A second paradigm which can be linked to mesolimbic dopamine activity is conditioned avoidance behavior. Chronic haloperidol, in the dosage and time course described above, was found to decrease the disruption caused by an acute dose. In addition, experienced, poor performing avoiders doubled their spontaneous, drug free avoidance rate after withdrawal from chronic haloperidol. Chronic clozapine did not produce an increase in avoidance rate.

In order to test dopamine sensitivity in the nigro-striatal system, we examined the ability of apomorphine to induce stereotypic movements. We found that chronic haloperidol, but not chronic clozapine, caused a significant increase in apomorphine induced chewing, sniffing and rearing.

Thus, it appears that clozapine can induce dopamine receptor supersensitivity only in behaviors mediated in mesolimbic areas, in contrast to haloperidol, which shows no apparent selectivity. These data may provide an explanation for the differences in action of the two drugs following long-term treatment in humans.

Inheritance of alcoholism and antisocial behavior in adoptees

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A sample of 56 male adoptees was studied to assess the relationship of biologic and environmental variables, childhood behavior and adult alcoholism. Adoptees were separated at birth from biologic relatives. All adoptees were interviewed with a structured psychiatric instrument which allowed Feighner criteria diagnoses to be made. Adoptive parents were interviewed about childhood behavior of the adoptee. Fifteen of the adoptees had biologic relatives with alcoholism.

Cluster analysis was used with childhood hyperactivity and aggression variables to determine whether certain behavioral clusters in childhood would correlate with development of alcoholism as an adult. Membership in any of the 4 clusters with significant numbers of hyperactivity or aggressive symptoms correlated with adult alcoholism when compared to the "normal" cluster. No relationship between biologic background and cluster membership was found.

To further examine the relationship between adult alcholism, biologic and environmental variables, and childhood behavior, multiple regression analysis was used. Two analyses were performed: (1) number of adult alcoholic symptoms was used as the dependent variable, (2) number of adult antisocial symptoms was used as the dependent variable. Results of the first analysis show that an alcoholic biologic relative and the number of adolescent antisocial symptoms significantly predict number of adult alcoholic symptoms. Results of the second analysis indicate that an antisocial biologic relative and the number of adolescent antisocial symptoms significantly predict the number of adult antisocial symptoms, but *not* the number of adult alcoholic symptoms. The results are consistent with a genetic factor in both adult alcoholic and antisocial behavior.

Biologic validation of diagnoses of depression

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The dexamethasone suppression test (DST) was used as an independent validating criterion to compare several systems of classifying depressed patients. The DST has face validity, predictive validity and construct validity for use as a laboratory marker of endogenous depression (ED). We studied 89 depressed outpatients by clinical criteria, Research Diagnostic Criteria (RDC) and St. Louis criteria. By clinical criteria 49 had ED and 42 had non-endogenous depression (NED). A simple version of the DST, requiring only one blood sample, correctly identified 40% of ED patients with a specificity of 98% and a diagnostic confidence of 95%. Differences in age, sex or severity of symptoms between ED and NED patients did not account for these results. Abnormal DST results were a function of the categorical distinction between ED and NED. By comparison, the diagnostic performance of the DST was weaker for the St. Louis category primary depression, and the RDC categories Major Depressive Disorder (MDD), and primary MDD. These were less selective and more heterogenous than

the clinical category ED. The clinical diagnoses of ED were supported in 98% of cases by the RDC, but 22% of RDC endogenous MDD diagnoses were not supported by clinical diagnoses. Abnormal DST results were found only in cases with both the clinical diagnosis ED and the RDC diagnosis endogenous MDD. Abnormal DST results were found in 42% of cases with definite endogenous MDD, in 14% with probable endogenous MDD, and in only 3% with absent endogenous MDD. We also found a significant association with a positive family history of depression.

We conclude (1) the DST is useful in the differential diagnosis of depressed outpatients; (2) the categories primary depression (St. Louis) and primary MDD (RDC) are more heterogenous than the clinical category ED, because these categories are diluted by cases diagnosed clinically as NED who have no neuroendocrine disturbance; thus they are probably less valid than the clinical category ED; (3) the present RDC have only moderate validity for the diagnosis of endogenous depression; (4) RDC diagnoses cannot substitute for careful clinical diagnoses in research studies; (5) the proper use of the RDC is to validate clinical diagnoses but not to generate diagnoses as a checklist function; (6) the clinical concept of endogenous depression has validity and should be retained in research studies of depression.

Suicide in professional women

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Women professionals have a high suicide rate. Women professionals have an increased lifetime prevalence of depression as compared to prevalence rates obtained from a community sample using similar assessment techniques and diagnostic criteria. However, the prevalence rate of depression in women physicians is lower, by far, than that predicted by PITT *et al.*, based on their careful data on the rate of suicide in women physicians. Reasons for this discrepancy will be discussed. Data on suicidal thoughts and attempts from 214 interviewed women M.D.'s and Ph.D's will be presented to support the hypothesis that suicide attempts are rare, so that suicide, when attempted is usually "successful".

Neurophysiology of individual motor units in psychotic patients

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Single-fiber electromyography (SFEMG) makes possible the relatively noninvasive study of individual nerve-muscle synapses and, when combined with H-reflex techniques, the study of relatively discrete events at spinal cord synapses between sensory and motor fibers. In view of the various hypotheses concerning abnormalities of synaptic transmission and of structural alterations of the nervous system in psychotic patients, we studied a series of schizophrenic patients using SFEMG techniques. Fiber Density (FD), the number of muscle fibers innervated by a single motor unit within a given area of muscle, was studied in the extensor digitorum muscle of 44 schizophrenic subjects. FD was significantly higher in the patient group compared with the normal control group. There was no correlation between FD and duration of illness, severity of illness, drug treatment, or length of hospitalization. However, 6 schizophrenic patients with tardive dyskinesia had significantly higher values for FD than did non-TD schizophrenics. This finding suggests that TD is associated causally with a neurotoxic effect of neuroleptic treatment, or that patients who develop TD have a pre-existing neuropathologic lesion which predisposes to the development of TD.

The latency jitter (variability response latencies) of single-fiber H-reflexes was studied in 21 schizophrenic subjects and 19 controls. Studies of conventionally recorded H-reflexes have indicated that certain psychotic patients have abnormalities of the recovery cycle of the H-reflex. With SFEMG methods, a normal tendency for H-reflex jitter to vary with stimulation rate was defined. In patients, a similar pattern of response was seen, but maximal jitter occurred at lower rates of stimulation. Similarly, the rate of stimulation at which reflex responses could not longer follow (drop-out point) occurred at a lower rate of stimulation in patients compared with controls.