Schizophrenia Symptoms

- Hallucinations
- Delusions
- Disorganized speech
- Disorganized behavior
- These are called "positive (+) symptoms" (abnormalities that have been 'added' to the person's behavior) & onset often sudden (acute)
- Respond to treatment

- Normal emotion lost
- Decreased motivation; apathy
- Decreased social interaction
- Decreased speech
- These are called "negative (-) symptoms" (normal behaviors that have decreased) & onset is gradual & then chronic
- Resistant to treatment

These may reflect 2 different pathological processes in brain.

Genetics of Schizophrenia - Family Studies

- Schiz. runs in families - you have increased risk if you have blood relatives with schizo
- Overall concordance in identical twins is ~45-50%, in fraternal twins its ~15-17%
- Identical twins with same handedness have a 92% concordance rate, that of those with opposite handedness is 25%
- BUT: Twins with same chorion 60% concordance (vs 11%) & fraternal twins more similar than other siblings. (Both of these support prenatal environmental factors are also important)

Characteristics

- Incidence around 1% of the US population
- Usual symptom onset in early adulthood; on average in teens or 20's for men, later 20's for women
- Somewhat more common & severe in men (7M/5F)
- Occurs worldwide but more common in western cultures & in urban environments

Genetics of Schizophrenia - Adoption Studies

- Adoptees with schizo are more likely to have schizo biological parents/relatives than schizo adoptive parents/relatives.
- A child of a schizo parent raised by a normal couple is more likely to develop schizophrenia than a child of normal parents raised by a schizo adopted parent.
- Have identified >70 genes more common in schizos, but these can vary with population sample.
- Schizos show 3X as many mutations or SNPs or "repeats" in genomes. (Note: our book calls repeats CNVs or copy number variations)
- Also, the older the father, the higher the risk of schizophrenia in his kids (sperm more likely to show mutations in genetic codes)
The **Vulnerability Model**

- Some threshold of causal forces must be exceeded in order for the illness to occur.
- Environmental challenges combine with a person's genetic vulnerability/predisposition to exceed that threshold.
- Environmental influences work in part by epigenetic means, affecting gene expression.

**Brain Anatomical & Functional Changes**

- Enlarged ventricles
- Smaller thalamus, prefrontal & temporal cortex, & hippocampus, especially on left side
- Abnormal communication between areas
- Loss of cells, smaller or disorganized cells in these regions
- Damage seems to precede diagnosis and is progressive early in life, but then levels off in adults
- Symptoms not apparent until the age where those brain areas mature & normally become fully functional

**SCHIZOPHRENIA IN IDENTICAL TWINS**

PET scans of 28-year-old male identical twins showing the enlarged brain ventricles in the twin with schizophrenia (right) compared to his well brother (left).

**PET Scans** - less frontal activity but may have increased hippocampal activity.

**Schizophrenia**

- Figure 14.9: Blood Flow in Normal and Schizophrenic Brains During Card Sorting (Frontal Lobe) Test.
- Figure 14.10: Brain Activation During Visual and Auditory Hallucinations in a Schizophrenic.

**Schizophrenia**

- Hallucinations associated with increased activity in sensory areas
- Nicotine
  - Normalizes auditory symptoms
  - Improves negative symptoms
  - 80% of schizophrenia patients smoke (may be self-medicating)
Neurodevelopmental Hypothesis of Schizophrenia

• Brain abnormalities associated with schizo begin **prenatally** or **neonatally**
• May relate to adverse prenatal/neonatal conditions as well as genetics
• Birth records of schizos show more "nonoptimal" signs during preg/labor (nutritional deficiencies, RH incompatibility, prematurity, delivery complications, low birth weight, illness during pregnancy, etc.) – all things that affect early development of CNS.
• Early childhood head injury also linked with schizo.
• Childhood home movies suggest some abnormalities in behavior may be detectable early on.

Season-of-Birth Effect (may help explain schizo in those w/o family history)

• 5-8% increase in risk of schizo in those born in winter, especially in winter-weather climates.
• Higher rate of schizophrenia in those born in winters of years with bad fall viral epidemics
• If an epidemic occurs in other seasons, there's more schizophrenia among those born 3 months later
• Probably not the virus but the fever it causes that affects CNS development (variety of viruses associated with increased risk). Fever decreases cell division.
• Schizo. more likely in those whose mom’s had rubella, herpes, or had a cat during pregnancy or right after.
• Antibodies to toxoplasma more common in schizos

Dopamine Hypothesis

Schizophrenia results from over-activity of dopamine in the brain

Support for DA theory:
DA Drug-Induced Psychosis

• amphetamine or cocaine use increases DA activity & can trigger a drug-induced paranoid psychoses
• excess l-dopa can cause symptoms of schizophrenia in Parkinson's patients
• amphetamine or l-dopa given to schizophrenics worsens their symptoms
• Higher levels of DA in some brain areas; about twice as many DA receptors in schizos – the more receptors/the more symptoms
• DA BLOCKERS treat schizophrenia
Schizophrenia
Relationship Between DA Receptor Blocking and Clinical Effectiveness of Schizophrenia Drugs.

“Typical” Antipsychotics or “Neuroleptics”
- phenothiazines like chlorpromazine (Thorazine)
- butyrophenones like haloperidol (Haldol)
- Block DA receptors throughout the brain

Main Side Effects
- Extrapyramidal Motor Disorders
  - Parkinson’s disease-like symptoms
  - A variety of other motor abnormalities, including:
    - Tardive dyskinesia - involuntary movements, particularly of the face and mouth
  - [https://www.youtube.com/watch?v=fLwZQBJs8fI](https://www.youtube.com/watch?v=fLwZQBJs8fI)

Newer Atypical Antipsychotics
- Prototype: Clozaril (clozapine)
- Block selected DA and 5HT2 receptors
- Fewer extrapyramidal side effects
- Helped previously unresponsive patients
- Improves “negative” symptoms; decreases suicides
- BUT can cause agranulocytosis in 1-2% so requires blood monitoring
- Other atypicals: risperidone (Risperdal); olanzapine (Zyprexa)
- These show less agranulocytosis, but increased risk of serious weight gain and diabetes.

Glutamate Hypothesis
- Underlying problem in schizophrenia is underactivity of glutamate (↓release, ↓receptors) especially in frontal lobe & limbic areas.
- This does not necessarily conflict with the DA hypothesis because these neurotransmitter systems interact & have opposite effects
- PCP (phencyclidine) blocks glutamate receptors & produces both positive and negative symptoms of schizophrenia. It induces long-lasting relapses in those with schizophrenia.
- Now working on meds to affect glutamate activity