S17 *Diagnostic interview for genetic studies rehability*

GENETIC EPIDEMIOLOGY OF SCHIZOPHRENIA

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All psychiatric disorders are aggregating in famillies. The etiological mechanism operating in families, however, remains widely obscure. Indirect evidence emerging from detailed analyses of the familial pattern of aggregation proposes that a) genetic as well as environmental components are relevant; b) a lack of diagnostic homogeneity of disorders is aggregating in the same family; c) clinical sub-types breeding true in families are unlikely to occur; d) the genetic component is unlikely to be represented by a single gene. Specific putative environmental factors for the multiple occurrence of psychiatric disorders in families have been explored. However, methodological limitations prohibit conclusive results on the specific nature of the predisposing environmental risk factors. The available tools for the identification of casual and/or susceptibility genes are more stringent. Previous claims of predisposing genes for schizophrenia did not pass the test of replication. Very recently, multiple susceptibility genes for schizophrenia were found in a replicable fashion. Current evidence emerging from genetic association and linkage studies in schizophrenia will be reviewed.

S18 *Schizophrenia: a new clinical narrative...*

SCHIZOPHRENIA: NEW CRITERIA FOR THE CLINICAL NARRATIVE

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Epidemiology, as it has been developed throughout these last years in psychiatry, has helped to outline clinical fields and diagnostic entities as well as to give importance to the phenomenon of comorbidity often underestimated in psychiatry. However, epidemiology has also brought to light new and troubling questions like those about the rate of young adult disorders and those concerning the patient's childhood which keeps its secret. Relating to schizophrenia, which remains an area of uncertainty, research in molecular genetics will no doubt bring important information over the next decades. Clinicians are still inconvenienced by the traditional description of schizohrenia which fails to take into account the elements of schizophrenia already present in childhood and adolescence. These elements could lead to interesting therapeutical possibilities. Epidemiology is the essential llink between those who work in fundamental research and those who are confronted daily with the patient as a person with his story, his desires, his regrets and memories.

S17 *Diagnostic interview for genetic studies rehability*

DIAGNOSTIC INTERVIEW FOR GENETIC STUDIES RELIABILITY

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The semi-structured Diagnostic interview for Genetic Studies (DIGS) was developed specifically for the assessment of major mood and psychotic disorders and spectrum conditions in genetic studies. It allows the assignment of a large spectrum of Axis I DSM-IV disorders and the collection of information on the chronology of comorbid disorders. The original interrater- and test-retest reliabilities were high for schizophrenia and mood disorders but markedly lower for schizoaffective disorders. Our research group has developed a French version and extensively tested its reliability in inpatients and outpatients from two sites. There are experienced clinicians, trained psychologists and psychiatrists with sessions and demonstration videos to ensure compatibility across sites. A first interview was performed in the presence of a co-rater to assess interrater reliability. The re-test interview was carried out 6 weeks later by an independent team member. Compared to the original English version, similarly high kappa coefficients for interrater reliability were found for mood disorders and schizophrenia and slightly higher kappas for schizo-affective disorders. In contrast, perhaps due to a longer interim period, the kappas for test-related reliability of mood disorders and schizophrenia were slightly lower than those reported for the original interview. The DIGS is a reliable diagnostic instrument for French-speaking regions.

S18 *Schizophrenia: a new clinical narrative...*

How to link clinical picture of schizophrenia with the neurodevelopmental hypothesis?

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The most commonly suggested pathogenetic view of schizophrenia has been, for the last ten years, the so-called neurodevelopmental hypothesis. This view heavily relies on epidemiological data pertaining to pre- and/or perinatal risk factors, as well as to developmental deviances and behavioral pecularities observed along childhood of future schizophrenics However, it has been so far difficult to link the neurodevelopmental hypothesis with the clinical picture of schizophrenia.
This link is, in our view, very problematic when the clinical picture of schizophrenia is restricted to descriptive, operationalist criteria. These derive mainly from overt, psychotic symptomatology, which is transient, state dependent, and thus cannot directly reflect an enduring biological substrate. We propose that clinical trait features underlying the whole range of the "schizophrenia spectrum disorders" are better candidates for elucidating the pathogenesis of the disease. However, such trait features are difficult to operationalize, because they pertain to the patient's inner experience. They reflect fundamental disturbances in self-experience and intersubjectivity. Recent advances in developmental psychology and insights in the ontogenesis of the CNS may help to clarify the neurodevelopmental hypothesis of schizophrenia by linking empirical data from these disciplines with premorbid and clinical trait features of schizophrenia spectrum disorders.

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