David Goldberg (London, United Kingdom), Kenneth S. Kendler (Richmond, USA)
08.30 - 10.00, Gasteig - Philharmonie

Monday, April 4, 2005

S-35. Symposium: Psychosocial aspects of depressive disorders in ethnic minority groups

Chairperson(s): Francis Creed (Manchester, United Kingdom), Christian Haasen (Hamburg, Germany)
14.15 - 15.45, Holiday Inn - Room 6

S-35-01

Prevalence of depression in people of Pakistani origin in U.K.

F. Creed. *University of Manchester, Manchester, United Kingdom*

Objective: To assess whether depression is more common in people of Pakistani origin than white Europeans living in U.K. To assess also whether the prevalence is associated with life stress.

Methods: Survey of population based sample of 928 people of Pakistani family origin and 947 white Europeans. Two phase study using Self-Report Questionnaire (SRQ) and SCAN diagnostic interviews to assess depression. Life Events and Difficulties Schedule for life stress.

Results: At baseline there was a higher prevalence of depression among Pakistani women (32%) compared with European women (19%), European men (13%) and Pakistani men (9%). Depression was particularly prevalent in older Pakistani women and was closely associated with severe social stress and lack of support. There was no difference in the course of depression over 6 months between the different ethnic groups.

Conclusion: The high prevalence of depression in Pakistani women is a result of severe social stress and lack of adequate social support.

S-35-02

Depression among migrants of Turkish and Russian origin living in Germany

C. Haasen. *University Hospital Eppendorf, Hamburg, Germany*

A depressive reaction to the stress associated to migration and the acculturation thereafter has been described in the literature. Furthermore, depressive syndromes among migrants are reported by clinicians to involve somatization more frequently, despite the fact that somatization has not been found to be more frequent in different regions of the world. There is insufficient evidence on the