that manifest in significant difficulties in acquisition and use of various learning abilities. LD were found in 10-20% of the general population. ADHD and LD share many common dysfunction characteristics in all daily activities. Studies show an overlap of 20-30% between the two disorders, and more psychometric disabilities, as well as a higher comorbidity rate and a lower SES status in adults who suffer from both than from LD alone. Yet, studies dealing with ADHD and LD comorbidity and its implication are few.

We wanted to examine ADHD frequency among students diagnosed as suffering from LD, and its correlation with other comorbidities, as well as to evaluate the efficacy of an ADHD screening questionnaire, and to estimate the rate of preliminary ADHD diagnosis and/or treatment in this group.

Methods: Population included 100 students, male and female, all aged 18 years old and above, studying in a specific center for LD. All students were diagnosed in the past as suffering from LD. No selection criteria had been administered. Methods were divided: 1) Screening questionnaire 2) ADHD assessment including: a structured interview (SCID), the Wender Utah Rating Scale (WURS), the adult ADHD self report scale (ASRS) and Test Of Variables of Attention (TOVA) with and without methylphenidate (MPH) challenge.

Results will be presented later

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Symposium: Endophenotypes of schizophrenia - recent findings and future prospects

S19.01

Cognitive endophenotypes: Why are we still trying to find them?

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Background: Despite a lot of initial enthusiasm and more than three decades of research, cognitive endophenotypes for psychiatric disorders are still to be found.

Methods: Based on a literature review and on our own research, we will analyse the reasons and consequences of this failure to find useful cognitive endophenotypes.

Results: Several commonly held ideas that proved to be over-optimistic, over-simplistic and finally false, have limited our ability to identify cognitive endophenotypes. Among those ideas, with deleterious methodological consequences, were the beliefs that neuro-cognitive validity is sufficient to ensure genetic validity, that cognitive measures and cognitive processes are equivalent and that cognitive processes have a simpler genetic architecture than psychiatric vulnerability. The perception of these initial errors modified our definition and expectations of cognitive endophenotypes and suggested ways to improve our chances to find them.

Several aspects of the study of cognitive endophenotypes demonstrated an initial excessive optimism, followed by disillusion and, now, a time for active search for realistic solutions. We will illustrate this process by an important feature for cognitive endophenotypes: the test-retest reliability. Although cognitive measures were initially considered stable, a systematic literature review revealed that most of them had problematic test-retest reliability. The use of such measures could lead to erroneous conclusions and limit their usefulness as cognitive endophenotypes.

Conclusions: Taking this parameter into consideration is important in selecting cognitive tests used to detect putative endophenotypes and in suggesting new approaches in the search for cognitive endophenotypes (for example the use of cognition questionnaires).

S19.02

Do putative endophenotypes go together? The case of schizotypy dimensions and neurocognitive domains

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Background and Aims: The extent and causes of covariance between schizotypy and neurocognition is not well-known yet. Certain models conceive their association as necessary for the construct validity of schizotypy, whereas others view them as independently contributing to a multivariate endophenotype. It is also not clear whether those at increased genetic risk for schizophrenia present stronger covariance, reflecting an extra latent source of variance. We analysed their association within relatives of schizophrenia patients defined with FIGS as Presumed Carriers -PC- of the genetic risk for schizophrenia, Presumed Non Carriers -PNC-, and controls.

Methods: 108 healthy relatives of schizophrenia patients and 72 healthy controls were assessed with the SCID-II and completed the SPQ-B. Neurocognitive assessment: Letter-Number Sequencing (LNS), WCST, CPT-IP, verbal fluency, and logical memory.

Results: Partial correlations adjusting for age and education showed that within PC-relatives self-rated negative schizotypy was associated with lower LNS and CPT-IP; positive schizotypy was associated with CPT-IP, and disorganization with memory and failure to maintain set. Schizoid symptoms had an association with failure to maintain set (though not perseveration) and paranoid symptoms with memory. Within PNC-relatives, negative schizotypy was associated with lower verbal fluency and more perseverative errors. Within controls, positive schizotypy was associated with perseverative errors and both positive and negative dimensions were associated with verbal fluency.

Conclusions: Results indicate a wider array of covariation between relatives with presumed higher genetic liability. A consistent pattern of

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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 antisaccade 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.

April 2008 Symposium: Drug dependence and gender

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

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