

of prefrontal dysfunction in schizophrenia with experimental paradigms that are thought to be sensitive to different prefrontal brain systems. We utilized neuropsychological tests that have been associated primarily with orbital (ventral) frontal and dorsolateral prefrontal system dysfunctions in nonhuman primates and human neurological patients. We also examined the association of these tests with reality distortion (positive), negative, and disorganization symptoms. We hypothesized that deficits on the Wisconsin Card Sorting Test (WCST), a putative probe of dorsolateral function, would be associated with negative symptoms, and that deficits on Object Alternation (OA), a putative orbital frontal probe, would be associated with disorganization symptoms. Participants were 15 schizophrenic outpatients and 18 normal controls. Patients performed significantly worse than controls on the WCST, OA, and Delayed Alternation, but not on classical Delayed Response. Among patients, the University of Pennsylvania Smell Identification Test (UPSIT), another orbital frontal probe, had a stronger inverse correlation with OA errors than with WCST errors. Bizarre behavior on the SAPS was significantly correlated with OA errors and with UPSIT performance, but was uncorrelated with WCST perseverations. These results partially replicated previous results by our group (Seidman et al 1995). Although far more attention has been given to dorsolateral prefrontal dysfunction in schizophrenia, the correlations of OA with the UPSIT and with bizarre behavior provide some convergent validity for the notion that orbital frontal dysfunction is also important in schizophrenia.

272. CHRONICITY AND NEUROPSYCHOLOGICAL DYSFUNCTION IN SCHIZOPHRENIA

I.C. Smet, R. Tandon, R.S. Goldman, L. Decker, G. Lelli, & S. Berent

Schizophrenia and Neuropsychology Programs, University of Michigan, Ann Arbor, MI 48109-0116

Much controversy exists as to whether or not schizophrenia is associated with progressive cognitive dysfunction over the course of the illness; we conducted a cross-sectional study to assess this question. We administered an extensive neuropsychological battery to 50 DSM-III-R schizophrenic inpatients shortly before discharge. The patients placed in one of three groups based on duration of illness: Group 1 - < 1 year (n=13); Group 2 - 1 to 10 years (n=16), and Group 3 - > 10 years (n=21). As expected, a significant difference in age was found between groups (mean age: Group 1 = 32.9 yrs., Group 2 = 32.8 yrs., Group 3 = 43.7 yrs.). There were no group differences in education level or clinical symptomatology as measured by the BPRS and SANS. The neuropsychological battery consisted of a comprehensive assessment of attention, memory, intellect, executive functioning, motor functioning, and perceptual abilities. Individual task performance was standardized using a normative reference group which adjusted for age, gender, and education. The findings revealed that patients with longer lengths of illness demonstrated significantly more impairment on measures of visuospatial memory (p=0.006) and executive functioning including Trailmaking, Part B (p=0.008) and number of errors on the Wisconsin Card Sorting Test (p=0.05). No other differences were observed between groups. These data suggest that chronicity of schizophrenic illness may be associated with deterioration of some aspects of neuropsychological functioning, although many neuropsychological deficits in schizophrenia may not progress through the course of the illness.

273. NEUROPSYCHOLOGICAL CORRELATES OF PREFRONTAL VOLUME IN SCHIZOPHRENIA

T. Lencz¹, R.M. Bilder¹, B. Bogerts², M. Ashtari³, H. Wu¹, J. M. Alvir¹, J. Schenkler¹, & J.A. Lieberman¹

¹Hillside Hospital Division of Long Island Jewish Medical Center, Glen Oaks, NY 11004; ²University of Magdeburg, Magdeburg, Germany; ³Long Island Jewish Medical Center, Glen Oaks, NY 11004

Abnormalities of the prefrontal cortex have been hypothesized to play a major role in the neurocognitive dysfunction of schizophrenia, particularly in deficits of attention, executive function, and working memory. The present study examined the relationship between magnetic resonance imaging (MRI) measures of prefrontal volume and measures of neuropsychological (NP) performance in a sample of 52 patients (M/F=31/21) in the first episode of schizophrenia. MR images were acquired on a 1.0 Tesla magnet using a 3D "FLASH" sequence yielding 3.1 mm contiguous coronal slices (in-plane resolution = 1mm x 1mm). Prefrontal volume included all gray and white matter anterior to the genu of the corpus callosum. Total cortical gray and white matter volume, excluding subcortical and ventricular spaces, was also measured. Regression analysis was used to obtain a standardized residual measure of prefrontal volume controlling for total cortical volume. An extensive NP battery was administered after clinical stabilization; composite scales were constructed for the following NP domains: language, memory, attention, executive, motor, and visuospatial functioning. The prefrontal residual measure was significantly correlated with the memory (r=.45, p<.01) and the attention (r=.27, p=.05) indices; correlations with the other NP indices were nonsignificant. The correlation between the prefrontal measure and the memory index remained significant after partialling attention (r=.36, p < .01). Residualized temporal lobe and premotor frontal lobe volumes were not significantly correlated with the attention or memory indices. Results support a relationship between prefrontal structure and attentional and memory function in schizophrenia.

274. MECHANISMS OF SELECTIVE ATTENTION IN SCHIZOPHRENIA

D.M. Barch, C.S. Carter, & P.C. Hachten

Clinical Cognitive Neuroscience Laboratory, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical School, Pittsburgh, PA 15213

Studies of selective attention in schizophrenia suggest a particular pattern of abnormal Stroop task performance among schizophrenia patients: increased facilitation as opposed to interference. Recent research suggests that this pattern reflects disturbances in higher level processes that control the allocation of attention to the processing of relevant, versus irrelevant, information present in a stimulus. However, it is not yet clear whether this disturbance impacts early, late, or multiple stages of information processing. If increased facilitation among schizophrenia patients reflects selective attention deficits only at later stages, such as response selection, then schizophrenia patients should display increased facilitation only when the neutral stimulus contains information that could compete for response production (e.g., a word). Alternatively, if disturbances in selective attention occur during earlier stages - instead of

or in addition to - later stages, increased facilitation should be present even with non-word neutral stimuli. To address these questions, we examined Stroop performance in DSM-IV schizophrenia patients and normal controls, using a range of neutral stimuli (color squares, non-color words, color words not in the response set). The findings suggest that disturbances in selective attention among schizophrenia patients operate at multiple stages during information processing.

275. DISTURBANCES OF AUDITORY LOCALIZATION AND TRAJECTORY DISCRIMINATION IN SCHIZOPHRENIA

R.W. Greene, B.F. O'Donnell, Y.A. Allaban, K.C. Stylianopoulos, & J.E. Allard

Department of Psychiatry, Brockton VAMC, Brockton MA 02401 and Harvard Medical School, Boston, MA

Evidence from single unit recording suggest that analysis of the position and trajectory of sounds in the environment by primates is mediated by neurons in the posterior superior temporal gyrus (STG). Gray matter of the posterior STG is reduced in schizophrenia, suggesting that patients might show disturbances in these types of auditory processing. We tested 14 male patients with schizophrenia and 12 control subjects on tests of sound localization, in which binaurally presented tones were louder on either the right or left side of the head, and trajectory determination, in which tones were perceived to move from one side to the other. All subjects were normal on audiometric evaluation. Patients with schizophrenia were less accurate than control subjects on both tests ($p < 0.01$, group main effect on ANOVA). In addition, there was a group X side interaction indicating that patients were worse for targets on the left side ($p = 0.02$), and a group X side X condition interaction ($p = 0.05$) indicating that this deficit was most severe for trajectories which terminated on the left side of the head. These findings suggest that patients with schizophrenia show deficits in tone localization, particularly for perception of trajectories moving from the right to the left side of auditory space, implicating neural circuits within posterior STG.

276. COMPUTER MODELING OF ADAPTIVE DEPRESSION AND ASYMMETRIC HEMISPHERIC PROCESSING

C. Webster

Duquesne University, School of Health Sciences, Pittsburgh, PA 15282

The DEP2 (Depression Emulation Program, version 2) computer model simulates vulnerability to depression and generation of resulting symptoms, while constrained by popularized hypotheses about asymmetrically distributed left and right hemispheric information processing (such as sequential-logical-analytical versus simultaneous-emotional-analogical dichotomies). Implemented with neural network, artificial intelligence, and control theoretic techniques, DEP2 extends a theory of adaptive depression (Webster, 1995) that provides a unified information processing account of ten depression symptoms and phenomena. DEP2's left hemispheric module relies on "locally" coded representations to generate slow sequential solutions to environmental problems, but becomes quick

with practice. DEP2's right hemisphere relies on "coarse" coded representations, operating in parallel to detect failure and retrieve similar material. In DEP2's undepressed state, both hemispheric modules work together to exploit environmental opportunities; in its depressed state, DEP2 withdraws from its environment while its right hemisphere retrieves similar failures for presentation to left hemisphere sequential problem solving so as to avoid future failure. DEP2 models a normal and adaptive depression that probably evolved due to advantages of withdrawal from noxious stimuli, followed by continued stimuli representation, processing, and elaboration. If clinical depression involves failed adaptation to environmental stress, then a model of successful adaptation, such as DEP2, might also be "broken" to suggest hypotheses relevant to abnormal and maladaptive clinical depression. Webster, C. (1995) Computer modeling of adaptive depression. *Behavioral Science*, 40, 314-330.

277. COGNITIVE IMPAIRMENT IN EUTHYMIC PATIENTS WITH BIPOLAR AFFECTIVE DISORDER

W.G. van Gorp^{1,2}, L.L. Altshuler^{1,2}, W. Dixon², & D.C. Theberge¹

¹V.A. Medical Center, West Los Angeles, CA 90073; ²University of California Medical Center, Los Angeles, CA

Although several studies suggest that individuals with bipolar disorder-I (BPI) have cognitive deficits, all but two subjects who were examined were acutely depressed or psychotic. This study sought to determine whether neuropsychological impairment was present in euthymic individuals with BPI independent of past alcohol abuse. Twenty four subjects with BPI, 11 of whom also had a prior history of alcohol abuse (none with use in the past 6 months), and 22 normal controls were studied. Subjects were administered a comprehensive battery of neuropsychological tests. Analysis of variance (ANOVA) revealed no differences across groups on age, education or estimated IQ. ANOVA revealed a significant main effect only for the California Verbal Learning Test (CVLT) and Wisconsin Card Sorting Test (WCST). For the CVLT, the BPI and BPI + alcohol groups performed significantly worse than controls. For the WCST, only the BPI + alcohol group achieved significantly fewer categories than the BPI or the control subjects. These results document lowered performance on measures of declarative learning and memory for subjects with BPI with and without alcohol abuse, suggesting a deficit in verbal learning and memory that cannot be explained solely by a history of prior alcohol abuse. The lowered performance by the subjects with BPI on the WCST can be attributed to alcohol abuse rather than BPI. The neuroanatomic substrate for these cognitive deficits remains unclear. Discussion will focus upon the neuroanatomic underpinnings for these findings as well as the role of medication in contributing to these results.

278. CLINICAL AND NEUROPSYCHOLOGICAL DEFICITS IN BIPOLAR AND SCHIZOPHRENIC PATIENTS

A. Smith, D. McKay, D. Schnur, S. Smith, M. Obuchowski, G. Osgood, & B. Cornblatt

Mt. Sinai School of Medicine, New York, NY 10029

The traditional assumption that bipolar disorder is less severe than schizophrenia has been increasingly challenged in the recent literature.