

effects, treatment optimization and development of new drugs. Several studies have demonstrated that clinical treatment with classical antipsychotics induces a high degree of D2dopamine receptor occupancy. For classical antipsychotics, distinct thresholds in D2occupancy have been shown for antipsychotic effect, prolactin increase and extrapyramidal side effects (EPS) respectively. The atypical antipsychotic clozapine induces a significantly lower striatal D2occupancy as compared to classical antipsychotics. The hypothesis of a 'limbic selectivity' for clozapine was recently tested with high resolution PET and the high affinity radioligand [¹¹C]FLB457. The finding of a low D2occupancy that was maintained also in extrastriatal regions did not support the hypothesis of a preferential limbic D2occupancy. PET studies of the novel antipsychotics risperidone and olanzapine have shown D2occupancy levels similar to those induced by classical antipsychotics. Further studies are needed to test whether D2occupancy thresholds for clinical effects differ between classical and novel antipsychotics.

S04.5

PET and antipsychotic drugs – future

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For many years PET using displacement studies of PET ligands bound to neuroreceptors has studied the pharmacological action of antipsychotic drugs. Using this approach it has been demonstrated that antipsychotic effects can be achieved by a number of neuroreceptor blocking properties.

During recent years, studies using electrical deep brain stimulation in neurological conditions, have demonstrated that electrical inhibition of very small localized intracerebral targets indeed can affect the function of vast areas of the brain. In a similar manner antipsychotic drugs may, despite different or selective receptor binding properties, affect certain functional domains of the brain, which are common for antipsychotic effects. To visualize such effects PET data have to be analysed differently, employing analysis of connectivity across brain networks such as the corticostriatal pathways. Using this approach it can be demonstrated marked differences between the healthy and schizophrenic states of brain connectivity. Typical and atypical antipsychotic drugs affect these deviations towards a more normalised state, albeit with some differences. Analysis of brain network connectivity in disease and of drugs are likely to expand understanding of the functional effects underlying the antipsychotic properties of various drugs.

S05. Personality disorders – an update

Chairs: L. Ekselius (S), J. Livesley (CDN)

S05.1

Developmental pathogenesis of personality disorder

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Multiple biological and psychosocial variables are associated with the development of personality disorder. Each variable appears to have a small effect and none appear to be either necessary or sufficient to cause personality disorder. Under these circumstances it seems more appropriate to refer to the factors that predispose to the development of personality disorder than to refer to causes.

Behaviour genetic studies indicate that genes and environment contribute to the aetiology of personality disorder and that all personality traits are heritable. It is not possible to distinguish between traits that are largely influenced by genetic factors and traits that are largely environmental in origin. Multiple genetic factors appear to be involved that differ in effect. Some influence the development of specific traits whereas others have wider effects influencing the development of clusters of traits. The broader genetic dimensions appear to be responsible for the clusters of traits that define the different patterns of personality disorder. Each genetic factor appears to involve multiple genes each contributing a small amount of phenotypic variance.

A similar picture emerges from studies of the psychosocial origins of personality disorder. Multiple factors are related to personality disorder including family dysfunction, deprivation, and trauma but none are invariably associated with personality disorder and specific links between different kinds of adversity and specific forms of disorder have not been identified.

These results reveal a complex picture of the aetiological of personality disorder. They suggest that studies of single variables or groups of related variables are unlikely to contribute to understanding pathogenesis. They also suggest the need to re-think our concept of the environment. The environment is not something independent of the individual. Instead individuals shape the environment to which they respond. A theory of the pathogenesis of personality disorder needs to explain the interaction between genetic predisposition and environmental adversity. In particular, it needs to explain the way genetic predisposition and the emerging personality shape the environment to which the individual responds and how this environment in turn influences gene expression and the emerging personality.

S05.2

Personality – different genes or differences in gene activation?

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Monoamine oxidase (MAO) activity in platelets correlates with personality (e.g. sensation seeking, impulsiveness). Low platelet MAO, as well as the personality traits associated with these, have been associated with e.g. type 2 alcoholism, criminality and violent behaviour. The transcription factor family AP-2 is a regulatory factor for prenatal development of monoaminergic nuclei as well as of monoamine turnover in the adult rat forebrain. The gene encoding AP-2b includes a polymorphic region, which is associated with e.g. personality as well as with impulsive binge-eating disorder. In both male and female AP-2 β genotypes homozygous with regard to a [CAAA]₅ repeat display significantly lower platelet MAO activity than the other genotypes. Thus, it seems likely that the personality disturbances, linked to low platelet MAO, should be associated with the presence of this AP-2 β gene allele. In this way, common transcription factors regulate the expression of midbrain monoamine structures as well as that of platelet MAO, thereby explaining the association between platelet MAO and personality (see Damberg et al., *Mol. Psych.* 6, 503, 2001).

S05.3

Genetics and suicidal behaviour

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Although a familial aggregation of suicide has been observed by many psychiatrists, the reason for this has until recently been