Although there is no full consistency across all studies, a series of loci on the genome overlap between several studies. Those consensus loci are: 1q, 5q, 6p, 6q, 8p, 13q, 18p and 22q. However, up to now not a single contributing gene has been identified. The multiplicity of these loci demonstrates that schizophrenia is not under the control of a single, causal gene; instead, multiple genes are operating in concert with environmental factors. It remains obscure if the contributing gene mutations are common with a multiplicity of pathogenic mutations for each case or if different subtypes of schizophrenia are each under the control of a subtype-specific major gene.

Current work is focussed on narrowing down the candidate regions by finding linkage disequilibrium to either anonymous markers or functional gene variants. Major progress has to be expected in this respect in due course.

S07.04
JOINT EFFECTS OF GENOTYPE AND ENVIRONMENT IN SCHIZOPHRENIA

P. Tienari. *Dept. of Psychiatry, University of Oulu, FIN-90210, Finland*

To an important degree, genetic effects on behavior come about because they either influence the extent to which the individual is likely to be exposed to individual differences in environmental risk or they affect how susceptible the individual is to environmental adversities. Adoption studies are able to distinguish the effects of environment from the effects of genes. A nationwide Finnish sample of schizophrenics' offspring given up for adoption (N = 186) was compared blindly with matched controls, who were adopted center dot Offspring of nonschizophrenic biological parents (N = 203). The adoptive families were investigated thoroughly using joint and individual interviews and psychological tests. The biological parents were also interviewed and tested. The Finnish adoption study has generated a large sample of adoptees; obtained standardized personal interviews and tests with all subjects whenever possible; used DSM-III-R criteria for all subjects; followed up adoptees who were initially not fully in the age of risk for schizophrenia and re-examined them with standardized diagnostic instruments. Our results support a genetic hypothesis for a schizophrenia spectrum that includes in addition to schizophrenia, nonaffective psychoses and schizotypal personality disorder. However, notable differences between the two groups only emerged in the families which were rated as disturbed. Thus the genetic effect, that is, the propensity for clinically serious psychiatric disorder in the adoptees, was expressed primarily in association with a disturbed adoptive family rearing-environment and was not present in association with a "healthy", possibly protective, adoptive family environment.

S07.05
ETHICAL IMPLICATIONS OF MOLECULAR-GENETIC RESEARCH IN PSYCHIATRY

M. Rietschel. *Department of Psychiatry, Univ. Bonn Sigmund-Freud-Str. 25, 53105 Bonn, Germany*

The etiology of schizophrenia and bipolar disorders is complex with genetic factors accounting for more than 50% of its variance. The aim of molecular genetic research is to identify vulnerability genes in order to gain insight in the pathophysiology. It is hoped that this will lead to better diagnosis, prevention and therapy of the disorders.

Besides those benefits, this progress may have serious ethical implications. Knowledge about vulnerability genes may influence disease concepts and self-awareness, (which may result in increased or decreased stigmatisation), privacy and confidentiality, family and life-planning.

In complex disorder the predictive value of vulnerability genes are limited, they only modify an "a-priori-risk". In monogenic disorder many disease genes have already been identified and a high degree of certainty can be achieved by predictive testing. Problems inherent to predictive testing in monogenic and complex diseases like psychiatric disorders will be discussed.

S08. Pharmacological relapse prevention in alcoholism – from animal models to clinical trials

Chairs: J.A.L. Boning (D), L.G. Schmidt (D)

S08.01
IS THERE A NEUROCHEMICAL BASIS FOR ALCOHOLISM AND RELAPSE? ANIMAL AND HUMAN STUDIES

R.J. Ward. *Unite de Biochimie, University Catholique de Louvain, 1348 Louvain-la-Neuve, Belgium*

Despite numerous neuochemical and molecular biological studies of alcohol abusers and experimental animal models, the pathophysiology and neuochemical basis for alcoholism remains poorly understood. The pharmacokinetics of ethanol clearance from the brain, predominantly by catalase (Ward et al., 2000) will have a profound effect upon the mesolimbic system, ethanol enhancing (Blanchard et al., 1993) and acetaldehyde (Ward et al., 1997) diminishing dopamine release from specific brain regions. In addition an association between a specific allele pattern of the dopamine D2 receptor to the marker hD2G1 in alcoholics differs from that of control subjects and is thought to be involved in the lower dopamine binding affinity to the receptor such that the individual would need to drink more ethanol to obtain the pleasurable effect initiated by dopamine release

It is clear that during chronic alcohol abuse the levels of most neurotransmitters are maintained within their normal concentrations and it is only during detoxification that such equilibrium is drastically disturbed. Excitatory amino acids, particularly glutamic acid, are increased during the initial stages of detoxification which is in part responsible for many of the unpleasant side effects observed in alcohol abusers during withdrawal, (Rossetti et al., 1995). The sulphonated amino acid taurine has been implicated in modulating such changes (Ward et al., 1999) which may be attributable to the alterations in both NMDA and GABA receptors as well as modulation of calcium homeostasis.

Despite the use of different animal models of ethanol sensitivity, tolerance and withdrawal as well as transgenic and knockout animals these have not helped to advance, to any considerable extent, our knowledge of the role of neurotransmitters and their receptors in chronic ethanol intoxication and withdrawal. However the use of agonists and antagonists of specific receptors have yielded a better insight into their role in alcohol intoxication and withdrawal and are the prime target of various pharmaceutical drugs now being developed for the treatment of alcoholism.

(1) Blanchard et al., *Alc Clin Exp Res* **17** 968–973 1993
(2) Rossetti et al., *Eur J Pharmacol* **283** 177–183 1995
(3) Ward et al., *Neuropharmacol* **36** 225–232 1997
(4) Ward et al., *Neurosci Res Comm*, 24 41–49 1999