111. FRONTAL CORTEX DYSFUNCTION AND SUBCORTICAL DOPAMINERGIC ACTIVITY IN SCHIZOPHRENIA SPECTRUM


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2-Deoxyglucose (2-DG) is an analog of glucose and inhibits intracellular glucose metabolism. By reducing cortical (including frontal) metabolic activity, 2-DG induces a physiologic stress which activates subcortical dopaminergic activity. Plasma homovanillic acid (pHVA) has been used as a marker of dopaminergic responsiveness to 2-DG and has been shown to be increased in response to 2-DG in schizophrenic patients compared to normal controls. We have pilot data on eleven schizotypal personality disorder (SPD) patients and six normal control subjects participating on this double-blind, placebo controlled paradigm of 40 mg/kg of 2-DG/placebo administered as a bolus infusion over 10 min. Two blood samples were drawn prior (baseline) and then at 15 min intervals starting at +15 min and ending at +135 min after infusion. Peak pHVA concentrations were defined as the highest value post infusion. The pHVA response was calculated as peak-baseline for active and placebo days. Preliminary analyses on four SPD patients and four normal controls include the following: the pHVA response on the drug day was 1.08 ± 0.9 for controls and 0.59 ± 0.8 for the SPD patients. For comparison purposes, on a similar paradigm at the NIMH, the pHVA response after 2-DG in schizophrenic patients is 2.6 ± 1.8. These data provide preliminary support for our hypothesis that SPD patients demonstrate reduced subcortical dopaminergic activation compared to normal controls following glucoprivation in contrast to schizophrenic patients who demonstrate increased responses. Analyses of the full data set will be presented.

112. TEMPORAL LOBE VOLUME IN SCHIZOTYPAL PERSONALITY DISORDER AND SCHIZOPHRENIA

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The volumes of the whole temporal lobe, the superior temporal gyrus and the corpus callosum were measured on MRI images from 27 patients with schizophrenia, 13 patients with schizotypal personality disorder (SPD) and 31 sex- and age-matched controls. The temporal lobe and superior temporal gyrus were traced on consecutive 1.2 mm thick SPGR coronal images from the anteriormost appearance of an uninterrupted temporal stem on each side to the posteriormost appearance of fibers in the crus of the fornix. From these consecutive slices, total and volumes relative to the whole brain were determined. Patients with SPD and schizophrenia had smaller temporal lobe gray matter primarily in the area outside the superior temporal gyrus. Correction for brain size diminished normal/schizophrenia differences but the normal/schizotypal differences remained, suggesting greater regional specificity for temporal lobe volume loss in schizotypal than schizophrenic patients. Higher scores on the Brief Psychiatric Rating scale and lower scores on verbal memory tasks were associated with temporal volume loss in patients with schizophrenia but not those with SPD. Temporal lobe gray/white volume correlations were positive in controls, non-significant in schizophrenic patients but negative in SPD patients. Both normal individuals and SPD patients showed significant correlations between the area of the posterior portion of the corpus callosum (which carries temporal interhemispheric connections) and the white matter volume of the temporal lobe.

These findings suggest that in schizophrenia, cognitive and psychotic symptoms may be related to combined temporal lobe gray and white matter decrease compared to controls, but that in SPD the symptoms are related to gray matter decrease with relatively intact white matter. This further suggests that in schizophrenia spectrum disorders, that enhanced connectivity may be a mechanism for the enhanced functioning in schizotypal patients compared to patients with schizophrenia.

113. COGNITIVE DEFICITS AND THE SCHIZOPHRENIA SPECTRUM

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Cognitive processing deficits have been identified as a core abnormality that SPD individuals share with schizophrenic patients. It has been hypothesized that impaired verbal learning and working memory may be a critical component of several of the more complex cognitive deficits found in schizophrenia-spectrum patients. The schizophrenia spectrum comprises a continuum from the chronically psychotic schizophrenic patients on one end to the patient who may meet one or two schizotypal criteria on the other. In DSM-III, patients were classified as meeting SPD if they met 4 out of 8 criteria compared to DSM-III-R where they meet 5 out of 9 criteria. The inclusion of an additional criterion for DSM-III-R was not made based on empirical data (Siever, Task Force for DSM-III-R). Cognitive impairment on DSM-III (Trestman et al, 1995) as well as DSM-III-R SPD patients (Bergman et al, 1996; Roitman et al. in press) have been reported. We were interested in exploring whether there is a threshold of clinical symptoms at which cognitive impairment is more likely to occur. 68 patients meeting criteria for one or more DSM-III-R personality disorders and 17 normal volunteers (NV) were tested on the California Verbal Learning Test (CVLT) where the total number of words recalled in trials 1 through 5 was the outcome measure. They were also presented with a pen and paper visuospatial working memory task (DOT test) consisting of 14 presentations of different dots (Keele et al, 1996). Distance error (in cm) is the average difference between the location where each stimulus was presented and the location where it was recalled to have been after a 30 sec delay. Patients who met two or less SPD symptoms (n = 28) performed similar to NV subjects (n = 17) recalling an average of 54.7 ± 7.1 words and having a distance error of 2.3 ± 2. cm compared to NV who recalled 58.5 ± 6.7 words and had a distance error of 1.6 ± 0.8 cm (both t-tests t < 12, p = ns). Patients who met 4 SPD symptoms (n = 8) performed similar on the cognitive tasks to those who met 5 or more SPD symptoms (n = 32) recalling 44.0 ± 12.3 words and having a distance error of 3.7 ± 3.0 compared to 46.6 ± 11.3 words and a distance error of 2.5 ± 1.8 cm for those with 5 SPD symptoms (both t-tests t < 1.1, p = ns). Hence, patients who met 4 or more SPD symptoms could be identified as schizophrenia spectrum and their performance was compared to NV performance. Indeed, spectrum patients performed significantly worse than NV recalling 46.1 ± 11.4 words (n = 40; t = 4.1, p = .001) and having greater distance error (2.7 ± 2.2 cm – t = 2.1, p < .05). These data support a threshold of 4 rather than 5 criteria of 9 for SPD. These results suggest that cognitive impairment lies in a continuum and that patients who meet 4 SPD traits share cognitive deficits similar to those who meet criteria for the full SPD diagnosis (5/9).