

# *Biological Psych*



*25 Things To Know*

Schizophrenia

25 disorders

# *Schizophrenia*

- Psychotic disorders
  - “The Schizophrenias”
  - 1% incidence
    - More likely in US & Europe
      - 10 to 100 times

# *Schizophrenia*

## ➤ Demographic Data

- Slightly more common in men
- Earlier onset
- More severe

# *Schizophrenia*

- Originally: *dementia praecox*
- Eugen Bleuler called it schiz  
–1911

# *Schizophrenia*

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

# *Schizophrenia*

## ➤ Symptoms vary

- Seem OK until share thoughts
- Sit without moving...for hours

# *Schizophrenia*

## ➤ Episodes

- Typical: not more than 6 weeks
- Symptoms come & go



# *Episodes*

- Lasts a few days
  - Feel agitated
  - Hallucinations
- Lasts a few months
  - Delusions

# *Schizophrenia*

- 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

OR

# *Schizophrenia*

- Positive symptoms
  - Happy symptoms?



# *Schizophrenia*

- Positive symptoms
  - Unique to schizophrenia
  - Not schiz without them



# *Positive symptoms*

## ➤ Delusions

- Unusual false beliefs
  - Martians are controlling me
  - Reading my mind
  - Thought insertion
  - “I killed someone”

# *Positive symptoms*

## ➤ Delusions

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

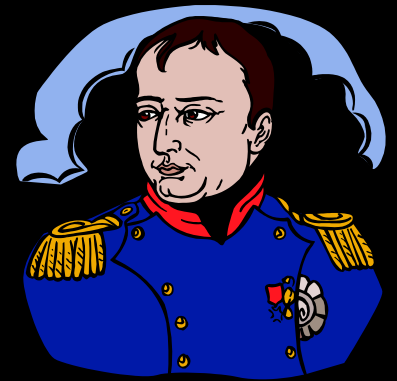


# *Positive symptoms*

## ➤ Delusions

– Believe you are someone else

– Often historical person



# *Positive symptoms*

## ➤ Delusions

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

# *Positive symptoms*

➤ Hallucinations



# *Positive symptoms*

## ➤ Hallucinations

- False sensory experiences
  - Hear voices not there
  - See things not there

# *Positive symptoms*

## ➤ Hallucinations

- Voices are most common

- Hear voices

- Talk to invisible person

- Voices talk to each other

# *Positive symptoms*

## ➤ Hallucinations

- See invisible objects or people
- Feel invisible fingers touching
- Smells

# *Positive symptoms*

➤ Thought disorders



# *Positive symptoms*

- Thought disorders
  - 1. Disorganized thinking
    - organizing thoughts
    - connecting thoughts
    - garbled talk



# *Positive symptoms*

## ➤ Thought disorders

### –2. Thought blocking

–Stop in middle of thought

–Feel thought taken out head

# *Positive symptoms*

## ➤ Thought disorders

### –3. Nonsense words

–Neologisms = new words

–Disorganized speech

–Rambling sentences

–Incoherent patterns

# *Positive symptoms*

➤ Movement disorders



# *Positive symptoms*

## ➤ Movement disorders

- Agitated movements

- Repeat motions over and over

- Catatonic = immobility

  - Rare—treated with drugs

# *Symptoms*

➤ Negative symptoms



# *Symptoms*

- Negative symptoms
  - Occur in other disorders
  - Flat affect
    - face immobile
    - monotonous voice



# *Negative symptoms*

- Similar to brain damage
  - poor control of eye movements
  - unusual facial expressions

# *Negative symptoms*

➤ Negative = lack of

–Lack of pleasure





# *Negative symptoms*

- Negative = lack of
  - Lack initiative & planning
  - Poor hygiene



# *Negative symptoms*

- Negative = lack of
  - Lack of persistence
  - Social withdrawal

# *Negative symptoms*

- Negative = lack of
  - Poverty of speech
    - Lacks fluidity of speech
    - Words don't flow
    - Don't talk much
      - Even when forced

# *Other Symptoms*

## ➤ Cognitive symptoms

- Difficult to notice

- Executive functioning

  - Trouble switching tasks

  - Trouble paying attention

  - Trouble with working memory

# *Other Symptoms*

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

# *Schizophrenia*

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

# *Schizophrenia*

- Abnormalities of perception
  - Schizophrenic Art
    - Dark silhouettes
    - Watchful eyes
    - Fragments

# *Characteristic of LSD*





# *Schizophrenia*

## ➤ Types

- 1. Disorganized
- 2. Catatonic
- 3. Paranoid
- 4. Undifferentiated

# *Schizophrenia*

## ➤ 1. Disorganized

- “Hebephrenic schizophrenia”
- Inappropriate thoughts & behav.
- Don't make sense

# *Schizophrenia*

## ➤ 1. Disorganized

- Severe

- Can't do routine daily activities

- bathing & meal prep

- Hard to understand what say

- Frustration, agitation, anger

# *Schizophrenia*

## ➤ 2. Catatonic

- Extremes

  - Coma-like daze

    - or

  - Talk in bizarre-hyperactive way

# *Schizophrenia*

## ➤ 2. Catatonic

- May last month+
- Easily treated with drugs
- Can be caused by non-schiz

# *Schizophrenia*

## ➤ 3. Paranoid

- Delusions

  - Someone trying to harm you

  - Hear voices

# *Schizophrenia*

## ➤ 3. Paranoid

- Not as many memory problems
- Okay concentration
- Handle daily life okay
- Suicide risk

# *Schizophrenia*

- 4. Undifferentiated
  - Not meet all criteria
  - Miscellaneous
  - Junk term



# *Causes*



# *Schizophrenia*

## ➤ Causal factors

- Genetics

- Dopamine

- Glutamate

- Brain Abnormalities

- Environment

- Infections

# *Genetics*

## ➤ Heritability

- Runs in families

- Environmental trigger?

# *Genetics*

- Old egg-sperm theory
  - Older parents more schiz children

# *Genetics*

- Children of schiz patients
  - Less than  $\frac{1}{2}$  become schiz
  - Inherit susceptibility to environmental factors?

# *Genetics*

- People without family history can develop schizophrenia

# *Genetics*

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

# *Genetics*

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



# *Genetics*

- Pure genetic effect = 100%
  - greatest environmental similarity
  - monozygote

# *Genetics*

## ➤ Adopted Children

- One study

  - 12.5% siblings in same environ.

  - None adopted had schiz

# *Genetics*

- Correlated factors
  - Women with schizophrenia
    - drink & smoke during preg?

# *Genetics*

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

# *Genetics*

## ➤ DISC1 gene

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

# *Genetics*

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

# *Combo*

➤ Genetics & Environment

# *Schizophrenia*

## ➤ Causal factors

- Heredity

- Dopamine

- Glutamate

- Brain Abnormalities

- Environment

- Infections



# *Schizophrenia*

- Dopamine hypothesis
  - Over-activity of DA synapses
    - In mesolimbic pathway?

# *Dopamine Hypothesis*

- DA agonists-antagonist effects
  - All treatment drugs block DA receptors

# *Dopamine Hypothesis*

- DA agonists-antagonist effects
  - Chlorpromazine
    - Originally used to prevent surgical shock

# *Dopamine Hypothesis*

- DA agonists-antagonist effects
  - Chlorpromazine
    - Dramatically effective
    - Reduces symptoms of schizophrenia

# *Dopamine Hypothesis*

- DA agonists-antagonist effects
  - DA agonists cause schiz sympts
    - Cocaine
    - Amphetamine
    - L-DOPA

# *Dopamine Hypothesis*

- DA agonists-antagonist effects
  - DA agonists cause schiz sympts
    - Elation, euphoria
    - Similar to start schiz. episode

# *Dopamine Hypothesis*

## ➤ Paranoid delusions

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

# *Dopamine Hypothesis*

- DA neurons release more DA?
  - Clozapine
    - atypical antipsychotic drug
    - blocks D<sub>4</sub> receptors
      - in nucleus accumbens
        - Part of the reward circuit



# *Dopamine Hypothesis*

➤ Caused by excess activity at some dopamine synapses

– Evidenced by

– Drugs that help

– Drugs that aggravate

# *Dopamine Hypothesis*

- Aggravaters
  - Cocaine
  - Amphetamine
  - LSD

# *Dopamine Hypothesis*

- Dopamine not cleaned up?
  - Schiz have twice as many  $D_2$  receptors occupied by dopamine as normal

# *Dopamine Hypothesis*

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

# *Schizophrenia*

## ➤ Causal factors

- Heredity

- Dopamine

- **Glutamate**

- Brain Abnormalities

- Environment

- Infections

# *Glutamate Hypothesis*

- Caused by poor glutamate functioning
  - dopamine inhibits glutamate
  - Mixed evidence

# *Glutamate Hypothesis*

## ➤ Schiz

- release less glutamate
  - in prefrontal cortex & hippocampus
- have fewer glutamate receptors

# *Glutamate Hypothesis*

## ➤ Phencyclidine (PCP)

- blocks NMDA glutamate receptors
- produces symptoms similar to schiz
- induces both negative and positive symptoms



# *Glutamate Hypothesis*

## ➤ Phencyclidine (PCP)

- Doesn't produce psychosis in preadolescents

- produces more severe symptoms than schiz

# *Glutamate Hypothesis*

- Risky to increase glutamate
  - Too widely used
- Don't stimulate directly

# *Glutamate Hypothesis*

- Working on glycine
  - amino acid
  - enhances NMDA effects
  - not effective antipsychotic
  - increases antipsychotics effects

# *Schizophrenia*

## ➤ Causal factors

- Heredity

- Dopamine

- Glutamate

- **Brain Abnormalities**

- Environment

- Infections

# *Brain abnormalities*

## ➤ MRI & CT studies

– Found loss of brain tissue in patients with schizophrenia

# *Brain abnormalities*

## ➤ Ventricles

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

# *Brain abnormalities*

## ➤ Mild Brain Abnormalities

- Less than average gray matter
- Larger than average ventricles
- Smaller thalamus
- left hemisphere slightly larger

# *Brain abnormalities*

- Worst in
  - left temporal lobe
  - frontal lobe



# *Brain abnormalities*

- Immature or poorly developed
  - dorsolateral prefrontal cortex
  - deficits in memory & attention

# *Brain abnormalities*

- Smaller cell bodies
  - in frontal cortex & hippocampus

# *Schizophrenia*

## ➤ Causal factors

- Heredity
- Dopamine
- Glutamate
- Brain Abnormalities
- **Environment**
- Infections

# *Environmental Causes*

- Famine during pregnancy
  - (especially thiamine deficiency)



# *Environmental Causes*

## ➤ Predictors

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

# *Environmental Causes*

➤ Neurodevelopmental hypothesis

– Schiz caused by abnormalities to nervous system during prenatal or neonatal periods

# *Environmental Causes*

- Prenatal and Neonatal
  - Mother's nutrition
  - Premature birth
  - Low birth weight
  - Complications during delivery

# *Environmental Causes*

- Rh-negative & baby Rh-positive
  - may trigger immunological rejection by mother
    - hearing deficits
    - mental retardation
    - twice usual probability of schiz
    - 2%



# *Environmental Causes*

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

# *Schizophrenia*

## ➤ Causal factors

- Heredity
- Dopamine
- Glutamate
- Brain abnormalities
- Environment
- **Infections**

# Schizophrenia

## ➤ Causes

– Flu (or other viral illness)



# *Schizophrenia*

- **Flu** (or other viral illness)
  - More likely if born during late winter and early spring



# *Schizophrenia*

- **Flu** (or other viral illness)
  - More likely in cities than countryside



# *Schizophrenia*

## ➤ Causes

- More likely far from equator
- Decreased winter temp?



# *Infections*

## ➤ Childhood infections

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

# *Diagnosis*





# *Diagnosis*

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

# *Diagnosis*

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

# *Diagnosis*

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

# *Drugs can help-hurt*



# *Drugs can help-hurt*

- Some drugs make it worse
  - Marijuana
  - Amphetamines
  - Cocaine

# *Drugs can help-hurt*

## ➤ Smoking

- 3x likely addicted to nicotine
- 90% in schiz
- Schiz worse during withdrawal

# *Drugs can help-hurt*

- Chlorpromazine (Thorazine)
  - 1<sup>st</sup> drug successful

# *Drugs can help-hurt*

## ➤ Antipsychotic drugs

- Primarily work by blocking dopamine receptors



# *Drugs can help-hurt*

## ➤ Phenothiazines

- class of neuroleptic drugs
- includes chlorpromazine

# *Drugs can help-hurt*

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

# *Drugs can help-hurt*

## ➤ Relapse

- Stop taking meds

  - Feel better, think don't need

  - Interact with other drugs

  - Interact with alcohol

# *Drugs can help-hurt*

- Antipsychotic medications
  - available since mid-1950's
    - Chlorpromazine (Thorazine)
    - Haloperidol (Haldol)
    - Perphenazine (Etrafon)
    - Fluphenazine (Prolixin)

# *Drugs can help-hurt*

- Antipsychotic medications
  - available since mid-1990's
  - "atypical" antipsychotics

# *Drugs can help-hurt*

- Antipsychotic medications
  - Clozapine (Clozaril)
    - psychotic symptoms
    - Hallucinations
    - breaks with reality

# *Drugs can help-hurt*

- Antipsychotic medications
  - Clozapine (Clozaril)
    - Side effect for clozapine
      - Agranulocytosis = loss of white blood cells

# *Drugs can help-hurt*

- Antipsychotic medications
  - Risperidone (Risperdal)
  - Olanzapine (Zyprexa)
  - Quetiapine (Seroquel)
  - Ziprasidone (Geodon)
  - Aripiprazole (Abilify)
  - Paliperidone (Invega)



# *Drugs can help-hurt*

- Antipsychotic medications
  - Old & new ones about equally effective

# *Drugs can help-hurt*

- Antipsychotic medications
  - Side effects
    - Worse when start
    - Last few days for most

# *Drugs can help-hurt*

## ➤ Antipsychotic medications

- Side effects

  - Dizzy when changing positions

  - Blurred vision

  - Drowsiness

# *Drugs can help-hurt*

- Antipsychotic medications
  - Side effects
    - Rapid heartbeat
    - Sensitivity to the sun
    - Skin rashes

# *Drugs can help-hurt*

## ➤ Antipsychotic medications

- Side effects

  - Major weight gain

  - Rigidity of joints

  - Muscle spasms

  - Restlessness

  - Tremors

# *Side Effects*

- Tardive dyskinesia
  - Caused by long term use
  - Can't control mouth muscles

# *Side Effects*

- Tardive dyskinesia
  - Tremors & involuntary move
  - Caused by prolonged blocking
    - Of dopamine receptors in basal ganglia

# *Drugs can help-hurt*

- Antipsychotic medications
  - Usually in pill or liquid form
  - Some are shots given monthly



# *Drugs can help-hurt*

## ➤ New Drugs

- Mesolimbocortical system

  - Where antipsychotics impact?

  - Set of neurons

  - Project from midbrain

    - tegmenum to limbic system

# *New Drugs*

- New drugs (atypicals)
  - Don't cause movement problems
  - Less intense effects on dopamine type D<sub>2</sub> receptors
  - Stronger effects at D<sub>4</sub> and serotonin 5-HT<sub>2</sub> receptors

# *New Drugs*

- Atypical antipsychotics
  - More effective?
  - Better with positive symptom
  - Not so much with negative
  - Don't improve overall quality of life any better

# *New Drugs*

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

# *New Drugs*

- Long-term drug treatment
  - Serious side effects
    - Similar symptoms to Parkinson's disease
    - Slow movement, lack of facial expression, general weakness

*Bye Bye*

