Schizophrenia
Schizophrenia: “Positive” Symptoms

- Active manifestations
  - Delusions
  - Hallucinations
- Obvious signs
- Distortions of normal behavior
- Exaggerations or excesses

- 50-70% experience
Schizophrenia: Positive Symptoms

- **Delusions**
  - Gross misrepresentations of reality
  - Disorder of thought content
  - Grandeur
  - Persecution

- Etiological views
  - Motivational
  - Deficit
Schizophrenia: Positive Symptoms

- **Hallucinations**
  - Sensory experience in absence of environmental stimuli or input
  - Can involve all senses
  - Most common: auditory
    - Meta-cognition
    - Own vs. others voice
    - Broca’s area
Schizophrenia: Positive Symptoms
Schizophrenia: **Negative Symptoms**

- **Absence or insufficiency of normal behavior**
- **25% experience**

- **Symptom Cluster**
  - Avolition (or apathy)
  - Alogia
  - Anhedonia
Schizophrenia: Positive Symptoms

Natural history of schizophrenia

Symptoms

- Premorbid: Mild motor, cognitive and social impairments
- Prodromal: Unusual psychotic-like behaviors
- Onset/deterioration: Positive, negative, cognitive, and mood symptoms
- Chronic/residual: Positive, negative, and cognitive symptoms

Stages

- Year: 10
- Year: 20
- Year: 30
- Year: 40
- Year: 50

© Wadsworth, Cengage Learning
Schizophrenia: “Disorganized Symptoms

- Erratic behaviors that affect many domains

- Speech
  - Cognitive slippage
  - Tangentiality
  - Loose associations/derailment

- Inappropriate affect/emotional expression

- Unusual behaviors
  - Catatonia
    - Wild agitation, waxy flexibility, immobility
Schizophrenia Subtypes

- **Paranoid Type**
  - Delusions and hallucinations
    - Grandeur or persecution
  - Intact cognitive skills
  - Intact affect
  - Little to no disorganized behavior

- Best prognosis

- Stronger familial link?
Schizophrenia Subtypes

- **Disorganized Type**
  - Marked disruptions
    - Speech
    - Behavior
  - Flat or inappropriate affect
  - Hallucinations and delusions
    - Fragmented
  - Develops early
  - Chronic
  - Few remissions
Subtypes of Schizophrenia (cont.)

- **Catatonic Type**
  - Unusual motor responses
  - Odd mannerisms
    - Echolalia
    - Echopraxia
  - Possible subtypes
    - Negative withdrawal
    - Automatic
    - Repetitive/echo
    - Agitated/resistive
Subtypes of Schizophrenia (cont.)

• **Undifferentiated Type**
  – Do not fit into other subtypes
  – Major symptoms
  – Fail to meet criteria

• **Residual Type**
  – One or more past episode
  – No major symptoms
  – Persistent, less extreme symptoms
    • Negative or bizarre beliefs
    • Social withdrawal
    • Inactivity
Cognitive Decline is a big problem too

Patients with Psychosis Lose about 1 SD of their General Intellectual ability (15 IQ points)

Other Psychotic Disorders

• **Schizophreniform Disorder**
  – Schizophrenic symptoms
  – Few months only
  – Associated with good premorbid functioning
  – Most resume normal lives

  – Prevalence = 0.2% (life)
Other Psychotic Disorders

Schizoaffective Disorder
- Symptoms of schizophrenia plus a mood disorder
- Disorders are independent
  - Delusions for 2 weeks in absence of mood

- Prognosis = similar to schizophrenia
  - Persistent
  - No improvement without treatment
Additional Psychotic Disorders

• **Brief Psychotic Disorder**
  – One or more positive symptoms
  – Lasts 1 month or less
  – Usually precipitated
    • Extreme stress
    • Trauma

  – Typically return to premorbid baseline
Other New Psychotic diagnoses

- Predominantly hallucinations/delusion

- Psychosis due to medical condition

- Substance/medication induced psychotic disorders
  - Psychosis due to drugs
Homeless

Approximately 200,000 individuals with schizophrenia or manic-depressive illness are homeless, constituting one-third of the approximately 600,000 homeless population.
Childhood Onset

- Ages <12 onset?
- Rare (1 in 40,000)
- Different than Prodrome
- Treatment is tough and outcome (prognosis) is not good
- Same as adult in terms of criteria except
  - in childhood-onset schizophrenia, the failure to meet expected social or academic milestones may be present, rather than a deterioration in functioning
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 = $\sim 1:1$
  - 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*

Low-risk, spectrum**

Low OPAS ratings
High OPAS ratings

36.8
5.8
4.8
5.3

* 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
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
Movement Abnormalities and Psychosis

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Representative Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypokinesia</strong> (associated with decreased DA activity in striatal pathways)</td>
<td></td>
</tr>
<tr>
<td>Akinesia – poverty of movement and movement initiation.</td>
<td>Parkinson’s Disease</td>
</tr>
<tr>
<td>Bradykinesia – slowness of movement.</td>
<td></td>
</tr>
<tr>
<td>Rigidity – uniform increase in resistance to passive movements about individual joints.</td>
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</tr>
<tr>
<td>Tremor – rhythmic, involuntary muscular contraction characterized by oscillations of a part of the body.</td>
<td></td>
</tr>
<tr>
<td><strong>Hyperkinesia</strong> (associated with increased DA activity in striatal pathways)</td>
<td>Huntington’s disease</td>
</tr>
<tr>
<td>Choreaathetoid – brief, irregular contractions that are not repetitive or rhythmic, but appear to flow from one muscle to the next.</td>
<td></td>
</tr>
<tr>
<td>Ballistic movements – violent or flinging movement.</td>
<td></td>
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<tr>
<td>Dystonia – sustained muscle contractions cause twisting and repetitive movements or abnormal postures.</td>
<td></td>
</tr>
<tr>
<td>Stereotypy – Movements of frequent repetition that serve no obvious purpose.</td>
<td></td>
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Low Striatal DA Activity

**Hypokinesia**

Slow Movements
Characteristic of Parkinson’s

Antipsychotic meds lower DA and can cause these movements (tardive dyskinesia).

High Striatal DA Activity

**Hyperkinesia and Psychotic Symptoms**

Spontaneous, Violent, Jerking, Non-instrumental Involuntary Movements Characteristic of Huntington’s or Schizophrenia

DA agonists used to treat Parkinson’s (levodopa) can result in drug induced hyperkinesias and in extreme cases, psychotic symptoms (Papapetropoulos & Mash, 2005).
DOPAMINE HYPOTHESIS

Normal
Neural Signal
Synapse
Neuro-Receptor
D

Untreated
D
D
D

With medication
D
D
D
M
M
D
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 show 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.
Risk Markers and the Neurodevelopmental Pathogenesis of Psychosis

OC Hypoxia example:

- Prenatal Insults
- Inherited Genetic Factors
- Genetic Mutations
- Congenital Vulnerability (DA Fontal-striatal Circuitry)
- Stress
  - Cognitive & Role Dysfunction
  - DA Hyperactivity
  - Brain Degenerative Processes
  - Gene Expression
  - HPA Hyperactivity

Adolescent Neuromaturation

Neuropathological Process

Brain Development

HPA & HPG activation

Gene Expression

Brain Degeneration

Cognitive & Role Dysfunction

DA Hyperactivity

Gene Expression

HPA Hyperactivity

Prenatal
Neonatal
Childhood
Adolescence
Young Adulthood

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**