

associations between psychotic-like dimensions and the brain functions tapped by neurocognitive tests did not emerge across groups.

### S19.03

Specific neurocognitive deficits are related to inferred genetic risk in unaffected parents of schizophrenic patients

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**Background and Aims:** Neuropsychological deficits are considered endophenotypes for schizophrenia, because they are not only found in patients but also in many of their unaffected relatives, albeit in attenuated form. It is not yet clear which of these deficits in relatives are related to genetic or to environmental causes. We tested effects of inferred genetic liability for schizophrenia on neurocognitive variables to address this problem.

**Method:** Twenty-eight patients with schizophrenia, 129 non-affected biological parents and 143 matched controls were assessed with an extensive neuropsychological test battery including tests of attention, memory, executive functioning and motor soft signs. Twenty-two parents had an ancestral history of schizophrenia and therefore were hypothesized to be more likely than their spouses without such a history ( $n = 17$ ) to carry a genetic risk for schizophrenia.

**Results:** Unaffected parents of schizophrenic patients showed significant deficits in a wide array of neuropsychological tasks and task domains. However, comparison of more likely and less likely carriers of illness-related genes showed specifically attentional and executive functioning, but not memory, to vary with degree of inferred genetic loading.

**Conclusions:** Attentional and executive (frontal) impairments vary with genetic loading for schizophrenia and can be considered true endophenotypes for this disorder. Consequently, these functions are particularly suited to evaluate the functional impact of candidate genes for schizophrenia in future studies.

### S19.04

Genetic and neuroimaging studies of antisaccade eye movements in schizophrenia

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An antisaccade is a rapid eye movement (saccade) made away from a visual stimulus. The task is a good measure of the conflict between an unwanted reflexive response (which must be inhibited) and a volitional response (which must instead be generated). Deficits on the anti-saccade task constitute a promising schizophrenia endophenotype. In this talk I will review studies that have demonstrated antisaccade deficits in sibling and twin pairs discordant for schizophrenia. I will then data from present recent investigations of association between antisaccade performance and candidate polymorphisms for schizophrenia and cognition. Finally, I will discuss results from an investigation of the relationship between brain function during eye movements and a single nucleotide polymorphism (SNP) in the catechol-O-methyltransferase (COMT) gene, a candidate gene for schizophrenia and brain function. The COMT val158met SNP (rs4680) was genotyped and the brain response during antisaccades was measured using fMRI in 36 healthy humans. Val158 carriers ( $N=24$ ) showed reduced BOLD response in ventromedial and dorsomedial frontal areas during antisaccades compared val158 non-carriers ( $N=12$ ). These findings suggest that COMT

val158met genotype may affect the brain response during antisaccades; the results may be compatible with a hypothesis on the role of COMT val158met genotype in tonic and phasic dopamine levels in cortex and measures of cognitive plasticity (e.g. antisaccades).

### S19.05

Sensitization to stress: An endophenotype for psychosis

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Increasing epidemiological evidence suggests that environmental stressors such as trauma and life events are associated with the development of psychosis. The underlying mechanism however remains unclear. Previous studies of our group have demonstrated that increased sensitivity to daily life stress is part of the underlying vulnerability for psychosis. It is therefore attractive to hypothesize that early trauma increases the risk for psychosis through sensitizing people for the small stresses of daily life. This hypothesis has been investigated in three different data sets (both general-population and clinical samples) using the Experience Sampling Method (ESM; a structured diary technique) to assess stress-reactivity in daily life defined as emotional and psychotic reactivity to stress. The results suggest that a history of childhood trauma sensitizes people to the stresses of normal life resulting in stronger emotional and psychotic reactions to stress. However, this sensitization process is most pronounced in subjects with an increased vulnerability for psychosis.

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## April 2008 Symposium: Drug dependence and gender

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### S47.01

Epidemiology of substance misuse, psychiatric comorbidity and gender

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Since substance use, misuse, harmful use and dependence are associated with considerable mortality and physical and psychological morbidity, the multiple and complex interactions of substance misuse with health will be explored.

Gender differences in substance use accrued from prevalence studies will be outlined and will be presented in the context of predisposing or complicating psychological symptoms or psychiatric syndromes. Observations that women are more likely to report a comorbid psychiatric condition than males, especially depression or borderline personality disorder but also impulsivity, aggression and disinhibition, anxiety, psychotic illness, post-traumatic stress disorder (as a result of early life stress and physical abuse) and eating disorders, will be examined in relation to the course and outcome of illness. Evidence for the high risk behaviours and chaotic life style that may be associated with comorbidity, such that self-harm may result, with eventual suicide, will be described.

In view of the fact that patients with comorbid conditions have poorer prognosis and place a heavy burden on services because of disengagement, high rates of relapse and re-hospitalisation, serious infections, and homelessness, unemployment, poverty, prostitution, violence, arrest and even imprisonment, it is important to have a grasp of the nature and extent of the problems so that patients can be sensitively managed. The likely impact of these conditions on women

and their social roles as mother and carer will be analysed as part of the need to develop effective services, which detect problems early and deliver appropriate interventions which are sensitively managed.

### S47.02

Aetiology of gender effects and dependence

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Epidemiological data show pronounced gender differences in the prevalence of substance use disorders (alcohol, sedatives, opioids, nicotine, psychostimulants, cannabinoids). Social, psychological and biological including genetic factors contribute to the gender differences. Several studies show in men a higher participation of genetic factors in the development of an addiction disease than in women, in which besides genetic factors other factors seem to be more prominent. The occurrence of psychic dependence with drug seeking behaviour is the outcome of a number of variables including sex hormonal, neuronal (dopamine and interactive transmitters f.e glutamate, GABA, serotonin, opioid peptides), genetic, developmental, age, neurodegenerative and environmental elements that interact to produce profound individual (gender) differences in both initial and longterm responsiveness to addictive drugs. Sex steroids, especially estrogens, are responsible for the synthesis and secretion of neuropeptides (eg opioids peptides), but also of the neurotransmitters dopamine, serotonin etc and may exert by these mechanisms and environmental interaction gender effects in addiction diseases. The diverse factors also have a significant impact on the accessibility to and effectiveness of pharmacological and psychotherapeutic treatment of different substance disorders in women and men.

Single representative results from animal and clinical studies especially on individual (genetic, sex hormonal, gender identification) differences will be presented which focus on key issues which may improve treatment effectiveness and models of service provision.

### S47.03

Gender aspects in the development and treatment of dependence

A. Heinz, J. Wrase. *Charite University Medicine, Berlin, Germany*

Women and men differ in the development of drug and alcohol dependence. In alcoholism, a phenomenon called "telescoping" has been described, i.e. women usually start later with excessive alcohol intake but develop neurotoxic effects (e.g. brain atrophy) earlier than men. On the other hand, estrogens may show neuroprotective effects, which has been postulated to explain relatively preserved serotonin transporter availability in female compared with male alcoholics. Once alcohol dependence is manifest, the relapse risk seems to be higher in women compared with men. Female patients usually report more emotional distress and reduced quality of life. They also show increased comorbidity with respect to anxiety and depression, while men more often display so-called "antisocial" personality traits. Borderline personality disorder also seems to be more frequent in women and may demand specific treatment options.

### S47.04

Substance dependence and pregnancy

N. Ebner, G. Fischer. *Medical University, Vienna, Austria*

The majority of women in drug treatment facilities are of childbearing age. According to a SAMHSA Report, four percent of women aged between 15 and 44, are pregnant while entering treatment

systems. These women represent a challenging patient population, that is in need of a comprehensive model of care, consisting of psychiatrists, psychologists, social workers, nurses and OBGYNs. Exposure to illegal substances during pregnancy may have consequences on the course of pregnancy and neonatal outcome. The fact that almost all patients showing up are also nicotine-dependent, should be taken into account, as neonatal withdrawal symptoms can be worsened. Furthermore, substance dependent women often find themselves in a situation of psychosocial instability. Prevalence of comorbid somatic (e.g. hepatitis C, malnutrition) and psychiatric disorders (PTSD, depression) is high. As these pregnancies are rated as "high-risk", prenatal checks should be undergone frequently. Recommended treatment for opioid-dependent, pregnant women is maintenance therapy with opioids. Post-delivery, 55 – 94% of infants exposed to substances in utero, may develop a neonatal abstinence syndrome (NAS). Incidence, time of onset and severity of NAS are associated with type of substances used. A standardized procedure of assessment and monitoring of NAS, as well as pharmacological and non-pharmacological treatment of these neonates is highly needed. By the means of a multi-professional treatment approach, the length of hospital stay may be shortened dramatically. In regard to a better future outcome, special aftercare (medical care plus psychosocial support) for mothers and infants should be provided, as well as further research.

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## Symposium: Nonverbal behaviour in psychiatric populations

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### S17.01

The clinical meaning of nonverbal behavior during psychiatric interviews

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The clinical phenomenology of psychiatric disorders includes both subjective psychological experiences and objective behavioral changes. Nevertheless, the diagnostic process in psychiatry is based almost exclusively on the evaluation of the psychological symptoms as voiced by the patient with virtually no use of direct observation of behavior. The weakness of such an approach to behavioral assessment has several negative consequences for clinical practice. It is difficult to estimate to what extent the findings of biological studies are confounded or invalidated by the fact that they are generally based on correlations between accurate physiological measurements and crude behavioral ratings, sometimes of the type "better/worse" or "much/less." Another negative consequence of psychiatry's neglect for direct observation of behavior is the difficulty of integrating animal and human data about the effects of drugs on behavior. If the clinical phenomenology of mental illnesses could be reformulated in ethological terms, the same, or similar, definitions could then be applied to the development of animal models, and analogs for specific behaviors might then become more feasible. Finally, the weakness of behavioral assessment in psychiatry has negative implications for clinical practice as well. Several studies have shown that the objective and quantitative recording of patients' behavior may sometimes yield different results from those obtained using rating scales or structured interviews. These findings cast doubt on the validity of routine psychiatric assessments and suggest caution in basing important clinical