Conclusions: The failure to show group differences at MRI scan time 1 may be because of our relatively small sample sizes or because the intrinsic group differences are hidden by the enlarging effect on the caudate nucleus with even a short period of neuroleptic exposure, and or of lithium. In future analyses, follow-up measures in this FE sample of SZ and psychotic affective subjects at MRI scan, time 2, will be of further interest to characterize more fully, over time, the effects of typical and novel neuroleptic and lithium medications on caudate nucleus volume. These effects may have functional consequences both in terms of efficacy and side effects such as EPS and tardive dyskinesia.

176. 2-HR POST-PRANDIAL GLUCOSE, LIPID, AND BODY MASS INDICES IN OLANZAPINE-TREATED SCHIZOPHRENIA PATIENTS BEFORE AND AFTER SWITCHING TO RISPERIDONE: A PROSPECTIVE TRIAL

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Background: The aim of the study was to determine the effect of switching from chronic olanzapine therapy to risperidone therapy on glucose metabolism, lipids, and body mass in schizophrenia patients.

Methods: Fasting blood glucose, insulin, total cholesterol and triglycerides, hip/waist girth and body mass index (BMI) were measured in 5 physically healthy patients (2M, 41±12.7 years old) with schizophrenia or schizoaffective disorder (15±7.3 years ill) on chronic (77±95 weeks) olanzapine therapy (20±3.2 mg/D). Patients then underwent oral glucose challenge with 75 g dextrose solution and 2-hr post-prandial glucose levels were measured. Olanzapine therapy was tapered and risperidone therapy was titrated over a week and maintained at stable doses (6.1±1.2 mg/D). Fasting blood glucose, lipid levels, body mass indices, and oral glucose challenge were repeated after patients were on stable doses of risperidone for 6 weeks. Measures (mean[SD]) on olanzapine therapy were compared with measures on risperidone therapy utilizing a paired t-test.

Results: Numerical decreases in 2-hr post-prandial glucose were found after risperidone therapy (2-hr glucose on olanzapine: 108.5 [48.1] mg/dL; on risperidone: 79.5 [19.7] mg/dL; $t=1.86$, $p<.16$). Similar decreases were observed for total cholesterol (olanzapine: 240.8 [64.3] mg/dL; risperidone: 201.0 [26.4] mg/dL; $t=2.04$, $p<.13$), LDL-cholesterol (olanzapine: 145.5 [40.5] mg/dL; risperidone: 122.0 [16.7] mg/dL; $t=1.8$, $p<.17$), and triglycerides (olanzapine: 199.8 [177.4] mg/dL; risperidone: 102.5 [76.4] mg/dL; $t=1.8$, $p<.17$). Although differences did not reach statistical significance, they were substantial and clinically significant for cholesterol and triglyceride levels in 3 of 5 patients and for response to glucose challenge in 2 of 5 patients. In contrast, hip girth increased on risperidone treatment with a trend towards statistical significance (olanzapine: 117.5 [25.0] cm; risperidone: 119.1[25.6] cm; $t= -2.60$ $p<.08$). Other measures, including fasting blood sugar, insulin levels, measures of insulin resistance, and BMI, were essentially unchanged.

Conclusions: These preliminary data suggest the possibility that a switch to risperidone therapy may improve repsonse to glucose challenge, cholesterol and triglyceride levels in olanzapine-treated schizophrenia patients, since some patients showed clinically significant improvements in these measures on risperidone. However, primarily due to the extremely small sample size, definite conclusions cannot be drawn at this time. Further data in an expanded sample of patients studied will be forthcoming.

177. STABILITY OF PREPULSE INHIBITION AND HABITUATION IN SCHIZOPHRENIA PATIENTS AND NORMAL COMPARISON SUBJECTS

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Background: Prepulse inhibition (PPI) and habituation of the human startle response are operational measures of sensorimotor gating. Numerous studies have found that schizophrenia patients exhibit deficient PPI and habituation compared to non-patients. Moreover, PPI impairments have been demonstrated in individuals within the "schizophrenia spectrum" such as schizotypal personality disordered patients and unaffected family members of schizophrenia patients, suggesting that PPI and startle habituation may be stable, trait measures for the information processing impairments observed in schizophrenia spectrum illness.

Methods: To examine the temporal stability of PPI and habituation, acutely ill schizophrenia patients and normal comparison subjects were tested at Time 1 and 14 days later at Time 2.

Results: Pearson correlations revealed that PPI was highly stable for patients ($r = .68$) and normal comparison subjects ($r = .83$), especially at the 120 millisecond interstimulus interval. This stability was also demonstrated for patients who were unmedicated at Time 1 and had been stabilized on antipsychotic medications at Time 2. A separate experiment was conducted with outpatient schizophrenia patients and revealed highly stable PPI (ICC=.65-.87) and startle habituation (ICC = .82) over three separate test sessions each one month apart, consistent with previous findings in normal subjects.

Conclusions: The results of these studies suggest that PPI and startle habituation are relatively stable over time and support the notion that PPI may be an important endophenotypic marker of sensorimotor gating disturbance.

178. CONTEXT DEPENDENT COGNITIVE FUNCTION IN SCHIZOTYPAL PERSONALITY DISORDER: A PRELIMINARY STUDY

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Background: Cognitive deficits in patients with schizotypal personality disorder (SPD) have been reported: SPD patients demonstrate impairments in working memory tasks, verbal learning tasks, attentional tasks and other tasks that involve overall executive function compared to healthy volunteers (HV). We investigated whether these impairments are consistent with deficits in context processing, in other words whether SPD patients cannot filter out 'irrelevant' information in tasks involving working memory.

Methods: 18 patients who met criteria for DSM-III-R SPD, and 19 healthy volunteers (HV) were tested on a neuropsychological battery that included the AX CPT and the N-back test developed by Cohen et al. For the CPT task, the integrity of context representation can be selectively examined through the relationship of AY to BX performance. It is predicted that intact context processing should lead to greater AY errors than BX errors, while impaired context processing should lead to relatively fewer AY errors but increased BX errors.

Results: Consistent with this model, SPD patients demonstrated significantly greater BX (17.8 +/- 26.5.) than AY (11.4 +/- 14.9) errors, while NC demonstrate greater AY (17.5 +/- 15.5) than BX errors (5.2 +/- 10.0-grp by condition interaction, $p<.02$). Moreover, SPD patients' performance was significantly impaired at the 2-back condition of the N-back test. Specifically, while both groups did not differ at the 0-back condition (HV: 97% +/- 4.3; SPD 96% +/- 4.05) at the 2-back condition SPD patients performance was significantly impaired (SPD: 82% +/- 9.8; HV: 92% +/- 5.0; group by condition interaction $p<.001$).

Conclusions: These results, which will be updated to include a larger sample and neuropsychological battery, are consistent with the hypothesis that SPD patients demonstrate impairments in working memory as they have difficulties in representing and maintaining context information as compared to normal controls.

179. OLANZAPINE IN THE TREATMENT OF SCHIZOPHRENIC PATIENTS WITH CATATONIC SIGNS AND SYMPTOMS

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Background: The term catatonia traditionally describes the manifestation of motor symptoms in psychotic diseases. The purpose of the present analysis was to investigate the efficacy of the new atypical antipsychotic compound olanzapine in a specific patient population suffering from significant catatonic signs and symptoms.

Methods: Data of 35 patients suffering from schizophrenia (DSM-IV), were collected from 7 different open-label and double-blind clinical trials, conducted in Eastern-European and some Middle-Eastern countries, according to a priori criteria of catatonic signs and symptoms. This particular patient population represents a very severe psychotic sample: mean PANSS total score ($\pm$SD) at baseline was 129.26 ($\pm$19.76). Across the different dose-scheduling trials, after 6 weeks of treatment the mean dose of olanzapine was 18.00 $\pm$2.89 mg/day.

Results: After one week of olanzapine treatment, PANSS total scores were decreased significantly (-13.14, $p<0.001$), as were scores after 6 weeks of olanzapine treatment (-45.16, $p<0.001$). A similar trend of changes was detected in the PANSS positive, negative and mood scores and in the BPRS total scores. A significant improvement in the a priori catatonic signs and symptoms composite score was also observed (-4.96, $p<0.001$).

Conclusions: The present data analysis suggests the efficacy of olanzapine in the treatment of severely ill schizophrenic patients with non-specified catatonic signs and symptoms.

180. NEONATAL HIPPOCAMPAL DAMAGE ALTERS PHYSIOLOGICAL RESPONSE PROPERTIES TO VTA STIMULATION IN THE ADULT RAT PREFRONTAL CORTEX

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Background: Neonatal ventral hippocampal lesions in rats result in a number of behavioral and neurochemical alterations resembling phenomena observed in schizophrenia. These changes are evident in adult, but not prepuberal, rats. Here we investigated the possibility of functional changes in the prefrontal cortex and mesolimbic dopamine system, which are known to be essential components in the pathophysiology of schizophrenia.

Methods: Ventral hippocampal lesions were performed at PD7-8 with bilateral injections of ibotenic acid. Control animals received a sham injection of vehicle. In vivo intracellular recordings were conducted from pyramidal neurons in the medial prefrontal cortex at either PD 28-35 (prepuberal) or PD$>$56 (adult). In addition, normal adult animals recieved similar lesions at PD$>$56 and were allowed to recover for two weeks prior to recording sessions.

Results: Prefrontal cortical pyramidal neurons of neonatally lesioned animals exhibited a bistable membrane potential similar to that observed in normal animals, with spontaneous fluctuations between a hyperpolarized down state and a depolarized up state. This was observed in both pre- and post pubescent groups. In animals lesioned as adults, up and down membrane potential states were absent. Electrical stimulation of the VTA with trains of pulses mimicking DA cell burst firing elicited a prolonged depolarization accompanied by a reduction in action potential firing. This was oberved in sham and prebubertal animals, as well as in normal animals. In the neonatally lesioned group recorded at PD$>$56, however, there was an increase in firing rate during the VTA-evoked depolarization.

Conclusions: Activation of mesocortical projections in animals with a neonatal ventral hippocampal lesion resulted in an abnormal response of PFC pyramidal neurons, characterized by increased firing. This could result in the loss of the normal modulation of synaptic responses and filtering of information that the DA innervation may have. This is the first demonstration of a functional alteration in adult animals following a neonatal hippocampal lesion. Given the control of dopamine systems by PFC afferents, it is possible that the abnormal mesocortical function reported here may in turn result in changes in subcortical dopamine, perhaps providing the substrate for the behavioral and biochemical changes seen in these animals.

181. INTACT SUCCESS-RELATED NEURAL ACTIVATION BUT DYSREGULATED UNCERTAINTY PROCESSING IN SCHIZOPHRENIA PATIENTS DURING DECISION-MAKING

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Background: Decision-making, i.e. selecting an action from a number of alternatives when the outcome is uncertain, is a complex process that is important for every day life. This study examined the effect of the degree of success and outcome uncertainty on decision-making and associated neural substrate activation in schizophrenia patients and normal comparison subjects.

Methods: Fifteen patients with the diagnosis of schizophrenia and fifteen age and education matched normal comparison subjects participated in this study. These subjects completed the two-choice prediction task during functional magnetic resonance imaging. Decision-making characteristics and activation of neural substrates was obtained at 20% error rate, 50% error rate, or 80% error rate.

Results: Success and uncertainty influenced the behavioral characteristics on the two-choice prediction task and the task-related activation in schizophrenia patients and normal comparison subjects. Behavioral characteristics during the two-choice prediction task did not reveal error-rate specific group differences, which does not support the hypothesis that either success or uncertainty results in different behavioral characteristics during decision-making in schizophrenia patients relative to normal comparison subjects. However, there was a significant interaction between group and error-rate in the premotor cortex, the dorsal anterior cingulate, and bilateral parietal cortex. In three of the four areas, the activation in normal comparison subjects was highest when the