The early gating in measure positively correlated with the amplitude of the P300 (r = .806, p (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 31P 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 vivo 31P NMR. Postmortem brain tissue (gray matter) was obtained from left frontal cortex of 5 schizophrenics and 5 controls. High resolution 31P NMR spectra were obtained at 121.65 MHz. Phosphatidylinositol (PI) was significantly 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 perinortem 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 neurophysiological 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 cognitive deficits through amelioration of prefrontal cortical dopaminergic (DA) hypofunction. There is evidence from our group and others that atypical antipsychotic agents, which augment cortical DA function, may ameliorate negative symptoms and neurocognitive deficits and reduce cigarette smoking in schizophrenics. Thus, evaluation of neuropsychological function in smoking abstinence 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 antagonizes DA and NE function], on neuropsychological function in schizophrenic (Bupropion SR) and control smokers (Selegiline) 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. VWM, 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.

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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