

# Big data solutions to mapping typical and atypical brain development



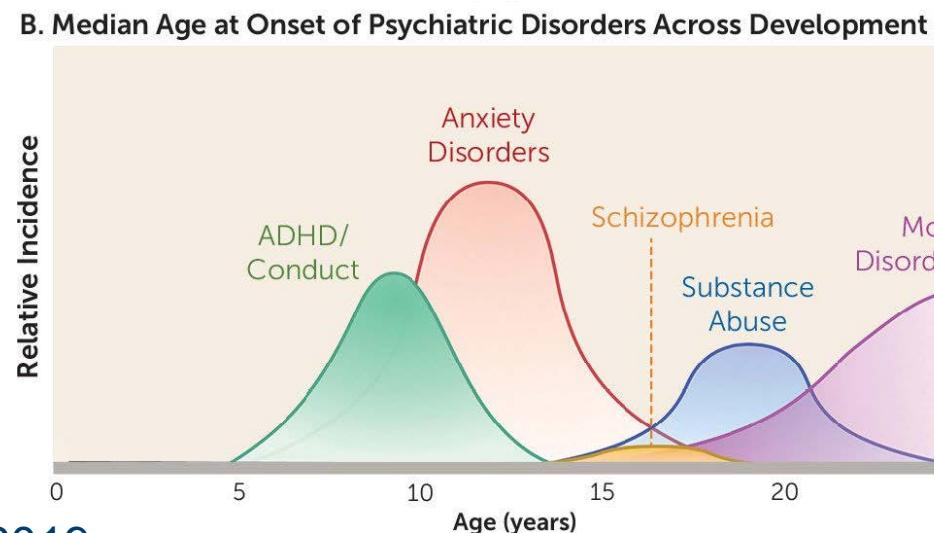
Richard A.I. Bethlehem  
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Brain Mapping Unit & Autism Research Centre  
University of Cambridge

# Typical and atypical brain development

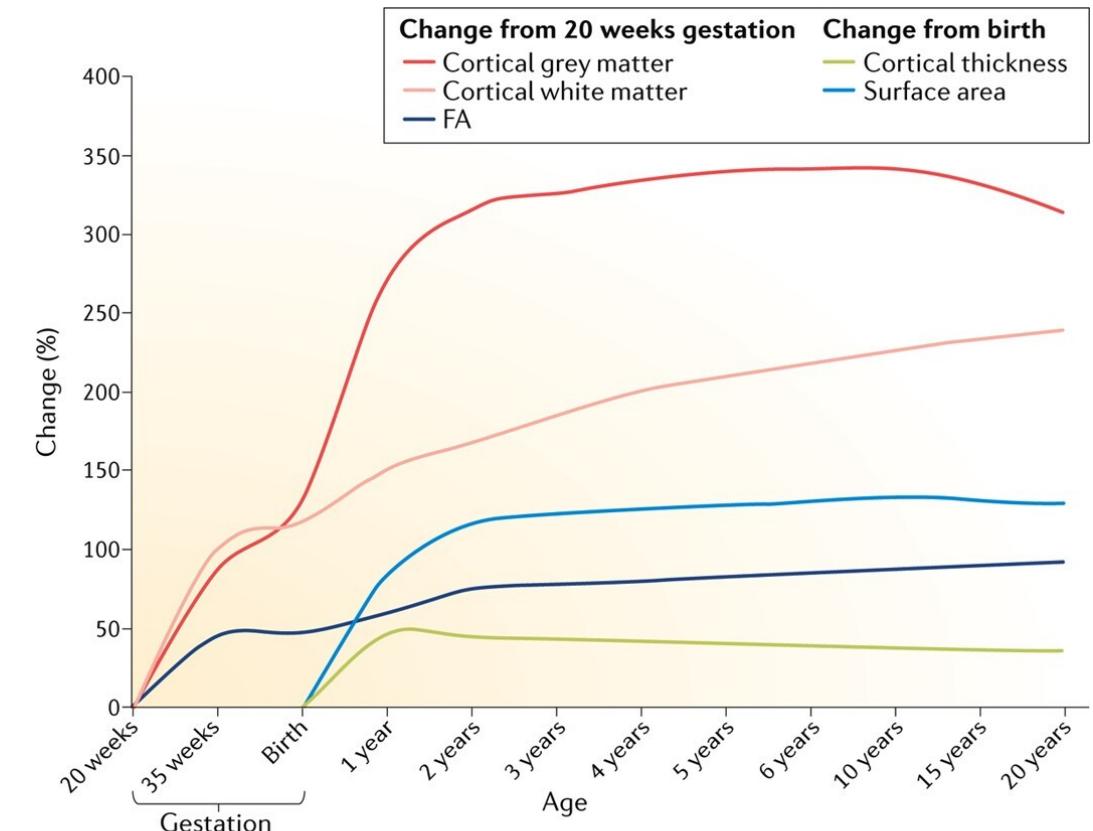
Table 1 Ages at onset for five categories of mental health disorder

	Projected lifetime risk, <sup>a</sup> % (s.e.)	Age at which % of projected lifetime risk attained, years <sup>b</sup>		
		25%	50% (median)	75%
Anxiety disorders	31.5 (1.1)	6	11	21
Mood disorders	28.0 (0.8)	18	30	43
Impulse control disorders	25.4 (1.1)	7	11	15
Substance use disorders	16.3 (0.6)	18	20	27
Any disorder	50.8 (1.2)	7	14	24

Jones 2013



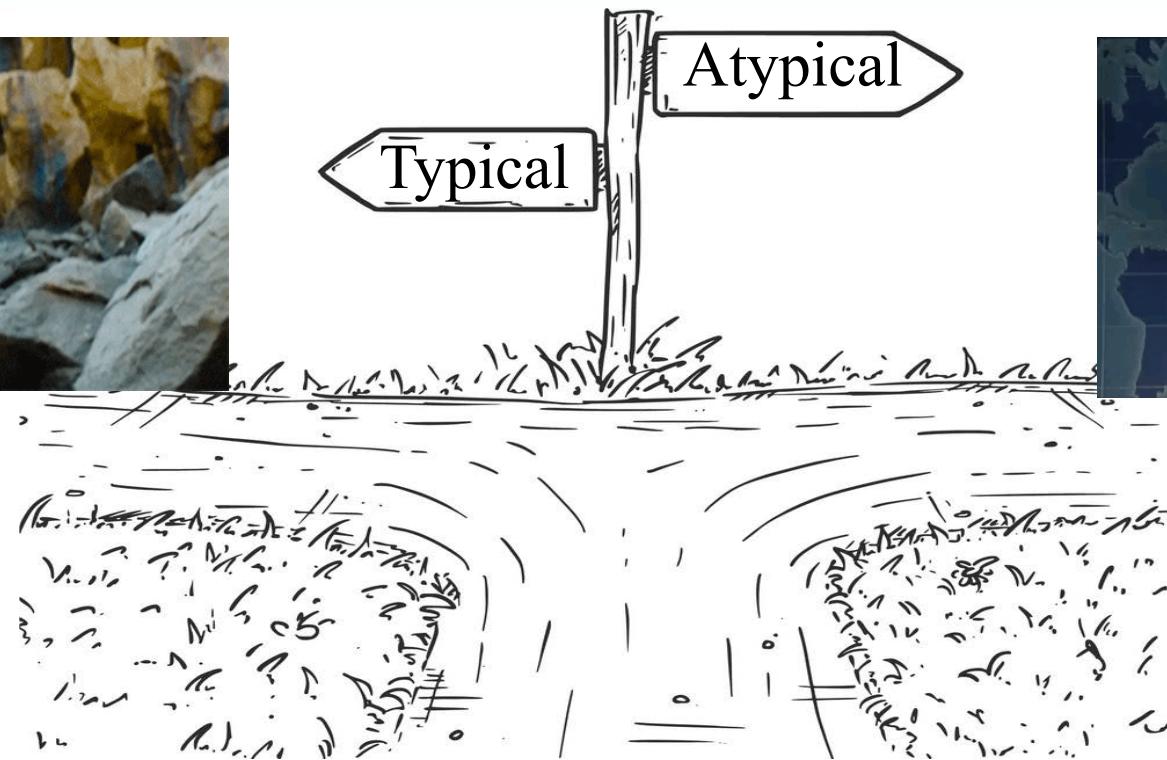
Meyer & Lee 2019



Nature Reviews | Neuroscience

Gillmore et al. 2018

# Typical and atypical brain development

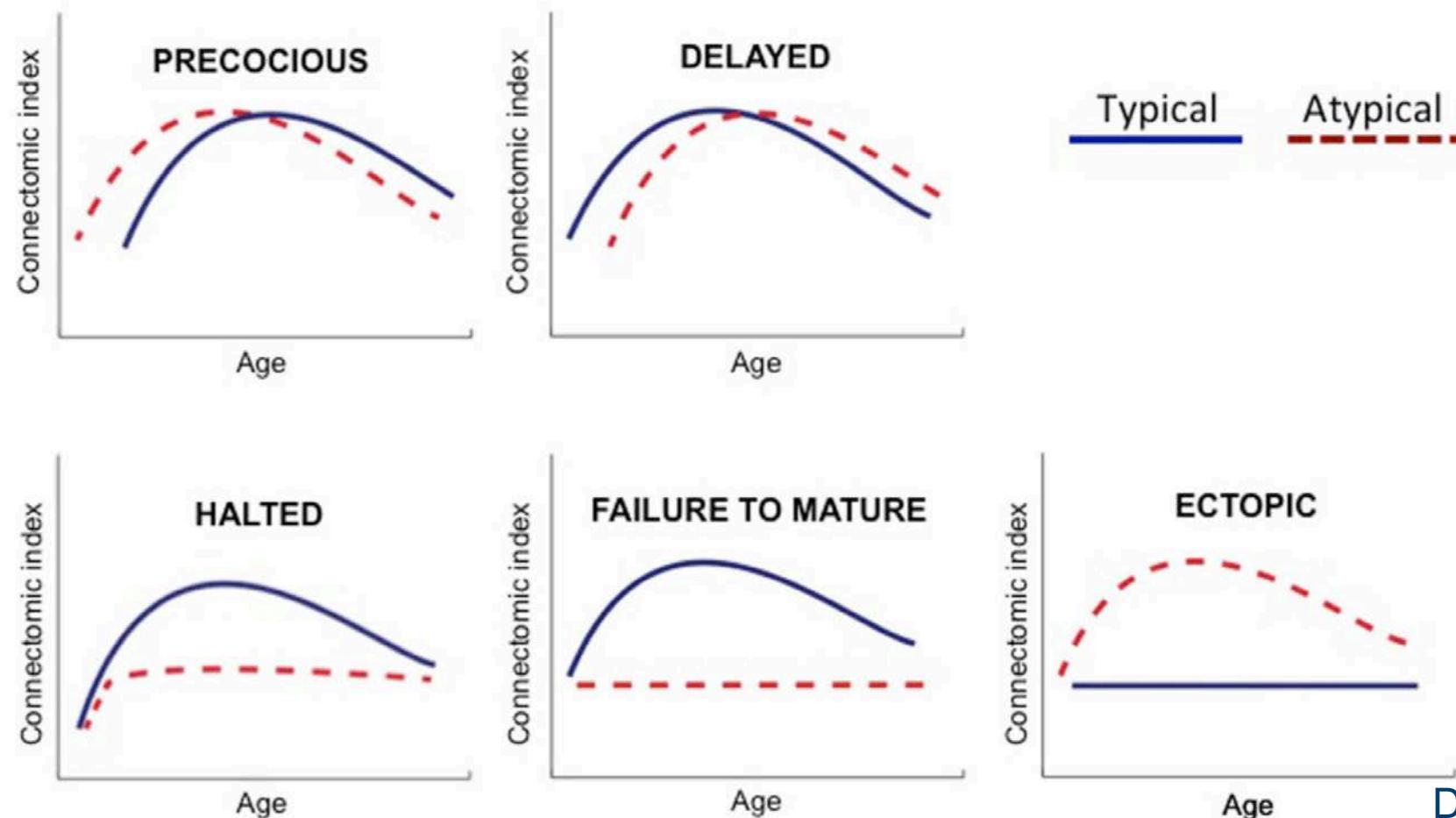


Why?

When?

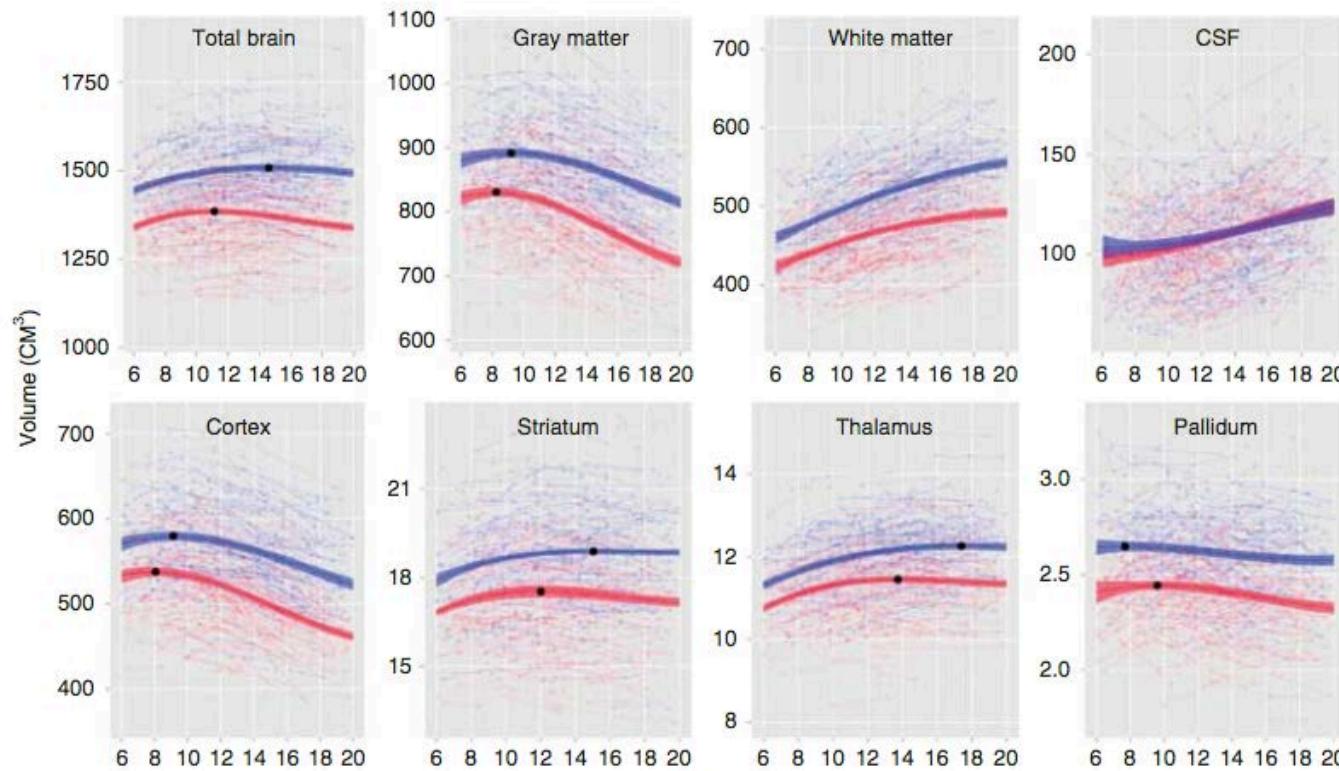
Where?

# How does the typical cortex develop

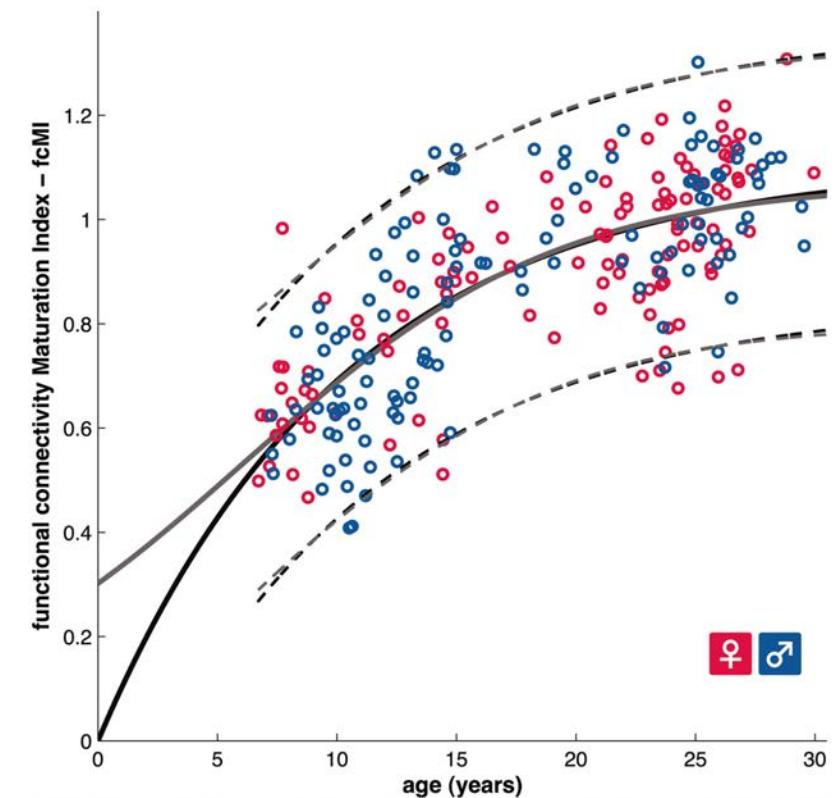


Di Martino et al. 2014

# How does the typical cortex develop

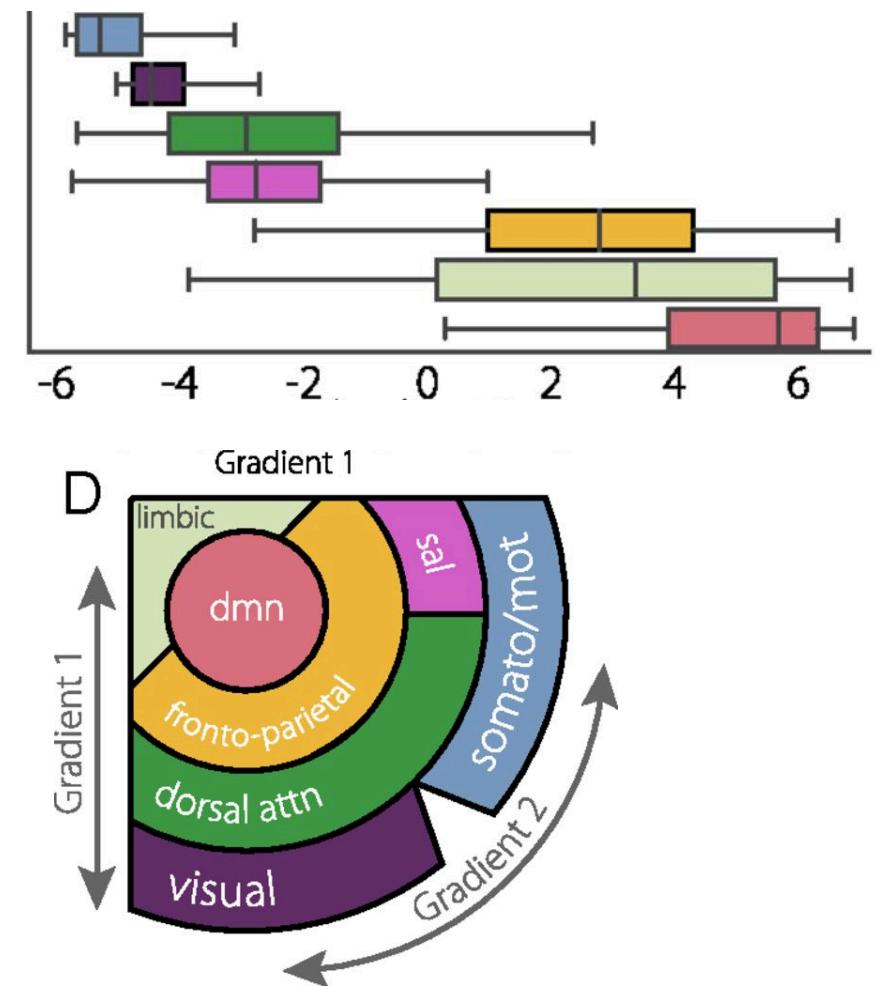
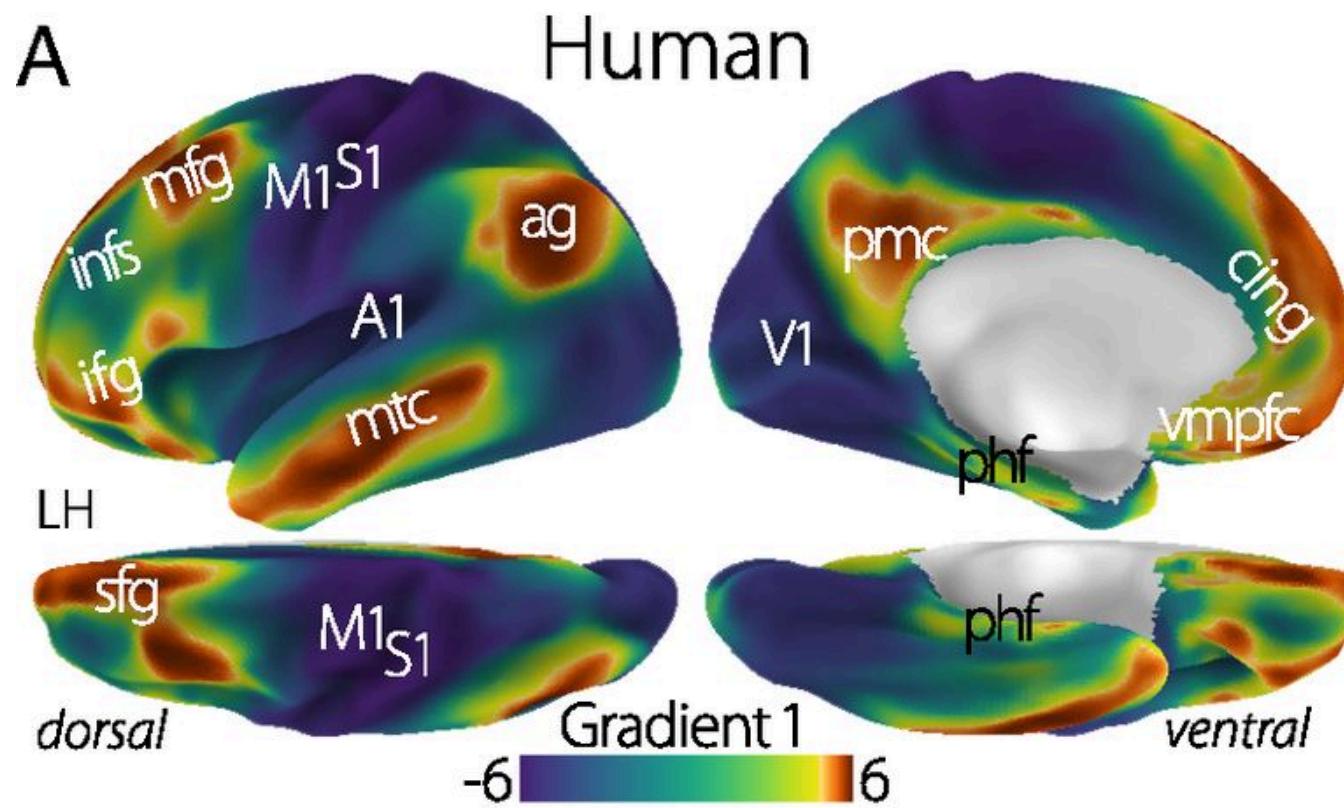


Raznahan et al. 2011



Dosenbach et al. 2010

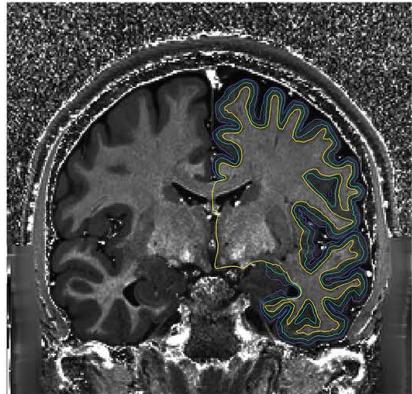
# What to measure



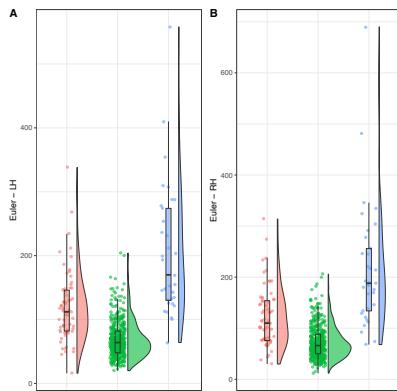
# Population and Methods



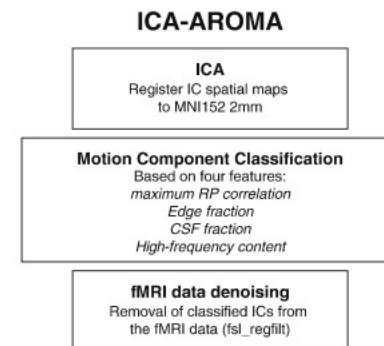
Structural  
processing



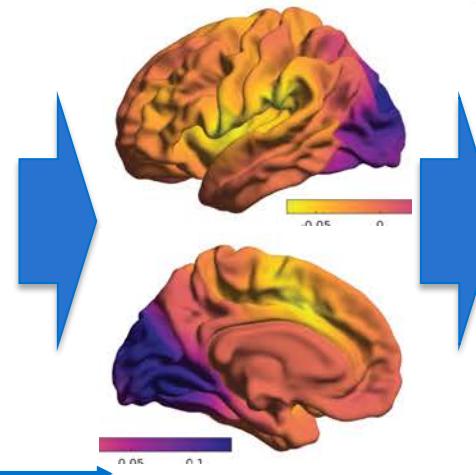
QC



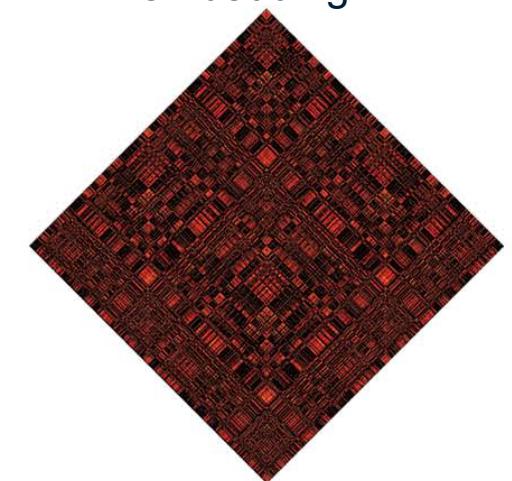
FC pre-processing  
+



Surface projection



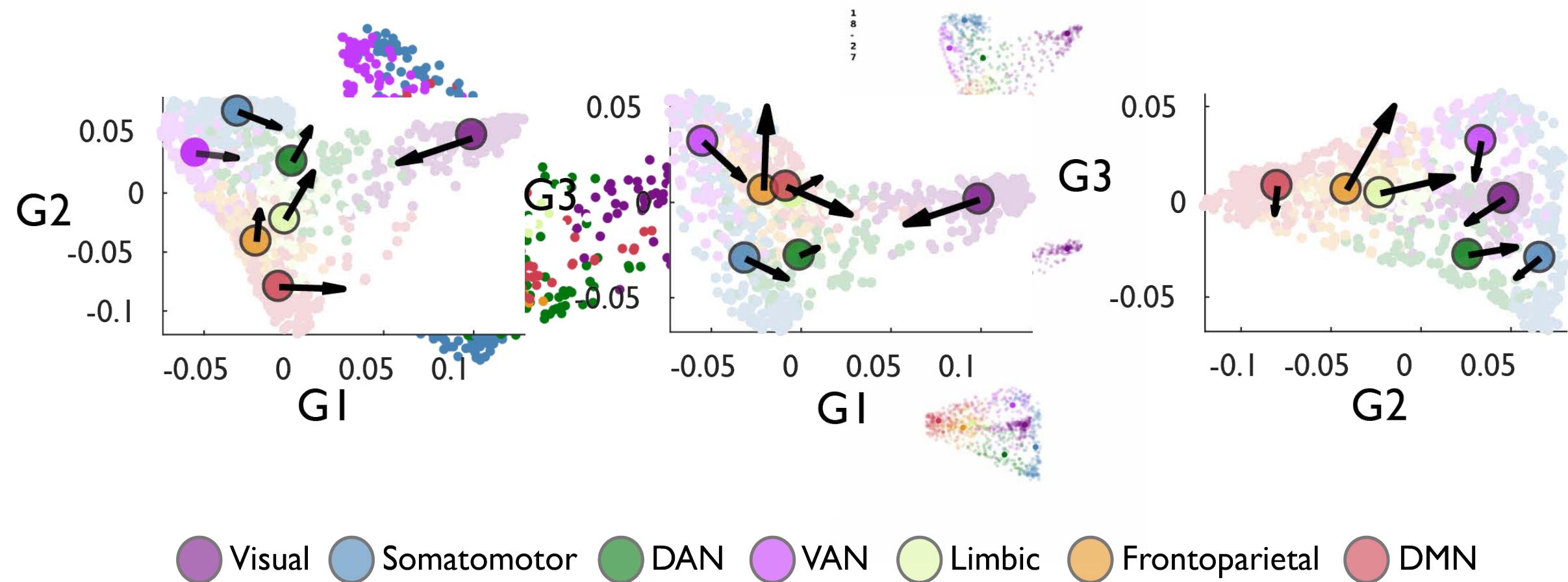
Diffusion  
embedding



# Regional age related effects on network topology

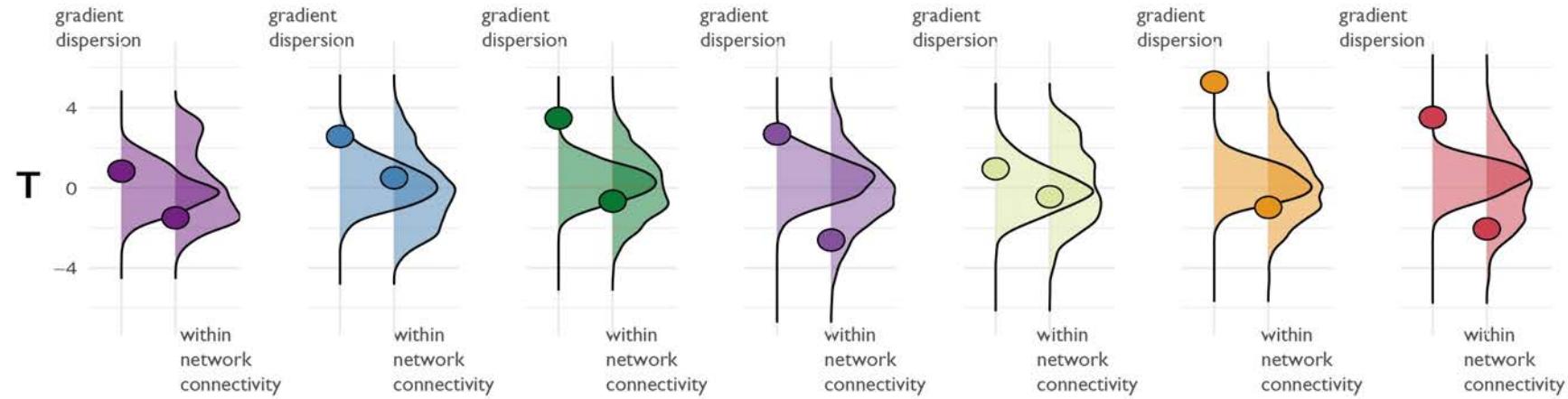


# Age related effects on network dispersion

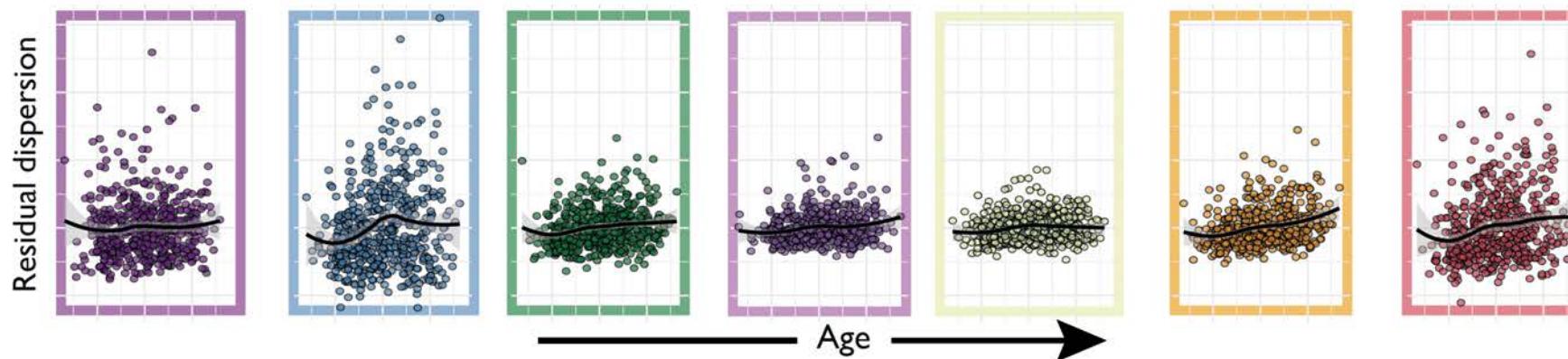


# Age related effects on network dispersion

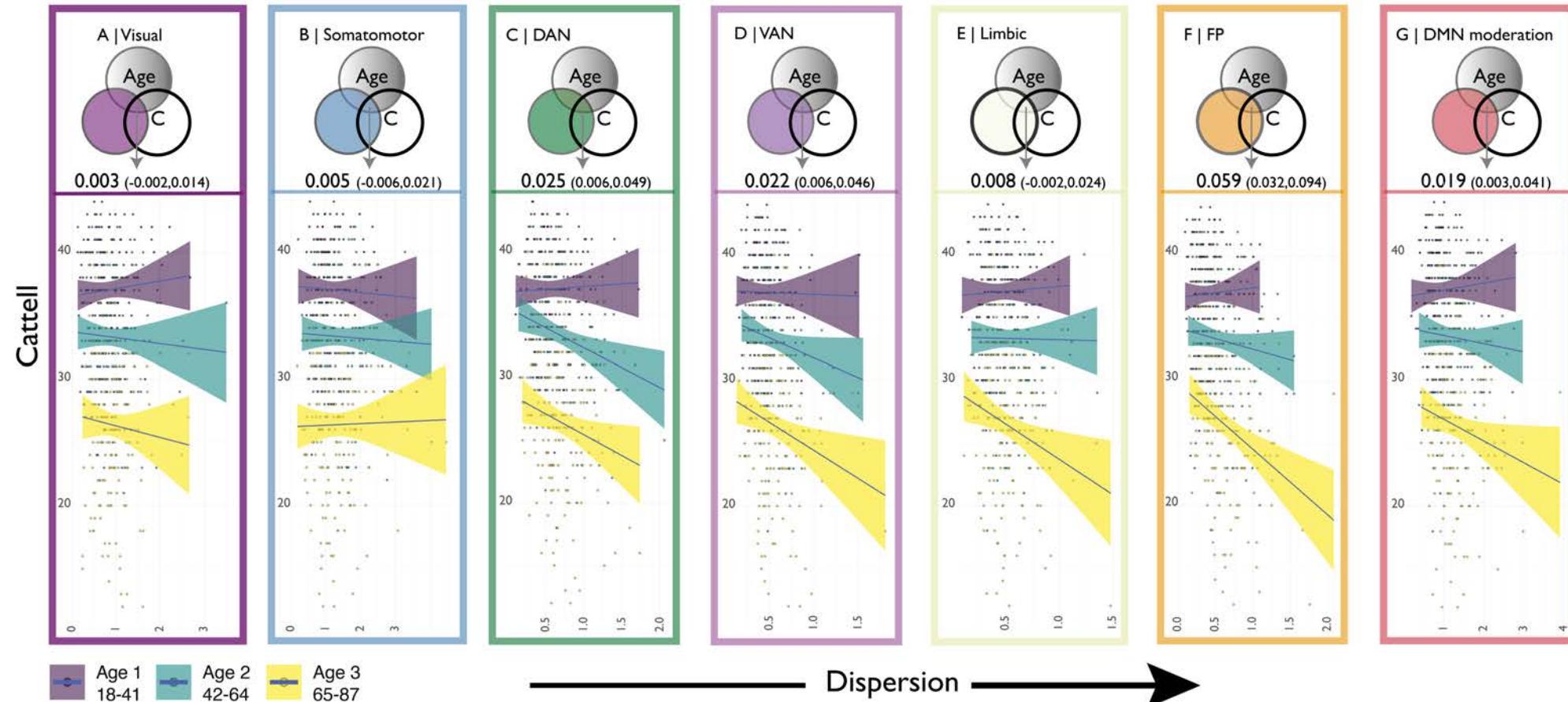
## A | Age related differences within functional networks



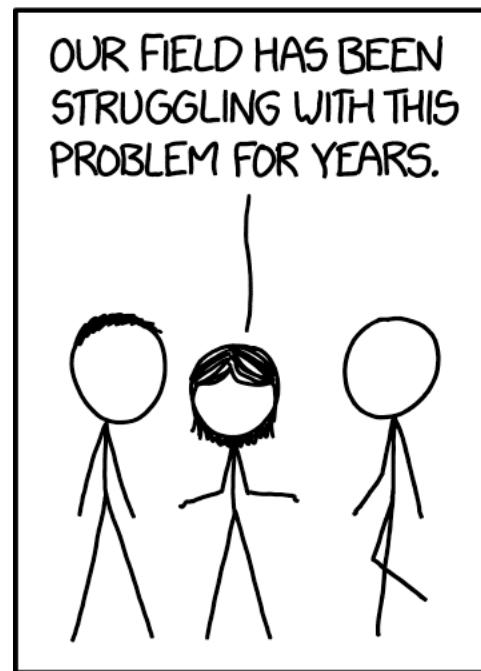
## B | Residual age related differences within functional networks



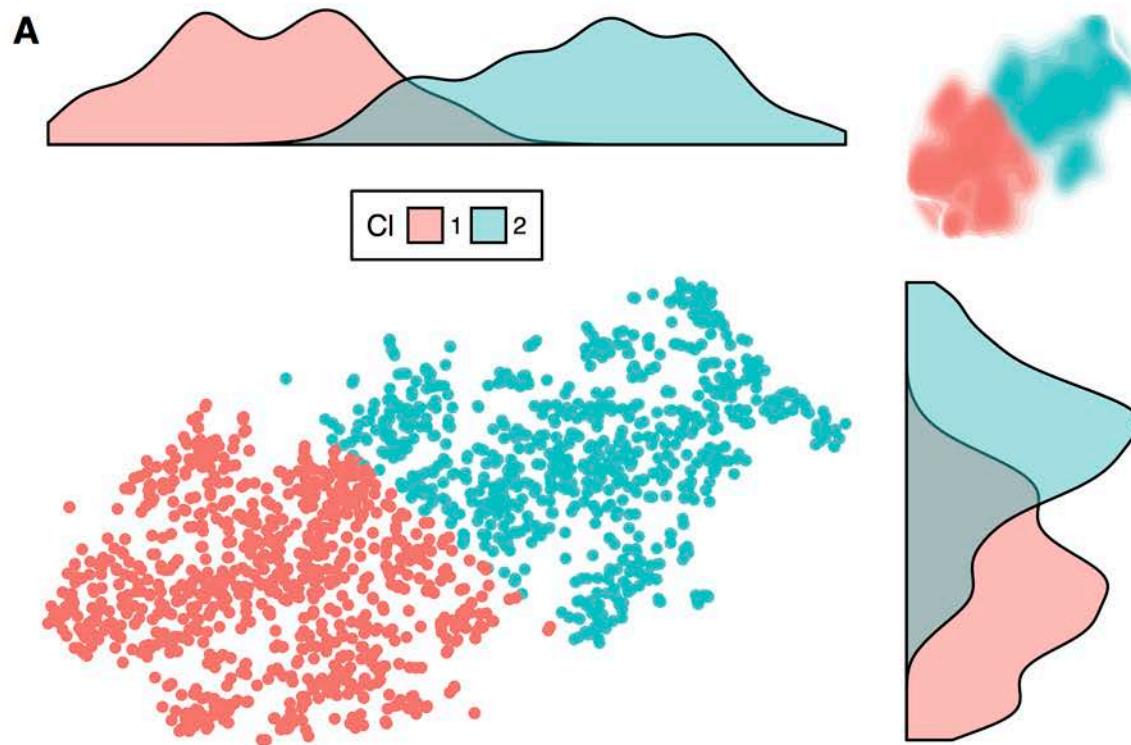
# Age related effects of network dispersion mediate intelligence



# So what is the problem?

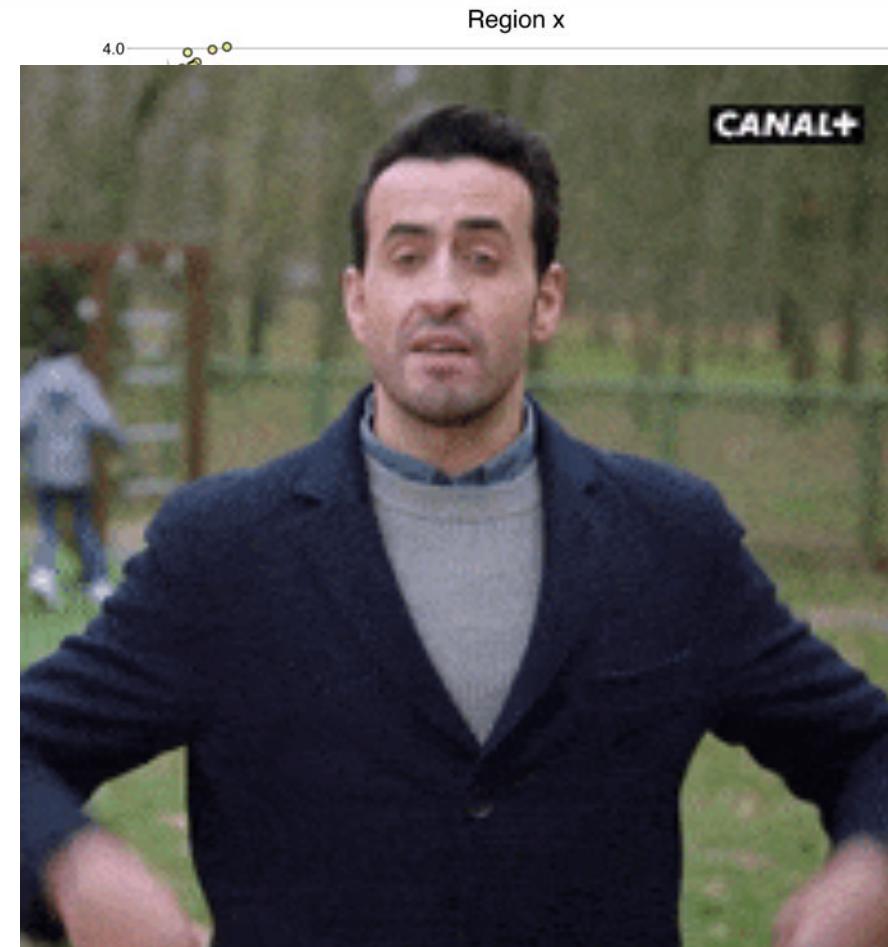
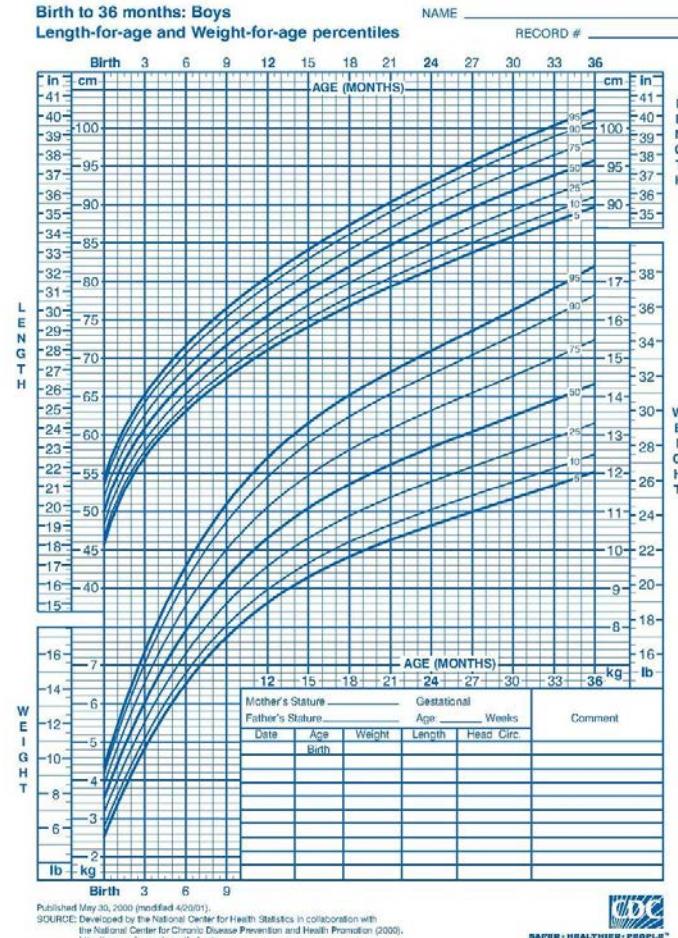


# Case-control vs heterogeneity



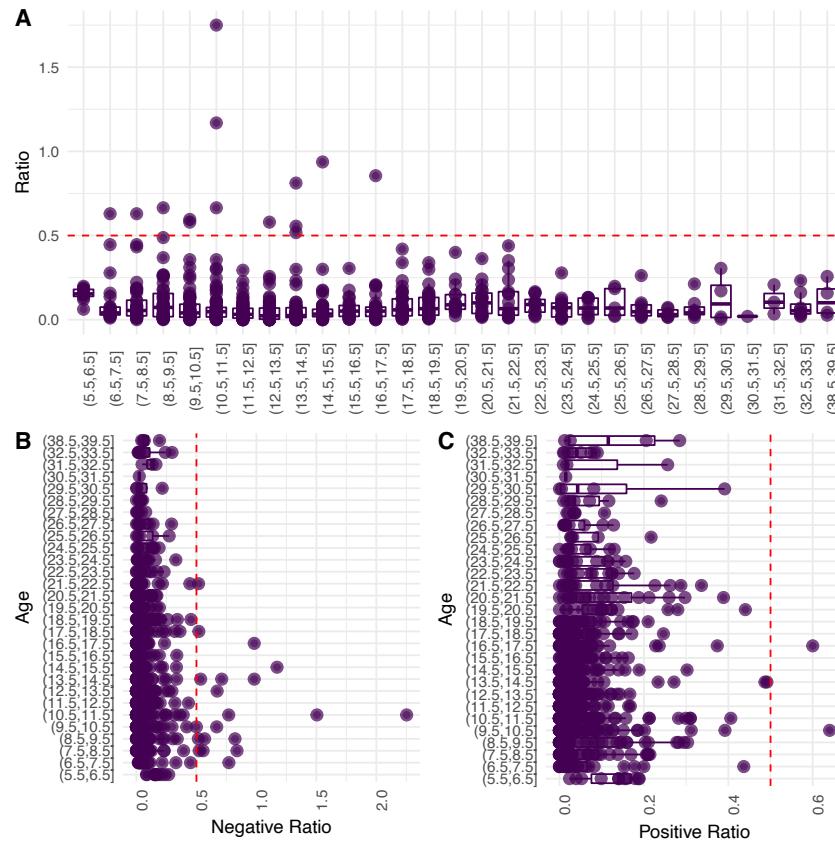
Bethlehem et al. 2019

# Normative models

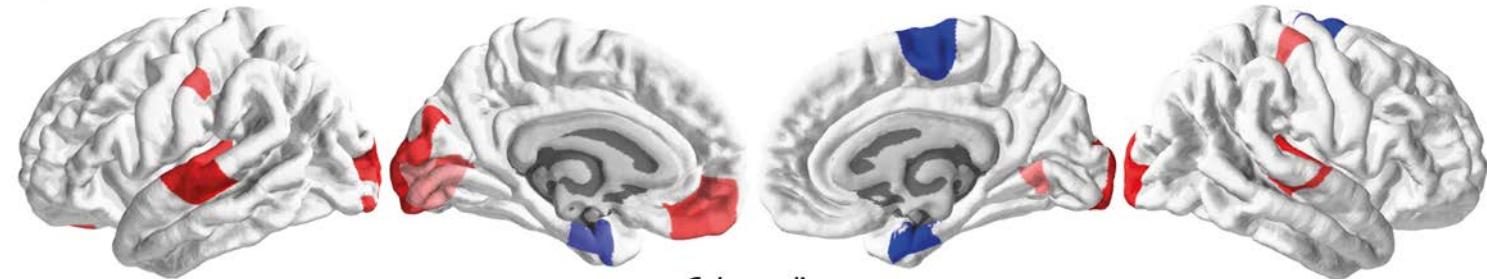


Bethlehem et al. 2019

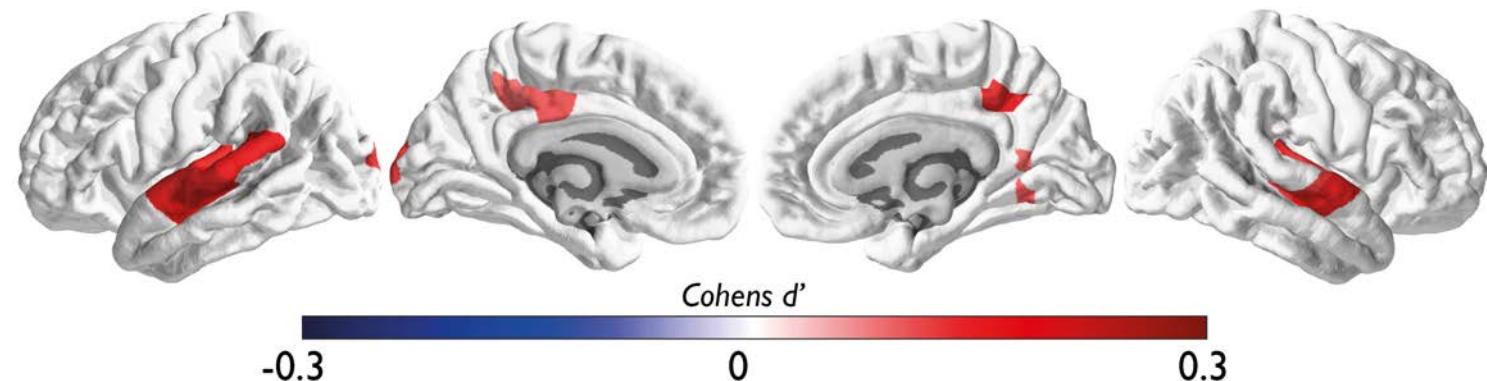
# Normative modeling – what is normal



**A|** Case-control linear mixed effects model



**B|** Case-control linear mixed effects model after outlier removal



Bethlehem et al. 2019

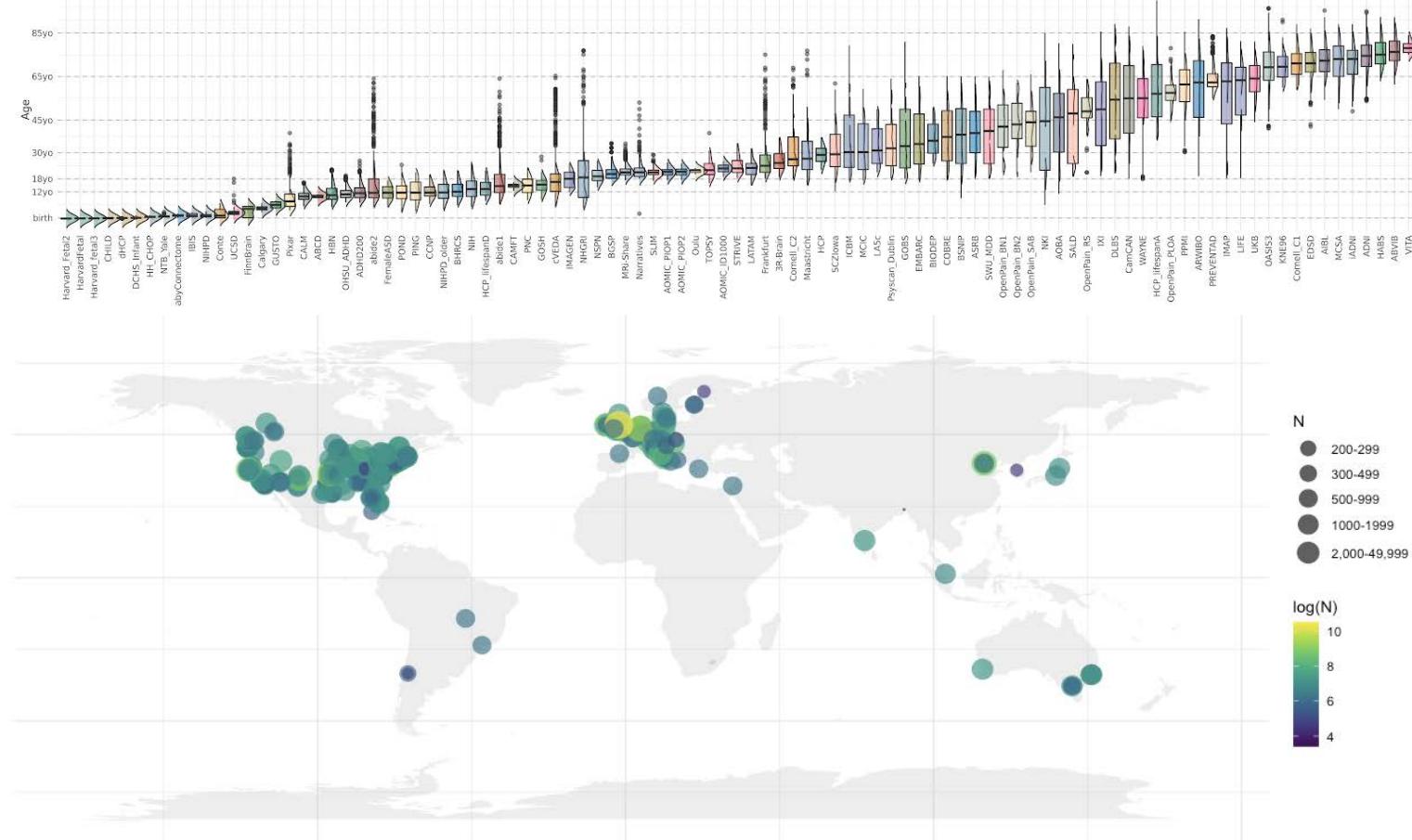
## Caveats

- Unlikely that there are uniform curves for every possible imaging metric
- Age range of available datasets → e.g. onset most likely earlier than current datasets cover
- Estimation from sparse & cross-sectional data → e.g. how reliable is the ‘norm’?



SCHOOL  
OF  
MEDICINE

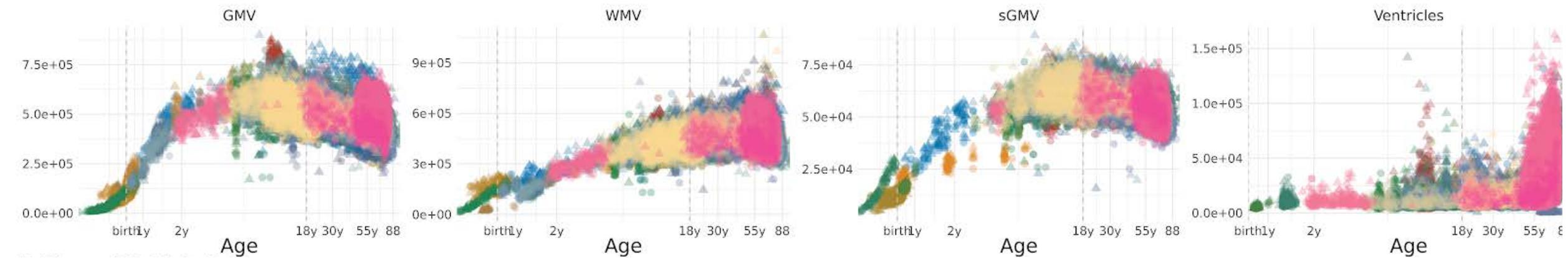
# The meaning of life(span)



Total	234913
<b>Total in Lifespan Study</b>	<b>143032</b>
Total Included/Processed/Downloaded	118806
Total Accessible	19717
Total Pending	53331
Total Replication	24226

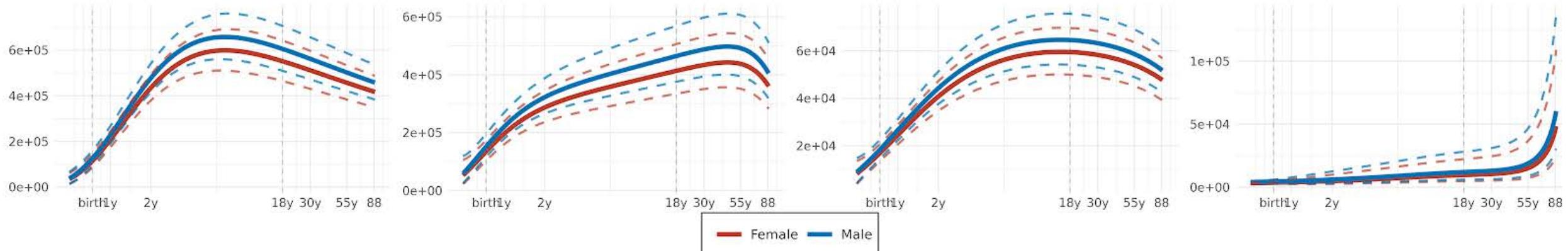
# The meaning of life(span)

B| Total tissue volume in mm<sup>3</sup>

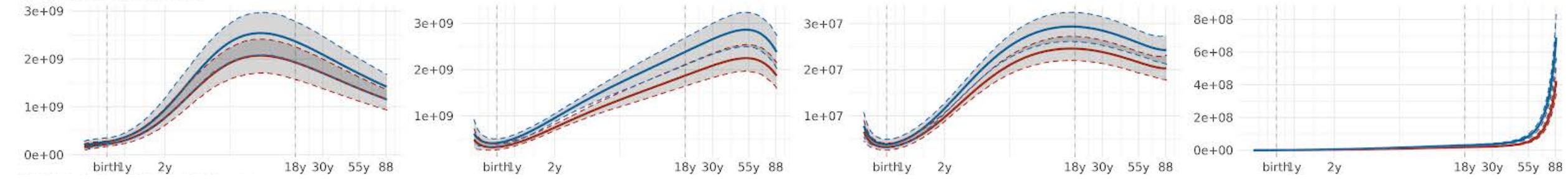


# The meaning of life(span)

C| Lifespan fitted trajectories

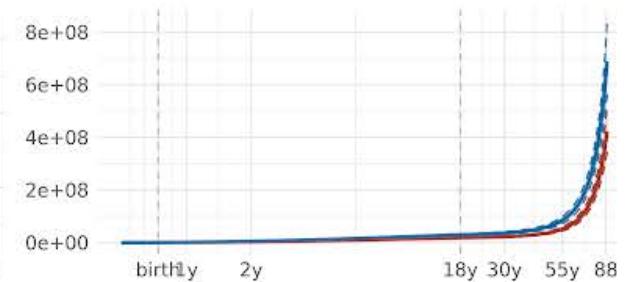
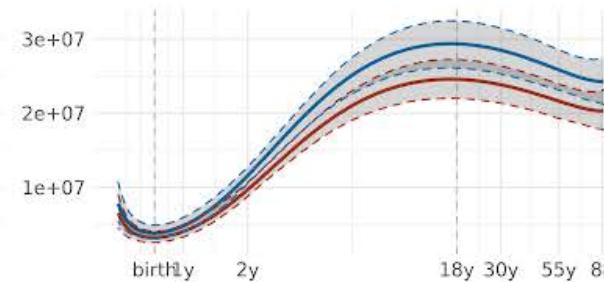
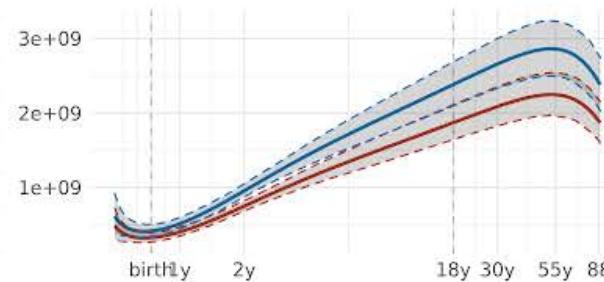
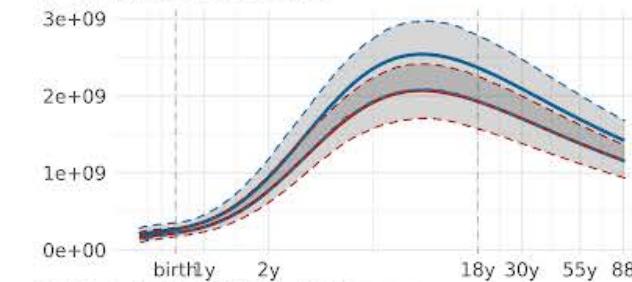


D| Population Variance

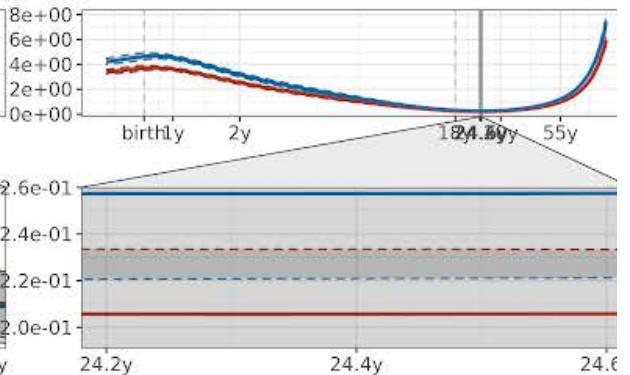
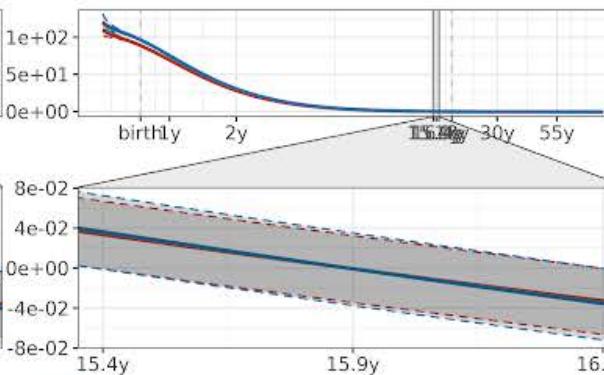
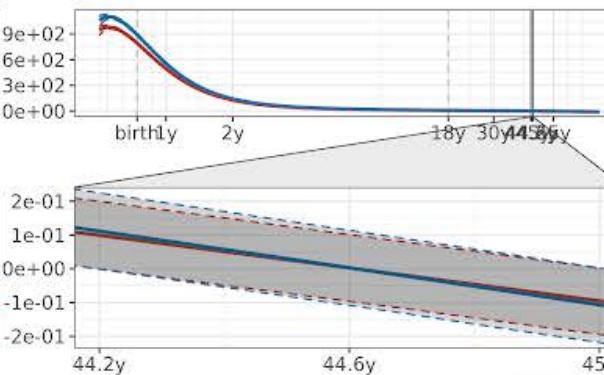
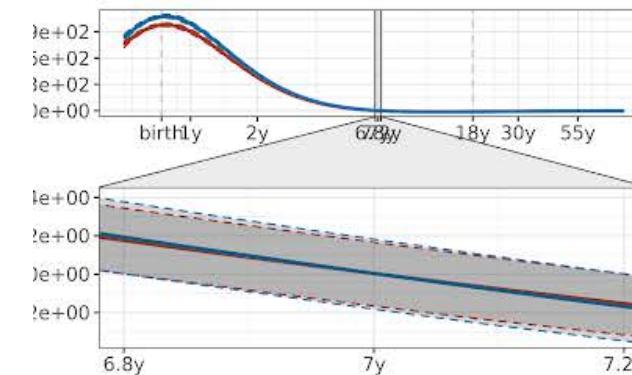


# The meaning of life(span)

D| Population Variance

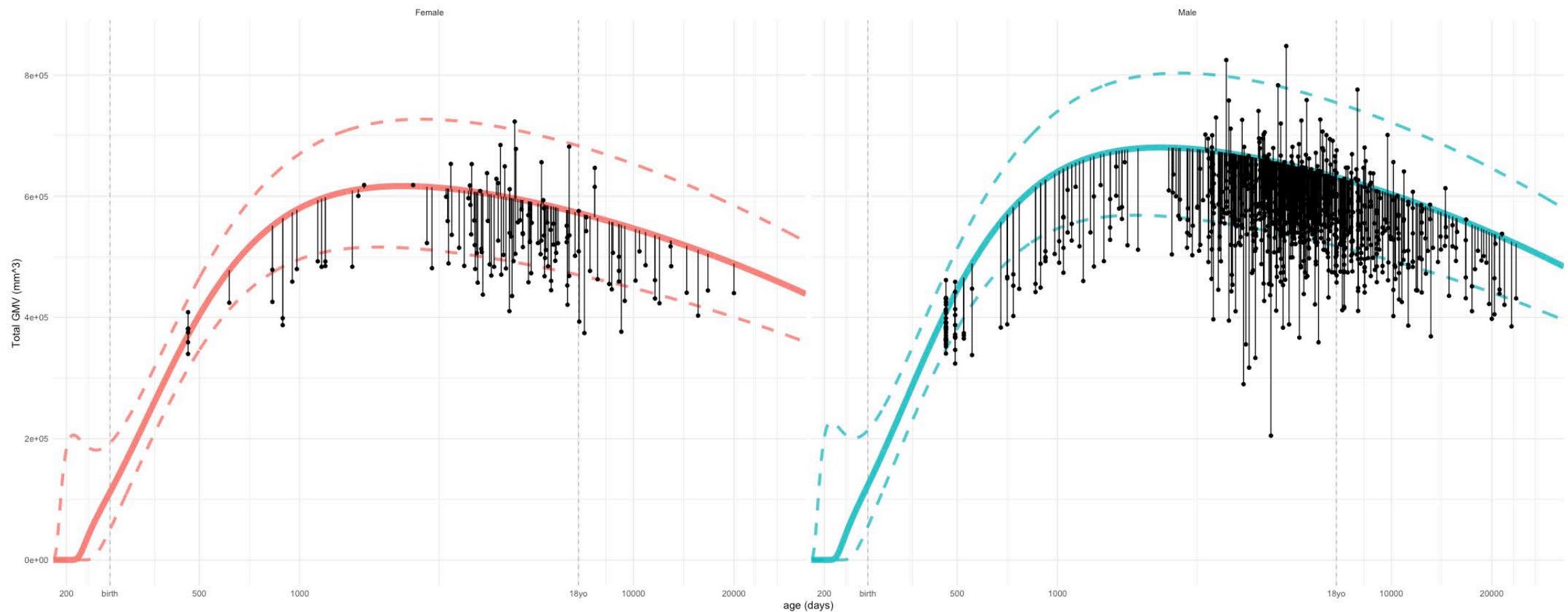


E| Population Rate of change

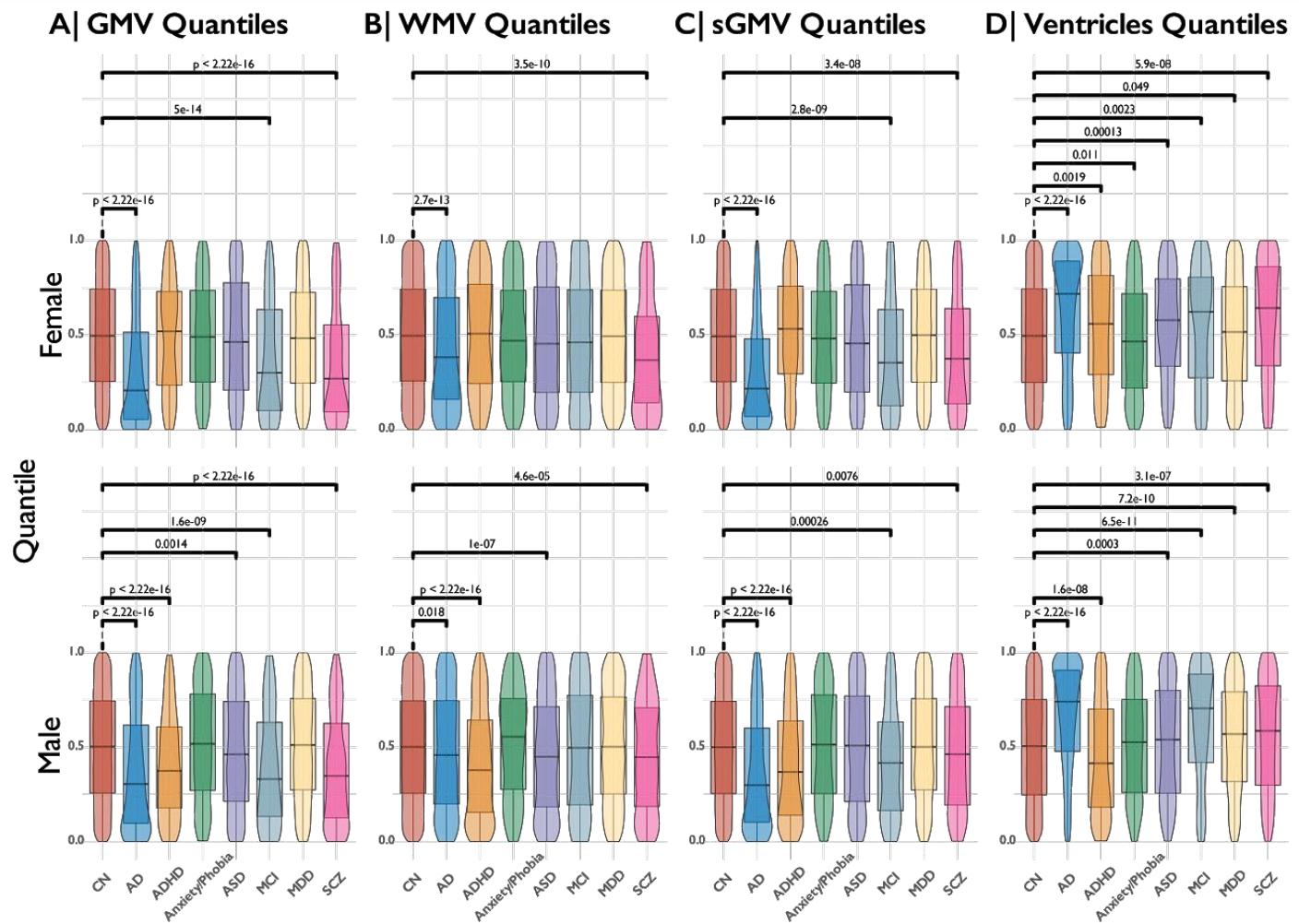


Female      Male

# Clinical utility

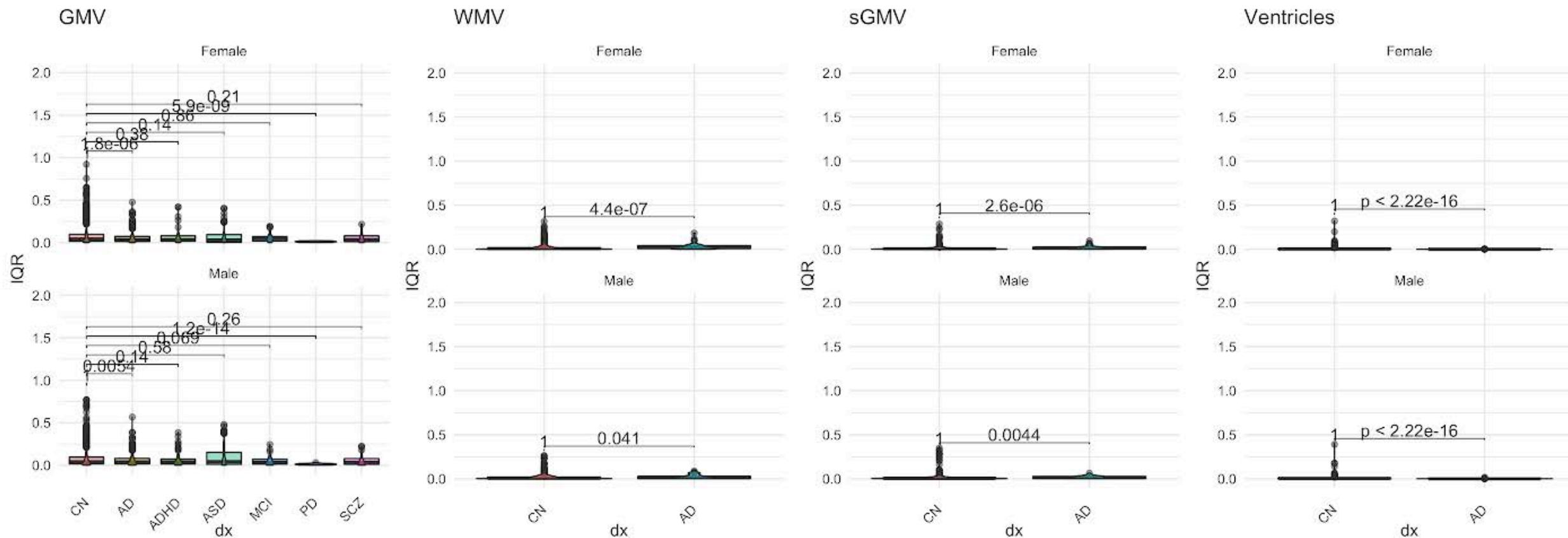


# Clinical utility



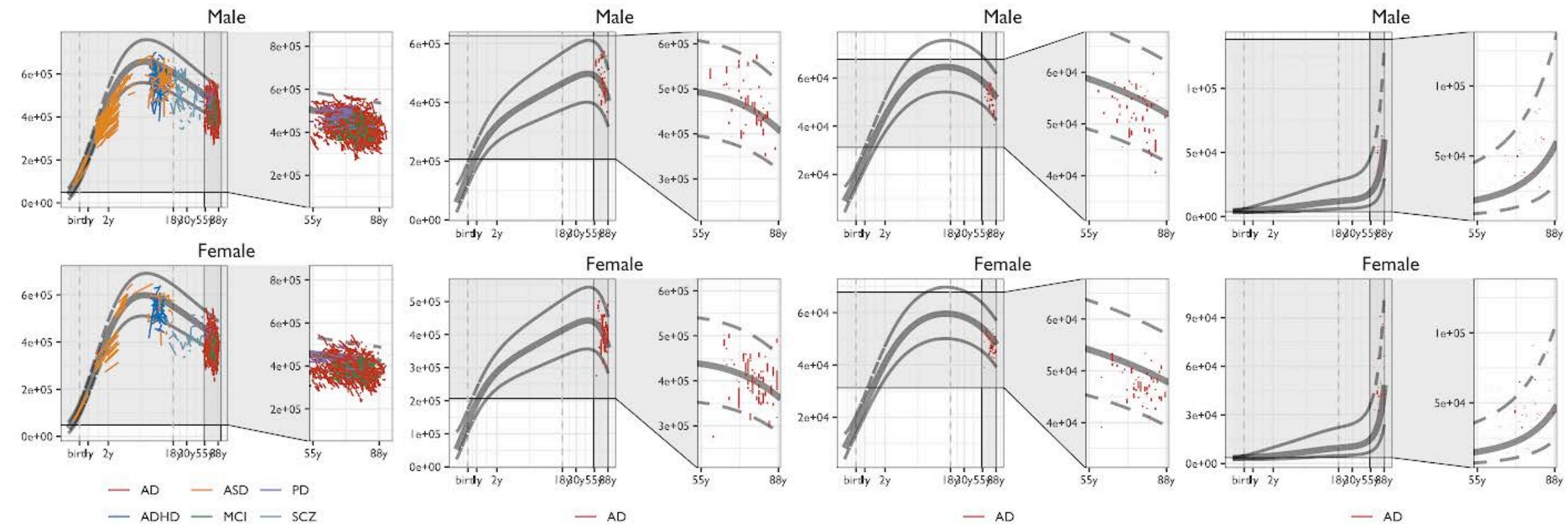
# What about stability

## A| Inter Quantile Range by Dx



# What about stability

## B| Longitudinal variation in mm<sup>3</sup>



# Lessons learned

- There is a lot of public data already available
- People are generally happy to share (simple) data
- We can learn a lot from simple features
- There is a lot of room to expand on this project!
- High performance computing is essential (650+TB and 1,450,000 CPU hours used to date)



# Thanks et al.

## Cambridge:

- Ed Bullmore
- Simon White
- Rafael Romero-Garcia
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## UPenn:

- Jakob Seidlitz
- Aaron Alexander-Bloch
- Jake Vogel

## MIT

- Kevin Anderson

## MNI

- Mallar Chakravarty
- Boris Bernhard
- Casey Paquola (now Julich)
- Gabriel Devenyi

## UCLA

- Michael Gandal

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# Questions

