THE STUDY OF SCHIZOPHRENIA VIA IN VIVO ^{31}P AND ^{1}H MRS

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Magnetic Resonance Spectroscopy (MRS) provides direct, non-invasive, localized access to cerebral metabolites. Consequently, MRS is ideal to investigate the "glutamatergic hypothesis" of schizophrenia. ^{31}P MR spectra from the left dorsal prefrontal cortex were acquired with a surface coil on a 2T Siemens whole body spectrometer on 9 never treated (NT) schizophrenic patients (2 have yet to meet the full DSM-III-R criteria) and on 10 appropriately matched controls. In addition, ^{1}H MR spectra from a volume element of 8 ml, positioned in the left dorsolateral prefrontal cortex, were acquired (STEAM, TE=20ms) on 6 NT schizophrenic patients and on 10 appropriately matched controls. From the ^{31}P MRS study, the phosphomonoester (PME) level significantly decreased ($p < 0.001$) while the phosphodiester (PDE, $p < 0.005$) and phosphocreatine (PCr, $p < 0.04$) levels and the calculated free $[Mg^{2+}]_{intra}$ ($p < 0.001$) all significantly increased in the NT schizophrenics compared to the controls. The ^{1}H MRS results have shown a significant decrease in level of glutamate (Glu, $p<0.001$) and aspartate ($p<0.002$) while the glutamine (Gln) level increased ($p < 0.001$) in the NT schizophrenics compared to the controls. However, no significant differences in levels were observed for the metabolites N-acetyl-aspartate (NAA), γ-aminobutyric acid, PCr plus Cr, taurine and choline-containing compounds.

The ^{31}P MRS results suggest neuronal degradation is present early in the illness of schizophrenia with the increase in catabolic and decrease in anabolic activity of the membrane phospholipid metabolism. The observation of an abnormal level of Mg^{2+}_{intra}, which has the potential to block the NMDA neuronal receptor channel, tends to implicate the glutamatergic neuronal system. The ^{1}H MRS results are also in keeping with this possibility. The decrease in Glu represents a reduction in its availability in the neurotransmitter pool and/or the metabolic pool. Normal levels of the neuronal marker, NAA, suggests theres no major neuronal cell loss. However, the increase in Gln reflects a reduction in dendritic proliferation of Glu neurons. Any process affecting prefrontal Glu neurons has potential to affect the descending prefrontal-striatal and -limbic glutamatergic pathways which would account for structural and functional abnormalities found in these parts of the brain in schizophrenic patients.

LONG-TERM FOLLOW-UP STUDY OF FRONTAL LOBOTOMY IN SCHIZOPHRENIA

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Data will be presented on 24 patients who were retrospectively diagnosed by three research psychiatrists, blind to the patient's current psychiatric status, as having schizophrenia prior to psychosurgery and compared with 10 similiarly diagnosed non-lobotomized age matched schizophrenics. Each patient has been evaluated with the Comprehensive Assessment of Symptoms and History, a structured interview that includes the Scales for the Assessment of Positive and Negative Symptoms. A battery of neuropsychological tests has also been given to them.

Quantitative measurements of the volume of the lobotomy lesions have been made from magnetic resonance images (MRI).

Data will be presented comparing the clinical outcome and neuropsychological test performance of patients who had the more extensive Freeman and Watts and Lyerly and Poppen procedures as quantified by MRI to the outcome of those who had the more conservative transorbital procedures of Freeman and Shanklin-Jones. The clinical outcome and neuropsychological data of all lobotomized subjects will then be compared to the age matched non-lobotomized schizophrenics.

CEREBRAL BLOOD FLOW ACTIVATION OF THE ANTERIOR CINGULATE GYRUS STUDIED WITH POSITRON EMISSION TOMOGRAPHY

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The anterior cingulate cortex has been implicated in schizophrenic pathophysiology and PET studies have implicated it as an anatomical locus involved in selective attention.

We studied 8 right-handed,healthy male subjects with $[^{15}O]$-H_2O PET to measure regional cerebral blood flow changes in response to a specific "activation" task designed to require attentional resources and activate the anterior cingulate gyrus. One of four letters (B, J, Q, Y) was presented visually every 1.5-2 sec. In the control task, the subjects responded by naming the letter (congruent mapping). In the activation task, subjects responded with a different letter than the one presented (incongruent mapping: Q for B, Y for J, J for Q, B for Y). We took the ~200 msec slower response time seen in the incongruent condition as an index of the demand on processing resources. Subjects underwent 6-8 PET scans, each acquired in 60-second frames, with a Siemens 931-08/12 scanner, alternating between the control and activation tasks. We transformed the images into stereotaxic space by an automated algorithm and generated statistical parametric maps of significant difference between the activation and the control tasks.

The largest area of significant positive activation occurred at the superior edge of the left anterior cingulate gyrus, suggesting the involvement of this region in tasks that demand controlled, attentional resources.