A within subjects ANOVA for TIME and DRUG (DP and PL) revealed that there was significant improvement on DP for neuropsychological tasks of verbal fluency (p = 0.07) and attention (p = 0.03). The serial IMRI data in four subjects were spatially normalized in Talairach space (Statistical Parametric Mapping) and then analyzed as a group. At all three time points during the verbal fluency task compared to rest there was significant activation in the occipital cortex and posterior cingulate (p < 0.001, extent threshold p < 0.05 for all imaging results). These posterior brain areas were the only areas of significant activation during the PL condition. However, during the DP condition there was also activation in the right dorsolateral prefrontal cortex as well as the anterior cingulate. Thus, uniquely while on DP augmentation, the schizophrenia subjects had a more normal pattern of activation of prefrontal cortex and cingulate.

58. 5-HT2A RECEPTOR BLOCKADE BY QUETIAPINE IS RELATED TO ITS SIDE EFFECT PROFILE

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Antagonist activity at serotonergic (5-HT2A) receptors may contribute to the novel therapeutic actions of atypical antipsychotic drugs. Six schizophrenic subjects and six healthy volunteer controls had a single photon emission tomography (SPECT) study using 123I-5-I-R91150, a selective 5-HT2A ligand, after at least 6 weeks quetiapine monotherapy at a mean (SD) dose of 350 mg (123) daily. Patients had a full clinical assessment before starting quetiapine and at time of scan. A SME 810 multidetector SPECT scanner acquired a whole brain multi-slice sequence at 120 minutes after injection of 180 MBq 123I-5-I-R91150. Region-of-interest templates were fitted to cortical and cerebellar regions. The ratio of activity in cortical areas relative to the cerebellum provides a measure of regional specific binding to 5HT2a receptors. Reduced frontal cortex:cerebellum ratio implies greater specific drug binding to 5HT2a receptors within the frontal cortex. Mean frontal cortex:cerebellum ratio in the quetiapine treated patients of 0.98 (SD = 0.09) was significantly lower than in healthy controls of 1.33 (p < 0.001). All patients showed improvement in either schizophrenic symptoms or movement side effects during the study. Mean frontal cortex:cerebellum ratio after quetiapine treatment was significantly negatively correlated with reduction in AIMS score (p = 0.025 Bonferroni corrected) or Simpson-Angus rating (p = 0.04 Bonferroni corrected), but not with the reduction in SAPS score (p = 0.4), SANS (P = 0.6) or MADRS score (p = 0.25). Significant in vivo cortical 5-HT2a receptor blockade by quetiapine may be relevant to its low propensity to induce extrapyramidal symptoms compared to typical antipsychotic drugs.

59. EXPANDING USE OF ATYPICAL ANTIPSYCHOTICS

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We are witnessing a period of rapid change in the pharmacotherapy of schizophrenia, as evidenced by the replacement of conventional antipsychotics by novel antipsychotics as the drugs of choice for first episode and maintenance therapy. More recently, use of novel antipsychotics has also expanded to beyond schizophrenia with potential efficacy in agitation/aggression, suicidality, and movement disorders which are features of other nonpsychotic psychiatric and neuropsychiatric disorders. To address this burgeoning clinical interest in a manner complementary to prescription use data, we sampled the perceptions and clinical experience across general and specialist psychiatrists in 2 U.S. states. Among 284 respondents, 97% had used risperidone, 93% olanzapine, 71% quetiapine and 66% clozapine in their clinical practice. The overwhelming majority of respondents (96%) favored the use of novel antipsychotics as first-line treatments for schizophrenia. Additionally, respondents considered these drugs to be of therapeutic value in dementia (94% of respondents), autism (78%), developmental delay/mental retardation (78%), and personality disorders (75%). The most frequently cited drawbacks to the expanding clinical use and profile of novel antipsychotics were cost, weight gain and the current lack of a long-acting intramuscular preparation. These findings confirm and extend the impression gained from prescription data of an increase and broad shift in the use of novel antipsychotics.

60. CRAVING REDUCTION AND CLOZAPINE RESPONSE IN PATIENTS WITH COMORBID SUBSTANCE ABUSE AND SCHIZOPHRENIA

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Accumulating evidence suggests that clozapine is efficacious in patients with schizophrenia and comorbid substance abuse (SA), with some data suggesting this effect occurs partly by attenuating drug craving. The present study examines in a prospective cohort the comparative efficacy of clozapine (mean dose 449 mg/day) in schizophrenic patients with and without active SA who are assessed at baseline, 6 weeks and 12 weeks for psychopathology, functional outcome, craving and drug use, medication tolerability, and plasma homovanillic (HVA) acid and 5-hydroxyindoleacetic acid (5HIAA). In a comparison of 22 SA and 22 nonSA patients who completed the 12-week trial, the SA patients were of older age at onset (25.1 yrs vs. 20.2 yrs; p = 0.029) but did not differ otherwise on baseline demographic, symptomatic or functional measures. At 12 weeks, mean PANS scores had declined comparably between SA (103.6—92.0) and nonSA (108.0—91.4) groups; similar patterns of response were evident for theQLS and GAF. Notably, 77% of SA patients were either not abusing or had diminished SA. These preliminary findings confirm clinical experience that many patients who commit to
clozapine therapy can achieve good outcome both with respect to treatment of psychosis and amelioration of SA. This presentation will focus on the relationships between craving (measured on the Minnesota Craving Scale), psychopathology, changes in HVA/SHHIAA, and treatment response to clozapine in SA patients.

61. EXTRACRANIAL SIZE IN PATIENTS WITH SCHIZOPHRENIA

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Much of the current literature from both neuroimaging and post mortem studies points to a reduction in intracranial size and cerebrum in schizophrenia. Intriguingly, there is also evidence for reduced extracranial size in infants at high risk for schizophrenia, while studies in adults with schizophrenia which have assessed head size have been inconclusive. Using head measures of circumference, length and width derived from caliper examination in both coronal and sagittal planes, we examined head size in 46 male controls (mean age 42 ± 9 years; 20 Caucasian, 26 African American) and 44 patients (mean age 40 ± 9 years; 18 Caucasian, 26 African American) with DSM-IV schizophrenia. In a linear regression model which entered race and diagnosis as independent factors and stature and elbow breadth as covariates, we found no evidence for reduced extracranial size in schizophrenia. These data suggest that the process(es) which underlie smaller brains in schizophrenia do not produce a corresponding reduction in head size.

62. LOW LEVELS OF ANTIBODIES TO CARDIOLIPIN IN FIRST EPISODE AND CHRONIC SCHIZOPHRENIA

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The objective of this study was to measure anticardiolipin antibodies (aCL) in major psychiatric diseases. In experiment 1, 96 subjects were evaluated: 20 first episode schizophrenic patients, [SCZ1] 20 chronic schizophrenia patients in acute exacerbation [SCZ2], 19 bipolar patients, 20 schizoaffective patients and 17 healthy age matched controls. In experiment 2 there were 97 subjects: 20 first episode schizophrenia patients [SCZ1], 60 chronic schizophrenia patients in acute exacerbation [SCZ2] and 17 healthy age matched controls. Diagnosis was according to DSM-IV guidelines. Serum samples were tested for aCL in parallel by enzyme linked immunosorbant assay in the presence of bovine serum. 6 positive control samples with high levels of aCL were run in parallel. Background binding to wells uncoated with cardiolipin (CL) was also measured.

In experiment 1, aCL levels were similar in the control, bipolar and schizoaffective groups. In contrast, aCL levels in the SCZ1 and SCZ2 groups were significantly lower than controls (p = 0.000002 and 0.00002 respectively).

Experiment 2 supported these results (p = 0.00002 for all schizophrenic patients versus controls). Interestingly, background levels in both experiments were higher in the schizophrenic groups than controls. Serum aCL levels are lower in schizophrenic patients, and especially in first episode cases, compared to controls. One possible explanation for the lower levels of aCL in schizophrenic patients is the consumption of these antibodies in an active phase of the disease. The higher background levels in these groups may indicate a high level of antibodies to some serum component in schizophrenic patients.

63. CYTOKINE PRODUCTION IN SCHIZOPHRENIC PATIENTS: DIFFERENTIAL EFFECT OF NEUROLEPTIC MEDICATIONS

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Patients with schizophrenia possess different immunological aberrations but their significance is not clear. In the present study the authors analyzed the production of cytokines in serum of 33 schizophrenic patients, before and after neuroleptic treatment, and 21 age and sex matched healthy controls. IL-1 receptor antagonist (IL-1ra), and IL-2 soluble receptor antagonist (IL-2sR) levels were evaluated by a sandwich enzyme immunoassay. No significant differences were found in serum levels of IL-1ra between schizophrenic patients and controls, but it was highly increased in schizophrenic patients after neuroleptic treatment (p < 0.017). Significant increased levels of IL-2sR was found in schizophrenic patients before and after treatment as compared to healthy controls (p < 0.02, p < 0.004, respectively). The present study supports evidence for immune activation in some schizophrenic patients and neuroleptic medications differently affect the production of various cytokines.

64. CORRELATIONS BETWEEN FOUR COMPONENTS OF SENSORY GATING

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Sensory gating refers to the brain’s ability to modulate its sensitivity to incoming sensory stimuli. This definition allows the concept of gating to include the capacity to inhibit irrelevant stimuli (gating out) and to dishabituate when novel stimuli are presented (gating in). Whether these measures reflect the same or different sensory gating components is not known. A high degree of correlation between these measures would indicate that they are reflecting the same process. Four components of sensory gating were examined in 36 normal volunteers: habituation (attenuation or gating out) and dishabituation (enhancement or gating in) of the P50 (early or preattentive gating) and of the N100 (late or early-attentive gating) EP amplitudes. Two conditions of the paired-click paradigm (S1 & S2) were used: identical pairs (gating out) and non-identical pairs (gating in). The P300 was recorded utilizing an odd-ball paradigm. All gating measures were calculated as the S2/S1 ratios. Pearson Correlations were: early in vs. early out = -.356, late in vs. late