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/SHIAA, and treatment response to clozapine in SA patients.

61. EXTRACRANIAL SIZE IN PATIENTS WITH SCHIZOPHRENIA

P.F. Buckley, L. Friedman, J.A. Jesberger, G.E. Jaskiw, S.C. Schulz

Department of Psychiatry, Case Western Reserve University, Cleveland, OH 44106

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

P. Sirota (1), I. Bogdanov (1), A. Katzav (2), R. Hershko (1), J. Chapman (2)

(1) Abarbanel Mental Health Center, Bat Yam and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; (2) Departments of Physiology & Pharmacology and Neurology, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

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 schizophrenic 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 = 0.0002 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

P. Sirota, M. Meiman, B. Epstein, I. Bogdanov, R. Hershko, R. Benatov

Abarbanel Mental Health Center, Bat Yam, and Sackler Faculty of Medicine, Tel Aviv, Israel

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

N.N. Boutros (1), D. Campbell (1), M. Torello (2)

(1) Yale University School of Medicine, (2) Capiital University, Columbus Ohio

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...
out \(=-0.90\), early in vs. late out \(=-0.061\), early out vs. late in = .195. The early gating in measure positively correlated with the amplitude of the P300 \((r = .806, p \text{ (two tailed)} < .02\). These data suggest that the four components of sensory gating may be reflecting different neural sensory processes and also suggest a possible influence of the early capacity to identify deviant input on amplitude of the P300.

### 65. 31P NMR OF PHOSPHOLIPIDS IN POSTMORTEM SCHIZOPHRENIC BRAINS

R.A. Komoroski (1,2), J.M. Pearce (1,2), W.S.T. Griffin (1), R.E. Mrak (1,2), C.N. Karson (1,2), M. Omori (3)

(1) University of Arkansas for Medical Sciences, Little Rock, AR 72205 USA; (2) Central Arkansas Veterans Healthcare System, Little Rock, AR 72205 USA; (3) Fukui Medical School, Matsuoka, Fukui 910-11, Japan

It has been hypothesized that schizophrenia arises from cell membrane abnormalities due to changes in phospholipid (PL) composition. Studies on erythrocytes and platelets suggest that alterations in membrane PL composition play a role in schizophrenia. It is essential to measure PL composition in the brain itself, which typically is only possible postmortem. In vivo \(^{31}\)P NMR of PL precursors and degradation products suggested changes in PL metabolism in the brain in schizophrenia, but solid-like PLs are not visible in typical in vivo NMR studies. Tissue PLs can be characterized according to headgroup and acyl-side-chain unsaturation using in vitro \(^{31}\)P NMR. Postmortem brain tissue (grey matter) was obtained from left frontal cortex of 5 schizophrenics and 5 controls. High resolution \(^{31}\)P NMR spectra were obtained at 121.65 MHz. Phosphatidyl ethanolamine (PE) was significantly higher in the schizophrenic group relative to controls \((p < 0.045)\). There were no differences between the two groups for other PL headgroups. The intensity of the PC peak representing molecular species with one saturated and one unsaturated acyl chain was higher in the schizophrenic group \((p < 0.043)\). These results support the notion that PL abnormalities occur in the brain in schizophrenia, and that fatty acid metabolism may be abnormal. These observations have the advantage that they pertain to brain itself, and not peripheral tissue. However, the possible confounding effects of antipsychotic medication and perinormal factors must be considered.

### 66. NEUROPSYCHOLOGICAL FUNCTION DURING SMOKING CESSATION IN SCHIZOPHRENIA


Division of Substance Abuse, Department of Psychiatry, Yale University School of Medicine and The Connecticut Mental Health Center, 34 Park St., New Haven, CT 06519

Schizophrenic patients have high co-morbid rates of nicotine dependence (58–88%) and well-characterized deficits in neuropsychological function. In particular, there is evidence that schizophrenic patients have abnormalities in executive function, response inhibition, visuospatial working memory, and attention and concentration. Cigarette smoking by schizophrenics may reduce negative symptoms and neurocognitive deficits and reduce cigarette smoking in schizophrenics. Thus, evaluation of neuropsychological function in cigarette smokers during a smoking cessation trial may yield important information on the effects of cigarette smoking and tobacco withdrawal on neuropsychological function in these patients.

Given the role of catecholamine mechanisms in nicotine dependence, the present study evaluated the effects of two catecholaminergic agents, Bupropion SR [a DA and norepinephrine (NE) reuptake inhibitor] and Selegiline [a monoamine oxidase B inhibitor which preferentially augments DA and NE function], on neuropsychological function in schizophrenic (Bupropion SR) and control smokers (Selegeline) participating in placebo-controlled smoking cessation pharmacotherapy studies. We have developed a computerized neuropsychological battery which includes the Wisconsin Card Sorting Test (executive function), Stroop Test (response inhibition), Continuous Performance Test (attention and concentration), visuospatial working memory and Serial Reaction Time (procedural memory). Schizophrenic subjects are known to have performance deficits on these tasks. Preliminary results indicate discrete baseline deficits in neuropsychological function (i.e. VSTM, Stroop Test) in schizophrenic vs. control smokers, and these changes in neuropsychological function are dependent on smoking status during the trial (i.e. abstinence vs. continued smoking) and study medication. Results from the complete sample of \(n = 30\) schizophrenic and \(n = 30\) healthy control smokers will be presented at the meeting.

This work was supported by the Department of Veterans Affairs VISN 1 MIRECC, a NARSAD Young Investigator Award (to T.P.G.) and USPHS grants K12-DA-00167, P50-DA-04060, P50-DA-84733 and P50-DA-09250.

### 67. NEUROPROTECTIVE ACTIONS OF OLANZAPINE IN RAT: CHOLINERGIC FUNCTION

S.P. Mahadik (1,5), A. Terry (2), W.D. Hill (3), D.R. Evans (1,4,5), J.L. Rausch (1,5)

Departments of (1) Psychiatry & (3) Anatomy, Medical College of Georgia; (4) Mental Health & (5) Research Services, VAMC, Augusta, and (2) School of Pharmacy, Univ. of Georgia, Athens, GA

Olanzapine (OLZ) treatment does not seem to induce extrapyramidal side-effects (EPS, i.e., drug-induced parkinsonism) similar to the haloperidol (HAL) treatment of psychotic patients. These EPS are indicative of the later development of serious abnormal involuntary movements, Tardive Dyskinesias (TD). In addition, olanzapine treatment seems to very significantly improve cognitive performance and decrease negative symptoms, particularly in patients previously treated with haloperidol. Haloperidol treatment in rats has been found to affect the brain, particularly the cholinergic system, and behavior. Therefore, the possible neuroprotective actions of OLZ against the haloperidol effects were studied in rats.

Three groups of rats (CON, HAL, OLZ) were treated for 45 days and 90 days. After 45 days of treatment, one third \((N = 15)\) of the rats in each of the HAL and OLZ groups were switched to OLZ and HAL, respectively, in order to determine the protective/restorative actions of OLZ against HAL effects. Cognitive performance was determined using Morris Water Maze, and then the alterations in CNS cholinergic system were determined by immunohistochemical method using antibody to choline acetyl transferase (anti-ChAT). The forty five days of treatment with either HAL or OLZ did not affect the cognitive performance. However, 90 days of HAL but not OLZ treatment significantly impaired cognitive performance and also reduced the swim speed. Furthermore, both 45 as well as 90 days of HAL treatment altered the cholinergic system: reduced number of ChAT reactive neurons, processes, varicosities and synapses indicating that the structural changes precede the behavioral effects. However, both 45 or 90 days of OLZ treatment did not...