efforts to measure quality of life in psychiatric patients and present reasons why quality of life should nevertheless be measured in psychiatric patients — reasons perhaps even more compelling in psychiatry than in other field of medicine.

S73. Psychiatric genetics and studies of relatives of psychotic patients

Chairmen: T Sharma, A Vita

NEURODEVELOPMENTAL MODEL(S) OF SCHIZOPHRENIA AND APPROACHES TO THEIR VALIDATION

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Several neurodevelopmental models have been proposed for schizophrenia: the early model which posits a fixed lesion during intra or perinatal life which interacts with normative postnatal maturation, a late model which implicates a primary derailment in postnatal peri-adolescent brain maturational processes, and a risk-diathesis model in which psychosocial risk factors interact with genetic vulnerability to cause the disorder.

In this paper, we critically evaluate each of these models; we propose that the facts best fit a continuous transaction model in which the schizophrenic syndrome results from a cascade effect of derailment in early and late maturational processes of brain development interacting with adverse humoral and psychosocial factors as well as protective factors continually during childhood and adolescence.

Finally, we will review the testable predictions generated by these models, and critically evaluate the various research strategies (i.e., the generic and biobehavioural high-risk strategies, follow back strategies, birth cohort studies, etc.) that will potentially further our understanding of the neurodevelopmental pathogenesis of schizophrenia. We suggest that an "enriched" high-risk paradigm (in which subjects at high genetic risk are further selected on the basis of neurobehavioural vulnerability markers) is likely to be a cost-efficient strategy for future high risk studies investigating the neurodevelopmental pathogenesis of schizophrenia.

LOSS OF DEVELOPMENTAL TORQUE IN FAMILIAL SCHIZOPHRENIA — A VOLUMETRIC MAGNETIC RESONANCE IMAGING STUDY USING UNBIASED STEREOLOGY

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The goal of the study was to determine whether familial schizophrenic patients and their unaffected first degree relatives differed from healthy subjects in regional cerebral asymmetries. Regional volumes corresponding to prefrontal, premotor, sensorimotor, occipitoparietal, and temporal lobes in each hemisphere were measured on contiguous 1.5 mm 3D MRI images in 28 patients, 55 relatives and 39 controls using a new software based on stereological principles and capable of unbiased volume estimation.

This study revealed a significant abnormality of cerebral hemispheric volume asymmetries in patients with schizophrenia. The healthy comparison subjects showed a systematic pattern of asymmetries, with prefrontal, premotor and temporal regions larger on the right and sensory motor and occipito parietal regions larger on the left. In contrast, the patients did not show this pattern; they had low absolute asymmetry of all regions and reversed asymmetry of the occipito-parietal and prefrontal regions. The loss of asymmetry was present in both dextral and non-dextral schizophrenic subjects. In addition, transmitting parents (presumed obligate carriers), who are themselves unaffected, showed the same reversal as the schizophrenic family members. The absence of normal cortical asymmetry in familial schizophrenia and the unaffected parents lends support to an early neurodevelopmental abnormality that is likely to be genetic in origin.

A PET STUDY OF WORD GENERATION IN OBLIGATE CARRIERS OF THE PREDISPOSITION TO SCHIZOPHRENIA

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Building on previously reported findings of a qualitatively different functional anatomy underlying word generation in chronic and acute [drug naive] schizophrenics and normal individuals we have studied presumed obligate carriers of the predisposition to schizophrenia. These individuals are drawn from multiply affected kindreds but are themselves clinically unaffected. We have used PET to measure regional cerebral blood flow (rCBF) in 11 obligates and 9 normal controls. Subjects were scanned while articulating words provided by the experimenter at a rate of 1 every 5 s, and also while articulating self-generated words at the same rate. The difference in rCBF between the two conditions indicates the pattern of cerebral activity associated with word generation. Obligates demonstrate a widespread pattern of aberrant activity within frontal systems associated with the execution of internally generated acts. These findings are consistent with theories implicating a heritable component to the brain dysfunction seen in schizophrenia.

SCHIZOPHRENICS AND THEIR ADOPTED-AWAY OFFSPRING. THE FINNISH ADOPTIVE FAMILY STUDY OF SCHIZOPHRENIA

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The National sample of the Finnish Adoptive Family Study of Schizophrenia consists of all adopted-away offspring (N = 183) of schizophrenic women hospitalized in Finland (N = 19447). The index offspring have been blindly compared with adopted-away offspring of nonpsychotic biological mothers. At initial assessment 345 (92%) out of total 376 adoptees (Index/controls) and their biological and adoptive parents and rearing families were interviewed and tested individually and jointly. At follow-up interviews (on average 15 years later) most of the adoptees available have been personally interviewed with PSE, SCID-2 and SIS schedules. DSM-III-R diagnoses have been given to the biological mothers and their adopted-away offspring.

There is more schizophrenia and "schizophrenia spectrum disorders" in adopted-away offspring of biological mothers with schizophrenia or with "schizophrenia spectrum disorders" as compared with control offspring. Schizophrenia Spectrum here is defined as

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