Schizophrenia and Other Psychotic Disorders II
## Table 13.3
COMPARISON OF BRIEF PSYCHOTIC DISORDER, SCHIZOPHRENIFORM DISORDERS, AND SCHIZOPHRENNIA

<table>
<thead>
<tr>
<th></th>
<th>BRIEF PSYCHOTIC DISORDER</th>
<th>SCHIZOPHRENIFORM DISORDERS</th>
<th>SCHIZOPHRENIA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration</strong></td>
<td>Less than one month</td>
<td>Less than six months</td>
<td>Six months or more</td>
</tr>
<tr>
<td><strong>Psychosocial Stressor</strong></td>
<td>Always present</td>
<td>Usually present</td>
<td>May or may not be present</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>Emotional turmoil; psychotic symptoms</td>
<td>Emotional turmoil; vivid psychotic symptoms</td>
<td>Emotional reactions variable; hallucinations</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Return to premorbid level of functioning</td>
<td>Possible return to earlier, higher level of functioning</td>
<td>Return to earlier, higher level of functioning is uncommon</td>
</tr>
<tr>
<td><strong>Familial Pattern</strong></td>
<td>No information; possible relationship to mood disorder</td>
<td>Possible increased risk of schizophrenia among family members</td>
<td>Higher prevalence of schizophrenia among family members</td>
</tr>
</tbody>
</table>
Prevalence and Cause of Schizophrenia

- **Prevalence = 1%**,  
  - 2% in urban environments

- **Course = Chronic**  
  - Moderate-to-severe lifetime impairment  
  - Life expectancy = less than average  
    - Suicide

- **Female : Male = ~1:1**  
  - Females  
    - Later age of onset  
    - Better outcomes
Prevalence and Cause of Schizophrenia

• Development
  – Early childhood clinical features
    • Mild physical abnormalities
    • Poor motor coordination
    • Mild cognitive problems
    • Social problems
Prevalence and Cause of Schizophrenia

• Development (cont.)
  – Diagnosis and treatment typically occur 1-2 years after symptom onset
  – Relapse and recovery
  – Most (78%) experience several episodes
  – Poor overall prognosis
  – High suicide rates- 10-15% completed suicides
Prevalence and Cause of Schizophrenia

• Cultural Factors
  – Does schizophrenia even exist?
    • Label for difficult, unusual people
  – Worldwide prevalence is similar
    • Course and outcomes are different
  – Higher prevalence in African Americans (U.S.)
    • Misdiagnosis
    • Bias and stereotyping
Neural Diathesis-Stress Model of Psychotic Disorders

- Inherited Constitutional Factors
- Acquired Constitutional Factors
- Stress (e.g., Life events/EE)
- Neuromaturational Processes
- Constitutional Vulnerability
- Psychotic Outcome
Causes of Schizophrenia: Genetic Influences

- **Twin Studies**
  - Genian quadruplets
    - Same genetics and environment (general)
    - Differences:
      - Ages of onset
      - Symptoms
      - Diagnoses
      - Courses
      - Outcomes

- **Importance of unshared environments**
Genetic and Environmental factors

Effects of genetic risk and family functioning on eventual schizophrenia-spectrum disorders

% of sub-sample

- High-risk, spectrum*: 5.8
- Low-risk, spectrum**: 4.8

Legend:
- Low OPAS ratings
- High OPAS ratings

*p < 0.001
**p = 0.582

Tienari, et al, BJM, 2004
Causes of Schizophrenia: Genetic Influences

- Adoption Studies
  - **Increased risk for children of biological mothers**
    - Schizophrenia = 5-fold increase
    - Schizophrenia or related disorder = 22-fold increase

- Offspring of Twins

MRI scans of 28-year-old male identical twins showing the enlarged brain ventricles in the twin with schizophrenia (right) compared to his twin (left).
Causes of Schizophrenia: Genetic Influences

- People with schizophrenia
- Relatives of people with schizophrenia who exhibit schizophrenia spectrum disorders
- Relatives of people with schizophrenia who do not exhibit schizophrenia spectrum disorders
- People who exhibit schizophrenia spectrum symptoms in the absence of a family history of psychotic illness
- People who do not exhibit schizophrenia spectrum symptoms and do not have a family history of psychotic illness
The accepted criteria that a biomarker must fulfill to be called an endophenotype include:

- The endophenotype is associated with illness in the population.
- The endophenotype is heritable.
- The endophenotype is primarily state-independent (manifests in an individual whether or not illness is active).
- Within families, endophenotype and illness co-segregate.

Endophenotypes
- Genes related to basic disruptive processes
  - Smooth-pursuit eye movement
    - Tracking deficits
  - Emotion identification
  - Sensory filtering
Causes: Neurobiological Influences

• The Dopamine Hypothesis
  – **Agonists**
    • Increase schizophrenic-like behavior
  – **Antagonists**
    • Reduce schizophrenic-like behavior

– Ex: Neuroleptics, L-Dopa, amphetamines
DOPAMINE HYPOTHESIS

Normal

Untreated

With medication

Neural Signal

Synapse

Neuro-Receptor

D D D

M M

D D D

M M

D D D

M M
Causes: Neurobiological Influences

- The Dopamine Hypothesis (cont.)
  - Overly simplistic
  - Problematic
    - Antagonists don’t always work
    - Slow response to meds
    - Little impact on negative symptoms
Causes: Neurobiological Influences

- **Current Theories**
  - Several neurotransmitters
  - Striatal $D_2$ receptors (excess) = too much DA received
  - Prefrontal $D_1$ receptors (deficit) = too little DA received
  - Glutamate (fast excitatory neurotransmitter)
    - drugs PCP and Ketamine act by inhibiting NMDA receptors (no direct effect on DA).
    - Because this causes delusions and hallucinations, it is believed that schizophrenia reflects diminished activation of NMDA receptors in the brain.
    - Mouse models: mice with diminished NMDA receptors sow altered social interactions, agitation and repetitive behaviors.
Causes: Neurobiological Influences

- **Brain Structure**
  - Enlarged ventricles
  - **Hippocampus volume** ↓
  - Reduced tissue volume
  - **Hypofrontality**
    - Dorsolateral prefrontal cortex
    - Low Dopamine activity in the front
Causes: Prenatal and Perinatal Influences

• **Viral Infections**
  – Influenza

• **Pregnancy complications**
  – Bleeding
  – Rhesus incompatibility

• **Delivery complications**
  – Anoxia

• Likely interact with genetics and environment
Causes: Psychological and Social Influences

- **Stress**
  - Activates vulnerability
  - Increases relapse risk

- **Family Interactions: Expressed Emotions (EE)**
  - Ineffective communication
  - High expressed emotion
  - Criticism, hostility, intrusiveness
  - Related to relapse risk
Cannabis

- Increases risk for developing Psychosis if you have a vulnerability (think: diathesis stress model)-
- Associated with earlier onset.
Review on Causes for Exam

• Genes
  – The more related you are to someone ill, the higher the likelihood
  – Endophenotypes are behaviors that may be used to identify risk genes
• Early prenatal virus in mother, pregnancy complication, birth complication heightens risk
• Enlarged Ventricles
• Dopamine Hypothesis (too much DA in basal ganglia)
• Hypofrontality (too little DA in the frontal cortex)
• Stress
• Family Environment (Expressed Emotion)
• Cannabis
Treatment: Biological Interventions

• Historical Treatments – 1930’s and 1940’s
  – Insulin coma therapy
  – Psychosurgery
    • Prefrontal lobotomies
  – Electroconvulsive therapy
Treatment: Biological Interventions

• **First Generation Antipsychotic Medications (Neuroleptics)**
  – First line treatment
  – Began in the 1950s
  – Decrease positive symptoms
  – Side effects: common, acute, permanent
    • Extrapyramidal
      – Parkinson-like
      – Tardive dyskinesia
  – Compliance problems
  – Doesn’t treat negative symptoms
Psychiatric Beds 1845-1995 in England

- Occupied Beds (000s)

Thorazine
Depot injections

• Administered intramuscularly

• Releases medicine slowly

• **Use for patients who are non-compliant**

• Used to only be available for typicals, but now available for atypicals
Atypical Antipsychotics

• Second Generation Antipsychotics

• Group of unrelated drugs that work differently from typical antipsychotics

• Lower affinity for D2 receptors and greater affinities for other receptors e.g. Serotonin and norepinephrine

• Better at reducing negative symptoms, fewer extrapyramidal side effects (helps additional patients with more negative symptom profiles)
Side effects of Atypicals

- **Metabolic syndrome**
  - Produce weight gain
    - Risk for heart attack!

- **High rates of diabetes**

- **Sedation**
Treatment: Psychosocial Interventions

• **Psychosocial Approaches**
  – Behavioral (i.e., token economies)
    • Inpatient units
  – Social and living skills training = Helps to combat disability
  – Behavioral family therapy = Lower EE
  – Vocational rehabilitation = Having Jobs help them do better all around

• **Necessary adjunct to medication**
Cognitive Remediation

• Developed to “work out” the parts of the brain that are disrupted in schizophrenia

• Patients engage in cognitive tasks (behavioral or computer programs)

• Tasks designed for Traumatic Brain Injury and Learning Disorder cases, not for schizophrenia
Rationale

• Verbal learning and memory disrupted in schizophrenia
  – Abnormalities in fronto-temporal cortical networks during verbal working memory, encoding, and retrieval

• More basic auditory processing also disturbed in schizophrenia, which is crucial for successful verbal learning and memory

• Cognitive training program that targets early auditory processing and verbal working memory
Training

• Set of computer exercises designed to improve speed and accuracy of auditory processing

• Exercises continuously adjust the difficult level, so user always responds correctly 85% of the time

• Correct trials are rewarded with points and animation
Examples:

- Exercise 1: users have to make gradually more difficult distinctions between different auditory frequencies, which are presented at increasing or decreasing time intervals.

- Exercise 2: users have to distinguish between two difficult to distinguish syllables.

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*The learner must perform a time-order judgment task and identify each of two successive frequency modulation sweeps as either “up” (sweep on left) or “down” (sweep on right). Sweep duration and interstimulus interval are modified parametrically as the learner’s performance improves.*
Review for Test

• First Generation Antipsychotics
  – Problems
• Second Generation Antipsychotics
  – Problems
• Depot Injections
• Psychosocial Rehabilitation
  – Token economy
  – Skills training
  – Family therapy
  – Vocational rehab
• Cognitive Remediation
Link

- http://www.youtube.com/watch?v=U6G0ZeoQfg8&feature=related
- http://www.youtube.com/watch?v=BWK3-E-Nqas&feature=related
- http://www.youtube.com/watch?v=loIW49liuV8