CHALLENGE STUDIES IN OBSESSIVE COMPULSIVE DISORDER: RECENT DEVELOPMENTS WITH MCPP AND PENTAGASTRIN

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Compounds with serotonin (5-HT) selective effects have been used in patients with obsessive compulsive disorder (OCD) to assess the functional status of brain 5-HT pathways in this disorder. Particularly, the provocation of behavioural and neuroendocrine responses by m-chlorophenyl piperazine (mCPP) has aroused great interest. Some investigators have reported a brief exacerbation of OCD systems following a single oral dose of mCPP, but the literature is not unequivocal in this respect. mCPP has also been used to examine the neuroendocrine responses in OCD patients. In healthy subjects, mCPP is associated with an elevation of plasma prolactin and cortisol, while in OCD patients both blunted and normal responses have been found.

To investigate the mechanism of action of mCPP, we have recently studied the effect of ritanserin, a 5-HT_2 antagonist, on the behavioural and neuroendocrine responses by mCPP in patients with OCD and healthy controls. Premedication with ritanserin completely antagonized the neuroendocrine effects of mCPP, suggesting a role for the 5-HT_2, receptor in the neuroendocrine response of this mixed 5-HT agonist.

To investigate the effects of mCPP on regional brain activity, we also evaluated the effects of acute oral mCPP (0.5 mg/kg) administration on the regional cerebral blood flow (rCBF) in patients and controls using the HMPAO-SPECT imaging technique. The most striking observation of this study was an augmented basal rCBF in the cerebellum of OCD patients. Administration of mCPP significantly reduced the rCBF in this area in patients, but not in controls. In control subjects, mCPP induced increases in rCBF in the basal ganglia and some cortical areas.

Pentagastrin is a new and interesting pharmacological agent, which can induce panic anxiety in panic disorder patients (PD). To evaluate the specificity of this CCK_B agonist to induce panic, we administered this compound to OCD patients. Seven OCD patients and seven control subjects were enrolled. In patients, but not in controls, a significant increase in anxiety was observed, resulting in a panic-like reaction in six out of seven OCD patients. No significant changes were noted in OCD symptoms. The data suggest that the panic-inducing properties of pentagastrin are not specific for PD patients and suggest a common biological abnormality for PD and OCD.

S55. Obstetric complications and markers for prenatal disturbance in schizophrenia

Chairmen: L Fañanás, A Lane

OBSTETRIC COMPLICATIONS AND PREMORBID COGNITIVE AND SOCIAL ADJUSTMENT IN SCHIZOPHRENICS AND THEIR SAME-SEX UNAFFECTED SIBLINGS

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Obstetric complications (OCs), premorbid emotional, social and cognitive dysfunctions could represent important factors in the development of schizophrenia due to a neurodevelopmental defect and could increase the vulnerability to schizophrenia (Murray, 1994, Zubin, 1986).

36 same-sex pairs of patients (schizophrenics, schizoaffectives) and their healthy siblings (no psychiatric diagnoses) have been diagnosed according DSM-III-R, using structured psychiatric interviews and a consensus of two psychiatrists. They have been compared in variables like OCs and in their premorbid emotional, social and cognitive functioning. Informations were also obtained by interviewing their mothers. Beside others the following scales were used: Family Assessment Measure (Steinhauser et al., 1984), "Giessen-Test" (Beckmann and Richter, 1979) and Parental Bonding Instrument (Parker et al., 1979).

First univariate analyses show differences in patients, compared to their siblings in birth weight on the 5% level and in two OC-classifications (Lewis et al., 1989, Parnas et al., 1982) on the 10% level of significance. In premorbid emotional (t-value = 3.09, $p = 0.005$), social (t-value = 4.81, $p = 0.000$) and cognitive functioning (z-value = −3.3, $p = 0.001$) patients show significant differences, compared to their siblings, too. Multivariate analyses (discriminant analysis) show correct classification of patients and their same-sex siblings of 96%.

These first results seem to confirm the concept of schizophrenia as a neurodevelopmental process (Murray et al., 1992, Murray, 1994).

OBSTETRIC COMPLICATIONS AND PRENATAL MALDEVELOPMENT: RESULTS FROM SWEDISH STUDIES

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While an increasing number of studies have shown an association between history of obstetric complications (OCs) and schizophrenia, the manner by which OCs may yield an etiopathological effect remains to be elucidated. Discrepancies in results obtained across studies may partially be due to the wide variety of methodological approaches currently in utilization. Increased knowledge concerning the role of OCs in the development of schizophrenia may be provided by studying the specific gestational timing of increased OCs and by testing hypotheses as to their possible origin. We have applied a newly developed OC assessment instrument (McNeil-Sjöström, 1995) which enables examination of several different phases of the reproduction to samples of singletons, MZ twins, and high-risk cases. Early pregnancy complications (PCs) were found to be related to increased incidence of minor physical anomalies (MPAs) in schizophrenic MZ twins. PCs were unrelated to findings of reduced head circumference at birth in schizophrenic singletons. These latter findings, reduced head circumference but no significant increase in PCs, have recently been replicated in patients with non-schizophrenic psychotic diagnoses. Our twin and singleton studies found significant increases in perinatal complications only, despite adequate PC reporting frequency. As our OC studies thus primarily indicate that histories of schizophrenics are characterized by perinatal complications, we have investigated the possibility that these may be the result of pre-existing abnormalities in the fetus. Our results show that schizophrenics with signs of prenatal abnormality (e.g. reduced head size, MPAs) did not have more labour/delivery complications (LDCs) than did other schizophrenics, and that LDCs were not related to PCs. Continued empirical study is clearly indicated in order to understand the origins of pre- and perinatal trauma and their role in the development of psychoses.