Effect of Clinical Doses of Fluoxetine on Psychological Variables in Healthy Volunteers By: Yevgenia Gelfin, M.D., Malka Gorfine, M.A., and Bernard Lerer, M.D. *American J Psychiatry* (1998), 155:290-29)

Objective: The authors sought to determine the effect of clinically equivalent doses of fluoxetine on mood and other psychological variables in normal subjects.

Method: Fifteen healthy volunteers received placebo for 2 weeks; fluoxetine, 10 mg/day, for 1 week; fluoxetine, 20 mg/day,for 5 weeks; and then an additional 2 weeks of placebo in the context of a single-blind study. The subjects were evaluated with a series of self-and observer-rated instruments.

Revariables: No significant effects attributable to fluoxetine were observed on any of the psychological variables examined. Minimal adverse effects were reported.

Conclusions: Significant mood-elevating and other psychological effects of fluoxetine would appear induced only when symptomatic targets exist.

Depression Among Concaine Abusers in Treatment: Relation to Cocaine and Alcohol Use and Treatment Outcome By: Richard A. Brown, Ph. D., Peter M. Monti, Ph. D., Mark G. Myers, Ph. D., Rosemarie A. Martin M. A., Timothy Rivinus, M.D., Mary Ella Dubreuil, R.N., L. C.D.P., and Damaris J. Rohsenow, Ph. D. *American J Psychiatry* (1998), 155:220 - 225

Objective: The authors investigated the theoretical and clinical role of depression among cocaine abusers in treatment.

Method: Eighty - nine cocaine - abusing patients underwent 2 weeks of substance abuse treatment. Posttreatment major depressive disorder, depressive symptoms before and after substance abuse treatment, and alcohol diagnoses were assessed and their relation to pretreatment substance use, cravings in high - risk situations, and 3-month follow - up status was examined.

Results: High rates of major depressive disorder were found but were unrelated to pretreatment substance use. The decrease in depressive symptoms during treatment was independent of major depressive disorder or alcohol diagnoses and predicted treatment attrition. Higher levels of depressive symptoms during treatment were associated with greater urge to use cocaine, alcohol, and other drugs in high - risk situations. Concurrent major depressive disorder and depressive symptoms did not predict cocaine use at follow - up. However, patients who had an alcohol relapse episode experienced more depressive symptoms during treatment than did those who abstained.

Conclusions: The results highlight the relationship of depression to alcohol use among cocaine abusers and suggest a need for further studies of the association between depression and substance use disorders.

Anonymity, Neutrality, and Confidentiality in the Actual Methods of Sigmund Freud: A Review of 43 Cases, 1907 - 1939 By: David J. Lynn, M.D., and George E. Vaillant, M.D. *American J Psychiatry* (1998), 155 : 163-171

Objective: The aim of historical study was to examine the methods actually used by Sigmund Freud in his practice of psychoanalysis in his mature years (1907 - 1939) and to assess the relationship between these methods and Freud's published recommendations concerning anonymity, neutrality, and confidentiality.

Method: The authors used both published and unpublished sources, including reports or autobiographies by analysands, interviews of analysands, letters by Freud, published works by Freud, and clinical records of subsequent treatment.

Results: Information concerning Freud's actual methods was found in 43 cases, including 10 clinical psychoanalyses, 19 didactic analyses, and 14 with combined clinical and didactic purposes. These 43 cases probably encompassed a majority of Freud's psychoanalytic hours during these years. Deviations from Frend's recommendations were found to the following extent: for anonymity, 43 cases (100%); for neutrality, 37 cases (86%); for confidentiality, 23 cases (53%). In addition, there were significant extra - analytic relations between freud and 31 of these analysands (72%).

Conclusions: Theses results show a substantial disparity between Freud's recommendations and his actual methods. Freud's prescribed method, between Freud's recommendations, was not tested or used in his practice. Freud's actual method was never explicitly described in his writings and cannot be replicated.

Comorbidity Between Abuse of an Adult and DSM - III - R Mental Disorders: Evidence From an Epidemiological Study By:Kirstie K. Danielson, Terrie E. Moffitt, Ph.D., Avshalom Caspi, Ph.D., and Phil A. Silva, Ph.D. *American J Psychiatry* (1998), 155 : 131 - 133).

Objective: The purpose of this study was to report the prevalence, risk, and implications of comorbidity between partner violence and psychiatric disorders.

Method: Data were obtained from a representative birth cohort of 491 young adults through use of the Conflict Tactics Scales and Diagnostic Interview schedule.

Results: Half of those involved in partner violence bad a psychiatric disorder; one - third of those with a psychiatric disorder were involved in partner violence. Individuals involved in severe partner violence bad elevated rates of a wide spectrum of disorders.

Conclusions: The findings support the importance of mental health clinicians screening for partner violence and treating victims and perpetrators before injury occurs.

Neurological Abnormalities in Schizophrenic Patients and Their Siblings By: baher Ismail, M.D., elizabeth Cantor - Graae, Ph. D., and Thomas F. McNeil, Ph.D. *American J Psychiatry* (1998), 155: 84 - 89

Objective: The aim of this study was to investigate the prevalence and type of neurological abnormalities in schizophrenic patients and their nonpsychotic siblings.

Method: A comprehensive neurological assessment, including evaluation of both hard and soft signs, was performed for 60 schizophrenic patients, 21 siblings, and 75 normal comparison usbjects.

Results: None of the comparison subjects scored higher than 6 on the neurological assessment scale, but a score of 7 or higher was given to 67% of patients and 19% of siblings . both patients and siblings scored significantly higher than comparison subjects on total neurological abnormalities, hard signs, soft signs, primitive reflexes, integrative sensory functions, and motor functions . The most conspicuous abnormalities were motor coordination problems and involuntary in the patients and cranial nerve deviations and mirror

movements in their siblings. levels of neurological abnormality were positively correlated within patient siblings pairs. The total battery and hard signs best discriminated patients from comparison subjects.

Conclusions: High levels of neurological abnormality characterize both schizophrenic patients and their siblings. The constellation of abnormalities and absence of overt psychopathology in siblings may represent the mildest form of disturbance within the schizophrenia spectrum. Levels of neurological abnormality covary positively in patients and siblings within the same family, suggesting common genetic and / or environmental pathogenic factors. An extended assessment battery provides optimal disrimination of patients from normal subject, and hard signs are more differentially associated with schizophrenia than are soft signs.

The neurological abnormality has no consistent localizing profile, and nearly all functional domains are involved .

Different Genetic Background of Schizophrenia Spectrum Psychoses: A Twin Study? By: Ernst Franzedk, M.D., and Helmut Beckmann, M.D. *American J Psychiatry* (1998) 155: 76-83

Objective: The authors report on a systematic twin study of index twins suffering from schizophrenia spectrum psychoses. Using different diagnostic systems, they examined twin concordance, family history, and the frequency and severity of the birth complications of 22 monozygotic and 23 dizygotic twin pairs.

Method: All twins in the region of Lower Franconia, Germany, born after 1930 and hospitalized for psychiatric disease were ascertained. The zygosity diagnoses were based on molecular genetic methodology and a zygosity questionnaire. two psychiatrists, wording independently, formulated diagnoses according to DSM - III - R criteria and Leonhard's nosology.

Results: There were substantially different concordance rates with regard to diagnostic subgroups, and monozygotic concordance was significantly higher than dizygotic concordance in only two of the following five subgroups (subgroups 1 and 3): 1) strict schizophrenia according to DSM - III - R: monzygotic, 85.7%, dizygotic, 25.0%; 2) schizophreniform, schizoaffective, and delusional (paranoid) disorders and psychotic disorder not otherwise specified according to DSM - III - R: monozygotic, 47.1%, dizygotic, 30.8%; 3) unsystematic schizophrenia according to Leonhard: monozygotic 88.9%, dizygotic, 25.0%; 4) systematic schizophrenia according to Leonhard; monozygotic pairs lacking, dizygotic, 0%; 5) cycloid psychoses according to leonhard:monozygotic,38.5%,dizygotic, 36.4%. In the case of cycloid psychoses and conditions less prominent in DSM - III - R schizophreniform, schizoaffective, and delusional (paranoid) significantly more severe birth complications than their healthy partners. Not one of the 37 monozygotic twins was diagnosed as having systematic schizophrenia, whereas six of the 25 dizygotic index twins received this diagnosis.

Conclusions: The results of the study suggest that schizophrenia spectrum psychoses may consist of clinically and etiologically heterogeneous subgroups with different genetic back grounds.

Self - Report Ratings and Informant's Ratings of Personalities of Depressed Outpatients By: R. Michael Bagby, Ph.D., Neil A. Rector, Ph. D., Kirstin Bindseil, B. Sc., Susan E. Dickens, M. Sc., Robert D. Levitan, M.D.,

and Sidney H. Kennedy, M.D. *American J Psychiatry* (1998), 155 - 437 - 438

Objective: This study sought to determine whether personality traits of depressed patients could be assessed similarly by informants and self - reports of the patients themselves.

Method: Forty - six depressed outpatients completed the self - report (first - person) version of the Revised NEO personality Inventory and nominated informants who knew them well to complete the third - person version of that instrument.

Results: Agreement between the self - ratings and informants ratings on the five factors of the inventory - neuroticism, extraversion, openness - to - experience, agrecableness, and conscientiousness -was high. The only significant difference between the self - ratings and informants ratings was on the extraversion scale, where the patients rated themselves as significantly more introverted than did the informants.

Conclusions: Informants ratings of personality are similar to self - report ratings of depressed patients. Depressed mood may not influence the self - report of personality traits.

Effect of a Haloperidol Challenge on Regional Brain Metabolism in Neuroleptic-Responsive and Nonresponsive Schizophrenic Patients By: Elsa J. Bartlett, Ed. D.., Jonathan D. Brodie, Ph. D., M.D., Philip Simkowitz, M.D., Ph. D., Ralf Schlosser, M.D., Stephen L. Dewey, Ph.d., Jean-Pierre Lindenmayer, M.D., Henry Rusinek, Ph.D., Adam Wolkin, M.D., Robert Cancero, M.D., ;and Wynne Schiffer, B.A. *American J Psychiatry* (1998), 155:337-343

Objective: .The CN5 metabolic response to a neuroleptic challenge in treatment-responsive and nonresponsive schizophrenic patients was measured in order to examine the relation between treatment outcome and the capacity to alter neurochemical function in response to acute receptor blockade.

Method: Positron Emission Tomography (PET) and [18 F] fluorodeoxyglucose (FDG) were used to measure regional cerebral metabolism in seven schizophrenic patients judged to have been responsive to drug treatment previously and seven nonresponsive schizophrenic patients after a drug-free period of at least 3 weeks (baseline) and again 12 hours after administration of 5.0 mg of haloperidol.

Results: The haloperidol challenge caused widespread decreases in absolute metabolism in the nonresponsive patients but not the responsive patients. These group differences reflect the findings on the second (challenge) scans, since metabolic values at baseline were not statistically different in the two groups. The pattern of decreased metabolic activity in the nonresponders after the haloperidol challenge is similar to that previously observed in normal subjects.

Conclusions: The metabolic response to drug challenge separates treatment responders from nonresponders and normal subjects. The results suggest that subtyping of schizophrenia (and other psychiatric disorders) can be achieved by measuring the physiological response to a pharmacologic challenge in vivo with chemical brain-imaging techniques.

Schizophrenia-Like Psychosis and Epilepsy: The Status of the Association? Perminder Sachdev, M.D., Ph.D., F.R.A.N.Z.C.P. *American J Psychiatry* (1998), 155:325-336

Objective: Current knowledge of the relationship between epilepsy and schizophrenia-like psychosis is examined,

and the proposed pathogenetic mechanisms are evaluated.

Method: The author provides am overview of the published literature on epilepsy and schizophrenia-like psychosis.

Results: The schizophrenia-like psychoses of epilepsy are inadequately categorized by the current classifications. Their categorization into ictal, psotictal, and interictal psychoses is clinically useful, but it does not imply distinct pathophysiology for each. The recent interest in postictal psychoses has opened an important avenue for research. Brief interictal psychoses, involving alternation between epilepsy and psychosis and accompanied by forced normalization, are uncommon. Many aspects of the relationship with chronic interictal psychosis remain controversial. The majority of investigators support a special but not exclusive relationship with mediobasal temporal lobe epilepsy, and left temporal bias receives only limited support. The chronic psychosis resembles schizophrenia phenomenologically. Some suggested risk factors are severe and intractable epilepsy, epilepsy of early onset, secondary generalization of seizures, certain anticonvulsant drugs, and temporal lobectomy. Different neuropathological studies suggest the presence of cortical dysgenesis or diffuse brain damage.

Conclusions: There are many mechanisms by which epilepsy may be associated with schizophrenia-like psychosis. It is likely that structural brain abnormalities, e.g., cortical dysgenesis or diffuse brain lesions, underlie both epilepsy and psychosis, and that the seizures modify the presentation of the psychosis, and vice versa, thus producing a clinical picture of both an affinity and an antagonism between the two disorders.

Positive and Negative Symptom Response to Clozapine in Schizophrenic Patients With and Without the Deficit Syndrome By: Robert W. Buchanan, M.D., Alan Breier, M.D., Brian Kirkkpatrick, M.D., Patricia Ball, R.N., and William T. Carpenter, Jr., M.D. *American J Psyhiatry* (1998), 155:751-760)

Objective: In a preliminary report, the authors observed that clozapine was superior to haloperidol in the treatment of positive and negative symptoms in stable outpatients with schizophrenia. In this final report, they examine the effects of clozapine on positive and negative symptoms in patients with and without the deficit syndrome to determine which patients receive the positive symptom advantage of clozapine and the extent of clozapine's therapeutic effects on negative symptoms. In addition, they examine the long-term effects of clozapine on positive, negative, and affective symptoms, social and occupational functioning, and quality of life.

Method: Seventy-five outpatients with schizophrenia, who met retrospective and prospective criteria for residual positive or negative symptoms, were entered into a 10 - week double-blind, parallel-groups comparison of clozapine and haloperidol. Patients who completed the double-blind study were then entered into a 1-year open-label clozapine study.

Results: For patients who completed the 10-week double-blind study, clozapine was superior to haloperidol in treating positive symptoms. This effect was not observed in the intent-to treat analyses. There was no evidence of any superior efficacy or long-term effect of clozapine on primary or secondary negative symptoms. Long-term clozapine treatment was associated with significant improvements in social and occupational functioning but not in overall quality of life.

Conclusions: For schizophrenic patients who are able to tolerate clozapine therapy, clozapine has superior efficacy for positive symptoms but not negative symptoms and is associated with long-term improvements in social and occupational functioning for patients with and without the deficit syndrome

Genome Scan of Schizophrenia By: Douglas F. Levinson, M.D., Melanie M. Mahtani, Ph.D., Derek J. Nancarrow, B.Sc., Donna M. Brown, M.S., Leonid Kruglyak, Ph.D., Andrew Kirby, B.A., Nicholas K. Hayward, Ph.D., Raymond R. Crowe, M.D., Nancy C. Andreasen, M.D., Ph.DDonald W. Black, M.D., Jeremy M. Silverman, Ph.D., Jean Endicott, Ph.D., Lawrence Sharpe, M.D., Ricard C. Mohs, Ph.D., Larry J. Siever, M.D., Marilyn K. Walters, M.S., David P. Lennon, M.A.P.S., Helen L. Jones, B.Nurs., Deborah A. Nertney, B.Sc., Mark J. Daly, B.S., Madeline Gladis, Ph.D., and Bryan J. Mowry, F.R.A.N.Z.C.P. *Am J Psychiatry* (1998), 155:741-750

Objective: The goal of this study was to identify chromosomal regions likely to contain schizophrenia susceptibility genes.

Method: A genomewide map of 310 microsatellite DNA markers with average spacing of 11 centimorgans was genotyped in 269 individuals-126 of them with schizophrenia-related psychoses-from 43 pedigrees. Nonparametric linkage analysis was used to assess the pattern of allele sharing at each marker locus relative to the presence of disease.

Results: Nonparametric linkage scores did not reach a genomewide level of statistical significance for any marker. There were five chromosomal regions in which empirically derived p values reached nominal levels of significance at eight marker locations. there were p values less than 0.01 at chromosomes2q (with the peak value in this region at D2S410) and 10q (D10S1239), and there were P values less than 0.05 at chromosomes 4q (D4S2623), 9q (D9S257), and 11Q (D11S2002).

Conclusions: The results do not support the hypothesis that a single gene causes a large increase in the risk of schizophrenia. The sample (like most others being studied for psychiatric disorders) has limited power to detect genes of small effect or those that are determinants of risk in a small proportion of families. All of the most positive results could be due to chance, or some could reflect weak linkage (genes of small effect). Multicenter studies may be useful in the effort to identity chromosomal regions most likely to contain schizophrenia susceptibility genes.