

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

Characteristics

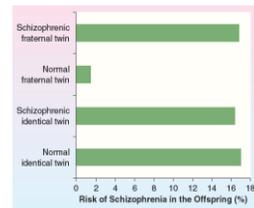
- Incidence around 1% of the US population
- Usual symptom onset in early adulthood; on average in teens or 20's for men, later 20's for women
- Somewhat more common & severe in men (7M/5F)
- Occurs worldwide but more common in western cultures & in urban environments

Genetics of Schizophrenia- Family Studies

- Schizo. 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)

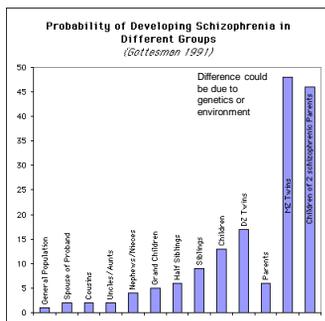
Schizophrenia

Figure 14.6: Risk of Schizophrenia in the Offspring of Normal and Schizophrenic Twins



Kids born to non-schizo member of identical twin pair have same risk as kids of twin with schizophrenia (17.4% vs 16.8% will develop schizo)(not true of fraternal). This suggests unaffected identical twins still have the "bad genes"

SOURCE: Based on data



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 3 X 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

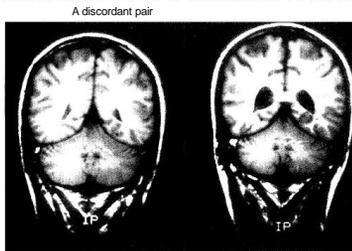
- Enlarged ventricles
- Smaller thalamus, prefrontal & temporal cortex, & hippocampus, especially on left side
- Abnormal communication between areas
- Loss of cells, smaller or disorganized cells in these regions
- Damage seems to precede diagnosis and is progressive early in life, but then levels off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

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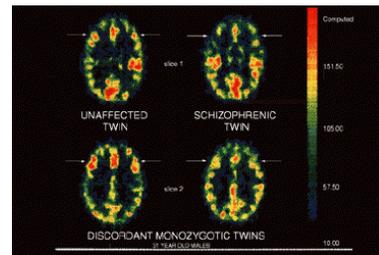
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SCHIZOPHRENIA IN IDENTICAL TWINS



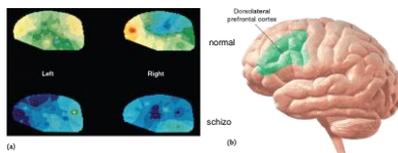
MR) scans of 28-year-old male identical twins showing the enlarged brain ventricles in the twin with schizophrenia (right) compared to his well brother (left).

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



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Figure 14.9: Blood Flow in Normal and Schizophrenic Brains During Card Sorting (Frontal Lobe) Test.

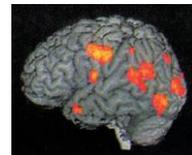


SOURCE: (a) From "Physiologic Dysfunction of Dorsolateral Prefrontal Cortex in Schizophrenia: I. Regional Cerebral Blood Flow Evidence," by D. R. Weinberger, K. F. Berman, and R. E. Zec, 1985, Archives of General Psychiatry, 41, 114-124.

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Figure 14.10: Brain Activation During Visual and Auditory Hallucinations in a Schizophrenic

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



SOURCE: From "A Functional Neuroanatomy of Hallucinations in Schizophrenia," by D. A. Silbersweig et al., Nature, 378, pp. 174-179. Reprinted by permission of Nature, copyright 1995.

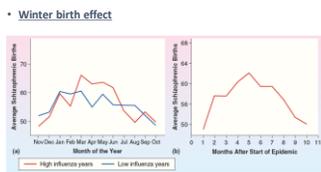
Neurodevelopmental Hypothesis of Schizophrenia

- 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 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

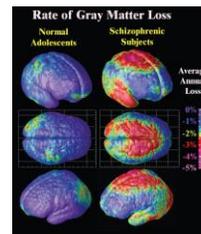
Figure 14.12: Relationship of Schizophrenic Births to Season and Influenza Epidemics in England and Wales (1939–1960).



SOURCE: From “Schizophrenia Following Pre-Natal Exposure To Influenza Epidemics Between 1939 and 1960,” by P. C. Sham et al., British Journal of Psychiatry, 160, pp. 461–466. Copyright 1992. Reprinted with permission of the publisher.

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Gray Matter Loss in Schizophrenic Adolescents.



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Dopamine Hypothesis

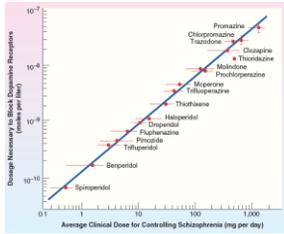
Schizophrenia results from or is associated with over-activity or over-response at DA synapses.

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

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Relationship Between DA Receptor Blocking and Clinical Effectiveness of Schizophrenia Drugs.

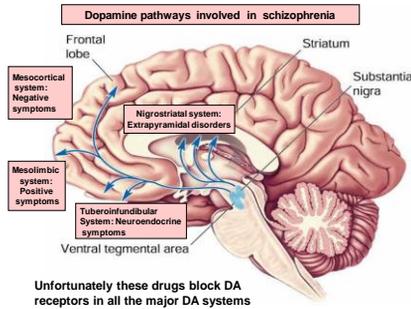


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“Typical” Antipsychotics or “Neuroleptics”

- 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>



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