# 260-2017-10-20-schizophrenia

Rick Gilmore

2017-10-19 11:36:33

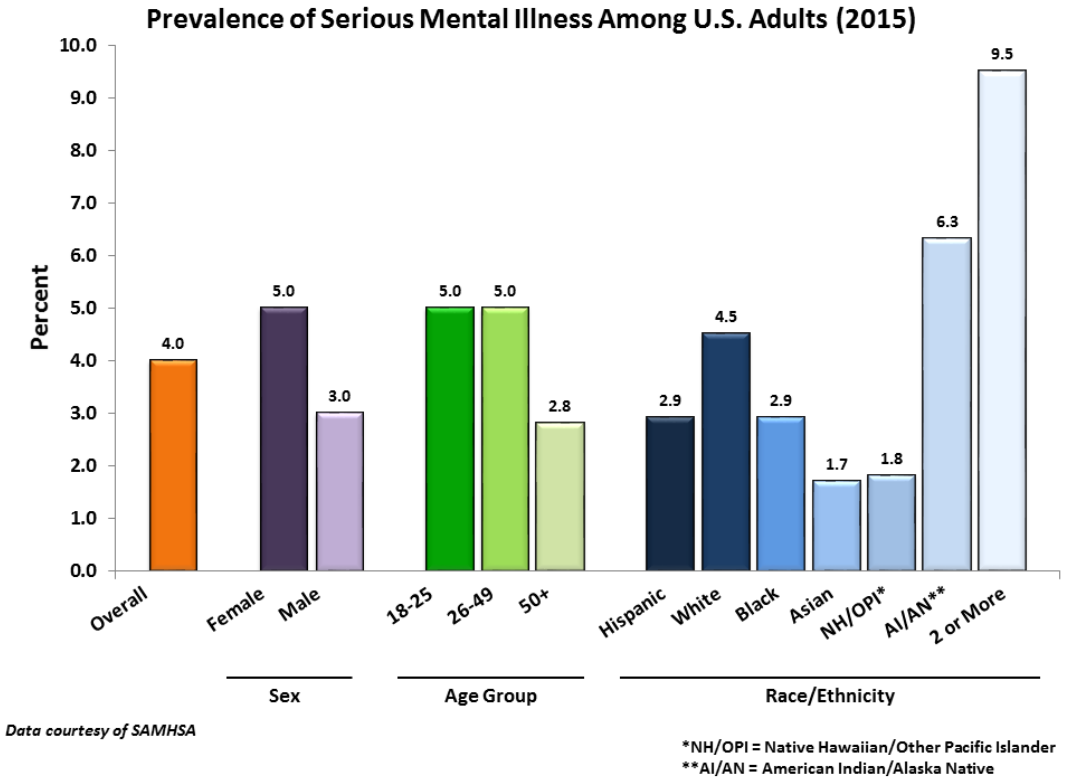
# Prelude

the kinks- you really got me

# Today's Topics

- Prevalence of mental illness
- Schizophrenia

# Mental illness lifetime prevalence



# Schizophrenia

Schizophrenia: Gerald, Part 1

# Simulating the Experience

Schizophrenia ABC 20-20 Documentary Part 2

# 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
  - Introduced “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)

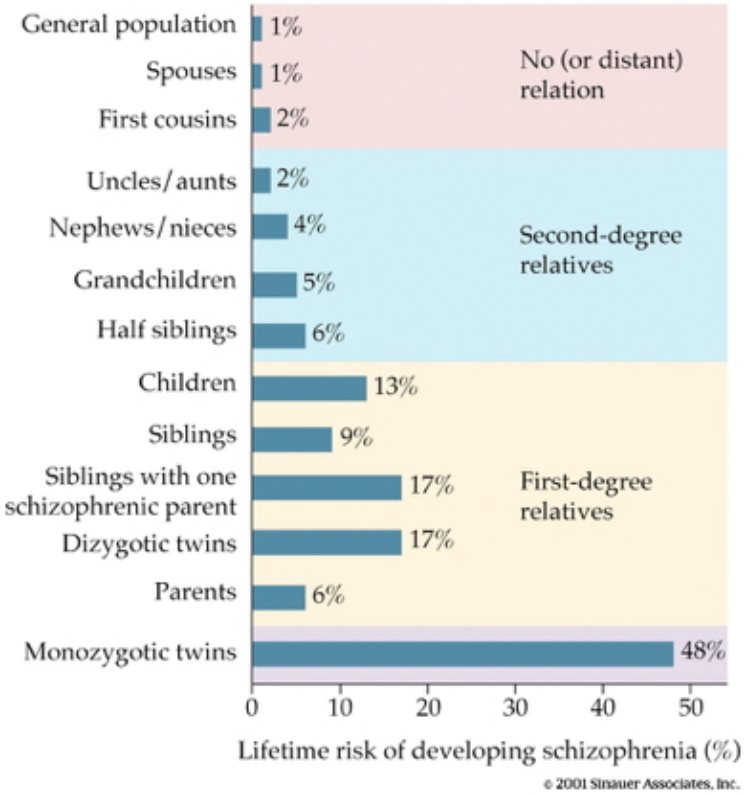
# Cognitive symptoms

- 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

# Genes associated with schizophrenia at higher than chance levels

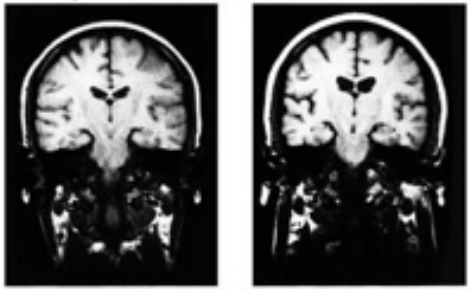
- , :
  - Part of major histocompatibility complex (MHC), cell membrane specializations involved in the immune system
- (dopamine D2 receptor), (Ca+ activated K+ channel), (metabotropic glutatmate receptor)

(Johnson et al. 2017)

# Ventricles larger, esp in males

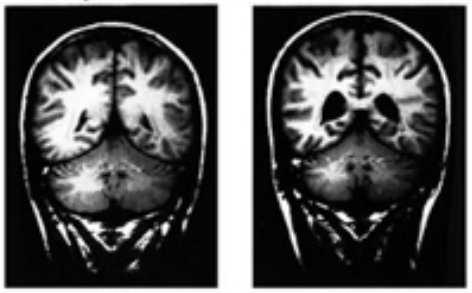
**MRI brain images of twins discordant for schizophrenia**

35-year-old female identical twins



Well Affected

28-year-old male identical twins

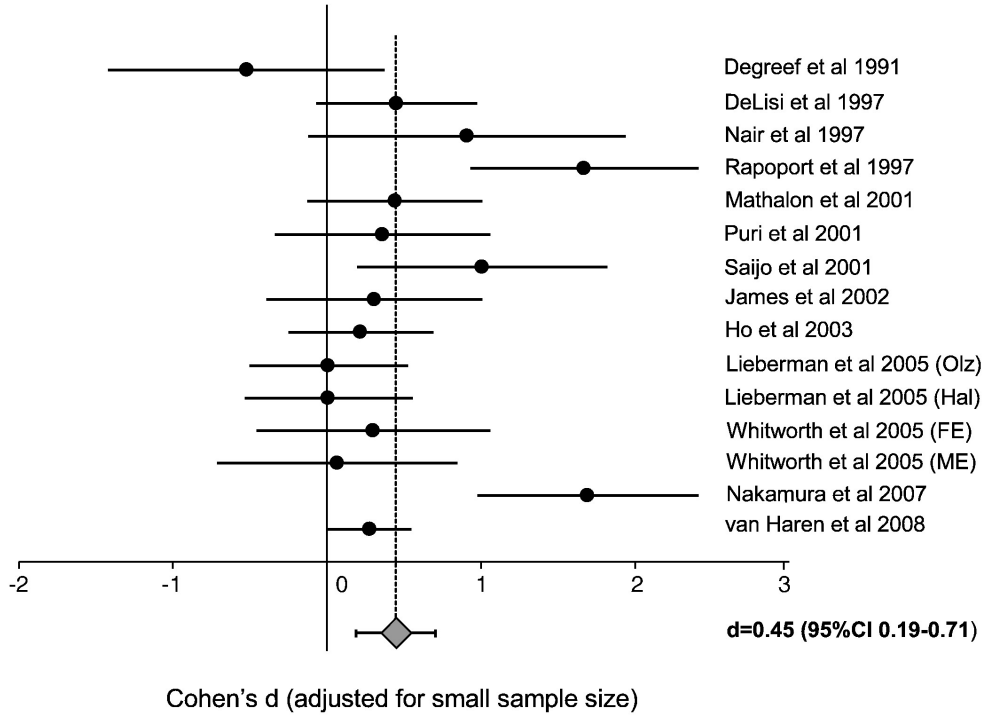


Well Affected

*BIOLOGICAL PSYCHOLOGY, Fourth Edition*, Figure 15.4 

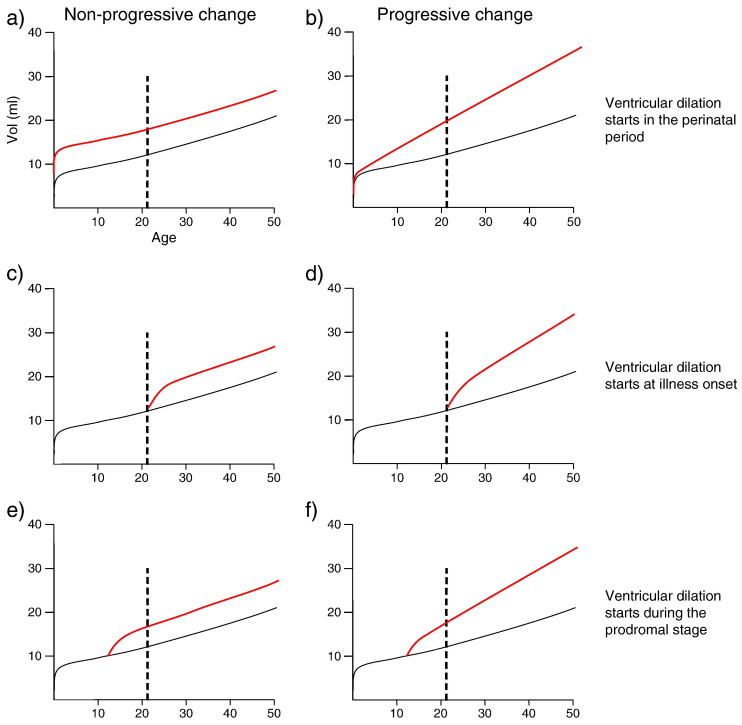
# Cause or effect?

Ventricular enlargement increases across time (Kempton et al. 2010)



# Enlargement precedes diagnosis?

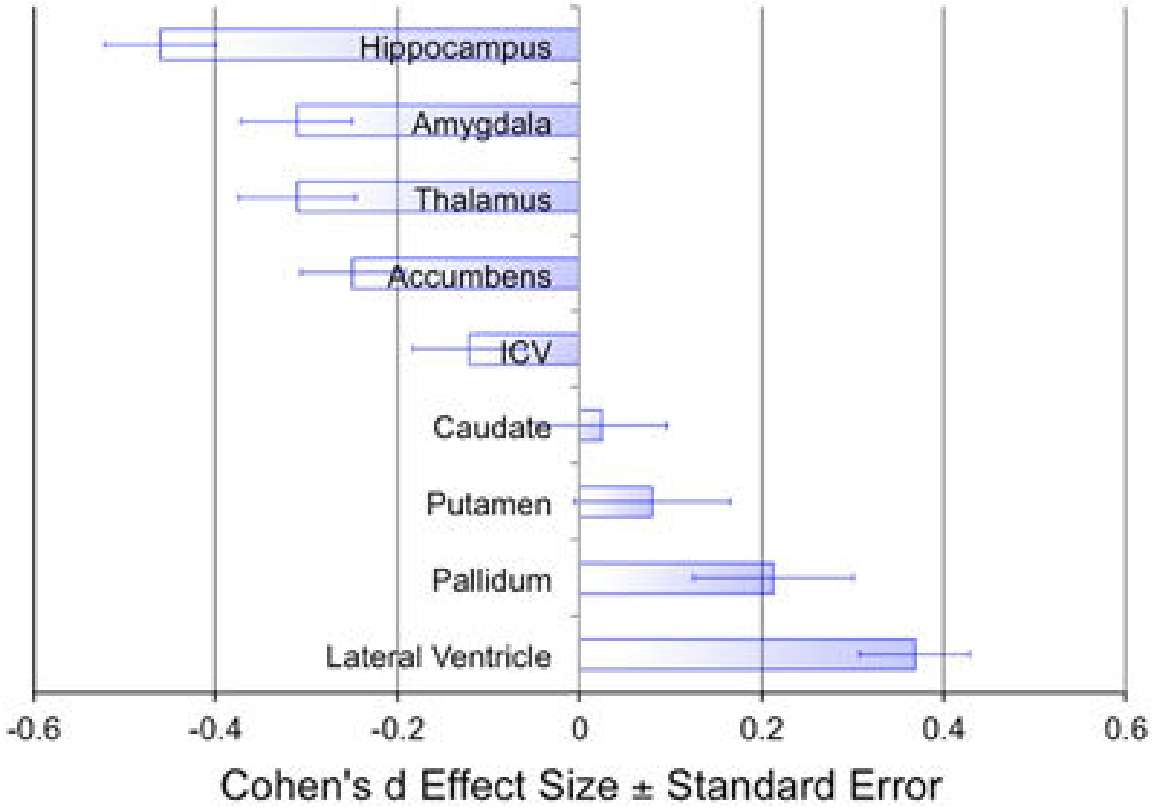
As in trajectories B or F




(Kempton et al. 2010)

# Hip and amygdala smaller

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




(Erp et al. 2015)

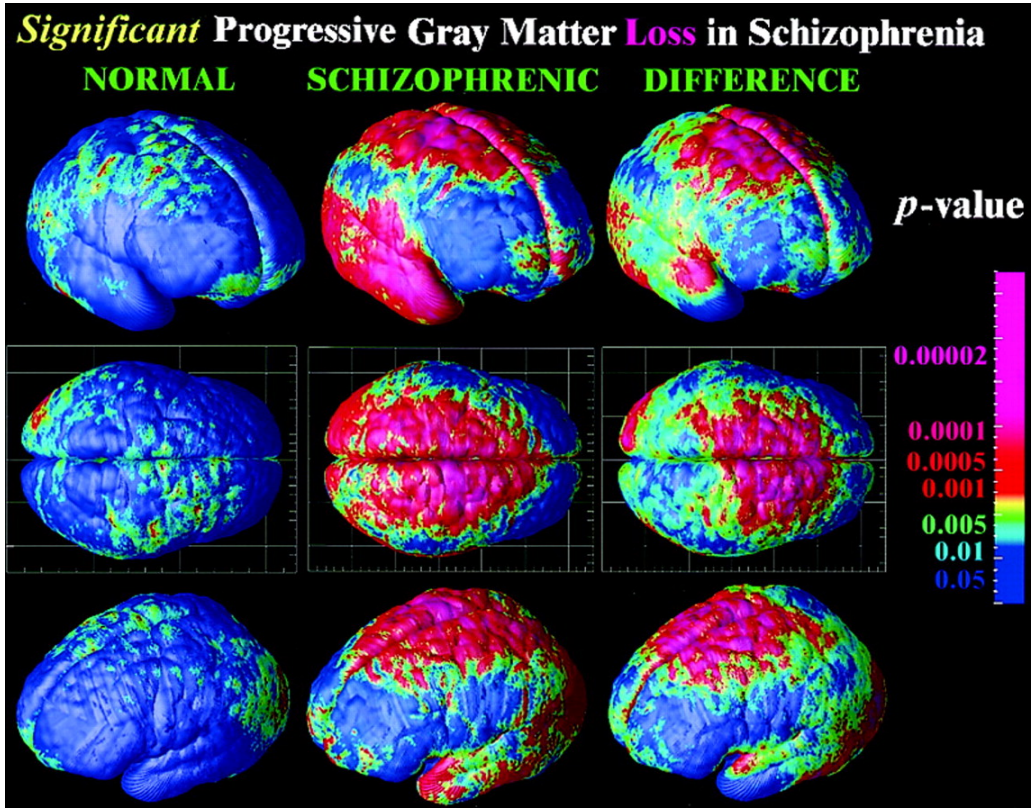
# (Jiao et al. 2017)

- 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)

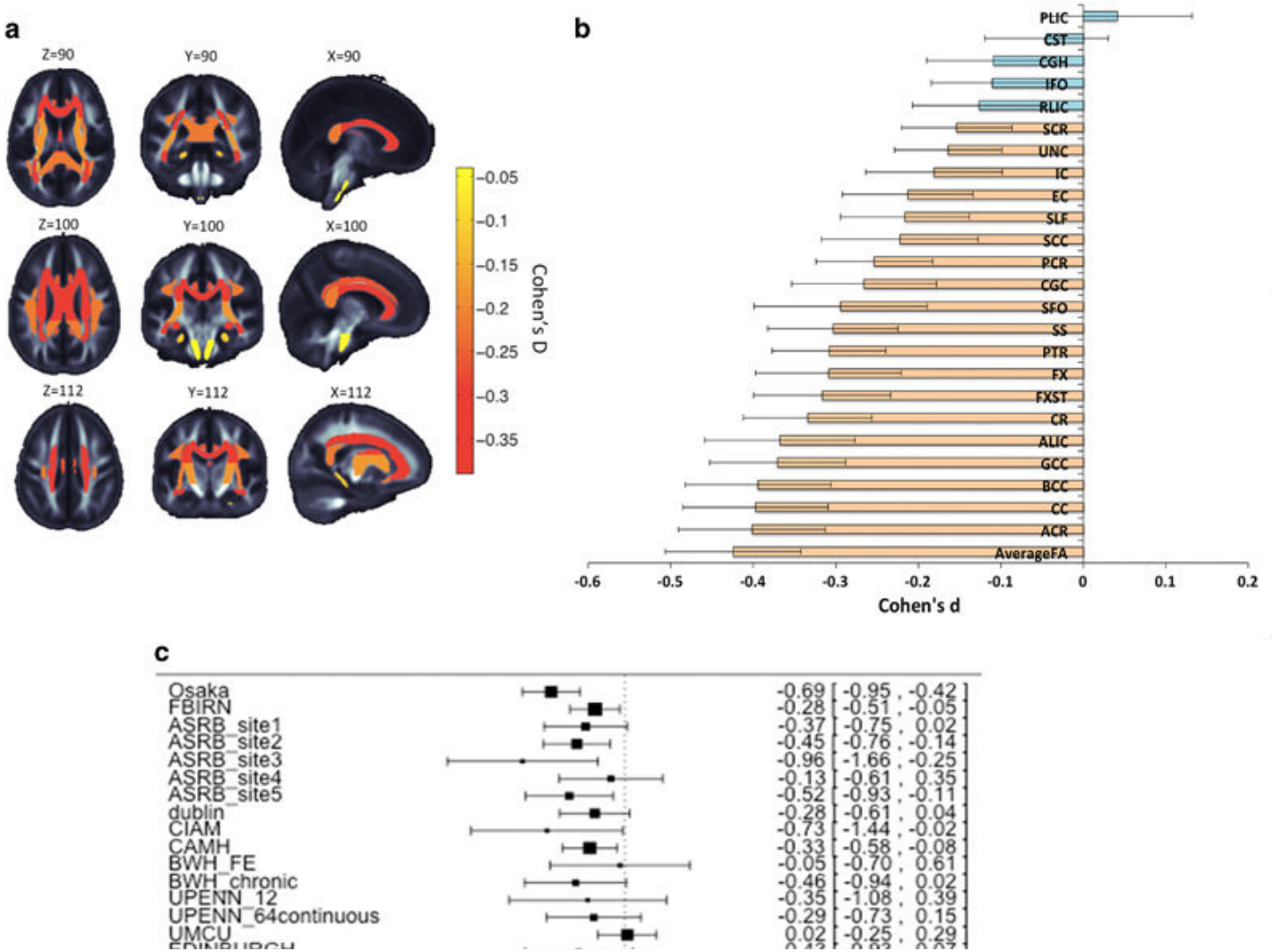
- Tmem108-deficient neurons form fewer and smaller spines.
- Tmem108-deficient mice display schizophrenia-relevant behavioral deficits.

# Rapid gray matter loss in adolescents?

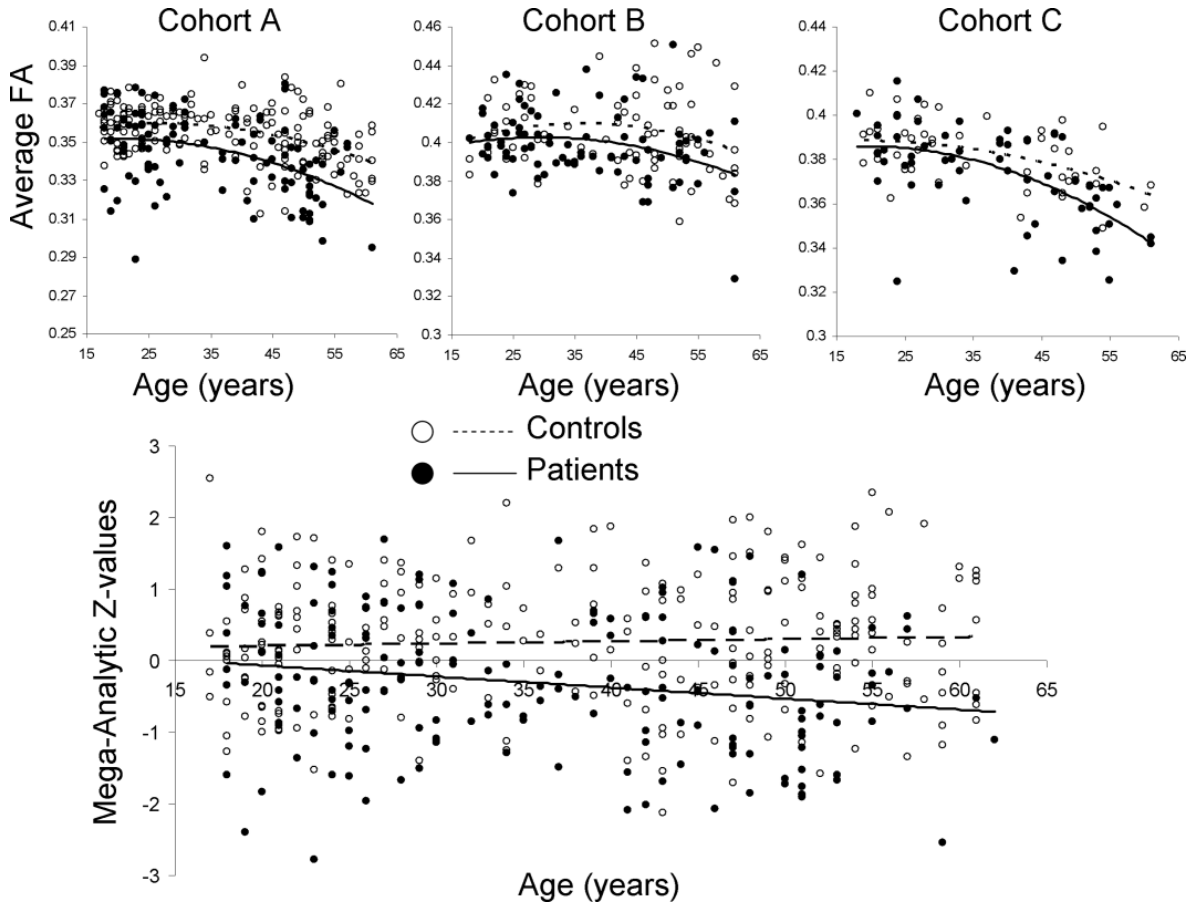



(P. M. Thompson et al. 2001)

# Widespread disruption in white matter connectivity

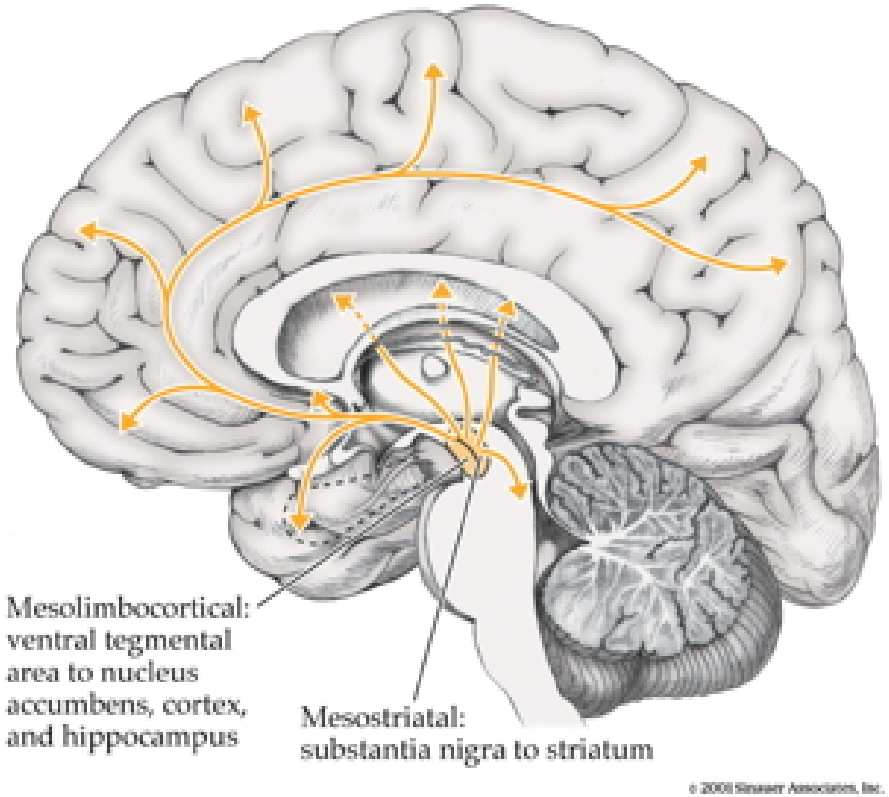


# White matter loss over age




(Kochunov et al. 2016)

# Dopamine hypothesis



# Evidence for DA hypothesis

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

# Tardive Dyskinesia a side effect of DA antagonists


https://2e.mindsmachine.com/ch/12/av/mm2e_1203_tardi

# Evidence against…

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

# Glutamate hypothesis

- drugs induce schizophrenia-like states
  - Phencyclidine (PCP), ketamine
  - NMDA receptor antagonists
- Schizophrenia == 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
- ~~Dopamine hypothesis~~ giving way to glutamate hypothesis
- Genetic (polygenic = multiple genes) risk + environmental factors

# Early life stress increases risk

- Urban vs. rural living
- Exposure to infection , 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 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
  - 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…

- Emotion, happiness, and reward

# References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