PSYCH 260/BBH 203

Schizophrenia

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Prelude

2:55

Today's Topics

- Quiz 3 next Tuesday (after class)
- Wrap-up on bipolar disorder
- Schizophrenia

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)

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

Historical background

- Bleuler
  - Coined term “schizophrenia” or “split mind”
  - NOT multiple personality disorder
- Kraeplin
  - 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)

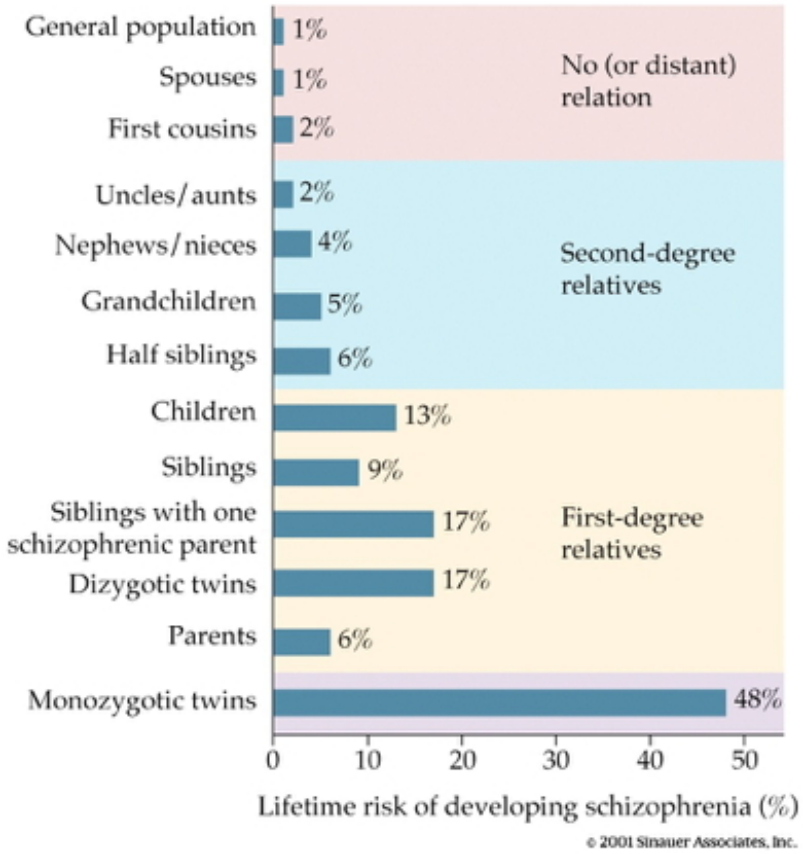
Cognitive symptoms

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

Biological bases

- Genetic disposition
- Brain abnormalities
- Developmental origins

Genetic disposition



But, no single gene…

Archival Report

No Evidence That Schizophrenia Candidate Genes Are More Associated With Schizophrenia Than Noncandidate Genes

Emma C. Johnson [a, b], Richard Border [a, b], Whitney E. Melroy-Greif [d], Christiaan A. de Leeuw [e, f], Marissa A. Ehringer [b, c], Matthew C. Keller [a, b]

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https://doi.org/10.1016/j.biopsych.2017.06.033

(Johnson et al., 2017)

Genes associated with schizophrenia at higher than chance levels

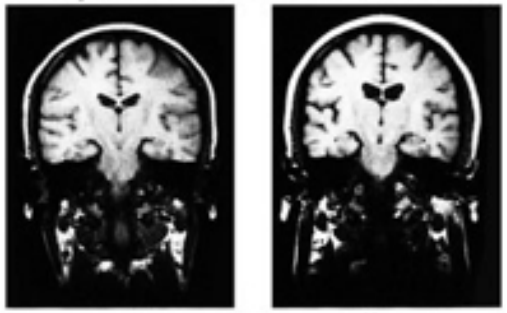
- *NOTCH4*, *TNF*:
    - Part of major histocompatibility complex (MHC), cell membrane specializations involved in the immune system
- *DRD2* (dopamine D2 receptor), *KCNN3* (Ca+ activated K+ channel), *GRM3* (metabotropic glutamate receptor)

(Johnson et al., 2017)

Ventricles larger, esp in males

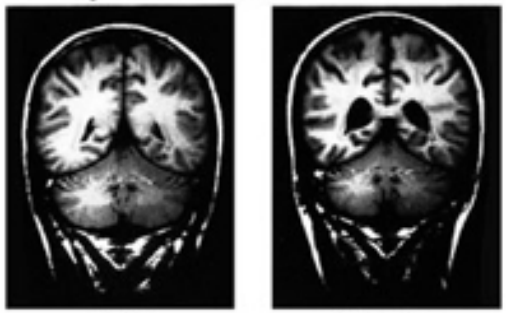
MRI brain images of twins discordant for schizophrenia

35-year-old female identical twins



Well Affected

28-year-old male identical twins

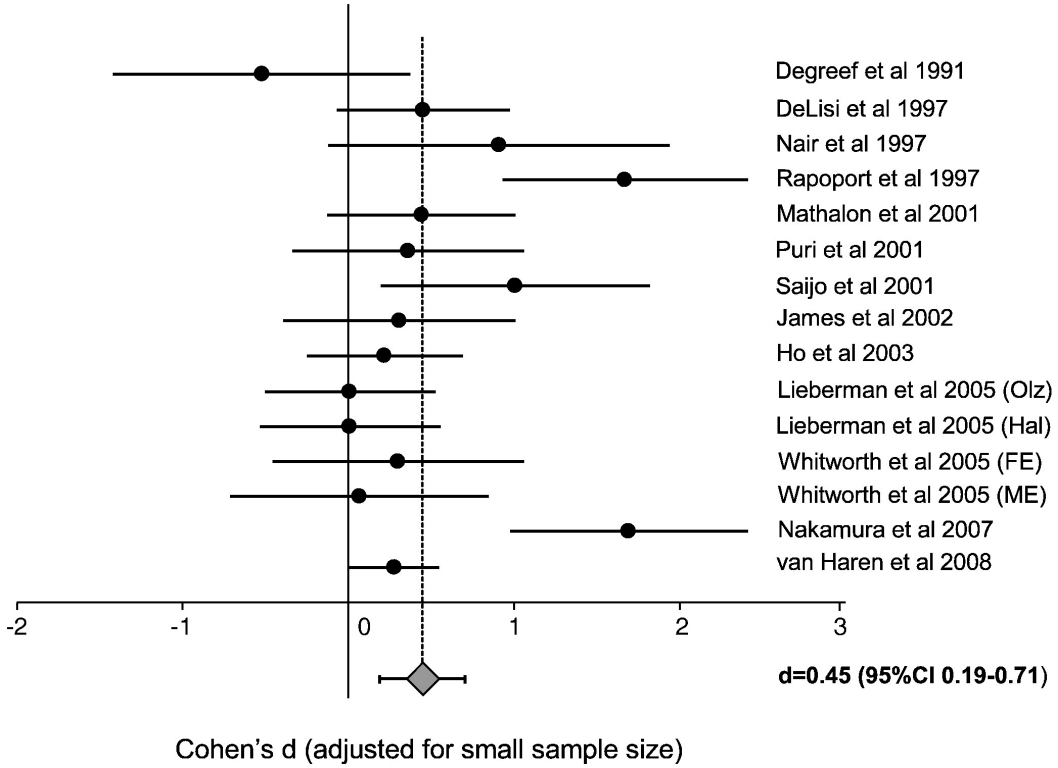


Well Affected

BIOLOGICAL PSYCHOLOGY, Fourth Edition, Figure 15.4

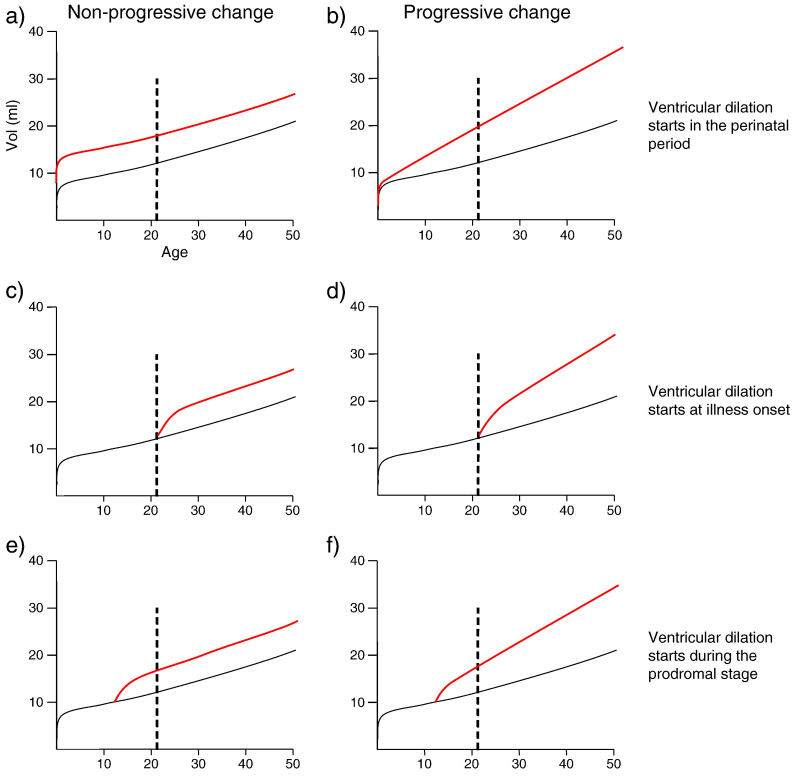
Cause or effect?

Ventricular enlargement increases across time (Kempton, Stahl, Williams, & DeLisi, 2010)



Enlargement precedes diagnosis?

As in trajectories B or F

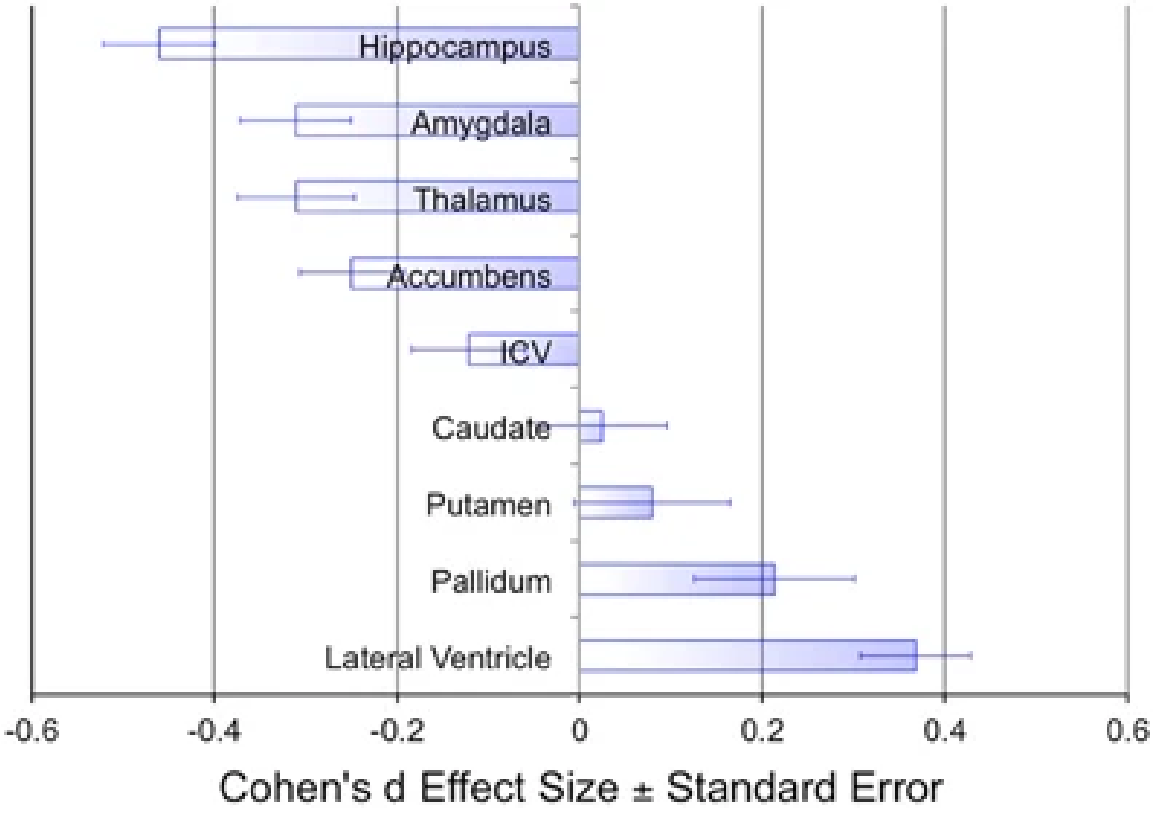


(Kempton et al., 2010)

Hippocampus, amygdala, thalamus, nucleus accumbens smaller

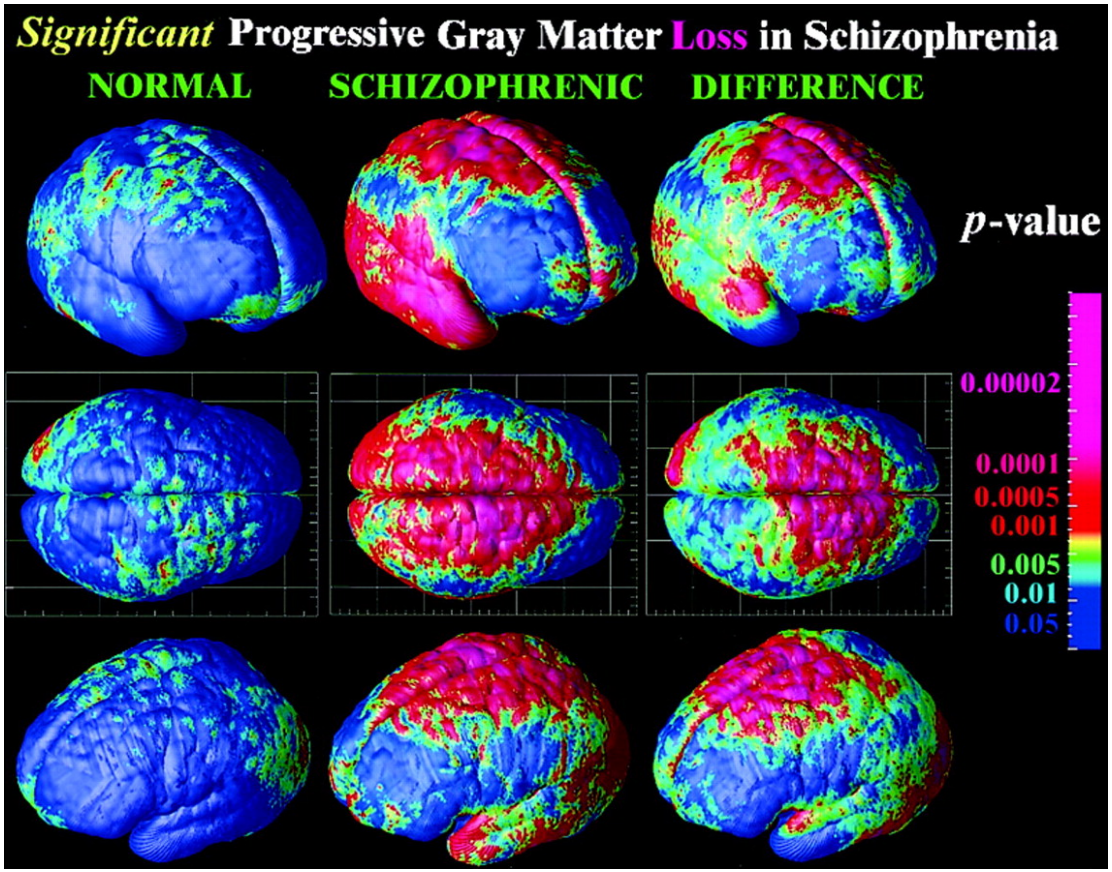
- Related to ventricular enlargement?
- Early disturbance in brain development?

(Erp et al., 2015)



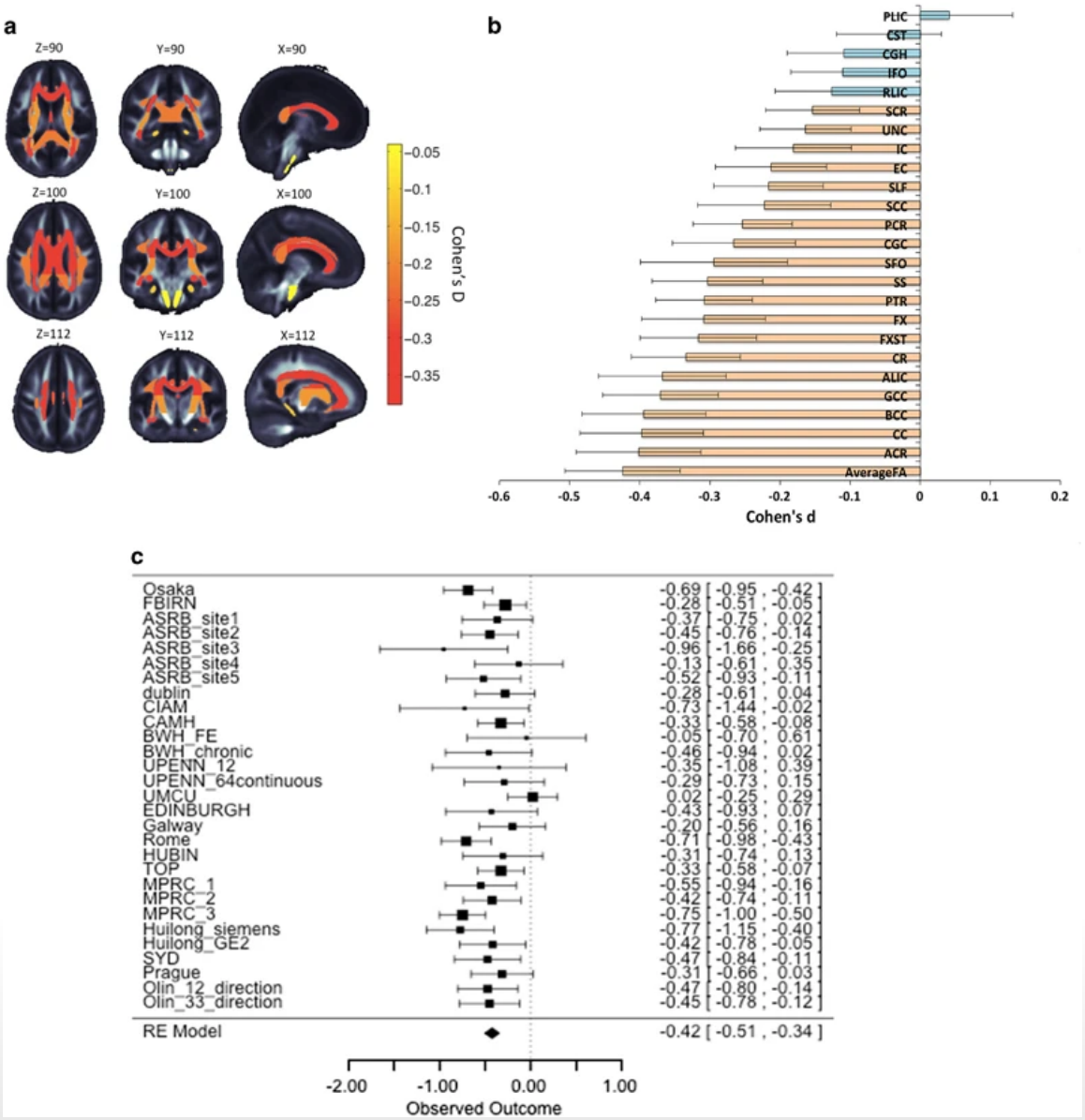
https://www.nature.com/articles/mp201563/figures/1

Rapid gray matter loss in adolescents?

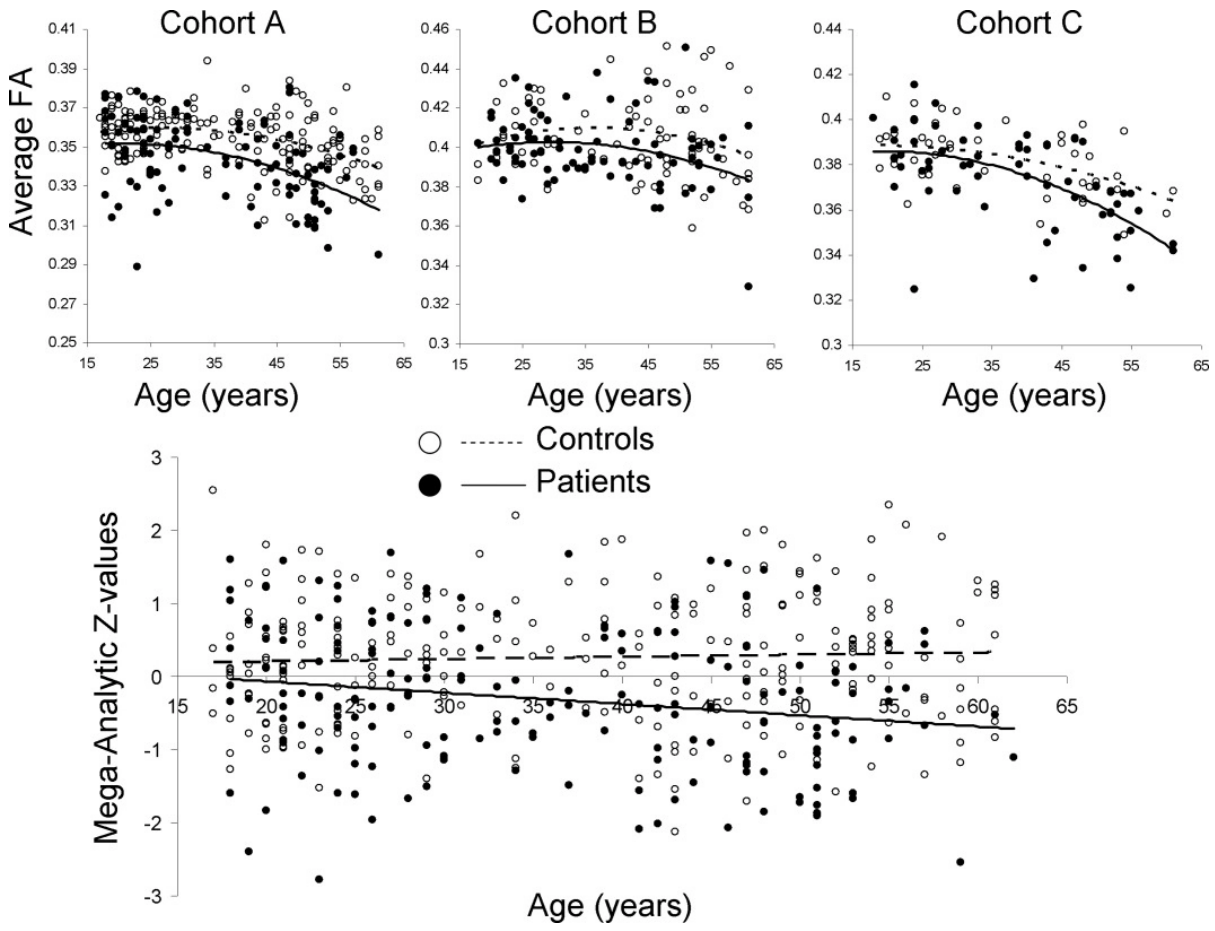


(Thompson et al., 2001)

Widespread disruption in white matter connectivity (Kelly et al., 2017)

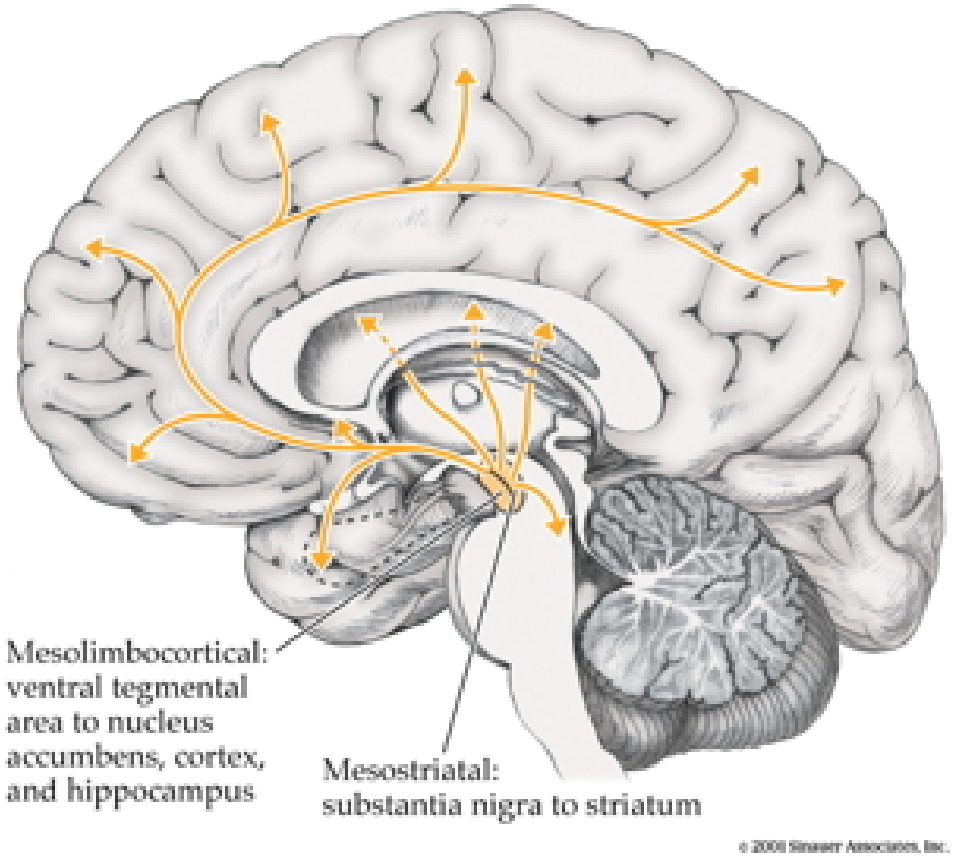


White matter loss over age



(Kochunov et al., 2016)

Dopamine hypothesis



Evidence for DA hypothesis

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

Tardive Dyskinesia a side effect of DA antagonists

https://www.youtube.com/watch?v=_UCaWSMddwA

Evidence against DA hypothesis…

- 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…
  - Phencyclidine (PCP), ketamine
  - NMDA receptor antagonists (NMCA glu + voltage-gated)
- …can induce schizophrenia-like states
- Schizophrenia == *underactivation* of NMDA receptors?
  - NMDA receptor role in learning, plasticity

Early life stress increases risk

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

(Levine, Levav, Pugachova, Yoffe, & Becher, 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
  - but *exposure during infancy (0-2 years) increased risk*
- Increased risk associated with an allele of a cortisol-related gene

Schizophrenia summed up

- Wide-ranging disturbance of mood, thought, action, perception
- Broad changes in brain structure, function, chemistry, development
- ~~Dopamine hypothesis~~ -> glutamate hypothesis
- Genetic (polygenic = multiple genes) risk + environmental factors
- One disorder or many?

Next time…

- Emotion, happiness, and reward
- Quiz 3 (after class)

References

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