81. A COGNITIVE, PERCEPTUAL, AND MOTOR STUDY OF HEMISPHERIC ASYMMETRY IN THE MAJOR PSYCHOSSES

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Studies have demonstrated asymmetric hemispheric dysfunction in patients with schizophrenia and bipolar disorder. However, few studies have compared directly the dysfunction in schizophrenia to that of bipolar disorder, and few have studied hemispheric asymmetries across modalities, which could address regional specificity of lateralized hemispheric dysfunction. We assembled a battery of assessments designed to measure lateralized hemispheric function of the following modalities: sensory information processing and arousal (dichotic listening, chair identification, consonant-vowel-consonant test), memory (Warrington recognition memory test), and motor (hand force instability, velocity scaling, reaction time). To date, 19 right-handed male patients with schizophrenia (N = 11) and bipolar disorder (N = 8) have been assessed to determine whether differences in lateralized performance appear across multiple modalities. Effect sizes between diagnostic groups were large for L-R (left minus right) scores for chair identification and velocity scaling and medium for hand force instability. In measures purported to reflect dopaminergic tone (velocity scaling and hand force instability), schizophrenia patients showed diminished right hemispheric function relative to the left, whereas bipolar patients showed diminished left hemispheric function relative to the right. In a measure purported to reflect hemispheric arousal (chair identification), the reverse was true: schizophrenia patients showed diminished left hemispheric function relative to the right, whereas bipolar patients showed diminished right hemispheric function relative to the left. These findings support the literature demonstrating a hemispheric imbalance in schizophrenia and bipolar disorder. They also suggest the possibility that the hemispheric dysfunction in psychosis is complex and may be related to either increased activity in one hemisphere or decreased activity in the other hemisphere. They also indicate that there may exist different mechanisms of hemispheric control, one responsible for motor activity and another for arousal.

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82. NEUROPSYCHOLOGICAL EVALUATIONS OF HIGH RISK ADOLESCENTS FOR SCHIZOPHRENIA

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Early detection is critical to the treatment and understanding of schizophrenia. Children of one schizophrenic parent have a 10–15% risk of having schizophrenia themselves, compared to the risk of 1% for the general population. Through research with children and adolescents at high risk for schizophrenia, it may be possible to find vulnerability markers, which would allow for a greater understanding of this disorder.

Schizophrenic adults have shown to have greater difficulties with executive functions and attention, which we are able to assess using neuropsychological testing. The Continuous Performance Test (CPT) and the Wisconsin Card Sorting Test (WCST) were administered to high-risk adolescents (n = 14, mean age 16.07 ± 2.02) and controls (n = 18, mean age 16.63 ± 1.63) between the ages of 13–19 in an ongoing study of neuropsychology and Magnetic Resonance Spectroscopy (MRS). Subjects were administered the Diagnostic Interview for Children and Adolescents or the Structured Clinical Interview for DSM IV (DICA or SCID), depending on age, to rule out any psychopathology. Statistical analysis using paired-t-tests showed significant differences in the General Assessment of Functioning (GAF) between the high risk and controls between the ages of 16–19 years old (p = .05), but not for the subjects ages 13–15. Results of the CPT showed trend differences in the number of commissions (p = .09), and rates of attentiveness (p = .18) with controls performing at a higher level. Differences were not found in the WCST scores. These results must be considered preliminary given the small sample size.

83. PHARMACOLOGY OF PSYCHOTIC-LIKE ABNORMALITIES EXPRESSED BY REELER HETEROZYGOUS MOUSE

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Reelin is not only essential for the normal development of the telencephalon and cerebellum, but this protein also exerts a continued neurotrophic function in the adult. Reelin and its mRNA are decreased by approximately 50% in the postmortem brain of schizophrenia patients (PNAS 95: 15718–15723, 1998) and bipolar patients with psychosis. Glutamic acid decarboxylase 67 (GAD 67), an enzyme critical for GABAergic function in the brain, is also decreased. Parallel to these findings in postmortem psychotic brain, we recently found in reeler heterozygous mouse (rel+/−): a) a 50% decrease of reelin mRNA and protein compared with wild type (rel+/+); b) a maldistribution of NADPH-d neurons in medial prefrontal cortex vs underlying white matter; c) neophobia on the elevated plus-maze, d) a deficient prepulse inhibition of startle, or PPI (NeuroReport 10: 1999); and e) a decrease in GAD 67 mRNA of more than 50% in frontoparietal cortex. Imidazenil is an allosteric modulator of the benzodiazepine binding sites located on GABA_A receptors and is devoid of sedation or of tolerance and dependence liability. In rel+/+ mice, a single dose of imidazenil increases prepulse inhibition of startle in a dose-dependent manner without affecting the overall level of startle. The effects of acute and chronic treatment with imidazenil compared with diazepam or saline controls on behavior and GABA function will be presented using the rel+/− mouse as a model for psychosis. Our experience with imidazenil suggests that it would be an ideal drug for future testing in psychiatric patients.

84. CLINICAL CORRELATES OF STRUCTURAL BRAIN ABNORMALITIES IN SCHIZOPHRENIA

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Although most longitudinal imaging studies suggest that structural brain abnormalities (SBA’s) in schizophrenics are not progressive, some