

the same neurobiological process. Recent examples of the success of a cytogenetic approach to studying mood disorders include the identification of an interstitial duplication of chromosome 15q associated with panic and phobic disorders in a family (Gratacos et al. 2001 *Cell*;106:367) and the analysis of a balanced reciprocal translocation in a large Scottish family that has identified two genes implicated in major psychiatric disorder, directly disrupted at the breakpoint on chromosome 1 (Millar et al. 2000 *Hum Mol Genet*;9:1415). This chromosome translocation segregates in a single large family with a phenotype that includes unipolar and bipolar affective disorder and schizophrenia (Blackwood et al. 2001. *Am J Hum Genet* 69:428). Analyses of families with chromosome rearrangements segregating with major mental illness are likely to implicate further genes whose disruption leads to mood disorders and the phenotypes associated with these rearrangements may help to clarify or redefine diagnostic categories.

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## S18. Gene–environment interplay

*Chairs:* P. McGuffin (GB), H. Ewald (DK)

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### S18.1

Genes and environment in ADHD

A. Thapar\*. *Child & Adolescent Psychiatry Section, Department of Psychological Medicine, University of Wales College of Medicine, UK*

There is now considerable evidence that Attention deficit hyperactivity disorder (ADHD) is strongly influenced by genetic factors. There have been a wealth of family, twin and adoption studies and now there is considerable international effort directed towards identifying susceptibility genes for ADHD. Early results look promising. Nevertheless the role of environmental factors and the question of how ADHD is best defined remain important issues. There is also increasing interest in the application of genetic findings in clinical settings with pharmacogenetic research aimed at examining what genetic factors influence treatment response. Recent and emerging research on the genetics of ADHD will be reviewed.

### S18.2

The role of personality in influencing genetic and environmental risk factors for major depression

A. Farmer\*. *SGDPRC Institute of Psychiatry, Denmark Hill, Camberwell, London, UK*

Personality factors such as extraversion or neuroticism could influence the way individuals respond to environmental adversity that could lead, in turn, to the development of an episode of depression. For example, subjects with high rates of neuroticism, may view the world as particularly threatening and hostile, and consequently may be unable to satisfactorily resolve the problems caused by an adverse life event. Alternatively, an extravert individual may indulge in risky activities, which have an attendant high risk of excess adverse events occurring, and who could be considered as leading “hazard-prone” life styles.

The role of personality will be considered in relation to the genetic vulnerability to depression in a sib-pair design. Depressed probands, their nearest aged siblings, healthy control probands and their nearest aged siblings were compared for the rates of depression in the 2 groups of siblings, and the number of different

types of life events experienced in a 12 month period by all four groups of subjects. In addition, the relationship between various measures of current mood, personality and life events will be discussed.

### S18.3

Genetic influences on autism

M. Rutter. *Social, Genetic and Developmental Psychiatry Research Centre, Institute of Psychiatry, London, UK*

Twin and family studies over the last quarter of a century have consistently pointed to a strong genetic influence on the liability to autism – a liability that extends beyond the traditional diagnosis of a seriously handicapping disorder, and which probably involves a relatively small number of susceptibility genes. During the last decade, several large-scale collaborative molecular genetic studies of autism have been established, with some partially replicated findings of gene loci. The paper will provide an update on the state of genetic knowledge and will consider the implications for our understanding of this multifactorial psychiatric disorder.

### S18.4

What do comorbidity studies with somatic disorders tell us about the etiology of schizophrenia?

O. Mors\*. *Institute for Basic Psychiatric Research, Risskov, Denmark*

It has proven very difficult to progress from evidence confirming a genetic contribution to the etiology of schizophrenia to evidence implicating the specific genes in the disease. At the same time the environmental risk factors have eluded us their discovery. The study of possible associations between somatic disorders and schizophrenia may generate hypotheses about the role of both genetic and non-genetic factors in etiology of schizophrenia: candidate chromosomal regions for schizophrenia may be identified, gene-environment interactions suggested and sources of natural selection in man illustrated. Comorbidity studies have usually been register based, since large data sets is needed to generate sufficient power to demonstrate significant, moderate increased or decreased relative risks. Results from an ongoing study in Denmark of associations between schizophrenia and other complex disorders such as autoimmune diseases (e.g. rheumatoid arthritis and type I diabetes) and also appendicitis will be presented. Methodological pitfalls such as selection bias will be discussed.

### S18.5

Genetic and non-genetic factors in bipolar affective disorder

H. Ewald. *Institute for Basic Psychiatric Research, Risskov, Denmark*

Developments in diagnostic instruments and criteria, molecular genetics, computer programs and statistics have helped to identify more than 10 candidate chromosome regions potentially containing genes which increase susceptibility to bipolar affective disorder. A number of research groups are now attempting to identify the specific risk genes in the most promising chromosome regions including chromosome 4p, 12q, 18 and 21. Increased knowledge of the neurobiology of the brain has also resulted in new candidate genes. Though no DNA sequence variation of relevance has yet been reported the draft sequence of the human genome and recent developments for high-throughput genotypings and other molecular genetic methods will facilitate this. Genetic mapping studies