

260-2017-03-13-schizophrenia

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Prelude

Today's Topics

- Prevalence of mental illness
- Schizophrenia

Mental illness lifetime prevalence

Schizophrenia

Simulating the Experience

Overview

- Lifetime prevalence ~ 1/100
- ~1/3 chronic & severe
- Onset post-puberty, early adulthood
- Pervasive disturbance in mood, thinking, movement, action, memory, perception

Screening (Yale PRIME test)

1. I think that I have felt that there are odd or unusual things going on that I can't explain.
2. I think that I might be able to predict the future.
3. I may have felt that there could possibly be something interrupting or controlling my thoughts, feelings, or actions.

<http://www.schizophrenia.com/sztest/primetest.pdf>

Screening (continued)

5. I get confused at times whether something I experience or perceive may be real or may be just part of my imagination or dreams.
6. I have thought that it might be possible that other people can read my mind, or that I can read other's minds.
7. I wonder if people may be planning to hurt me or even may be about to hurt me.

Historical background

- Bleuler
 - Introduced “schizophrenia” or “split mind”
 - Not multiple personality disorder
- Kraepelin
 - Dementia Praecox and Paraphrenia (1919)

- Emphasized developmental and hereditary origins

“Positive” symptoms

- “Additions” to behavior
- Disordered thought
- Delusions of grandeur, persecution
- Hallucinations (usually auditory)
- Bizarre behavior

“Negative” symptoms

- “Reductions” in behavior
- Poverty of speech
- Flat affect
- Social withdrawal
- Impaired executive function
- Anhedonia (loss of pleasure)
- Catatonia (reduced movement)

Cognitive symptoms

- Memory
- Attention
- Planning, decision-making
- Social cognition
- Movement

Biological bases

- Genetic disposition
- Brain abnormalities
- Developmental origins

Genetic disposition

Ventricles larger, esp in males

Hip and amygdala smaller

- Related to ventricular enlargement?
- Early disturbance in brain development?

(Jiao et al. 2017)

- Dentate gyrus (DG) in hippocampus critical for spatial coding, learning and memory, and emotion processing.
- DG dysfunction implicated in schizophrenia.
- Gene linked to schizophrenia, Transmembrane protein 108 (Tmem108) enriched in DG granule neurons
- Tmem108 expression increased during postnatal period critical for DG development.

(Jiao et al. 2017)

- Tmem108-deficient neurons form fewer and smaller spines.
- Tmem108-deficient mice display schizophrenia-relevant behavioral deficits.

Rapid gray matter loss in adolescents?

(Thompson et al. 2001)

Dopamine hypothesis

Evidence for DA hypothesis

- DA (D2 receptor) antagonists (e.g. chlorpromazine)
 - improve positive symptoms
- *Typical antipsychotics* are DA D2 antagonists
- DA agonists
 - amphetamine, cocaine, L-DOPA
 - mimic or exacerbate symptoms

Tardive Dyskinesia a side effect of DA antagonists

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Evidence against...

- New, *atypical antipsychotics*
 - (e.g. Clozapine) INCREASE DA in frontal cortex, affect 5-HT
- Mixed evidence for high DA metabolite levels in CSF

Glutamate hypothesis

- *Psychomimetic* drugs induce schizophrenia-like states
 - Phencyclidine (PCP), ketamine
 - NMDA receptor antagonists
- Schizophrenia == *underactivation* of NMDA receptors?
 - NMDA receptor role in learning, plasticity
 - DG neurons in (Jiao et al. 2017) were glutamate-releasing.

Schizophrenia summed up

- Wide-ranging disturbance of mood, thought, action, perception
- Broad changes in brain structure, function, chemistry, development
- Genetic risk + environmental factors

Early life stress increases risk

- Urban vs. rural living
- Exposure to infection *in utero*, other birth complications

(Levine et al. 2016)

- Children (N=51,233) of parents who born during Nazi era (1922-1945)
- Emigrated before (indirect exposure) or after (direct exposure) to Nazi era
- Children exposed to direct stress of Nazi era in utero or postnatally
 - Did **not** differ in rates of schizophrenia, but
 - Had higher rehospitalization rates

(Debost et al. 2015)

- Danish cohort (n=1,141,447)
- Exposure to early life stress
 - *in utero* did **not** increase risk of schizophrenia, but
 - during 0-2 years increased risk
- Increased risk associated with an allele of a cortisol-related gene

Next time...

- Bipolar disorder

References

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