Schizophrenia

Dr. Fred Rose

Nature of Schizophrenia and Psychosis: An Overview

• Schizophrenia vs. Psychosis
  – Psychosis – Cluster of disorders; hallucinations and/or loss of contact with reality
  – Schizophrenia – A type of psychosis
• Affects 1 in 100 persons, $65 Billion annually
• Historical Background
  – Emil Kraeplin – 1896; Used the term dementia praecox, focused on onset and outcomes
  – Eugene Bleuler – 1911 he introduced the term “schizophrenia” or “splitting of the mind”
Prevalence of Schizophrenia

- **Prevalence of 1% worldwide**
  - 2 x Alzheimer’s
  - 5 x Multiple Sclerosis
  - 6 x Insulin-dependent Diabetes
  - 60 x Muscular Dystrophy

- **Schizophrenia Is Generally Chronic**
  - Moderate-to-severe lifelong impairment
  - Life expectancy is slightly less than average

- **Equal Gender Distribution**
  - Women - better long-term prognosis
  - Onset differs between men and women

Gender differences in onset of schizophrenia in a sample of 470 patients

Howard et al., 1993
Diagnosis: DSM IV

• Symptoms (2 or more):
  – Delusions (content)
  – Hallucinations
  – Disorganized speech (form)
  – Disorganized or catatonic behavior
  – Negative symptoms (flat affect etc.)

• Social/Occupational Dysfunction

• Duration: 6-months (1 month of symptoms)

• Not caused by substances

• Not Schizoaffective/Mood Disorder

The “Positive” Symptoms

• Active manifestations of abnormal behavior or distortions of normal behavior

• Delusions - 90%
  – Somatic: “Snake living inside my abdomen”
  – Grandeur: “Chosen by God”
  – Persecution: “‘They’ are monitoring me”
  – Manifestations: Thought broadcasting, ideas of reference, thought withdrawal
The “Positive” Symptom Cluster

• **Hallucinations**
  – Sensory events without environmental input
  – Auditory are the most common (can be any sensory modality)
  – Normal volume, known, external, negative
  – Speech vs. auditory processing studies

Some major language areas of the cerebral cortex
The “Negative” Symptom Cluster

• Absence or insufficiency of normal behavior

• Spectrum of Negative Symptoms
  – Avolition (or apathy) – Inability to initiate and persist in activities
  – Alogia – A relative absence of speech
  – Anhedonia – Inability to experience pleasure or engage in pleasurable activities
  – Flat affect – Show little expressed emotion, but may still feel emotion

“Disorganized” Symptoms

• Severe and excess disruptions in:

• Speech
  – Cognitive slippage – Illogical and incoherent speech
  – Tangentiality – “Going off on a tangent” and not answering a question directly
  – Loose associations or derailment – Taking conversation in unrelated directions
“Disorganized” Speech

“I have also killed my ex-wife, [name], in a 2.5 to 3.0 hours sex bout in Devon Pennsylvania in 1976, while two Pitcairns were residing in my next room closet, hearing the event. Enclosed, please find my urology report, indicating that my male genitals, specifically my penis, are within normal size and that I’m capable of normal intercourse with any woman, signed by Dr. [name], a urologist and surgeon who performed a circumcision on me in 1982. Conclusions: I cannot be a nincompoop in a physical sense (unless Society would feed me chemicals for my picture in the nincompoop book).”

“Disorganized” Symptoms

• Affect
  – Inappropriate affect (e.g., crying when one should be laughing)

• Behavior
  – Disruption in goal directed behavior
  – Decline in routine daily functioning
  – Catatonia – Spectrum from wild agitation, waxy flexibility, to complete immobility
Symptoms of Schizophrenia

<table>
<thead>
<tr>
<th>Positive (Type I)</th>
<th>Negative (Type II)</th>
<th>Disorganized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thematic Delusions</td>
<td>Avolition (apathy)</td>
<td>Grossly Bizarre Behavior</td>
</tr>
<tr>
<td>Thematic Hallucinations</td>
<td>Alogia (Poverty of Speech/Content)</td>
<td>Incoherent hallucinations or delusions</td>
</tr>
<tr>
<td>Bizarre Behavior</td>
<td>Anhedonia</td>
<td>Disorganized Affect</td>
</tr>
<tr>
<td></td>
<td>Flat Affect</td>
<td>Disorganized Speech</td>
</tr>
<tr>
<td></td>
<td>Asociality</td>
<td></td>
</tr>
</tbody>
</table>

Lenzenweger, Dworkin & Wethington (1991)

Subtypes of Schizophrenia

• **Paranoid Type**
  – Intact cognitive skills and affect, and do not show disorganized behavior
  – Hallucinations and delusions thematic (e.g., grandeur or persecution)

• **Disorganized Type**
  – Marked disruptions in speech, behavior, affect
  – Fragmented hallucinations and delusions
  – Develops early, tends to be chronic, lacks periods of remissions
Subtypes (cont.)

- **Catatonic Type**
  - Unusual motor responses and odd mannerisms (e.g., echolalia, echopraxia)
  - ? Need for consistency
  - Tends to be severe and quite rare

- **Undifferentiated Type**
  - Symptoms, but don’t meet criteria for another type

- **Residual Type**
  - One past episode of schizophrenia
  - Continue to display less extreme residual symptoms (e.g., odd beliefs)

Problems with Diagnosis

“Schizophrenia appears to be a disorder with no particular symptoms, no particular course, no particular outcome and which responds to no particular treatment” [Bentall, 1990]

- **Heterogeneity of symptoms**
  - Symptoms change as the disorder develops
  - Schizophrenics ‘slip back into reality’

- **Treatment response varies**

- **Is it a unitary disorder?**

- **Is it distinct from normal experience?**
Other Psychotic Disorders

• Schizophreniform Disorder
  — Schizophrenic symptoms for less than 6 months
  — Associated with good premorbid functioning; most resume normal lives

• Schizoaffective Disorder
  — Symptoms of schizophrenia and a mood disorder
  — 10-year outcome better than Schizophrenia (Harrow et al., 2000)

Other Psychotic Disorders

• Delusional Disorder
  — Delusions without other major schizophrenia symptoms
  — May show other negative symptoms
  — Type of delusions include erotomanic, grandiose, jealous, persecutory, and somatic
  — This condition is extremely rare
Additional Disorders with Psychotic Features

- **Brief Psychotic Disorder**
  - One or more positive symptoms of schizophrenia
  - Usually precipitated by extreme stress or trauma
  - Lasts < 1 month

- **Shared Psychotic Disorder**
  - Delusions from one person manifest in another person
  - Little is known about this condition

- **Schizotypal Personality Disorder**
  - May reflect a less severe form of schizophrenia

Genetics Influences

- **Family Studies**
  - Inherit a tendency for schizophrenia
  - Schizophrenia increases risk in other family members

- **Twin Studies**
  - Risk of schizophrenia in MZ twins ranges from 15% to 65%, with an average of 28% (Fuller-Torrey, 1994).
  - Risk of schizophrenia drops to 6% for dizygotic twins

- **Adoption Studies**
  - Risk remains high in adopted children with a biological parent suffering from schizophrenia
Risk of developing schizophrenia

Gottesman, 1991

Genetic Influences (cont.)

• *Summary of Genetic Research*
  – Risk of schizophrenia increases as a function of genetic relatedness
  – Multiple genes involved
  – One need not show symptoms of schizophrenia to pass on relevant genes
  – Schizophrenia has a strong genetic component, but genes alone are not enough
Genetic Influences (cont.)

- Genes scattered 15 of 23 chromosomes have been implicated
- Most important:
  - Neuregulin 1: NMDA, GABA, & Ach receptors
  - Dysbindin: synaptic plasticity
  - Catechol-O-methyl transferase: DA metabol.
  - G72: regulates glutamatergic activity
  - Others: myelination, glial function
- Paternal age: more cell divisions in sperm

Biological Markers

- *Smooth-Pursuit Eye Movement*
  - Tracking a moving object visually with the head kept still
  - Tracking is impaired in persons with schizophrenia, including their relatives
Etiology

- *The Dopamine Hypothesis*
  - Overactivity of dopamine (DA) neurons in the brain causes schizophrenia
The Dopamine Hypothesis

• **Support**
  – Drugs that block dopamine receptors reduce positive receptors
  – Amphetamines, which increase dopamine, create positive symptoms
  – High number of D2 receptors in schizophrenic brains

• **Problems**
  – Dopamine antagonists don’t treat negative symptoms
  – Time lapse - immediately in brain but no improvement for 2 weeks
  – Parkinson’s disease (but…)
    • Substantia-Nigra, Caudate-Putamen - PD
    • Ventral Tegmentum, Nucleus Accumbens, Septal area - Schiz.
  – Neuroleptics increase D2 receptors
  – PET scan studies inconclusive
The Dopamine Hypothesis

• **Revised:**
  – **Overactivity** of dopamine neurons in the mesolimbic pathway may cause positive symptoms.
    • Antipsychotics which block dopamine receptors *lessen* positive symptoms
  – but...

The Dopamine Hypothesis

• **Revised:**
  – **Underactivity** of dopamine neurons in the mesocortical pathway in the prefrontal cortex may cause negative symptoms.
    • Antipsychotics have *little or no* effect on negative symptoms.
Other Neurobiological Influences

- **Structural and Functional Abnormalities in the Brain**
  - Enlarged ventricles and reduced tissue volume
    - Inverse relationship between ventricle size and response to medication
  - Abnormal neural migration
  - Gray matter loss in adolescence
  - Hypofrontality – Less active frontal lobes (a major dopamine pathway)
Enlarged Ventricles in Schizophrenia

Source: Daniel Weinberger, M.D.
(f) Normal control

(g) A patient with schizophrenia

Rate of gray matter loss

Normal adolescents  Adolescents with schizophrenia

Average annual loss

0%  -1%  -2%  -3%  -4%  -5%
Functional changes in brain

• Hypofrontality hypothesis
  – Discordant twins: low frontal blood flow only in affected twin
  – Cognitive Flexibility
    • Schizophrenics can’t shift attn. to other criterion
    • Functional imaging: frontal lobe activity lower at rest, esp. in right hemisphere, does not increase during task.
    • Drug treatment increased activation of frontal lobes
Psychosocial Influences

• **The Role of Stress**
  – May activate underlying vulnerability and/or increase risk of relapse

• **Family Interactions**
  – Families of people with schizophrenia show ineffective communication patterns
  – High expressed emotion in the family is associated with relapse

• **The Role of Psychological Factors**
  – Likely exert only a minimal effect in producing schizophrenia
Gene-Environment Interaction

  - Children of schizophrenic and “normal” mothers adopted out at birth
  - Tracked family communication patterns

<table>
<thead>
<tr>
<th>Schizo. Risk</th>
<th>Communication</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Poor</td>
</tr>
<tr>
<td>Low</td>
<td>Good</td>
</tr>
</tbody>
</table>

- Lowest Impairment!
- High Impairment
- No Impairment

Medical Treatment

- Antipsychotic (Neuroleptic) Medications
  - Dopamine antagonists are often the first line of treatment for schizophrenia
  - Began in the 1950s
  - Most medications reduce or eliminate the positive symptoms of schizophrenia
  - Acute and permanent extrapyramidal and Parkinson-like side effects are common
  - Poor compliance with medication is common
  - Risperdal, Olanzapine are “atypical” neuroleptics with better side-effect profile than “Thorazine”
Psychosocial Treatment

• *Psychosocial Approaches: Overview and Goals*
  – Behavioral (i.e., token economies) on inpatient units
  – Community care programs
  – Social and living skills training
  – Behavioral family therapy
  – Vocational rehabilitation

• *Psychosocial Approaches Are Usually a Necessary Part of Treatment*

Summary

• *Schizophrenia Includes a Spectrum on Cognitive, Emotional, and Behavioral Dysfunctions*
  – Positive, negative, and disorganized symptom clusters

• *DSM-IV-TR Divides Schizophrenia Into Five Subtypes*

• *Other DSM-IV-TR Disorders Include Psychotic Features*

• *Genetic, Biological, and Environmental Causative Factors Have Been Implicated for Schizophrenia*

• *Successful Treatment Rarely Includes Complete Recovery*