Psychotic disorders
“The Schizophrenias”

1% incidence
More likely in US & Europe
10 to 100 times

Slightly more common in men
Earlier onset, more severe

Originally: dementia praecox
Eugen Bleuler called it schizophrenia in 1911

Starts as teens or early adult
Typical onset 16 to 30
Uncommon onset over 45

Symptoms vary
Seem OK until share thoughts
Sit without moving…for hours

Episodes
Typical: not more than 6 weeks
Symptoms come & go
Lasts a few days
Feel agitated
Hallucinations
Lasts a few months
Delusions

Range of severity
Hospitalized
Meaningful lives in communities

3-Factor Model
Disorganized thinking
Distorted thinking
Delusions & hallucinations
Disconnected mind-motor
Spontaneous movement
Fluid speech
Self control
Positive symptoms

Unique to schizophrenia
Not schiz without them

Delusions

Unusual false beliefs
Martians are controlling me
Reading my mind

Thought insertion
“I killed someone”

Behavior controlled by
People on TV or movies
Special messages
Magnetic waves
Aliens

Believe you are someone else
Often historical person

Someone out to get you
Paranoid delusions
Spying, plotting, cheating

Hallucinations

False sensory experiences
Hear voices not there
See things not there

Voices are most common
Hear voices
Talk to invisible person
Voices talk to each other

See invisible objects or people

Feel invisible fingers touching

Smells

Thought disorders

1. Disorganized thinking
organizing thoughts
connecting thoughts
garbled talk

2. Thought blocking
Stop in middle of thought
Feel thought taken out head

3. Nonsense words
Neologisms = new words
Disorganized speech
Rambling sentences
Incoherent patterns

**Movement disorders**
- Agitated movements
- Repeat motions over and over
- Catatonic = immobility
  - Rare—treated with drugs

**Negative symptoms**
- Occur in other disorders
- Flat affect
  - face immobile
  - monotonous voice
- Similar to brain damage
  - poor control of eye movements
  - unusual facial expressions

**Negative = lack of**
- Lack of pleasure
- Lack initiative & planning
  - Poor hygiene
- Lack of persistence
- Social withdrawal
- Poverty of speech
  - Lacks fluidity of speech
  - Words don’t flow
  - Don’t talk much
  - Even when forced

**Cognitive symptoms**
- Difficult to notice
- Executive functioning
  - Trouble switching tasks
  - Trouble paying attention
  - Trouble with working memory

**Disturbed emotions**
- Hyperemotional
- Depressed
- Flat affect (no emotion)

**Abnormalities of perception**
**Schizophrenic Art**
- No foreground-background diff
- Obsessed with certain objects (skulls)
- Emotionally distant
Types of Schizophrenia

1. Disorganized
   “Hebephrenic schizophrenia”
   Inappropriate thoughts & behav.
   Don't make sense
   Severe
   Can’t do routine daily activities
   bathing & meal prep
   Hard to understand what say
   Frustration, agitation, anger

2. Catatonic
   Extremes
   Coma-like daze
   or
   Talk in bizarre-hyperactive way
   May last month+
   Easily treated with drugs
   Can be caused by non-schiz

3. Paranoid
   Delusions
   Someone trying to harm you
   Hear voices
   Not as many memory problems
   Okay concentration
   Handle daily life okay
   Suicide risk

4. Undifferentiated
   Not meet all criteria
   Miscellaneous
   Junk term

Causes of Schizophrenia

Genetics
   Heritability
   Runs in families
   Environmental trigger?
Old egg-sperm theory
Older parents more schiz children

Children of schiz patients
Less than ½ become schiz
Inherit susceptibility to environmental factors?

People without family history can develop schizophrenia

Why likely genetic component
Men & women about equal
Men slightly more
Men have earlier onset
Men have more severity
About 1% worldwide

Runs in families
1% in general population
10% when parent or sibling
15% in fraternal twin
50% when identical twin

Pure genetic effect = 100%
greatest environmental similarity
monozygote

Adopted Children
12.5% siblings in same environ.
None adopted had schiz

Correlated factors
Women with schizophrenia
drink & smoke during preg?

Not one single gene
10+ genes are more common in schizophrenics

DISC1 gene
(disrupted in schizophrenia 1)
Controls production of dendritic spines
Controls generation of new neurons in hippocampus

Other genes linked to
brain development
glutamate synapses
hippocampus & prefrontal cortex connections

Combo
Dopamine hypothesis

Over-activity of DA synapses
In mesolimbic pathway?

DA agonists-antagonist effects
All treatment drugs block DA receptors
Chlorpromazine
  Originally used to prevent surgical shock
  Dramatically effective
  Reduces symptoms of schizophrenia

DA agonists cause schiz sympts
Cocaine
Amphetamine
L-DOPA
Elation, euphoria
Similar to start schiz. episode

Paranoid delusions
Maybe caused by increased DA input to amygdala
involved with emotional responses for aversive events

Clozapine
  atypical antipsychotic drug
  blocks D4 receptors
  in nucleus accumbens
    Part of the reward circuit
  Caused by excess activity at some dopamine synapses

Evidenced by
  Drugs that help
  Drugs that aggravate

Aggravaters
Cocaine
Amphetamine
LSD
  Dopamine not cleaned up?
  Schiz have twice as many D2 receptors occupied by dopamine as normal

Dopamine not sole cause
  Drugs that block dopamine receptors
    do so immediately
    but effects on behavior build up gradually over 2 or 3 weeks
Glutamate Hypothesis

Caused by poor glutamate functioning
dopamine inhibits glutamate

Mixed evidence

Release less glutamate
in prefrontal cortex & hippocampus
have fewer glutamate receptors

Phencyclidine (PCP)
blocks NMDA glutamate receptors
produces symptoms similar to schiz
induces both negative and positive symptoms
Doesn’t produce psychosis in preadolescents
produces more severe symptoms than schiz

Risky to increase glutamate
Too widely used
Don’t stimulate directly
Working on glycine
amino acid
enhances NMDA effects
not effective antipsychotic
increases antipsychotics effects

Brain Abnormalities

MRI & CT studies
Found loss of brain tissue in patients with schizophrenia

Ventricles
Relative size of lateral ventricles
2+ size of control subjects

Mild Brain Abnormalities
Less than average gray matter
Larger than average ventricles
Smaller thalamus
Left hemisphere slightly larger

Worst in
left temporal lobe & frontal lobe
Immature or poorly developed
dorsolateral prefrontal cortex
deficits in memory & attention

Smaller cell bodies
in frontal cortex & hippocampus
Environmental Causes

**Famine during pregnancy**
(especially thiamine deficiency)

**Predictors**
- More likely if mother underweight
- More likely if low birth-weight
- More likely if Rh incompatible

**Neurodevelopmental hypothesis**
Schiz caused by abnormalities to nervous system during prenatal or neonatal periods

**Prenatal and Neonatal**
- Mother’s nutrition
- Premature birth
- Low birth weight
- Complications during delivery
- Rh-negative & baby Rh-positive may trigger immunological rejection by mother
- hearing deficits
- mental retardation
- twice usual probability of schiz
  - 2%

**Season-of-birth effect**
Winter, slightly greater
- Nutrition
- viral infections
- fever and influenza

**Infections**

**Flu (or other viral illness)**
- More likely if born during late winter and early spring
- More likely in cities than countryside
- More likely far from equator
- Decreased winter temp?

**Childhood infections**
- Such as toxoplasma gondii
- memory disorders, hallucinations, and delusions
- bacteria only reproduces in cats
- more likely to have a pet cat

**Diagnosis of Schizophrenia**

Confused with drug abuse
- Can’t show abuse causes schiz
- More likely to abuse drugs
Self medication
Makes treatment less effective

**Prodromal = pre-symptoms**
Self-isolation
Increased unusual thoughts
Increased suspicions
Family history of schiz

**Self-diagnosis as bipolar**
Or something “less sever”

**Drugs can help-hurt**
**Some drugs make it worse**
- Marijuana
- Amphetamines
- Cocaine
- Smoking
  - 3x likely addicted to nicotine
  - 90% in schiz
  - Schiz worse during withdrawal

**Some drugs make it better**
**Chlorpromazine (Thorazine)**
- 1st drug successful
**Antipsychotic drugs**
- Primarily work by blocking dopamine receptors
**Phenothiazines**
- class of neuroleptic drugs
- includes chlorpromazine

**Try several medications**
- Not all work the same for all
- Best combination, right dose

**Relapse**
- Stop taking meds
  - Feel better, think don’t need
- Interact with other drugs
- Interact with alcohol

**Antipsychotic medications**
available since mid-1950's
- Chlorpromazine (Thorazine)
- Haloperidol (Haldol)
- Perphenazine (Etrafon)
Fluphenazine (Prolixin) available since mid-1990's "atypical" antipsychotics
Clozapine (Clozaril) psychotic symptoms
Hallucinations; breaks with reality Side effect for clozapine
Agranulocytosis = loss of white blood cells
Risperidone (Risperdal)
Olanzapine (Zyprexa)
Quetiapine (Seroquel)
Ziprasidone (Geodon)
Aripiprazole (Abilify)
Paliperidone (Invega)

Old & new ones about equally effective
Side effects
Worse when start
Last few days for most
Dizzy when changing positions
Blurred vision
Drowsiness
Rapid heartbeat
Sensitivity to the sun
Skin rashes
Major weight gain
Rigidity of joints
Muscle spasms
Restlessness
Tremors
Tardive dyskinesia
Caused by long term use
Can’t control mouth muscles
Tremors & involuntary move
Caused by prolonged blocking of dopamine receptors in basal ganglia

Antipsychotic medications
Usually in pill or liquid form
Some are shots given monthly
New Drugs
Atypical medications
Mesolimbo-cortical system
Where antipsychotics impact?
Set of neurons
Project from midbrain tegmentum to limbic system
Don’t cause movement problems
Less intense effects on dopamine type D₂ receptors
Stronger effects at D₄ and serotonin 5-HT₂ receptors

**More effective?**
Better with positive symptom
Not so much with negative
Don’t improve overall quality of life any better

**Long-term drug treatment**
**Antipsychotic drugs not cure**
Don’t fully treat condition
Don’t work for 1/3 of patients

**Serious side effects**
Similar symptoms to Parkinson’s disease
Slow movement, lack of facial expression, general weakness