Schizophrenia and the Psychoses
Taking leave of one’s senses

Students of schizophrenia need to study and understand:

- Clinical presentation via case studies
- Terms and Definitions
- Biological features
- Prognosis and treatment
- Hospitalization, institutionalization, community care and homelessness

Important terms
Psychosis: lack of contact with reality

- The ability to perceive and respond to the environment is significantly disturbed

Other terms:
- formal thought
- ideas of reference
- illogical thinking (alogia)
- avolition
- loosening of associations
- derailment

- The most florid “hallmarks” of psychosis are hallucinations and delusions

Important terms

- **Hallucinations**: perceptions that are experienced in the absence of external stimuli, or with altered/distorted sensation.
  - auditory, visual, somatic, gustatory, olfactory
### Important terms

- **Delusions**: strange, unusual, or unique interpretations of perception, sensation and/or reality that are held despite evidence to the contrary. Usually represent interpretations of distorted sensation and hallucinations. Often represent interpretations of hallucinations.
  - examples: delusion of being controlled, grandiose delusion, delusion of reference, somatic delusion, persecutory delusion*, command delusion*
  - *of most concern for potential self-harm

### Important terms

- Core psychotic symptoms involve difficulties in
  - content of thought,
  - form of thought,
  - perception,
  - affect,
  - sense of self,
  - volition, and
  - psychomotor behavior.

### The psychoses or “thought disorders”

- Psychosis may be substance-induced, caused by brain injury, or by brain disease.
- **Many disorders have psychotic features:**
  - Brief reactive psychosis
  - Delusional (paranoid) disorder
  - Schizophreniform disorder • Schizotypal disorder • Schizoaffective disorder • Bipolar disorder • OCD • Post-partum psychosis
  - ..., and psychotic features are occasionally present in many other disorders

### The psychoses or “thought disorders”

- Although many disorders and conditions have psychotic features, Schizophrenia is the characteristic psychotic disorder
ICD Definition of schizophrenia

"...fundamental and characteristic distortions of thinking and perception, and affects that are inappropriate or blunted. Clear consciousness and intellectual capacity are usually maintained although certain cognitive deficits may evolve in the course of time. The most important psychopathological phenomena include thought echo; thought insertion or withdrawal; thought broadcasting; delusional perception and delusions of control; influence or passivity; hallucinatory voices commenting or discussing the patient in the third person; thought disorders and negative symptoms.

DSM definition of schizophrenia

The presence of two or more characteristic psychotic symptoms during an active phase that lasts for at least one month:
- delusions
- hallucinations
- disorganized speech (e.g., derailment/incoherence)
- grossly disorganized or catatonic behavior
- negative symptoms (affective flattening, avolition, alogia).

At least one Sx must be 1, 2, or 3
Marked decrease from previous levels of social/occupational functioning.
Continuous signs of the disturbance for at least 6 months.

Case study:

- "George Bush is dead"

Prevalence

Schizophrenia affects 0.2 to 1.5% of adult humanity. This low rate seems to be cross-cultural.
Worldwide prevalence estimates range between 0.5% and 1% of persons with schizophrenia. Among people who eventually develop schizophrenia, 9 out of 10 men will develop it by age thirty, but only 2 out of 10 women. People with schizophrenia pose a high risk for suicide. Approximately one-third will attempt suicide and, eventually, about 1 out of 10 will take their own lives.

Three dimensions/types of schizophrenia:
- Paranoid
- Catatonic
- Disorganized (hebephrenic)

These were once separate Dxs, but the "truth" of schizophrenia is that many people present with some elements of all three of these; their manifestations vary by episode and with time, so the DSM has abandoned these distinctions for the purpose of diagnosis.

Positive, negative and psychomotor symptoms
- Positive symptoms:
  - Delusions, disorganized thinking and speech, heightened perceptions, hallucinations, excessive/inappropriate affect
- Negative symptoms
  - Poverty of speech, alogia, blunted affect, avolition, social withdrawal, catatonia
- Psychomotor:
  - Awkward movements, repeated grimaces, odd gestures ...
  - Extreme forms are called catatonia and include stupor, rigidity, posturing, or excitement

Type I and Type II schizophrenia
- Type I schizophrenia:
  - Primarily positive symptoms
- Type II schizophrenia
  - Primarily negative symptoms
- Type I schizophrenia is characterized by better adjustment prior to the disorder, later onset of symptoms, and greater likelihood of improvement
Typical development of schizophrenia:
The course of schizophrenic disorders varies extensively:
- can be continuous, or episodic with progressive or stable deficit, or there can be one or more episodes with complete or incomplete remission.
- typical course is a prodromal phase, followed by an active phase, and then a “residual” phase. Prodromal symptoms are typically evident in late adolescence, and active symptoms in early adulthood.

Typical development of schizophrenia:
Life courses with SCZ
- some people get worse
- some stay at roughly the same level of difficulty
- some improve, but people rarely return to normal premorbid functioning (cf. w/text:)
The text notes that “One-quarter of patients fully recover” but other studies of people with hard-core symptoms have lower full recovery rates.
The general consensus is that even “fully” recovered people remain vulnerable to subsequent episodes.

FACTS on schizophrenia:
Schizophrenia runs in families, and much vulnerability is probably hereditary
- or it is associated with congenital abnormalities
- Schizophrenia is related to abnormal cortical brain functions that usually include much frontal lobe dysfunction
- Schizophrenia is related to structural cortical abnormalities

FACTS on schizophrenia:
the neuroleptic or anti-psychotic drugs are partially effective.
- almost all of these drugs inhibit the activity of dopamine in the brain (and probably affect the disordered regulation of glutamate, GABA and serotonin).
- the dopaminergic areas affected link sensory perceptions to memories, movement, attention and emotions
FACTS on schizophrenia:

- First prominent symptoms usually occur in late adolescence and early adulthood (median age, males: 24, females: 26),
- Stress makes the symptoms worse

Schizophrenia outcomes

SCZ is a disabling and chronic condition
- Death by accidents and suicide has been found to be as high as 25% by the age of 45
- Victimization is common
- Depending on the level of social care, homelessness is common (roughly 60% in the USA)
- Schizophrenia requires multiple forms of intervention and care

Genetic aspects: Gottesman and Shields’ (1982) review of numerous studies

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Morbid risk (concordance rate) (%)</th>
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<tbody>
<tr>
<td>Genetically unrelated</td>
<td>2.3</td>
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<tr>
<td>Second or degree relatives</td>
<td>&lt;4.2</td>
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<tr>
<td>First degree relatives with SCZ:</td>
<td></td>
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<tr>
<td>Parents</td>
<td>5.6</td>
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<tr>
<td>Fraternal twin</td>
<td>9.0</td>
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<tr>
<td>Siblings</td>
<td>10.1</td>
</tr>
<tr>
<td>Children</td>
<td>12.8</td>
</tr>
<tr>
<td>Identical twin</td>
<td>50.0</td>
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<tr>
<td>Children of two parents with SCZ</td>
<td>46.3</td>
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Concordance rates vary considerably, with highest morbidity rates found with studies of “hard” symptoms.

Viral and gestational aspects:

- People with schizophrenia are more likely to have been born in late winter or early spring
- Pregnant women are more likely to have children who eventually develop schizophrenia, if during the early or middle trimester of their gestation the mothers
  - Have herpes, or
  - Get viral influenza or strep throat, meningitis, or other viruses
- Frontal lobe damage in childhood
- Some people with early onset of HIV develop schizophrenia-like symptoms in advanced stages of AIDS
<table>
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<th>Best prognosis for schizophrenia is associated with:</th>
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<tr>
<td>- adequate premorbid social functioning,</td>
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<td>- absence of a premorbid personality disorder,</td>
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<td>- abrupt onset,</td>
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<td>- onset precipitated by an external stressor,</td>
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<td>- late onset (esp. mid-life),</td>
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<td>- availability of aftercare in the community.</td>
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<td>- Positive and supportive family attitude</td>
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<th>Medications for schizophrenia</th>
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<tbody>
<tr>
<td>- Large class of &quot;neuroleptic&quot; medications (&quot;antipsychotics&quot; or &quot;major tranquilizers&quot;)</td>
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<td>Mechanism of action #5: receptor blockade</td>
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<tr>
<td>- post-synaptic neurons have localized receptors in and around dendrites</td>
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<tr>
<td>- these receptors respond to neurotransmitter release from presynaptic neurons.</td>
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<tr>
<td>- this response triggers membrane changes and ion flow in post-synaptic neurons</td>
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<td>Mechanism of action #5: receptor blockade</td>
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<tr>
<td>- medications (and some toxins) can reduce receptor activity by</td>
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<tr>
<td>- blocking receptor sites and</td>
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<tr>
<td>- metabolizing excess neurotransmitter at receptor sites</td>
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<tr>
<td>- the effect is &quot;receptor blockade,&quot; a reduction in the amount of stimulation that occurs in post-synaptic neurons</td>
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<tr>
<td>- effectively reducing excitation</td>
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</table>
**Medications for schizophrenia**

- Medications for schizophrenia inhibit excessive activity of dopamine in the brain, usually by blocking dopamine receptor blockade.
- Main targets are subclass of DA receptors called D₂ receptors, which are mesolimbic and mesocortical neurons.

**Medications for schizophrenia**

- Side effects of these medications
  - the most notable side effect is tardive dyskinesia.
  - Kinetic/motor malignancy syndromes (lasting stiffness)
  - In as many as 1% of patients, particularly elderly ones, conventional antipsychotic drugs produce a neuroleptic malignant syndrome – a severe, potentially fatal reaction

**Theories of schizophrenia**

- Social, environmental and family dysfunction hypotheses
- Biological hypotheses:
  - genetic and congenital
  - the dopamine hypothesis
  - abnormal brain structure
  - frontal lobe damage
- Newest advances in research are focusing on:
  - dysfunction of inhibitory circuits (gamma synchrony)
  - inefficient task-related prefrontal activation
  - working memory impairment

**Theories of schizophrenia**

- Could there be a combined structural brain physiology theory? yes ... these are (cf. text)
  - neurodegenerative theory and
  - neurodevelopmental theory
adolescent development
gone awry
- most theorists agree that schizophrenia emerges in early adulthood due to abnormalities in adolescent brain development ("development gone awry"): synaptic pruning, dendrite and axon migration, frontal lobe development, stress and hormonal changes

adolescent development
gone awry
- worsening behavior, oddities, idiosyncrasies, volitional problems in middle adolescence
- first active phase in early adulthood
- residual phases often with increasing passivity and amotivational and syndromes.

adolescent development
gone awry
- increased adherence to limitations and decrease in externalizing behavior in middle adulthood ("improvement")
- stabilization with degeneration in seniority
- this very clear course suggests a gradual degeneration in brain control functions suggestive of neurodegenerative theory

Schizophrenia as degeneration
- traditional views of schizophrenia characterize the disorder as a degenerative and worsening process, as indicated by
  - the onset of negative symptoms
  - premorbid symptoms in late adolescence
  - active phases just after the final stages of adolescent brain development
  - inability to return to premorbid levels of functioning
Schizophrenia as degeneration
- degenerative and worsening process, continued...
- progress into avolitional/amotivational and hebephrenic syndromes
- increasing dopamine sensitivity
- associated onset of other mental disorders
- life-long social problems
- deteriorated frontal lobe autopsies
- these observations are the basis for neurodegenerative theory

Schizophrenia as degeneration
- implications of neurodegenerative theory:
  - treatment manages symptoms, primarily through suppression
  - treatment is tertiary and life-long
  - improvement is temporary
  - worsening is due to deterioration, not treatment
  - treatment emphasizes medication and medical services

but ... neurodegenerative theory ignores some neuroscience facts:
- brain damage is overcome by adaptational processes, neuroplasticity
- learning is an accumulative process throughout adulthood
- brain adaptations to lesions and other insults are gradual
- most changes are continuous with rapid changes in early childhood and adolescence
- these rapid changes occur in SCZ

A new perspective: neurodevelopmental theory
- Argues that SCZ is a developmental process.
- Brain development (particularly in adolescence) both creates and adapts to these difficulties.
- Symptoms are attempts to adapt.
- Appropriate time and learning can result in adaptational success in adulthood.
A new perspective: **neurodevelopmental theory**

- Implications of neurodevelopmental theory:
  - Schizophrenia can be prevented
  - Treatment manages symptoms, primarily through compensation and recovery
  - Neuroplasticity is encouraged
  - Learning of new skills is necessary
  - Worsening is due to stress and lost opportunities
  - Improvement is due to adaptation, compensation and healthy living

Comparison of neurodegenerative and neurodevelopmental theory

<table>
<thead>
<tr>
<th>Neurodegeneration:</th>
<th>Neurodevelopmental:</th>
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<tr>
<td>SCZ processes represent deterioration that begins in early adulthood</td>
<td>SCZ processes represent development gone awry, originating in early childhood</td>
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<tr>
<td>Prevention efforts unlikely to work</td>
<td>Prevention efforts likely to reduce severity of outcome</td>
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<tr>
<td>Pattern of SCZ with aging represents decay process</td>
<td>Pattern of SCZ with aging represents adaptation to Sx</td>
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<table>
<thead>
<tr>
<th>Neurodegenerative</th>
<th>Neurodevelopmental</th>
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<tr>
<td>Positive symptoms are reactions to negative symptoms</td>
<td>Positive symptoms create and worsen other Sx</td>
</tr>
<tr>
<td>Decrease in positive symptoms with age represents further deterioration</td>
<td>Decrease in positive symptoms with age represents coping</td>
</tr>
<tr>
<td>Emphasis on receptor blockade in medication</td>
<td>Emphasis on sedation of kindling and other control mechanisms in medication</td>
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<tr>
<td>Family/community efforts at maintenance</td>
<td>Family/community efforts at skill development</td>
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Recovery

- Families
- Improved systems of care
- The work of E. Fuller Torrey MD
- Growing emphasis on recovery-based approaches. The recovery model emphasizes a personalized, holistic, patient-directed approach to treatment and rehabilitation (Frese et al., 2009).
- The recovery movement
### Treatments for schizophrenia

- Multiple modalities of intervention and care.
- Combined drug treatment with psychotherapy, family support and rehabilitation services are best.
- Psychotherapy and case management aimed at social skills development, insight in symptom management, assistance in self-care, vocational development.
- Cognitive-behavioral therapy?

### Psychosocial interventions facilitate

- Supported living, housing, efforts at independent living.
- Participation in day hospital or supervised vocational programs.
- Vocational rehabilitation.
- Treatment for substance abuse.
- "Assertive" community treatment (ACT).
- **"integrated systems of care."**

### Conclusions