linked to schizophrenia. We will present data from a group of 45 SPD subjects who were assessed on a specific set of information processing tasks including startle prepulse inhibition, P50 event related potential sensory gating, visual backward masking, visual contrast sensitivity, oculomotor measurement, choice, and neuropsychological measures. Preliminary analyses show strong but selective relationships between many of the information processing measures. These results suggest that some of the measures may collectively identify a vulnerability to schizophrenia. In addition, there appear to be subgroups of SPD subjects with deficits across multiple measures. The significance of these findings will be discussed.

118. PPI IN UNMEDICATED AND MEDICATED ACUTELY PSYCHOTIC SCHIZOPHRENIA PATIENTS

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The present study was designed to extend our understanding of sensorimotor gating in acutely psychotic schizophrenia patients and to assess the relationship between gating deficits and neuroleptic treatment. Many studies support the hypothesis of a schizophrenia-linked deficit in sensorimotor gating with an associated vulnerability to psychosis. One way to assess sensorimotor gating in humans is through prepulse inhibition (PPI) of the startle blink reflex. PPI occurs when a weak prestimulus presented 30 to 500 milliseconds prior to a startling stimulus results in a dampening of the blink reflex. In animal studies, activation of D2 dopamine function in the limbic forebrain produces deficits in PPI that model the PPI deficits seen in schizophrenia patients. Blockade of the D2 receptors restores prepulse inhibition. Recently, there has been a report that clozapine-treated schizophrenia patients showed normal levels of PPI compared to patients treated with typical neuroleptics. The same group has also found that haloperidol disrupted PPI in normal males leading to the conclusion that hypo and hyperdopaminergic states may lead to PPI deficits. However, it remains unclear if there is an interaction between medication status, acuity and symptom state in the mediation of PPI. The strategy used in this study to address this question was to assess a sample of schizophrenia patients all of whom are within 48 hours of admission to an acute psychiatric hospital.

In this study, PPI was measured in acutely psychotic schizophrenia patients within 48 hours of admission. Sixteen patients were unmedicated while the other 13 were being treated with an antipsychotic medication, eleven patients were treated with atypical antipsychotic medications. Subjects were clinically assessed with the PANSS to quantify symptoms. The medicated versus unmedicated subjects were not significantly different on any of the symptom measures. PPI was measured in a paradigm using three prepulse to pulse intervals (30, 60 and 120 msec). There were no differences between the two groups for any of the three conditions, nor was there a relationship between symptoms and PPI for either group or when the groups were combined. These findings support the interpretation that symptom acuity is a more powerful mediator of PPI than medication status in schizophrenia patients.

119. SUSTAINED HALOPERIDOL OPPOSES APOMORPHINE AND PHENCYCLIDINE-INDUCED STARTLE GATING DEFICITS

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Both dopamine (DA) agonists and NMDA antagonists produce prepulse inhibition (PPI) deficits in rats that model PPI deficits in schizophrenia patients. While DA agonist effects on PPI are reversed by acute treatment with either “typical” high potency D2 DA antagonists or “atypical” antipsychotics, PPI deficits produced by phencyclidine (PCP) are preferentially reversed by acute treatment with “atypical” antipsychotics. Acute effects of antipsychotics may not accurately model the more clinically relevant effects of these drugs, that emerge after several weeks of continuous treatment. In the present study, sustained treatment with haloperidol via subcutaneous minipumps blocked the PPI-disruptive effects of the DA agonist apomorphine and attenuated the PCP-induced disruption of PPI. Restoration of PPI in apomorphine-treated rats was evident within the first week of sustained haloperidol administration; a partial but statistically significant reversal of PCP effects on PPI did not develop until weeks 2-3 of haloperidol treatment, was not observed for treatment weeks 4-6, then re-emerged in the seventh week of sustained haloperidol treatment. The delayed emergence and re-emergence of anti-PCP effects of haloperidol suggests that the brain substrates responsible for the DAergic and NMDA regulation of PPI are differentially sensitive to acute and chronic effects of antipsychotics.

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120. REGULATION OF SENSORIMOTOR GATING IN RATS BY HIPPOCAMPAL NMDA: ANATOMICAL LOCALIZATION

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Prepulse inhibition (PPI) of the startle reflex is a measure of sensorimotor gating that is reduced in humans with certain neuropsychiatric disorders, including schizophrenia, and in rats after manipulations of limbic cortico-striato-pallido-pontine circuitry. We have reported that PPI is reduced after specific manipulations of the hippocampal complex (HPC) in rats, but the mechanisms for these effects remain poorly understood. For example, dopaminergic substrates clearly regulate PPI, but the PPI-disruptive effects of intra-HPC carbachol or NMDA are not reversed by D2 receptor antagonists. This study examined the anatomical specificity within the HPC of the PPI-disruptive effects of NMDA infusion. Startle magnitude and PPI were assessed after acute bilateral infusion of NMDA (0, 0.4 or 0.8 µg) into the dorsal subiculum (DS), the ventral subiculum (VS) or the entorhinal cortex (EC), in a within-subject design with order balanced across groups. A dose-dependent disruption of PPI was observed after NMDA infusion into the VS or EC, but not the DS. These findings demonstrate the importance of the ventral, but not the dorsal HPC, in the glutamatergic regulation of PPI. The proximity of the VS and EC preclude simple conclusions regarding the relative role of