findings lend support to Cornblatt et al. (1992) model of sustained attention deficits as a pathway towards the development of social indifference and isolation.

FC11.04

A CLUSTER ANALYTIC STUDY OF NORMAL ADOLESCENTS WITH NEURODEVELOPMENTAL, NEUROCOGNITIVE, PERSONALITY AND SOCIAL RISK FACTORS FOR SCHIZOPHRENIA SPECTRUM DISORDERS

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Background: Schizophrenia is thought to have a neurodevelopmental origin, which would explain the early signs of abnormality found in pre-schizophrenics. We wanted to see how certain risk factors for schizophrenia including signs of neurodevelopmental disturbance cluster in individuals from the general population.

Methods: Data for this analysis come from a biobehavioural high-risk study of adolescents from the general population initiated in 1993. Two phases have been conducted so far (T1 and T2). We did a hierarchical cluster analysis with 97 subjects (mean age 17.65, SD = 0.77) to identify subgroups on the basis of T2 (1998) markers for schizophrenia spectrum from several domains: neurodevelopmental (dermatoglyphics), neurocognitive (CPT-IP, verbal and spatial memory, WCST), personality (4 schizotypal dimensions), and social behaviour. After constituting the groups we compared them on T1 (1994) variables.

Results: Four clusters were determined. From these, Cluster I (n = 29) was characterised by a predominance of boys, more negative schizotypy, poorer verbal memory and attention, and more developmental instability. A MANOVA showed that only 4% of the variance was left unexplained (Wilks Lambda 0.04, p = 0.0001). When compared on T1 variables, this cluster showed to have significantly more negative schizotypy, teacher-rated internalising symptoms, neurological soft signs (trend), and in a 25% parents reported delivery OC_s . The remaining clusters were also clearly interpretable.

Conclusions: We have found in a sample of 'normal' adolescents a subgroup of subjects in which markers for schizophrenia spectrum phenomenology coaggregate very similarly to what has been found in population cohort studies as the antecedents of the neurodevelopmental type of schizophrenia: negative features, signs of perinatal disturbances, and neurocognitive abnormalities. Whether this subgroup is at heightened risk to show axis I or II symptoms compared to the others will be evaluated soon in a third phase with clinical interviews.

FC11.05

HUBIN – HUMAN BRAIN INFORMATICS: A CLINICAL DATABASE PROJECT FOR MULTIDISCIPLINARY RESEARCH IN SCHIZOPHRENIA

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Schizophrenia represents a tragedy for patients and relatives, and a serious problem for society. The HUBIN database project – Human Brain Informatics Center – concerns the establishment of a relational database at the Karolinska Institute on human brain data in schizophrenia and in healthy volunteers. The HUBIN research

program represents an international research collaboration investigating multiple dimensions concerning the etiology and pathophysiology of schizophrenia. The HUBIN database study combines molecular genetic, phenotypic, brain imaging (MR, PET), and environmental high quality data for representative schizophrenia patient populations and healthy control subjects. Major HUBIN studies are conducted on one of the world's largest siblingpair study of schizophrenia and on a large representative sample of patients with schizophrenia and normal comparison subjects. The HUBIN database project is now entering its second phase in which data from more than 2000 clinical and biological variables from more than 3000 patients and a similar number of healthy control subjects are entered into the database. With this approach we will search for new evidence regarding genetic and environmental mechanisms for the etiology and pathophysiology in the group of schizophrenia patients. Data mining procedures are used to search for relations between patients and volunteers, which in turn will be used for the generation of new hypotheses with regard to both etiology and pathophysiology. The database will also be used for a detailed characterization of the variability of a large number of entities of importance for the human brain and its functions in relation to health and psychiatric disorders.

FC11.06

A UNIFIED HYPOTHESIS OF SCHIZOPHRENIA BASED ON GLUTATHIONE DEFICIT

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We have previously investigated teh concentrations of amino acis, dopamine and serotonin metabilites, N-acetylaspartate and N-acetylaspartylglutamate in teh cerebrospinal fluid (CSF) of drug naive or drug free schizophrenic patients (Table 1) in whom long-term changes secondary to previous antipsychotic treatment could be excluded. Among the 26 compounds analysed, we reported a decrease in γ-glutamylglutamine (γ-Glu-Gln; Do et al., 1995). This γ-glutamyl dipeptide is most probably synthesised from GSH by the enzyme γ-glutamyl-transpeptidase, which transfers the γglutamyl moiety of GSH to an amino acid (Fig1). We therefore determined the GSH (Glutathione) concentration of the same CSF samples.

Methods:

<u>MRS</u>

- Use of a double quantum coherence filter technique (DQC) based on coherence pathqay filtering with static field gradients in combination with spatial selection of a single volume. The strongly coupled dysteine CH2 compound of GSH (multiplet at 2.9 ppm) was found to be the most suitable target for spectral editing.
- The sequence was implemented on a Philips Gyroscan ACS NT 1.5 Tesla whole body scanner equipped with a transmit/receive birdcage resonator (Philips Medical Systems, Best, The Netherlands).
- 9 male inpatients (age range: 19 to 43.6 years); DSM-III-R: Schizophreniform (n = 3), schizophrenic disorder (n = 6); 3 patients were treated with neuroleptic medication in the past, 4 were drug-naive, 2 drug-free for at least 6 months.

AMDP, PANSS, SANS, SSCL-16, SCL 90 served as psychopathological rating scales.