71. ELEVATED DOPAMINE-INDUCED Gs PROTEIN MEASURES IN PATIENTS WITH SCHIZOPHRENIA

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Heterotrimeric G proteins play a pivotal role in post-receptor information transduction and were previously implicated in the pathophysiology and treatment of mood disorders. Changes previously detected in G protein levels in postmortem brains of patients with schizophrenia could reflect effects of antipsychotic medication. The present study aims at quantitatively and functionally evaluating receptor-coupled G proteins in mononuclear leukocytes obtained from 23 untreated patients with schizophrenia and 30 healthy subjects, in an attempt to unravel a pattern of G protein measures in schizophrenia distinct from patterns previously described in mood disorders. Dopamine-enhanced guanine nucleotide binding capacity to Gs protein through D1 or D5 receptors in mononuclear leukocytes of untreated patients with schizophrenia was significantly increased in comparison with healthy subjects. β-adrenergic and muscarinic receptor-coupled G protein functions, as well as Gsα, Giα and Gβ immunoreactivities were similar to healthy subjects. These findings, distinctive for schizophrenia, unrelated to drug treatment, and differential from previous findings in mania and depression, may potentially help to differentiate between the major psychoses: schizophrenia vs. manic-depressive illness after the first psychotic episode.

72. A GENETIC VARIANT OF CCK PROMOTER REGION MAY LINK TO NEGATIVE SYMPTOM OF SCHIZOPHRENIA

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The finding that neuropeptide cholecystokinin (CCK) co-localized with dopamine in central nervous system has made CCK an important candidate gene for schizophrenia research. Several previous studies have found reduced CCK level in cerebrospinal fluid of schizophrenia patients. A more recent study reported a marked decrease of CCK mRNA in the frontal and temporal cortex of schizophrenia. In present study, mutation screens were carried out on the CCK gene by means of single strand conformational polymorphism (SSCP). A C to T substitution was found in transcription factor Sp1 binding site of the CCK promoter region. Such variation can affect the gene expression by altering the transcription factor binding capacity to Gs protein through D1α receptor in mononuclear leukocytes of untreated patients with schizophrenia was significantly increased compared with healthy subjects. β-adrenergic and muscarinic receptor-coupled G protein functions, as well as Gsα, Giα and Gβ immunoreactivities were similar to healthy subjects. These findings, distinctive for schizophrenia, unrelated to drug treatment, and differential from previous findings in mania and depression, may potentially help to differentiate between the major psychoses: schizophrenia vs. manic-depressive illness after the first psychotic episode.

73. BCL-2 PROTEIN REDUCED IN SCHIZOPHRENIC TEMPORAL CORTEX

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Schizophrenia is an illness in which both neurodevelopmental and neurodegenerative processes have been implicated, yet the underlying pathophysiology remains elusive. Active apoptosis (programmed cell death) and altered Bcl-2 proteins have been documented in neurodegenerative disorders including Alzheimer’s disease. Involvement of apoptosis has also been hypothesized in schizophrenia. Apoptosis is regulated by Bcl-2 family proteins. Bcl-2 is a neuroprotective protein that inhibits apoptosis and can regenerate damaged CNS neurons. We hypothesized that Bcl-2 protein levels are altered in schizophrenic brain. Using ELISA, Bcl-2 protein was measured in postmortem temporal cortex (Brodmann area 21) from the Stanley Foundation Neuropathology Consortium in control, schizophrenic, bipolar, and depressed patients, n = 15 per group (matched on age, gender, and post-mortem interval). A priori, the primary analysis was limited to control versus schizophrenic specimens, given our underlying hypothesis. Bcl-2 levels were 25% lower in schizophrenic temporal cortex (21.9 ± 2.8 U/mg protein, mean ± SEM) compared to control (29.3 ± 2.1 U/mg protein) by Student’s t test (p = 0.046). In a secondary analysis we compared all samples. While Bcl-2 levels in all diagnostic groups were decreased compared to controls (schizophrenia < bipolar < depressed), ANOVA analysis was not statistically significant. Individual levels did not correlate with cumulative neuroleptic exposure. Interestingly, by combining schizophrenic and bipolar groups and separating them on neuroleptic naïve (n = 4) vs neuroleptic treated (n = 26) status, Bcl-2 levels in the treated group were higher (p = 0.034), demonstrating a potential neuroprotective role for neuroleptics. In conclusion, reduced Bcl-2 protein suggests a vulnerability to neurodegeneration through pro-apoptotic insults and/or atrophy in schizophrenic temporal cortex.

74. INHIBITORY DEFICITS IN STATE HOSPITAL SCHIZOPHRENIA PATIENTS

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Negative priming measures have been used extensively to evaluate sequential attentional processes in patient populations. Negative priming is a normal slowed reaction time to select items that were previously ignored. We have previously reported that unmedicated schizophrenia outpatients fail to exhibit normal negative priming (NP), while at the same time exhibiting within-trial inhibition equivalent to controls (Salo, Robertson & Nordahl, 1996). Previous studies have also reported that neuroleptic medication normalizes NP in outpatients and increases NP effects in controls (Beech, 1990; Salo, 1997). Since all of these studies were conducted with high functioning outpatients, it was of interest to conduct the same experimental procedure with chronic state hospitalized patients. In this study we tested 12 outpatients, 12 hospitalized inpatients and matched controls on a computerized Stroop negative priming paradigm. Both patient groups were medicated and matched on age, education and parental level of education. The controls were matched to