School, Pittsburgh, PA; 3Vermont State Hospital, Waterbury, VT; 4Highland Drive VA Medical Center, Pittsburgh, PA

We examined lexical priming in 75 medicated and 25 unmedicated DSM-III-R schizophrenics, 10 depressed controls, and 28 normal controls. Our sample population and experimental design were chosen to address mediation and methodological issues related to lexical priming and the assessment of automatic components of processing in schizophrenia. Word naming was used instead of lexical decision to provide more precise measures of automatic processing, given the status of this construct in previous theorizing about schizophrenic language deficits. We used five SOAs to systematically examine the time course of priming among schizophrenics. Our results indicated that at shorter SOAs (200, 300 msec), medicated schizophrenics displayed enhanced priming compared to other groups, while priming among unmedicated schizophrenics was similar to normal and depressed controls. At longer SOAs (700, 950 msec) unmedicated schizophrenics did not display significant priming effects, while normal and depressed controls did. Medication dosage in chlorpromazine equivalents was positively correlated with priming at all SOAs other than 950 msec. These results suggest that previous reports of enhanced priming in samples of medicated schizophrenic subjects may have been influenced by the effects of antipsychotic medications. The normal priming displayed by unmedicated schizophrenics at the shorter SOAs suggests that automatic components of priming operate normally in unmedicated schizophrenics. In conjunction with the lack of significant priming effects at the longer SOAs among unmedicated schizophrenics, these results suggest that it may be more relevant to focus on disturbances in strategic or higher-level components of language processing in schizophrenia.

143. HYPOFRONTALITY AND WORKING MEMORY DYSFUNCTION IN SCHIZOPHRENIA

J.D. Cohen1, R. Ganguli2, C. Carter1, J. Brur2, T. Nichols3, M. DeLeo2, & M. Mintun2,3
1Clinical Cognitive Neuroscience Laboratory, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical School; 2Department of Psychiatry, University of Pittsburgh Medical School; 3Department of Radiology, University of Pittsburgh Medical School, Pittsburgh, PA 15213

Hypofrontality, indexed by reduced glucose metabolic rate or blood flow, is a common though not uniform finding in studies of schizophrenia. We studied patients with schizophrenia and matched normal controls using a procedure designed specifically to tap working memory, a function commonly attributed to the prefrontal cortex. Regional cerebral bloodflow (rCBF) was measured during performance of a nonspatial memory task, and compared to rCBF during a simple target detection task, which controlled for non-memory-related factors involved in performance. In normal subjects this procedure produces a reliable increase in rCBF in the dorsolateral prefrontal cortex bilaterally. Despite the fact that patients showed significant impairment on performance in the memory task (but not the control task), they did not show decreased prefrontal rCBF response. In fact, patients showed a tendency toward increased prefrontal rCBF; however, patients did fail to activate the right inferior temporal cortex and the precuneus, as compared to controls. Since the blood flow changes observed during cognitive activation studies are typically associated with presynaptic metabolic activity, our results may still be consistent with prefrontal dysfunction in schizophrenia. The activation observed in PFC may be due to intact afferents to this area, while PFC units themselves may fail to respond. This, in turn, could account for the failures of activation observed in other regions, such as inferior temporal cortex. If such an interpretation is correct, these results have significant implications for neuropathological hypotheses based upon changes in rCBF observed in functional brain imaging studies.

144. MODELING MEMORY-GUIDED TASKS IN SCHIZOPHRENIA

S.D. Forman1,2 & J.D. Cohen2,3
1Highland Drive VA Medical Center, Pittsburgh, PA 15206; 2Clinical Cognitive Neuroscience Laboratory, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical School, Pittsburgh, PA 15213; 3Department of Psychology, Carnegie Mellon University, Pittsburgh PA 15213

We have used the asymmetric diffusion learning algorithm to model visually and memory-guided saccadic eye movements. A growing body of evidence from primate experiments indicates a role for frontal cortex in the maintenance of memory representations needed to support delayed responses. The system is clinically interesting because schizophrenic patients show deficits in memory-guided but not in visually guided eye movements. Specific neural modeling achievements include single- and multiple-hidden layer models of the oculomotor delayed-response and antisaccade task. These models produce qualitatively similar behavior to primate experiments, under both control conditions and putative catecholaminergic manipulations in the prefrontal cortex. In addition this modeling space has led to a new understanding of how certain representations could be developed and sustained in the prefrontal cortex. The key result is the manner by which memory representations are chosen and maintained as the result of sequential input through circuits. Unlike earlier models requiring specific recurrent circuitry to create a population of "memory cells," in this model maintenance of memory representations is an emergent property from an interaction between the circuit architecture and the input dynamics.

145. VALIDITY STUDIES IN FUNCTIONAL MAGNETIC RESONANCE IMAGING: APPLICATION TO SCHIZOPHRENIA

S.D. Forman1,2, J.D. Cohen2,3, D.P. van Kammen1, T.S. Braver3, R.J. Orr3, & J. Gurklis1
1Highland Drive VA Medical Center, Pittsburgh, PA 15206; 2Clinical Cognitive Neuroscience Laboratory, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical School, Pittsburgh, PA 15213; 3Department of Psychology, Carnegie Mellon University, Pittsburgh, PA 15213

Functional magnetic resonance imaging (fMRI) is a new technique for investigating cognitive function. Before fulfilling its promise for longitudinal, noninvasive investigation in individual normal and schizophrenic subjects, several methodological questions must be addressed. How does one avoid false-positive results in the face of thousands of multiple comparisons, while still maintaining adequate power to detect small, task-related changes? Does activation remain stable over time? How does the pattern of brain activation seen in fMRI compare to that seen with other methods, such as PET? First, we present a method for identifying significant areas of neural activity, which improves power by 3-4-fold over standard approaches used in functional imaging without sacrificing false-positive protection. This is accomplished by using the size as well as the intensity of a putative activated region to distinguish true signal from noise. Second, we tested longitudinal reliability of fMRI activation maps using a series of test-retest studies of frontal cortical activation in normal subjects performing a working memory task. We found a voxel-wise correlation between studies ≥ 0.6 (n = 3 subjects; ~10,000 voxels/subject). We also present one subject, studied in the same task in both PET and