

(BDQ). They were also interviewed using a semi-structured schedule focussed on the phenomenon of bodily change. Each subject was also asked to attempt an estimation of the size of body parts on a linear presentation.

All groups over-estimated their body size, with females significantly more so than males. Apart from a non-significant trend for female schizophrenics to over-estimate to a greater extent, there was no difference between any of the groups, including controls. On the BSQ and BDQ, there was no difference between the schizophrenic group and controls, even though the semi-structured interviews in the patient group indicate quite marked distortions of body experience, suggesting that the standard instruments are not sensitive enough in rating the subjective experience in schizophrenic patients. There was no correlation between the BPRS, SANS, and HBS ratings in the patient group and the ratings on BSQ and BDQ.

These findings will be discussed in relation to theoretical issues in the study of subjective experiences in schizophrenia, and the methodology appropriate to this domain of disability.

## **Obstetric complications in schizophrenia**

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A large number of studies examining obstetric histories of schizophrenic patients have reported that schizophrenics are more likely to have a history of obstetric complications than are non-schizophrenic controls. Although it is not known exactly how obstetric complications may be related to the pathophysiology of schizophrenia, it has been hypothesized that, via hypoxic mechanisms, they may cause cell loss to key brain areas that have been implicated in the pathophysiology of schizophrenia. One way to investigate this hypothesis is to compare schizophrenics with and without a history of obstetric complications using indices that are purported to reflect hypoxic-related injury (e.g. MRI measures of brain areas known to be sensitive to hypoxia, neurologic measures, and neuropsychological data). Finding differences on these measures between schizophrenics with and without obstetric complications would support the validity of obstetric complications as a risk factor for schizophrenia, and would provide preliminary data on a possible pathophysiological mechanism.

We have, using age and sex matched sibling controls and blind ascertainment of obstetrical data, collected obstetrical data on 56 schizophrenic patients and 129 of their non-schizophrenic siblings. In our preliminary analyses, we were unable to find significant differences between total patients ( $N=56$ ) and their siblings ( $N=129$ ) and age and sex matched patient-sibling pairs ( $N=36$  matched pairs), on incidence of definite, total, or equivocal complications. In addition, we found no significant differences among schizophrenics with and without definite obstetric complications on measures hypothesized to be sensitive to hypoxia-related events (i.e., MRI volumetric measures of the hippocampus, caudate, amygdala and prefrontal cortex; premorbid adjustment measures; and neuropsychological and neurological measures). However, when we used less stringent criteria (i.e., (OC) positives ( $N=10$ ) vs (OC) negatives, equivocals, and questionables ( $N=19$ ), we found that the OC+ group had a larger percentage of perseverative errors on the Wisconsin Card Sort ( $OC+ = 26.6 \pm 6.3$  vs  $OC- = 11.7 \pm 3.5$ ,  $p < 0.01$ ).

Our study fails to support the hypotheses that: 1) obstetric complications are increased in schizophrenic patients compared to their siblings; and 2) that obstetric complications may be related to the pathophysiology of schizophrenia by means of hypoxic mechanisms. This might be explained by the sample sizes, the sensitivity of the measures employed, and the difficulties involved when relating retrospective history of birth complications to the absence or presence of "significant" early hypoxia. Future analyses will include larger subject populations, as well as a normal control group, in order to more definitely address the possible mechanistic role of obstetric complications in schizophrenia.

## **Negative symptoms, neuropsychological findings, and ventricular enlargement in schizophrenia**

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In 1976 Johnstone and Crow were the first to report findings suggesting a relationship between negative symptoms, neuropsychological impairment, and ventricle-brain ratio (VBR) in schizophrenia. Since that time several authors have expanded the list of clinical phenomena associated with negative symptoms, including premorbid schizoid traits, poor response to treatment, and unfavorable prognosis. Indeed, negative symptoms, neuropsychological dysfunction, and increased VBR were suggested to characterize a possibly distinct subgroup of schizophrenic patients. Recently these relationships have been challenged. Andreasen (1990) in a recent reappraisal suggested that although negative symptoms could be used to dichotomize schizophrenic patients along certain variables, VBR was unrelated. Bilder and his colleagues (1988) studying deterioration in schizophrenia, suggested that CT scan abnormalities may be associated with relatively *high* premorbid neuropsychological function, as well as greater clinical deterioration. Thus, these seemingly inseparable clinical phenomena may be related in a much more complicated way than previously thought. In an effort to further evaluate these relationships, 23 medication-free chronic schizophrenics (DSM-III-R, RDC), admitted to the University of Michigan Schizophrenia Program, were studied. Patients were rated at base-line and four weeks post-treatment with the SANS, BPRS, and HRSD, to assess negative, positive and depressive symptoms respectively. Cognitive function was assessed via a comprehensive neuropsychological battery that included WAIS-R, Wisconsin Card Sorting test, Trails A and B, Wechsler Memory Scale, and others. Computerized tomography (CT) of the brain was performed and VBR was determined via computer-enhanced video digital planimetry. The results, contrary to previously published work, demonstrated no relationship between ventricle size and negative symptoms or neuropsychological impairment. Indeed VBR was positively correlated with education ( $p < 0.06$ ) and full scale IQ ( $p < 0.1$ ). Negative symptoms were negatively correlated with full scale IQ, verbal IQ, reaction time, Wisconsin Card Sorting performance, and Tactual Performance Test scores ( $p < 0.05$ ), as well as, Wechsler Memory Scale ( $p < 0.05$ ; pretreatment only), Selective Reminding Test performance, and finger tapping, ( $p < 0.01$ ). These relationships tended to be stronger for post-treatment ("deficit") negative symptoms. Pretreatment BPRS ratings were inversely related to Wechsler Memory Scale scores ( $p < 0.05$ ); post-treatment BPRS ratings were negatively correlated only with Wisconsin Card Sorting perseverative responses ( $p < 0.08$ ) and Tactual Performance Test memory scores ( $p < 0.06$ ). HRSD ratings were not associated with any neuropsychological test scores. The findings of this study suggest that, similar to other researchers, negative symptoms (especially "deficit" symptoms) are associated with global neuropsychological impairment. However, contrary to previous reports, VBR was not related to cognitive impairment or negative symptoms, and indeed may be related to relatively good cognitive performance. These results are consistent with Bilder et al. (1988), suggesting that greater deterioration, rather than global cognitive impairment, is associated with VBR.

## **Development of cognitive and electrophysiological measures of selective attention for genetic linkage studies of schizophrenia**

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Traditional approaches to the genetics of schizophrenia have been limited by the failure of this disease to fit a classical Mendelian transmission mode. The problem may be related to the predominant use of diagnostic classification as the sole definition of schizophrenic phenotype. Linkage analyses with DNA markers may ultimately depend on an expansion of the schizophrenic phenotype to include associated psychological and psychophysiological traits. The goal of this approach is to uncover traits which tend to segregate in the families of schizophrenics but show a more classical pattern of inheritance. We have employed genetic and developmental research strategies in our ongoing studies of information processing in twins and in schizophrenics and their families. Assessments include a series of visual attention tasks and electrophysiological recordings. Preliminary investigations revealed that visual selective attention and P300 amplitude are heritable, stable components of CNS functioning. Current studies of large Utah families with multiple incidence of schizophrenia suggest that poor selective attention and reduced P300 amplitude may be useful phenotypic markers for linkage analyses.