

PSYCH 260

Schizophrenia

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2021-10-21 08:30:44

Prelude

the kinks- you really got me



2:55

Today's Topics

- Wrap-up on [bipolar disorder](#)
- Schizophrenia

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
 - Coined term “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)

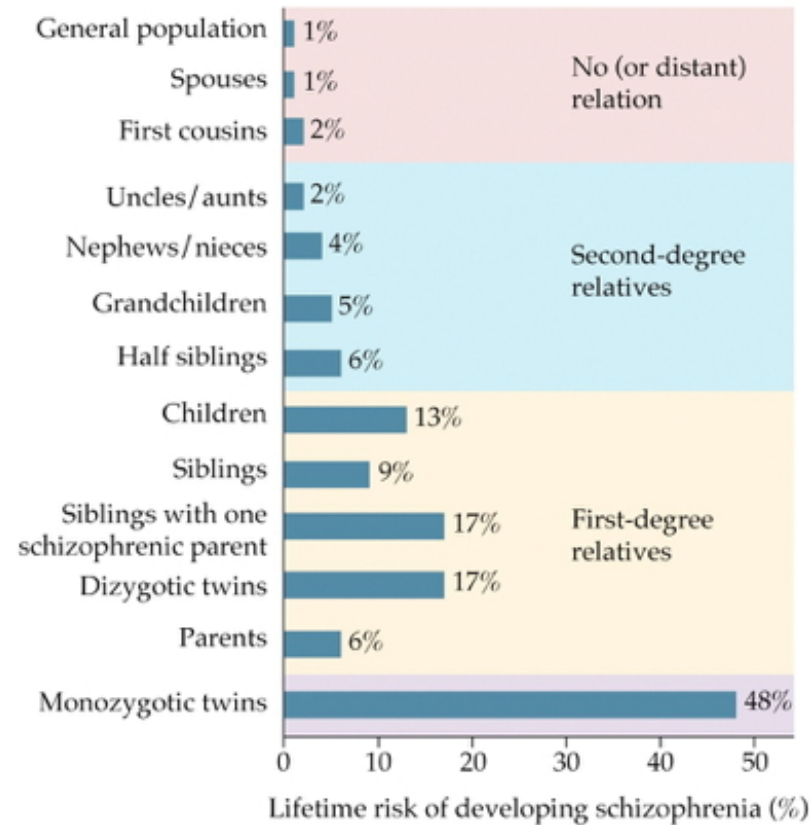
Cognitive symptoms

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

Biological bases

- Genetic disposition
- Brain abnormalities
- Developmental origins

Genetic disposition





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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>

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(Johnson et al., 2017)

Genes associated with schizophrenia at higher than chance levels

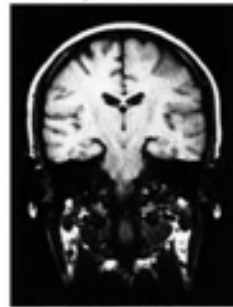
- *NOTCH4*, *TNF*:
 - Part of major histocompatibility complex (MHC), cell membrane specializations involved in the immune system
- *DRD2* (dopamine D2 receptor), *KCNN3* (Ca⁺ activated K⁺ channel), *GRM3* (metabotropic glutamate receptor)

(Johnson et al., 2017)

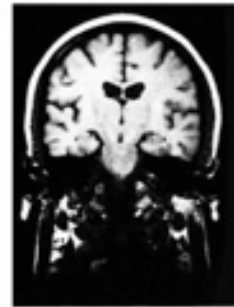
Ventricles larger, esp in males

MRI brain images of twins discordant for schizophrenia

35-year-old female identical twins

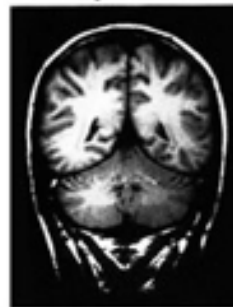


Well



Affected

28-year-old male identical twins



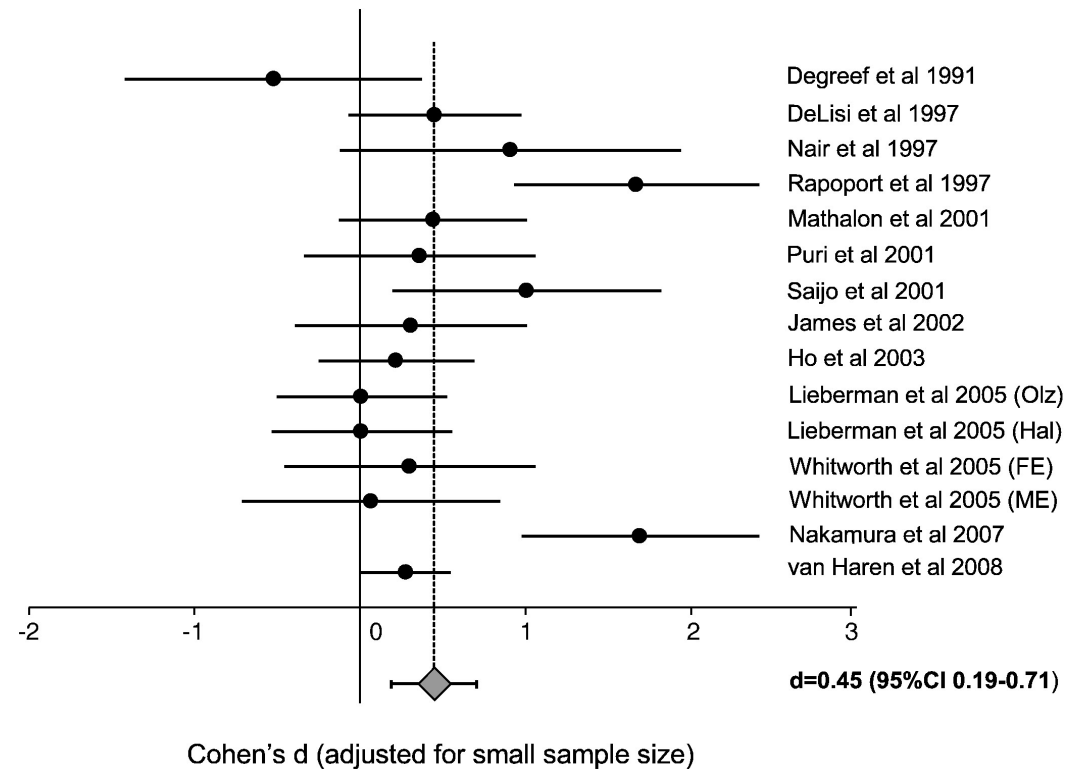
Well



Affected

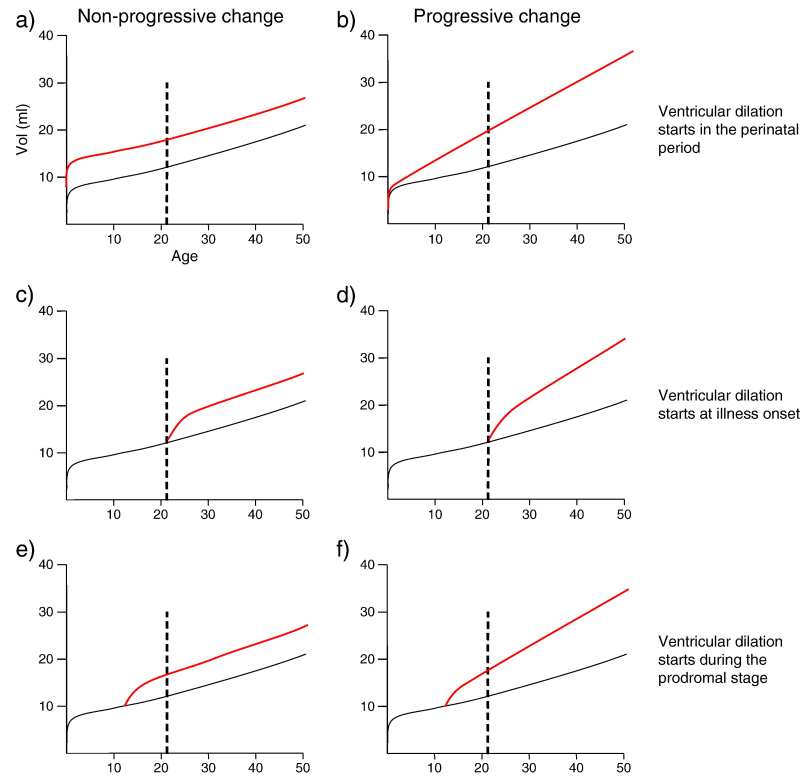
Cause or effect?

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



Enlargement precedes diagnosis?

As in trajectories B or F

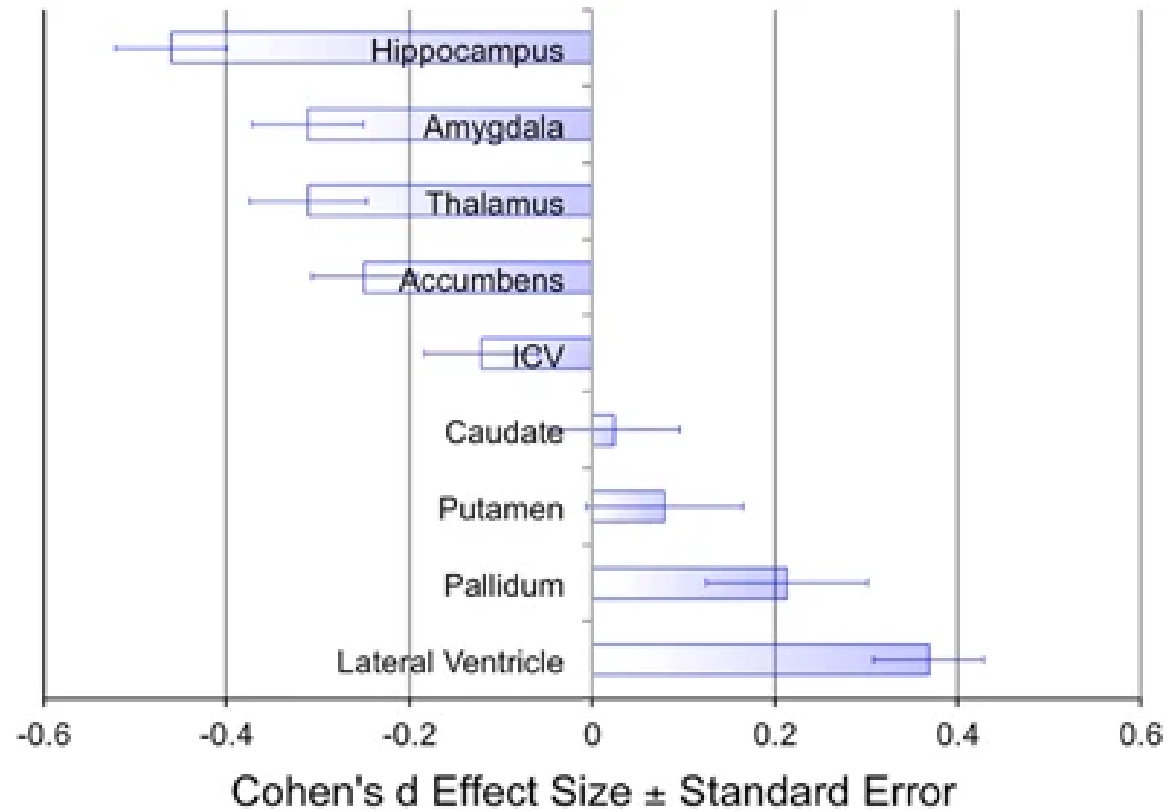


(Kempton, Stahl, Williams, & DeLisi, 2010)

Hippocampus, amygdala, thalamus, nucleus accumbens smaller

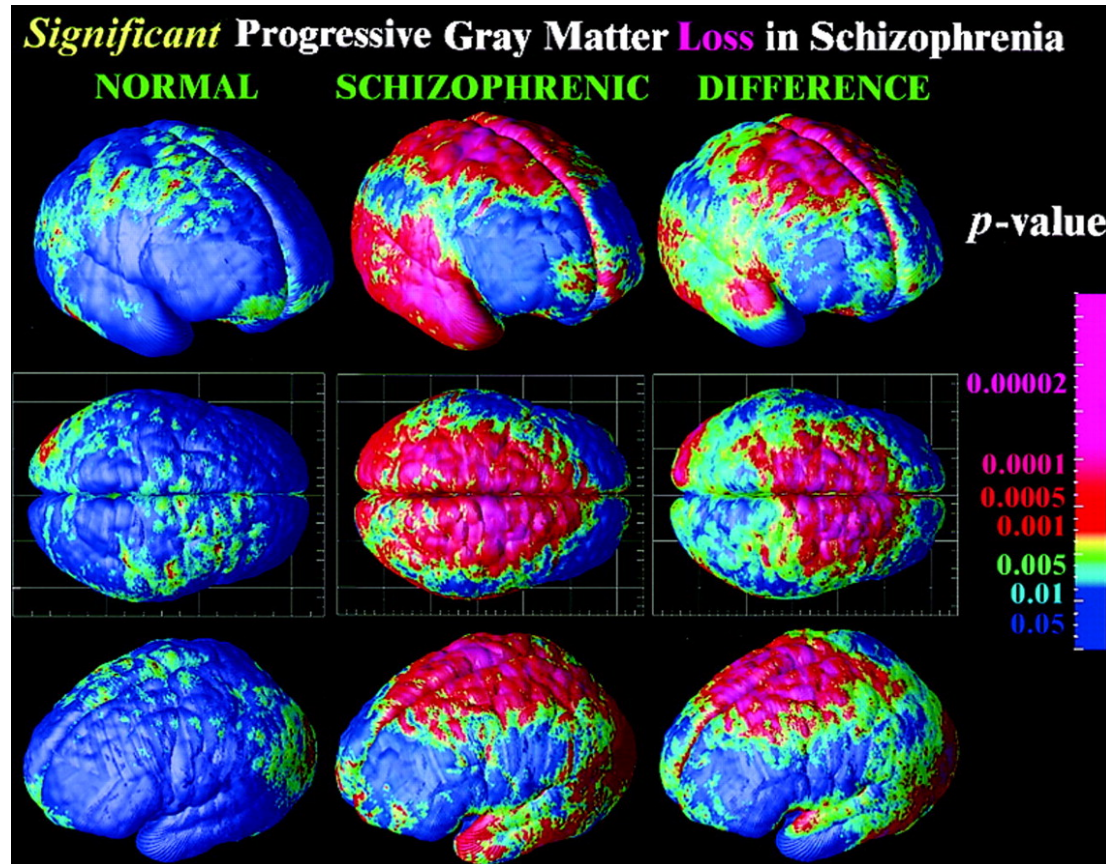
- Related to ventricular enlargement?
- Early disturbance in brain development?

(Erp et al., 2015)



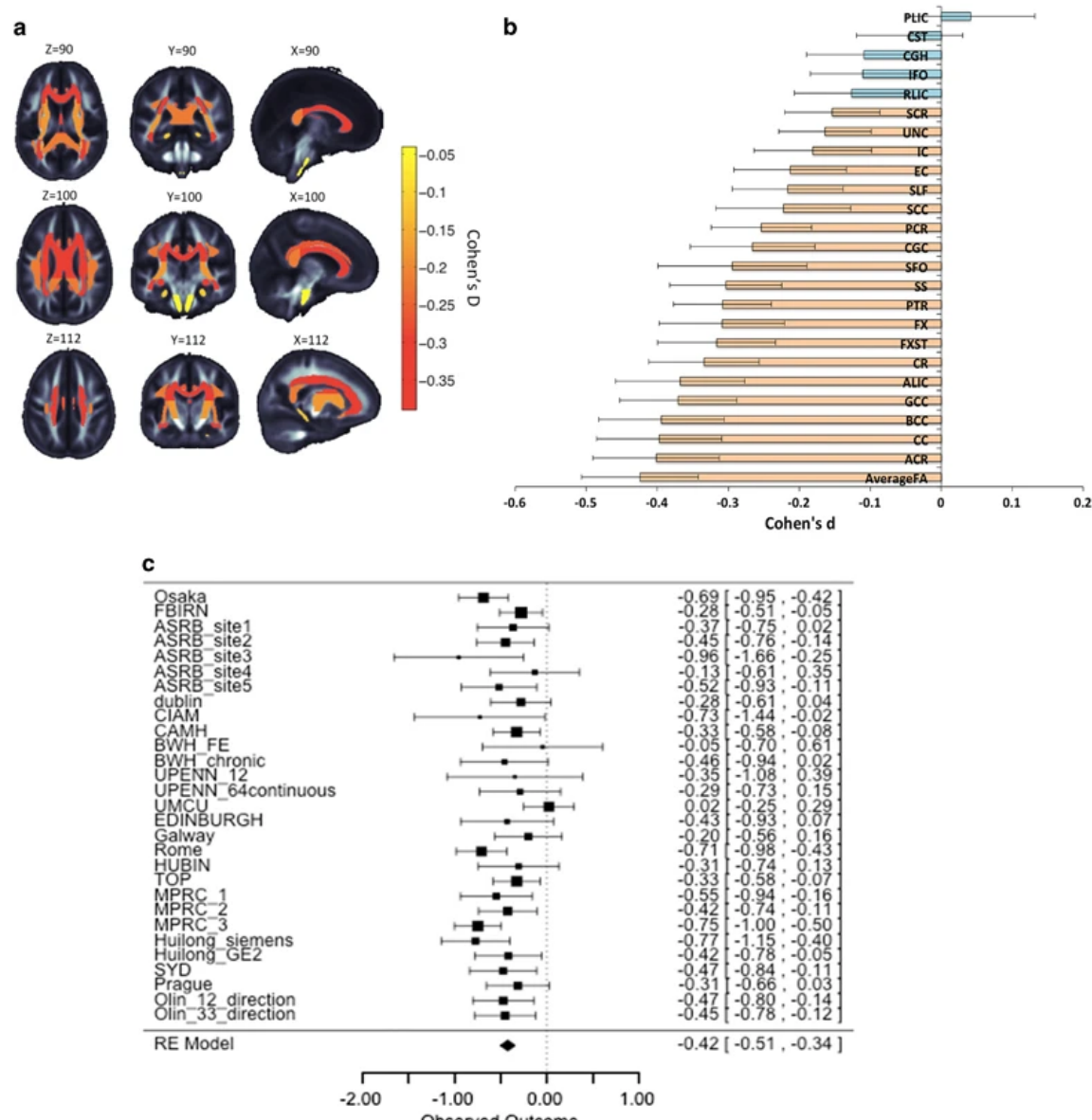
<https://www.nature.com/articles/mp201563/figures/1>

Rapid gray matter loss in adolescents?

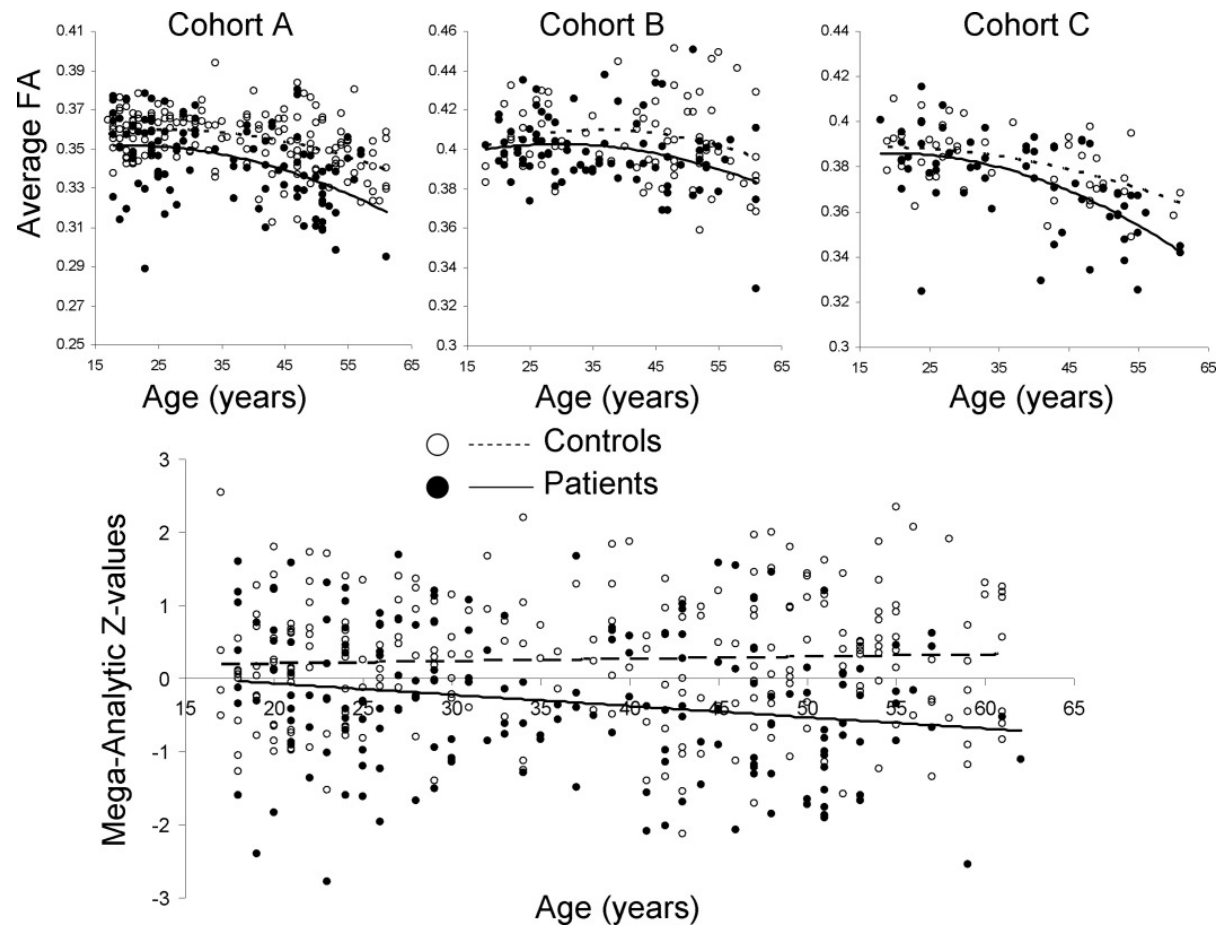


(Thompson et al., 2001)

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

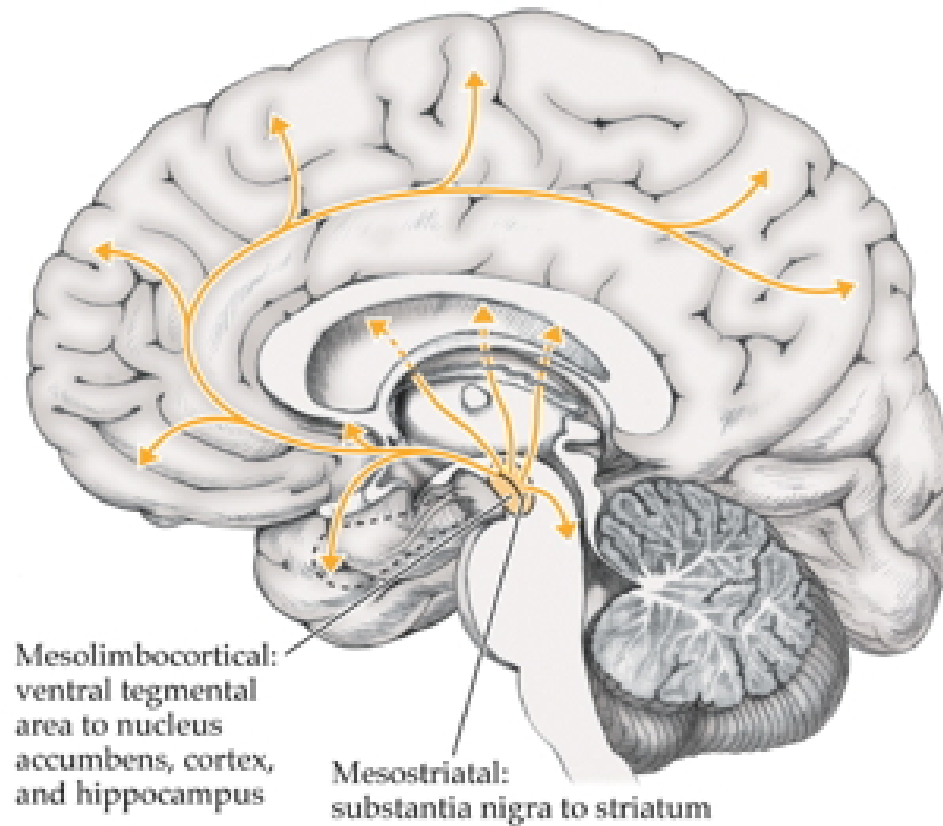


White matter loss over age



[\(Kochunov et al., 2016\)](#)

Dopamine hypothesis



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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

Meet Jeff, Living With Tardive Dyskinesia (TD)



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
- ...can induce schizophrenia-like states
- Schizophrenia == *underactivation* of NMDA receptors?
 - NMDA receptor role in learning, plasticity
 - Dentate gyrus neurons in [\(Jiao et al., 2017\)](#) were glutamate-releasing.

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

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