Outlines for Unit 2 - Schizophrenia and Psychotic Disorders

Instructor: June Sprock
Unit 2 - Schizophrenia and Psychoses

Reading: Ho, Black & Anderson (2004) Ch 5 from Hales & Yodofsky

I. Introduction

A. Reading: Nicholson & Neufeld, 1993; Tsuang, Stone & Faraone, 2000 (pp 1041-1043); Jones & Cannon, 1998 (pp 16-19); Rivas-Vazquez et al., 2000 (p 631)

B. Case examples

C. Symptoms
   1. psychosis: hallucinations, delusions
   2. disturbed affect - flat, inappropriate
      Kring et al (’93): study of schiz watching videos – experienced emotions, not express
   3. thought disorder (disorder of associations)
   4. deterioration in functioning
   5. Positive vs. negative symptoms: Strauss et al (’74); Crow (’80, ’85)
      Positive sx: presence of abnormal behavior (e.g., hallucination)
      Negative sx: absence of normal behavior (e.g., flat affect, social withdrawal)
      Ciompi (’80), Zubin (’89) - negative sx may be a tx artifact
      Rivas-Vazquez et al. (2000): primary vs secondary negative sx

D. Historical roots
   1. Kraepelin
      a) dementia praecox - "early onset dementia"
      b) 3 subtypes: paranoid, hebephrenic, catatonic
   2. Bleuler
      a) coined term "schizophrenia" (splitting of mind); fundamental defect
      b) saw as a group of disorders
      c) 4 fundamental symptoms - "4 A’s" - in order of importance
         1) disordered Associations = thought disorder
         2) disordered Affect (flat, inappropriate)
         3) Ambivalence
         4) Autism
      d) emphasis on theory/cause as opposed observation of signs (Kraepelin)
3. subsequent emphasis on thought disorder; Rorschach; not diagnostic of schiz

4. Schneider
   a) Schneiderian symptoms - bizarre delusions, hallucinations

   1) thought broadcasting
   2) thought insertion
   3) thought withdrawal
   4) delusions of control or influence

   b) Hit rate using Schneiderian "first rank" sx:
      high rate of true and false negative
      low rate true and false positive

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Schneiderian sx</th>
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<tbody>
<tr>
<td>Schizophrenic</td>
<td>yes</td>
</tr>
<tr>
<td>Not Schizophrenic</td>
<td>15%</td>
</tr>
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<td></td>
<td>5%</td>
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E. American History

1. DSM-II (1968)
   a) 10 subtypes of schizophrenia (see Table 1): concerns with these 2 subtypes:
      1) simple: negative sx only and deterioration (to differentiate from schizoid): Deficit type in DSM-IV Appendix
      2) latent: pre-psychotic or borderline schiz: borderline and schizotypal today
      3) May relate to schiz spectrum (schizoid, schizotypal - predispose to schiz, evidence for genetic relationship to schiz: relates to theories of etiology: Meehl’s schizotaxia (1962); Tsuang et al’s (2000) reformulation

   b) United States-United Kingdom Diagnostic Project (Cooper, Kendall & Sartorius, 1966-1968) - Americans overdiagnose schiz

Table 1: Subclassification of Schizophrenia

<table>
<thead>
<tr>
<th>Kraepelin</th>
<th>DSM-II</th>
<th>DSM-III and III-R</th>
<th>DSM-IV and IV-TR</th>
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<tbody>
<tr>
<td>Paranoid</td>
<td>Paranoid</td>
<td>Paranoid</td>
<td>Paranoid</td>
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<tr>
<td>Catatonic</td>
<td>Catatonic</td>
<td>Catatonic</td>
<td>Catatonic</td>
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<tr>
<td>Hebephrenic</td>
<td>Chronic Undifferentiated</td>
<td>Disorganized</td>
<td>Disorganized</td>
</tr>
<tr>
<td>Residual</td>
<td>Residual</td>
<td>Undifferentiated</td>
<td>Undifferentiated</td>
</tr>
<tr>
<td>Childhood</td>
<td></td>
<td>(no separate dx for children)</td>
<td>Residual</td>
</tr>
<tr>
<td>Acute</td>
<td></td>
<td>Not schiz: Brief Psychotic Disorder or</td>
<td>Brief Psychotic Disorder or</td>
</tr>
<tr>
<td>Schizoaffective</td>
<td></td>
<td>Schizophreniform Disorder</td>
<td>Schizophreniform Disorder</td>
</tr>
<tr>
<td>Simple</td>
<td></td>
<td>Not schiz: Schizoaffective Disorder</td>
<td>Schizoaffective Disorder</td>
</tr>
<tr>
<td>Latent</td>
<td></td>
<td>Not schiz: probably Schizoid</td>
<td>Schizoid or Deficit type schiz</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(Appendix)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Schizotypal or Borderline</td>
</tr>
</tbody>
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2
2. Feighner criteria (1972) and RDC (1975) - narrowed definition
   (Both required deterioration; RDC - added Schneiderian sx)


4. Dichotomous (2 category) classifications in literature
   a) Process (chronic) vs. Reactive (acute): based on onset and course
      Process: poor premorbid, gradual continued deterioration, no stressor
      Reactive: good premorbid, onset rapid, in response to stressor
   b) Poor vs. Good Prognosis/poor vs. good Premorbid - Phillips (1953)
   c) Type 1 (positive symptom) vs Type 2 (negative symptom): Crow (1980)
   d) Nicholson & Neufeld (’93)- positive sx vs negative sx: are continuums
   e) Can view these categories as dimensions: (see Table 2)

<table>
<thead>
<tr>
<th>Basis of dimension</th>
<th>Process</th>
<th>Chronic</th>
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<tbody>
<tr>
<td>Cause/course:</td>
<td>Good Prognosis</td>
<td>Poor Prognosis</td>
</tr>
<tr>
<td>Course:</td>
<td>Good Premorbid</td>
<td>Poor Premorbid</td>
</tr>
<tr>
<td>Outcome:</td>
<td>Positive Symptom</td>
<td>Negative Symptom</td>
</tr>
<tr>
<td>Symptoms:</td>
<td>Type I (Type II or Deficit type)</td>
<td></td>
</tr>
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5. New in DSM-IV (and DSM-IV-TR)Appendix:
   a) Alternative dimensional descriptors for schiz:
      1. 3 dimensions:
         a) psychotic (like positive sx)
         b) disorganized
         c) negative (deficit)
      2. After usual subtype and course, specify absent, mild, moderate, severe for each dimension; can specify for current or lifetime or both
   b) new proposed categories:
      1. Simple Deteriorative Disorder (Simple Schizophrenia):
         a) only negative sx with progressive decline (decline =not schizoid pd)
         b) diagnosed as: Unspecified Mental Disorder (Simple Deteriorative Disorder)
      2. Postpsychotic Depressive Disorder of Schizophrenia:
         a) major depressive episode during residual phase of schiz
         b) diagnosed as: Depressive Disorder NOS (Postpsychotic Depressive Disorder of Schizophrenia)
II. Schizophrenia: Description
A. Reading: Nicolson & Neufeld (1993); Tsuang et al. (2000); Lopez et al. (2004); also see: Lewis (2004)

B. Phases
1. prodromal (negative sx)
2. active (positive sx): ≥ 1 mo
3. residual (negative sx)
4. total ≥ 6 mo

C. Subtypes and Dimensions
1. Subtypes in DSM-IV and IV-TR
   a. Paranoid
   b. Catatonic: stupor, rigidity, waxy flexibility, excitement
   c. Disorganized
   d. Undifferentiated
   e. Residual (case)

2. Evidence for subtypes and alternative dimensional approach
   a. evidence for paranoid strongest (Nicolson & Neufeld, 1993)
   b. problem: subtypes change over time
   c. Liberman (1995) 2 courses of chronic schiz:
      1) increased neg sx
      2) increased disorganized, catatonic sx
   d. Nicolson & Neufeld ('93): 2 dimensions:
      1) severity of disorder: paranoid(milder) to non-paranoid
      2) severity of symptoms: milder to more severe
   e. Tsuang, Stone & Faraone (2000): dimensional view:
      1) some elements of psychosis shared across disorders (Crow’s ideas)
      2) schizophrenic spectrum - a dimensional approach, based on etiology rather than
description; genetic relationship between schizotaxia (pre-psychotic schiz proneness,
negative sx, neuropsych deficits) and schiz; theory of etiology but also classification
   f. DSM-IV Appendix
      1) alternative dimensional descriptors for schiz: 3 dimensions, rate according to severity:
absent, mild, moderate, severe; current/lifetime; in addition to basic subtypes, specifiers
      a) psychotic: like positive sx of Type I
      b) disorganized
      c) negative (deficit): like neg sx, Type II
2) proposed subtypes in DSM-IV appendix:

a) Postpsychotic Depressive Disorder of schiz: major dep episode during residual phase of schiz (dx as Mood Disorder NOS)

b) Simple Deteriorative Disorder (simple schiz): neg sx only + deterioration (like Type II)

D. Course

1. Early onset of schizophrenia: teens, early 20s (except small group women with late onset)

2. Zubin & Spring (1977): about 50% recover, 40% have episodes with partial recovery between episodes, 10% chronic

3. Ciompi (1988) 37 yr. longitudinal study of 289 schizophrenics according to type of course (simple or undulating), type of onset (acute or chronic) and outcome (good recovery or moderate-severe impairment):

<table>
<thead>
<tr>
<th>COURSE</th>
<th>Acute</th>
<th>Chronic</th>
</tr>
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<tbody>
<tr>
<td>Simple</td>
<td>good recovery</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>impaired</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td>13%</td>
<td>35%</td>
</tr>
<tr>
<td>Undulating</td>
<td>good recovery</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>impaired</td>
<td>12%</td>
</tr>
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</table>

Most common patterns in Ciompi study:
25% Acute onset, undulating course, good recovery (or only mild sx)
25% Chronic onset, simple course, moderate-severe impairment
Equally divided between acute and chronic onset
Equally divided between good recovery and moderate-severe impairment
About equally divided between simple and undulating course

4. Other studies (from book chapter):
   a. Iowa 500 (followed 500 schiz from 1930s and 1940s through early 1970s: 20% doing fairly well but over 50% incapacitated
   b. Chesnut Lodge study (McGlashan, 1984): followed 1950s through early 1980s: 28% living independently
   c. Methodological probs many of these studies; several recent data re-analyses of older studies, one came out within past year re-analyzing Bleuler’s outcome data

E. Prognosis

1. Good prognostic features: good premorbid, acute onset in resp to stressor, anxiety or depression (why?), positive sx, family hx mood disorders, female
2. Poor prognostic features: poor premorbid, slow onset (no stressor), absence of emotional upset, neg sx, fam hx of schiz, male; also substance abuse – high rate in schiz, may worsen sx


4. Depression and suicide - depression a good prognostic sign, but increased risk suicide
   a. Fenton et al. (1997):
      1) lower risk suicide: prominent neg sx, nonparanoid (usually considered poor prognosis)
      2) higher risk: positive sx, paranoid, absence of negative sx (usually good prognosis)
      also: young, male, awareness of illness, severe/chronic/meds

   b. Zisook et al. (1999): depression very common in schiz;
      1) no consistent sex diffs in dep;
      2) depressive sx correlated with positive sx, not negative sx

   c. APA Guidelines (2004): dep & suicide important management issue; high risk in schiz

   d. Lewis (2004): usually thought that insight about illness associated with increased risk
      1) proposes that hopelessness and pessimism, not realistic insight assoc with SI in schiz
      2) proposes therapy can be used to increase insight but reduce risk of suicide in schiz; can increase insight while maintaining hope
      3) general risk factors in schiz similar as others: depression, hx of SI/Attempts
      4) times of increased risk: discharge, acute phase, partial insight, paranoid and hostility towards tx providers
      5) need distinguish between neg sx, depression, anosognosia (organic, inability recognize illness) vs denial, mourning (loss of functioning)

5. Families and High Expressed Emotions (High-EE):
   a. Giron & Gomez-Beneyto (1998): 2 year followup study
      1) associated with lower rates of relapse: empathic family
      2) associated with increased relapse: family with poor empathy; also pt’s negative sx; unemployment; poor premorbid adjustment; poor tx compliance

   b. Lopez et al. (2004): most research focuses on role of negative emotions, need look at positive emotions in the family, role of cultural factors
      1) compared 2 studies of family functioning and schiz relapse: Mex-Am and Euro-Am
      2) looked at family attributions of control, positive and negative affect, relapse
      3) Mex-Am: family warmth most predictive of course
      4) Euro-Am: family criticism (blame, neg emotions) most predictive of course
      5) implications for treatment (e.g., contact with family, family therapy)
III. Schizophrenia in a Diverse Society
A. Reading: Szymanski et al., 1995; Leung & Chue, 2000; Trierweiler et al., 2000; Kuno & Rothbard (2002); Lopez et al. (2004)

B. Gender differences in schizophrenia
   1. Szymanski et al (1995): differences in course, outcome: women better tx response, outcome, older age onset (even in 40s) – small group of women with late onset
   2. Goldstein (1988): key study – 10 yr study; women shorter hosp stays, fewer rehosp, better premorbid, better course (less severe) and outcome
   3. Castle et al (1994): women better premorbid, later onset, better prognosis
   5. Hafner et al (‘95) women later onset
   6. Andia et al (’95): women receive lower meds, more paranoid and disorganized types, better functioning (education, married, living independently, working), fewer psychosocial probs - even when have equal sx to men
   7. Salem & Kring (1998): men earlier onset; poorer premorbid social and intellectual functioning; poorer course, response to meds, and outcome
   8. Castle et al. (1998): men earlier onset, different type of schiz with different etiologies
   9. Goldstein et al. (1998): men more neuropsychological impairment, women’s impairment more limited and verbal processing ok
   10. Explanations:
       a. estrogen protects, acts as antipsychotic
       b. periuterine development- faster in women so less chance periuterine trauma,
       c. biological indicators may differ: less structural brain abnormalities female schiz
       d. However, findings mixed - Patton et al (1994)- no differences in brain morphology
       e. Salem & Kring (1998): men more structural abnormalities suggesting neurodevelopmental subtype of schiz; proposed:
          1) men more prone to neurodevelopmental type of schiz with poor prognosis, more obstetric complications, less family hx schiz or mood disorder;
          2) women more prone to disorder related to fam hx affective disorder, better prognosis
       f. Castle et al (‘95)- increased hx maternal influenza female schiz; may be different factors in development of schiz for men and women
   10. Miller (1997): women with schiz have additional issues related to sexuality, reproduction, family planning
       a. increased risk of unwanted pregnancy, HIV
       b. complications of pregnancy including use of antipsychotic meds
c. Postpartum exacerbations
d. challenges of parenting

11. Canuso et al., 1998: reviewed literature on women and schizophrenia
   a. Better premorbid, later onset, more + sx (men more - sx), better tx resp
   b. May have more side effects meds: hyperprolactinemia (increased prolaction?);
      less a prob for new atypicals but increased fertility can be a problem
   c. Substance abuse (but less than male schiz except possibly tobacco)
   d. Estrogen affects sx: may account for lower doses antipsychotics needed, increased TD
      post-menopause, increased risk of relapse during pregnancy and post-partum
   e. Psychosocial issues: motherhood, victimization, homelessness (more men, but
      higher % homeless women have SMI)

12. Leung & Chue (2000) review:
   a. men: earlier onset, poorer premorbid, more neg sx, more cog deficits, increased structural
      and neurophysiological basis of schiz, families more critical and high-EE more an effect
   b. women: more affective sx, auditory halluc, persecutory dels, faster and better resp meds
      at lower doses, less smoking and substance abuse
   c. more mixed conclusions; points out methodological probs in studies; no evidence for diffs
      in fam hx, obstetric complications, neurological soft signs
   d. Estrogen has structural effects (dimorphism of brain structures, pruning, lateralization)
      and functional (modifying neurotransmitters, lessening psychotic sx)
   e. Neurodevelopmental model: accounts for sex diffs: men more prone to
      neurodevelopmental probs; sex hormones plus psychosocial sex differences mediate sex
      difference

   a. men dx’ed earlier, more deficit sx, more smoking and sub abuse, more mortality due to
      suicide, homicide
   b. women: more comorbid non-psychotic dx (mood, eating, personality), better compliance
      and therapeutic alliance, need lower dose meds due to diffs in age, ht and weight, body fat,
      (except pregnancy); concerns about meds during pregnancy, nursing (like Canuso)


C. Racial bias in schizophrenia and mood disorders
   1. Strakowski et al (1993): blacks receive more dx schiz, higher doses antipsychotics
      Record review of 231 public hospital pts

   2. Adibempe (1986); Jones & Gray (1986): earlier reviews; blacks overdx with schiz,
      underdx with mood disorders; whites more likely dx with psychotic mood disorders

   3. Explanations:
      a. social distance: DeHoyos & DeHoyos: admissions notes longer for whites,
         young, middle class, college students - most similar to med students
b. Diffs in sx: blacks more delusions, halluc, paranoia of system, misinterp as paranoid schiz; receive more meds - side effects meds look like neg sx schiz

1) Hanson & Klerman: white clins more accurately perceived dep sx in whites

2) Vitols et al: black pts more dels, halluc; less predictive of psychotic dx; in whites, dels, halluc more associated with schiz

3) Dassori et al (1995)- Hispanics from diff cultural groups showed diff sx patterns; cultural factors affect sx presentation

4) Scott & Gaitz; Welner et al: blacks showed less affect – interp as flat affect

c. Cultural basis for suspiciousness misinterpreted as paranoid (blacks 2x rate of paranoid type)

d. Biased tests:
   1) MMPI-2: Blacks higher on scales 8 and 6
   2) MCMI: Antisocial, Paranoid, Psychotic Thinking

e. Garb (1996)- clinicians have race and sex stereotypes about dtic categories

4. Trierweiler et al., 2000: study of nearly 300 psychiatric pts, mostly African-American
   a. increased diagnosis schiz among African-American pts
   b. increased attributions of halluc, paranoid sx African-American pts
   c. increased attributions of dysphoria, elevated mood (and w/ negative sx) non-African-American pts
   d. logistic regression showed differential decision making models for pts based on race
   e. suggests sx are differently weighted in likelihood of dx schiz according to race

   a. examined antipsychotic prescription in >2500 Medicaid pts with schiz for African Americans vs Caucasians

   b. found African Americans prescribed: more traditional antipsychotics, fewer atypicals (newer meds, fewer side effects, more effective tx-resistant schiz, more expensive), more depot meds (long-acting, for non-compliance)

   c. above held up even when control for differences in service use (Caucasians more continuity of care – more frequent, longer term services)

   d. not look at clinical characteristics (could explain some of differences)

6. Lopez et al. (2004): ethnic differences in effect of course, High-EE affect on outcome; need consider cultural diffs in role of family support and influence on course, implications for tx
   a. Mex-Am: family warmth most predictive of course
   b. Euro-Am: family criticism (blame, neg emotions) most predictive of course
IV. Theories of Etiology of Schizophrenia

A. Reading: Jones & Cannon (1998); Kapur (2003); Siever & Davis (2004); also see: Tsuang et al. (2000) and Leung & Chue, 2000

B. Theories of etiology:
1. divided up theories for clarity: nearly everyone recognizes are multiple factors in the etiology of schiz and that schiz is a heterogeneous disorder

2. Current theories: genetic vulnerabilities and biological factors such as viruses result in dysregulation of neurotransmitters, other neuroanatomical abnormalities that interact with each other and with maturation and environmental factors

3. Current theories recognize schiz is a heterogeneous disorder with different factors involved for diff types

C. Biological theories of etiology:
   a. Family studies: 1 parent schiz:10-12%, both schiz:35-45%

   b. Twin studies: concordance (not incidence or prevalence!!) -
      1) Why compare MZ (identical) to DZ (fraternal) twins?
      2) Concordance for MZ 3 x DZ, MZ 35-65 x unrelated persons
      3) Jones & Cannon (1998): all major twin studies show concordance for MZ twins (53%) > DZ twins (15%) – suggest overall heritability estimate of 68% for liability for schiz

   c. Adoption studies:
      1) Wender et al. (1974): cross-fostering: adopted child w/schiz adoptive parents little increased risk of schiz
      2) Slater & Crowe (1971): 65% concordance MZ twins raised apart
      3) Jones & Cannon (1998): several major European studies, all show increased risk of schiz depending on degree of biological relatedness, regardless of degree of contact with the relatives

      4) what do these data suggest about the role of genetics and environment??

   d. Gottesman & Shields (1982)- multifactorial polygenic inheritance model: multiple genes interact to produce a liability, when exceeds threshold, schiz develops (is actually an interactive or threshold model)

   e. little evidence for "sporadic" schiz (no family hx or biological diathesis):
      Gottesman & Bertelson (’89): healthy twin passes genetic contribution to offspring

   f. currently recognize the role of multiple genes in combination; also recognize environmental factors important – if all genetic, what would concordance rate be for identical twins?

   g. Stress diathesis models: polygenic inheritance of vulnerability to schiz with associated neuropsych deficits, interact with environment, maturation to -> schiz
1) Meehl’s (1967) schizotaxia model

2) Tsuang et al. (2000): also proposes a schizotaxia model: inherited vulnerability to schiz (neg sx, neurocognitive deficits)

3) Jones & Cannon (1998): schizotypy (like schizotypal pers dis) not schizophrenia is inherited based on linkage (within family) and association (across family) studies; genetics about 70%, environmental about 20-30%

4) Siever & Davis (2004): also focus on schiz spectrum, especially genetic relationship schizotypal pd and schiz; hypothesize that psychotic sx (positive sx) and deficit sx (negative sx and cognitive impairment) have independent heritability in development of schizotypal pd and schiz

2. Biochemical (neurotransmitters)

a. Dopamine theory: increased DA receptors or sensitivity to DA; drug evidence:

   1) amphetamines: release DA -> cause or exacerbate psychosis

   2) antipsychotics: block DA receptors -> reduce sx; some evidence D2 receptors involved; however, mostly help positive sx, not all pts improve (suggesting what??)

   3) DA theory may be more applicable for type I (positive sx) than type II (negative sx or deficit type)

   4) site of DA receptor abnormalities: hypothesized in striatem/nucleus acumbens and limbic connections (part of neuroanatomical models)

   5) Kapur (2003): role of DA in increased salience of stimuli, cognitions, results in delusions; links biology with phenomenology; antipsychotics reduce saliency of the stimuli

b. serotonin (5-hydroxytryptamine or 5-HT): long speculation involved;

   1) newer atypical antipsychotics act on 5-HT

   2) functional relationship with dopamine - if block 5-HT receptors can modify DA levels in certain brain regions

   3) recognizing interconnection these neurotransmitters

c. GABA (gamma amino butyric acid): some suggest GABA involved; part of some neurodevelopmental models

3. Structural and Other Neuroanatomical Theories: focus on structural CNS abnormalities; link to CNS insult and/or genetic predisposition and neurotransmitters; recognize interaction with development, environment; support for these theories: neurological, physical, cognitive deficits, imaging and psychophysiological studies

a. Subtle neurological abnormalities: EEG, neurological, physical: provide support

b. L Hemisphere prob: abnormal L EEG and L perf; schiz L handed: sugg lateralized deficits
c. pre-frontal cortex (PFC): considerable evidence of impairment in PFC:

1) impairment in cognitive tasks requiring PFC: attention, abstraction, problem solving, lang, also see in relatives of schiz (milder) suggesting genetic basis

a) Green (1996) review - schiz have widespread cognitive deficits: need look at more specific deficits to predict outcome, need to address in cognitive remediation:

1> verbal memory most associated with outcome
2> vigilance (attention) associated with social problem solving and skill acquisition
3> deficiencies act as “neurocognitive rate limiting factors” in outcome

b) Spaulding et al. (1999): gross cog deficits associated with the acute phase but can use cog assessment to predict post-acute and chronic functioning

1> some aspects of cog funct improve over time even during post-acute phase
2> lateralized deficits in schiz: however, vary: suggets is heterogeneous group
3> pts with L lateralization poor outcome
4> 2 factors in analysis of cog deficits of schiz: verbal and spatial processing; are inversely related - improvement in one assoc with none in other
5> cog tx may have benefits beyond behavioral and other standard techniques

c) Siever & Davis (2004): similar cog deficits schiz and relatives or schizotypals suggest frontal and temporal lobe dysfunction: working memory, episodic (verbal) memory, executive functioning (reviews studies using Wisc Card sort, other neurocog tasks) but schizotypal less than schiz

2) Imaging studies (and post-mortem) suggest reduction in prefrontal cortex and/or enlarged ventricles: cortical atrophy CT

a) however: 1/4 schiz not have, is small reduction in size cortex in schiz

b) Chua & McKenna (1995); Weickert & Kleinman (1998): conclude is the consistent neurological finding, but Jones & Cannon (1998) suggest highly inconsistent findings

c) Some suggs may pertain more to type II schiz (negative sx or deficit type)

d) May be a consequence of schiz (a marker not cause), or tx, or other factors

e) Siever & Davis (2004):

1) structural imaging suggest temporal, frontal lobes impaired in schiz: Increased CSF, reduced volume; also the striatum (DA) and thalamus (higher level integration) affected

2) functional imaging: PET and SPECT (computer tomography): looks at blood flow, glucose usage during cognitive tasks; supports PFC involved in schiz


3) Psychophysiology:
   a) Andreasen (1998): researchers still looking for the fundamental cog processing
deficits in schiz: P50 studies (evoked brain wave reflecting attention, abnormal
suppression of distracting stimuli), eye tracking studies: abnormal for schiz
spectrum pts and relatives of schiz; may be markers for schiz

   b) Siever & Davis (2004): review research on backward masking tasks, failure of P50
suppression (ability to modulate sensory stimuli to prevent sensory overload and cog
disorganization), pre-pulse inhibition (ability inhibit startle response), P-300 evoked
potentials, attention and CPT: some heritable, see with schiz, their relatives, schizotypal;

d. Obstetric Complications frequently found in schiz (Zomberg et al., 2000) (also sex
differences discussed earlier)
   1) Jones & Cannon (1998): 2-9% of schiz liability due to various pregnancy
and birth complications (fetal hypoxia); might interact with genetic liability

   2) maternal influenza (and winter pregnancies) and schiz and schiz spectrum

e. Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis
   a) due to increased maternal stress resulting in increased release of cortisol
and hippocampal dysplasia (abnormal cells);

   b) Walker’s neurodevelopmental model: HPA dysregulation interacts with
maturation

f. Integrative Models of Neurotransmitters/Structural/Physiological Deficits

   1) Weickert & Kleinman (1998): hypofrontality (abnormality in prefrontal cortex)
(PFC) may relate to neurotransmitters:
   a) altered GABA and its regulating enzyme (GAD)

   b) abnormal glutamate neurons of PFC

   c) abnormal pre-and post-synaptic serotonergic transmission (because
clozapine [atypical antipsychotic] acts on serotonin as well as DA)

   d) also abnormal D2 receptors

   e) focus is on neuroanatomy (striatum/nucleus acumbens, limbic connections, PFC) but
problem is neurochemical - D2, GABA, glutamate, serotonin receptors

   f) recognizes interaction between anatomy and neurochemistry: most modern
theories comprehensive

   2) Neurodevelopmental models (e.g., Walker’s): lesion (due to toxins, genetics, injury,
infection, virus, in limbic system and prefrontal cortex (PFC), that remains inactive until
maturation (Walker); actually an interactive model (CNS abnormalities interact with
environment, maturation)

   3) Woods (1998) found support for a progressive developmental disorder model in which
developmental mechanism (apoptosis, pruning) go awry (as opposed to prenatal
developmental abnormalities or a neuro-degenerative model)
4. Summary of Biological theories:
   a. Most are actually theories of vulnerabilities to schiz, not the cause of schiz; similar milder
deficits in schizotypal and unaffected relatives of schiz
   b. Etiology may depend on the subtype (although findings mixed):
      1) Type I (positive sx): more associated with neurochemical dysfunction - DA;
      2) Type II (negative sx): more associated with structural - enlarged ventricles
      3) Siever (1994): deficit type (negative sx) associated w/ abnormal brain structure;
alteration in DA assoc w/ psychotic (positive) sx
   c. Most recognize the interaction of biological vulnerability (especially genetic) with
environment, and the interaction of neuroanatomy, neurotransmitters and
development

C. Psychological theories
   1. Generally older theories, less support; now recognize is a biological component;
however, familial factors (apart from genetics), stress interact with biological predisposition; purely
psychological causes unproven, few advocate today
   2. Psychoanalytic: failure form bond, trust between mother and child;
      Also, schizophrenic (Arieti, Frank, Fromm-Reichman): Little support for this older theory!
   3. Family/systems theories: also older theories; recognize need a broader approach
      a. Communication problems: are older theories - been revised to high EE theory
         1) Jackson & Haley: communication is paradoxical, contradictory
         2) Wynne & Singer (1965): communication is ambiguous or fragmented
         3) Laing (1965) - same as above plus mystification (denial of the child's
thoughts and feelings)
         4) Rund (1995) found communication problems in parents of schiz
      b. Role distortions: Lidz - schism and skew: also an older theory
      c. High expressed emotion: newer version of family theories: more a theory of
relapse and prognosis than cause of the disorder: more support than earlier theories:
         1) Wing (1972): high EE 50-60% relapse
         2) Weisman et al (1993): HEE families blame the pt
         3) Leff et al (1982); Penn & Mueser (1996): tx helps reduce high EE and relapse
         4) Giron and Gomez-Beneyto (1998): family’s lack of empathy related to
increased pt relapse over 2 year study
         5) Lopez et al. (2004): need consider culture: warmth (positive outcome Mex-Am) vs
blaming/criticism (negative outcome Euro-Am): high-EE more relevant for Euro-Am

4. Behavioral theory: also, more a theory of maintenance and exacerbation of sx rather
   than etiology or cause:
   a. social learning (poor role models)
   b. classical and operant conditioning: attention for bizarre behavior or poor social
skills results in little success, withdraws
5. Theories of Social factors: poverty, low SES, low education; cause vs social drift
   a) Jablensky & Kalydjieva (2003): relationship of schiz to urban setting; problem: multiple variables: DK if psychosocial, biological/environmental exposure
   b) also related to immigration

6. Negative life events (Ventura et al. 1989) assoc w/relapse; actually an interactive theory (in vulnerable individuals)

7. Existential: Schizophrenia (or actually psychosis) is a way of coping with an unreasonable environment: not a widely accepted theory

8. Overall: evidence for psychological factors – especially the role of HEE, stress, negative life events, social factors contribute to development of schiz, course, outcome, but not necessary or sufficient to cause schiz: suggest interactive theories

D. Interactive theories: vulnerability and stress-diathesis
   1. biological + psychological factors both contribute to disorder; biological can be environmental as well as genetic, neurochemical and neuroanatomical; most current theories recognize is complex

   2. Meehl's (1962) schizotaxia theory: schizotaxia, not schizophrenia inherited, called a schizotype - has inherited basic neurological deficit that makes prone to schiz) schiz only develops depending on stress, environment); 1st of these theories


   4. Zubin & Spring's (1977, 1987) vulnerability model: biological + psych factors determine vulnerability; interacts with environment, the more vulnerable, the less stress needed to develop schiz

   5. Liberman et al. (1989) stress diathesis approach: biol + psych vulnerability + stress -> sensory overload, onset of psychosis or relapse unless treated

      a) combination of genetic (multiple genes) + environmental factors results in liability for schiz
      b) Genes can be specific to schiz or nonspecific and general (acts as modifying factor - e.g., risk for depression); environmental factors general liability
      c) liability normally distributed; when liability exceeds threshold, develop schiz

      a) elaboration of Walker's Neurodevelopmental model
      b) as a result of hypothalamic-pituitary-adrenal (HPA) axis hyperactivity, there is increased vulnerability to environmental stimuli and stress: are overwhelmed by stimuli, more vulnerable
8. **Jones & Cannon (1998):** Genetic liability for schizotypy interacts with developmental and environmental events (see table in article)
   a) schizotypy: inherited neurological defect, associated cognitive difficulties
   b) genetics – about 70% of liability for schiz; rest, environment
   c) environmental factors:
      1) pre- and peri-natal events such as hypoxia, maternal influenza,
      2) season and place of birth
      3) childhood developmental delay, CNS
      4) older: heavy marijuana use, immigration

9. **Tsuang et al. (2000):** schizotaxia model:
   a) views psychosis as a dimension across diagnostic categories; end state
   b) Meehl’s schizotaxia: inherited vulnerability to schiz
   c) defines schizotaxia by: neg sx, neuropsychological deficits
   d) study of schiz spectrum, and specifically individuals with schizotaxia needed to tease out genetic, physiological basis of schiz

11. **Siever and Davis (2004):** schiz spectrum model:
    a) uses studies of genetics, psychophysiology, cognitive/neuropsych, structural and functional imaging, neurochemical to support spectrum relationship for schiz
    b) schiz and schizotypal pd share common genetics that result in temporal cortex vulnerable to insults
    c) other genetic and/or environmental factors buffer schizotypal pd from loss of frontal volume and subcortical sensitivity to DA to lessen vulnerability
    d) schizotypal: increased frontal reserves, more resistant to temporal lobe abnormalities; use compensatory mechanisms; (e.g., higher intelligence)
    e) both schiz and schizotypal have abnormalities in thalamic nuclei, but PFC abnormalities primarily in schiz
    f) buffers that protect schizotypal: increased PFC capacity and therefore able to compensate, reduced subcortical responsiveness to DA, better striatal modulation of DA
V. Treatment of Schizophrenia

A. Reading: APA Practice Guidelines (2004); Rivas-Vazquez et al. (2000); Bustillo et al. (2001); Hogarty et al. (1995); Lewis (2004)

B. Biological treatments: APA (2004); Rivas-Vazquez et al. (2000)

1. Traditional antipsychotic medication (see Table 3)
   a. Mechanism of action:
      1) Dopamine antagonists: have an affinity for, bind to, or block D_2 receptors:
         thought to result in overall decrease at dopamine receptors (D_1-D_5)
      2. Atypical (newer) antipsychotics also affect serotonin receptors (5-HT_2A)
         which affect dopamine certain parts of brain (different 5-HT receptors
         increase, decrease dopamine)

   b. Effects of traditionals: agitation 1st, del/halluc next; neg sx last (if at all)

   c. treatment strategies: 6 wk trial; 6 mo-1 yr after sx respond

   d. Hogarty et al. study of effectiveness & relapse (up to 68% relapse within 1 yr)

   e. Gilbert et al ('95): relapse when dc antipsychotics: 3xs higher relapse (sooner) if
      DC meds; more so for men, nonparanoid, young, poorer social skills, on higher
      dose

   f. Equipotent doses (see Table 3): supposed to be equally effective, but are not –
      some pts respond better to certain antipsychotics

   g. Side effects (see DSM-IV Ch: “Other Conditions...” codes for med side effects)
      1) Low potency agents (chlorpromazine):
         a) Anticholinergic - autonomic NS, dry mouth, constipation etc.
         b) Antihistaminic - sedation, weight gain
         c) Anti-α-adrenergic: orthostatic hypotension (faint when stand up)

      2) High potency agents (haloperidol):
         a) Extrapyramidal (EPS) - extrapyramidal tract - smooth muscle movement;
            neg r w/ Anticholinergic side effects because requires a balance between
            dopamime and acetylcholine; more with high potency meds; restless, muscle stiffness;
            b) acute dystonia severe type

      3) Tardive dyskinesia (10-40% mild sx 2 yrs use): movements mouth, hands
         a) Kane & Smith, 1982: 15% with chronic use
         b) Robinson et al., 1986: 41% chronic schiz some TD
         c) Andreasen (1998): typical antipsychotics increase basal ganglia: may
            relate to TD

   4) Neuroleptic malignant syndrome: 1%, 20% fatal, usually in older pts and those
      with medical problems

   5) Debate over longterm maintenance on antipsychotics
Table 3
Antipsychotic Medications

I. Therapeutic Equivalents of Common Traditional Antipsychotics

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Equipotent Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thorazine</td>
<td>Chlorpromazine</td>
<td>100mg</td>
</tr>
<tr>
<td>Mellaril</td>
<td>Thioridazine</td>
<td>100mg</td>
</tr>
<tr>
<td>Loxitane</td>
<td>Loxapine</td>
<td>15mg</td>
</tr>
<tr>
<td>Navane</td>
<td>Thiophthixene</td>
<td>5mg</td>
</tr>
<tr>
<td>Stelazine</td>
<td>Trifluoperazine</td>
<td>5mg</td>
</tr>
<tr>
<td>Haldol</td>
<td>Haloperidol</td>
<td>2mg</td>
</tr>
<tr>
<td>Prolixin</td>
<td>Fluphenazine</td>
<td>2mg</td>
</tr>
</tbody>
</table>

II. Profile of Side-Effects for Selected Traditional Antipsychotics

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>BP</th>
<th>EPS</th>
<th>Sedation</th>
<th>Anticholinergic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haldol</td>
<td>LOW</td>
<td>HIGH</td>
<td>LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>Loxitane</td>
<td>LOW</td>
<td>LOW</td>
<td>LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>Navane</td>
<td>LOW</td>
<td>HIGH</td>
<td>LOW/LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>Prolixin</td>
<td>LOW</td>
<td>HIGH</td>
<td>LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>Stelazine</td>
<td>LOW</td>
<td>HIGH</td>
<td>LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>Trilafon</td>
<td>LOW</td>
<td>HIGH</td>
<td>LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>Mellaril</td>
<td>LOW</td>
<td>LOW</td>
<td>HIGH</td>
<td>HIGH</td>
</tr>
<tr>
<td>Thorazine</td>
<td>LOW/HIGH</td>
<td>LOW</td>
<td>HIGH</td>
<td>LOW</td>
</tr>
</tbody>
</table>


a. definition of atypical: more serotonin (5-HT$_{2A}$) effects, also blocks D$_2$ but less than 5-HT or traditional meds: therefore lower EPS and other side effects, more effect on neg sx than traditional, may help make more amenable to other tx (psychological), may help cog sx more than traditional

b. Specific atypical (also called second generation) antipsychotics:

1) Clozapine (Clozaril): First, introduced 1989
   a) high 5-HT$_{2A}$ and lower D$_2$ (affinity for D$_2$, other receptors)
   b) 30% drug resistant pts improve, fewer side effects
   c) expensive monitoring
   d) side effects: agranulocytosis: suppress production WBC

2) Risperidone: (Risperdal) Janssen, 1994
   a) high 5-HT$_{2A}$ and lower D$_2$ (but higher than Clozaril) (also affinity for other receptors)
   b) for drug resistance pts, relatively fewer side effects (although high EPS, other sx at high doses)
   c) Mander & Meibach (’94) reduces + and - sx of schiz

3) Olanzapine (Zyprexa) - Eli Lilly, 1995
   a) high 5-HT$_{2A}$ and relatively high D$_2$ (higher than clozapine)
b) may help drug resistant pts, also helps with compliance because few side effects

4) Quetiapine (Seroquel) - most recent, 5-HT_{2A} > D_{2}
   a) somewhat more side effects
   b) may need higher dose because of lower dopamine effect

5) Others:
   a) Ziprasidone (Zeldox) - Pfizer, 1996, potent 5-HT_{2A} binding, moderate D_{2}
   b) Serindole (Serlect): also potent 5-HT_{2A} binding

6) advantages:
   a) better compliance, since fewer side effects and broader tx effect
   b) helps with neg sx
   c) helps with cognitive sx, cognitive functioning (Harvey & Keefe, 2001)
   d) better able cooperate with tx programs; may improve insight
   e) more expensive in the short-term, less in the long term since reduce rehospitalization
   f) Andreasen (1998): opposite effect basal ganglia than typicals (why less TD)

3. Compliance and decanoates: long-standing problem; depot forms several antipsychotics

4. Adjunctive medications - lithium, benzodiazepines, antidepressants and MAOIs

5. ECT - electroconvulsive therapy; effective, use with antipsychotics, but high rate relapse

C. Psychological treatments: increasingly seen as useful – especially multimodal approaches (e.g., personal therapy, assertive community therapy), cognitive-behavioral, family therapy, and supportive employment

1. Individual therapy:
   b. Glass et al. (1988)
   c. Treatment recommendations (shorter, more frequent sessions; focus on reality testing; later, education about disorder; help with compliance and recog of relapse; avoid intensive uncovering therapies - can lead to deterioration effects)
   d. Used as part of the multimodal treatments (e.g., personal therapy)

2. Group therapy
   a. Traditional/Yalom group, deterioration effects
   b. Educational, supportive
   c. Social skills training (Eisler et al.): effective for specific behaviors, problems with generalization; best if target: simple behaviors, use overlearning, needs modeling; Mueser et al (’95): long term, linking to external contingencies in environment more effective
3. Family therapy:
   b. Goldstein & Miklowitz ('95): fam th+meds>meds alone
   c. help family increase understanding of dx, reduce family stress, provide support, teach management skills, recognition of relapse
   d. 1-2 yrs; with medication, other resources - OT, RT, VR


5. Token economies - operant conditioning; usually with above, in therapeutic communities

   a) social skills training effective for specific behaviors
   b) family therapies good for high EE families, prevent relapse
   c) cognitive therapy:
      1) process approach: focus on cognitive processes: cog rehab- results unclear, needs further research
      2) content approach: changing responses to content dysfunction (e.g., pt's responses to delusions, hallucinations)

7. Bustillo et al. (2001): update on psychosocial tx: research since Penn & Meuser
   a) family therapy: positive results for preventing relapse and rehosp, no effect other outcome (social function, employment) or positive or negative sx; concluded should be made available most pts
   b) assertive community tx: same as family therapy; recommended for pts w/ frequent relapse, without family support
   c) social skills training: improve social skills, not prevent relapse, not help other sx, not help with competitive employment; may improve adaptive functioning
   d) cognitive behavior therapy (content approach): improves psychotic sx: delusions, hallucinations
   e) supportive employment progs (place and train models): helps obtain competitive employment; rapid placement with ongoing support, for those who want to work
   f) Hogarty's Personal Therapy: preliminary evidence improves social functioning

8. Lewis (2004): psychotherapy to increase insight but reduce suicidal risk
   a) proposes that hopelessness and pessimism, not realistic insight assoc with SI
   b) therapy can be used to increase insight while maintaining hope
D. Combined Treatments: Liberman et al (1989) - additive effects of psychotherapy and medication

1. **Hogarty’s Personal Therapy**: multimodal approach: Hogarty et al. (1995)
   
   a) emphasizes tx according to stage of illness
   
   b) importance of helping with affect dysregulation (loss of control or regulation of mood): promotes awareness, addresses coping styles, probes current affect
   
   c) Educational: recognizes neuropsychological/cognitive deficits, directive
   
   d) Structure the environment
   
   e) Works with medical – use minimally effective dose of meds (reduced side effects that impair functioning, increase compliance)


1. Phases of disorder and treatment:
   
   a) **Acute**: assessment (reason for relapse, SI, medical), choice of tx: antipsychotics and adjunctive meds (decision tree figure to help); psychosocial: reduce stimulation and stress - structured environment; goals: rapidly reduce sx and return to functioning
   
   b) **Stabilization**: continue to reduce sx: meds at dose for > 6 mos, reduce stress, psychosocial: less structured, education for pt and family, help adjust to community
   
   c) **Stable**: ongoing assessment, psychiatric management, antipsychotics - balancing side effects w/ preventing relapse; psychosocial tx: family, supported employment, social skills, assertive community

2. Issues to consider: rapport, education, tx adherence, family, psychosocial approaches

3. Traditional vs new antipsychotics (olanzapine)

4. Relevant clinical features to consider
   
   a) subtypes, deficit (negative) sx
   
   b) substance use and related disorders: nearly ½ of schiz (harm reduction, abstinence, relapse prevention, rehab)
      
      1) Akerele & Levin (2002): high rate of alcohol and other sub abuse schiz, esp men
      
      2) hypothesize are self-medicating due to reduce DA in parts of PFC associated with neg sx and resulting anhedonia; schiz may use substances to increase DA, but this increases positive sx
      
      3) Smoking also reduces neg sx, increases positive sx
      
      4) May be genetic basis to affect of nicotine on brain in schiz and relatives that interacts with DA abnormalities
   
   c) depression: in acute phase: usually improve with antipsychotics; if pervasive or late phase (post-psychotic dep of schiz) use antidepressants
   
   d) suicide risk: increase frequency of visits, monitoring for signs
e) aggressive behaviors: minority of schiz

f) demographic factors:
   1) gender and pregnancy and meds
   2) age: 20% late onset (>40) and small % very late onset; also effects/side effects meds with older pts
   3) cultural and race: effects dx, tx, metabolism meds
   4) homelessness and outreach efforts
VI. Overview of Other Psychotic Disorders

A. Reading: Maxmen Ch 9; Kendler & Walsh, 1995; Sanjuro-Hartman et al. (2001); Fear & Libretto (2002)

B. Schizophreniform: sx >1 mos but less 6 mos; sx like schizophrenia
   1. better prognosis:
      b. Coryell & Tsuang (1982) worse prognosis than brief psychotic, more than 1 mo associated with poorer prognosis
      c. 1/2-1/3 ->schiz; 1/3-1/2 ->recover

   2. Kendler & Walsh (1995): family hx schiz but less than for schiz pts

   3. Acute onset; emotional turmoil/mood sx

   4. Same tx schiz

   5. Strakowski (1994)
      a) heterogeneous dx: includes new onset schiz, schizoaffective, atypical mood disorder, remitting nonaffective psychosis (intended meaning)
      b) limited usefulness; use NOS instead


C. Brief psychotic disorder - < 1 mo
   1. often in response to stressor, rapid onset

   2. sx: confusion/perplexity; aggressive, SI, labile

   3. predisposing: personality dis (erratic, possibly odd/eccentric cluster); young

   4. tx: structure w/ no meds or short term meds

D. Schizoaffective disorder - both psychotic and mood sx
   1. Schiz + mood sx concurrent, both prominent (not postpsychotic depressive disorder of schiz);

   2. no period mood sx without psychotic sx (not mood dis w/ psychotic features) but at least 2 weeks schiz sx without mood sx


   4. subtype of schizophrenia: Bleuler (1920); Coble (1953), DSM-II (1968)

   5. Models of schizoaffective disorder (See Table 4)
6. Depressed vs bipolar types
   a. schizodepressed: later onset; worse prognosis, variable course, fam hx schiz
      tx: antipsychotic plus antidepressant; Keck et al (1996)-risperidone
      particularly effective (perhaps serotonin =DA??); also ECT
   b. schizomanic: younger onset, more women; better prognosis; fam hx mood disorder
      tx: antipsychotics plus lithium

Table 4  
Models of Schizoaffective Disorder

<table>
<thead>
<tr>
<th>Theory</th>
<th>Schizophrenia</th>
<th>Mood Disorder</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>subtype schizophrenia</td>
<td>X</td>
<td></td>
<td>Older, fam hx schiz, poor outcome</td>
</tr>
<tr>
<td>subtype mood disorder</td>
<td></td>
<td>X</td>
<td>Newer, fam hx mood dis, good outcome, r</td>
</tr>
<tr>
<td>in between</td>
<td></td>
<td>X</td>
<td>Fam hx both, outcome in between, r to</td>
</tr>
<tr>
<td>both</td>
<td>X</td>
<td>+</td>
<td>antidep, lithium, antipsych</td>
</tr>
<tr>
<td>heterogeneous:</td>
<td>X</td>
<td></td>
<td>same as above</td>
</tr>
<tr>
<td>schizodepressed</td>
<td></td>
<td>X</td>
<td>fam hx schiz, poor outcome, antipsychotics</td>
</tr>
<tr>
<td>schizomanic</td>
<td></td>
<td></td>
<td>fam hx mood dis, good outcome, lithium</td>
</tr>
<tr>
<td>not exist</td>
<td>X</td>
<td>OR</td>
<td>really schiz or mood disorder, misdx'ed</td>
</tr>
</tbody>
</table>

E. Delusional disorder - only delusions, nonbizarre (much of research outside of US)

1. later onset; women; immigrants and low SES

2. Kendler & Walsh (1995)- small number of pts, no family hx schiz their study

3. Manschreck: later onset women, poss familial, diff tx; not as resp to antipsychotics
   as schiz - resistant to therapy because unaware of problem

4. Monro & Mok ’95 agree but sugg good tx resp to pimozide (Opler et al, 1995);
   Others less positive result (Silva et al., 1999)

5. Resp to atypical neuroleptics: clozapine, risperidone (Songer & Roman, 1996;
   Buckley et al, 1994)

6. Wada et al. (1999): response to clomipramine (antidepressant) in pimozide-
   resistant pts with somatic type of DD; hypotheses??

7. Serretti et al. (1999): factor analysis sx of 108 pts with DD; sugg heterogeneous
   disorder; found 4 independent factors: depressive sx, hallucinations, delusions, irritability

8. Yamada et al. (1998): type depends age of onset: persecutory - oldest,
   somatic type - youngest onset

F. Shared psychotic disorder (induced psychotic, shared paranoid, folie a deux)
1. Glassman et al. (1987) - folie a famille case

2. Rare, possibly women, MR and demented, impressionable, original one w/ delusion is dominant personality; adverse social/environmental circumstances; family hx of disorder

3. Harmon & Rames ('94): twins, twin who developed it had Histrionic pd

4. Goldman et al ('92): son from mother; mother dominant; tx antipsychotics

5. Dippel et al (1991) folie a six: persecutory delusions in women spread to husband, 2 sons, sister-in-law, nephew; woman very dominating; no family hx (unusual)


G. Substance induced and due to a general medical condition
1. Temporal relationship; conforms to known effects of substance, medical condition

2. Atypical presentation: sx, course, absence of family hx

3. Opler et al ('95): tx underlying condition (cause)