



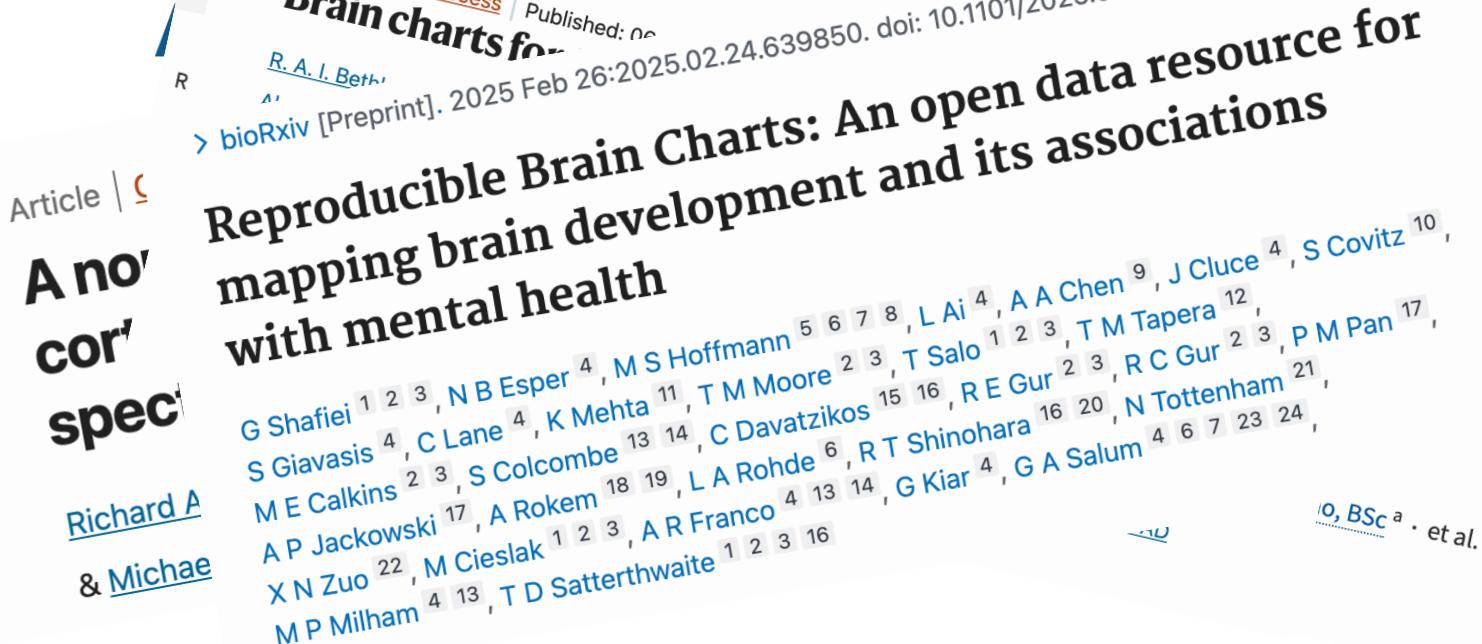
BRISBANE
OHBM 2025 JUNE
24-28

**Charting the velocity of
brain growth and
development**

Dr. Johanna M.M. Bayer

I have no disclosures.

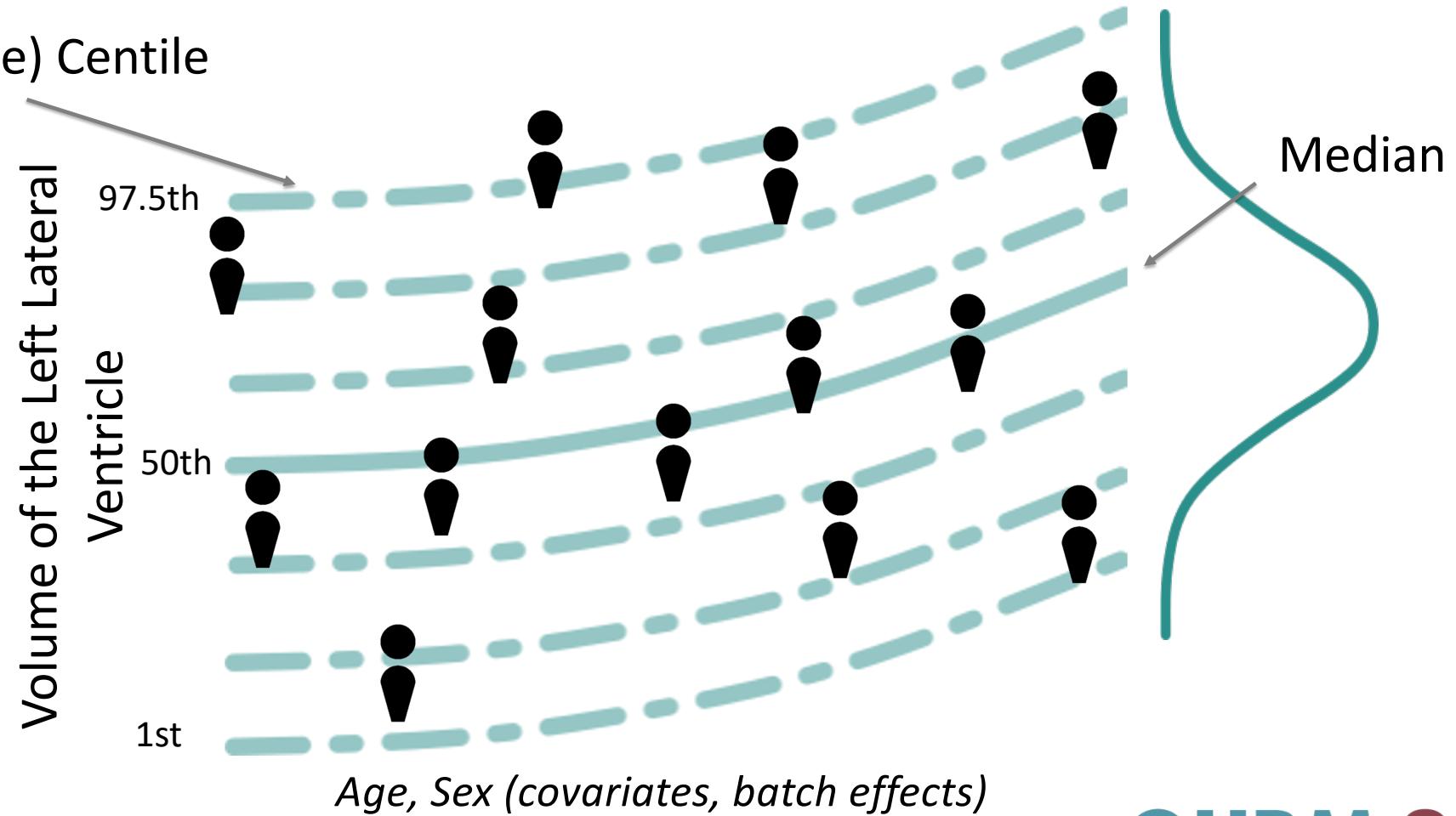
Normative Modelling: A Dream Story



OHBM 2025

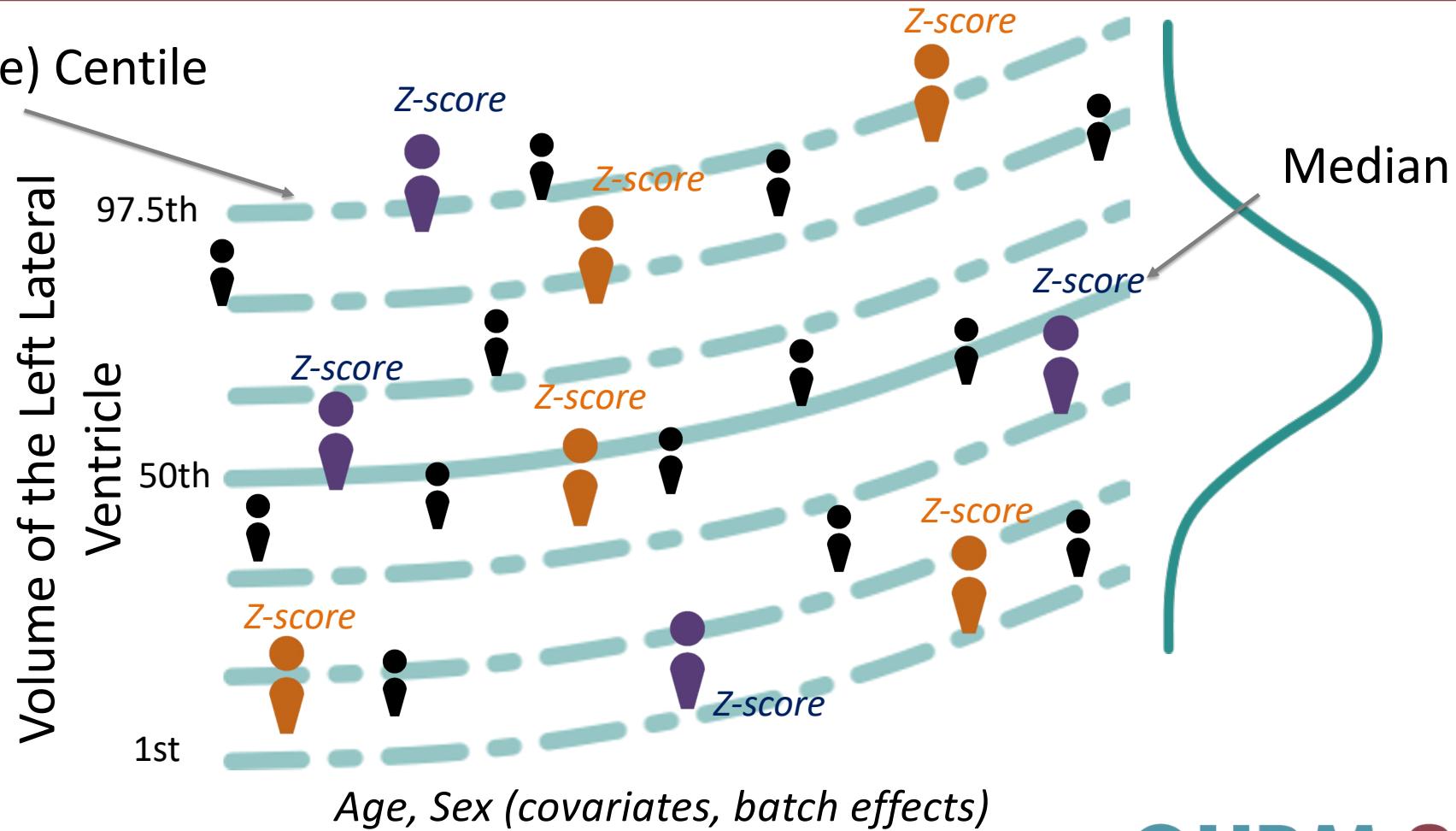
Cross-sectional normative models

(Distance) Centile



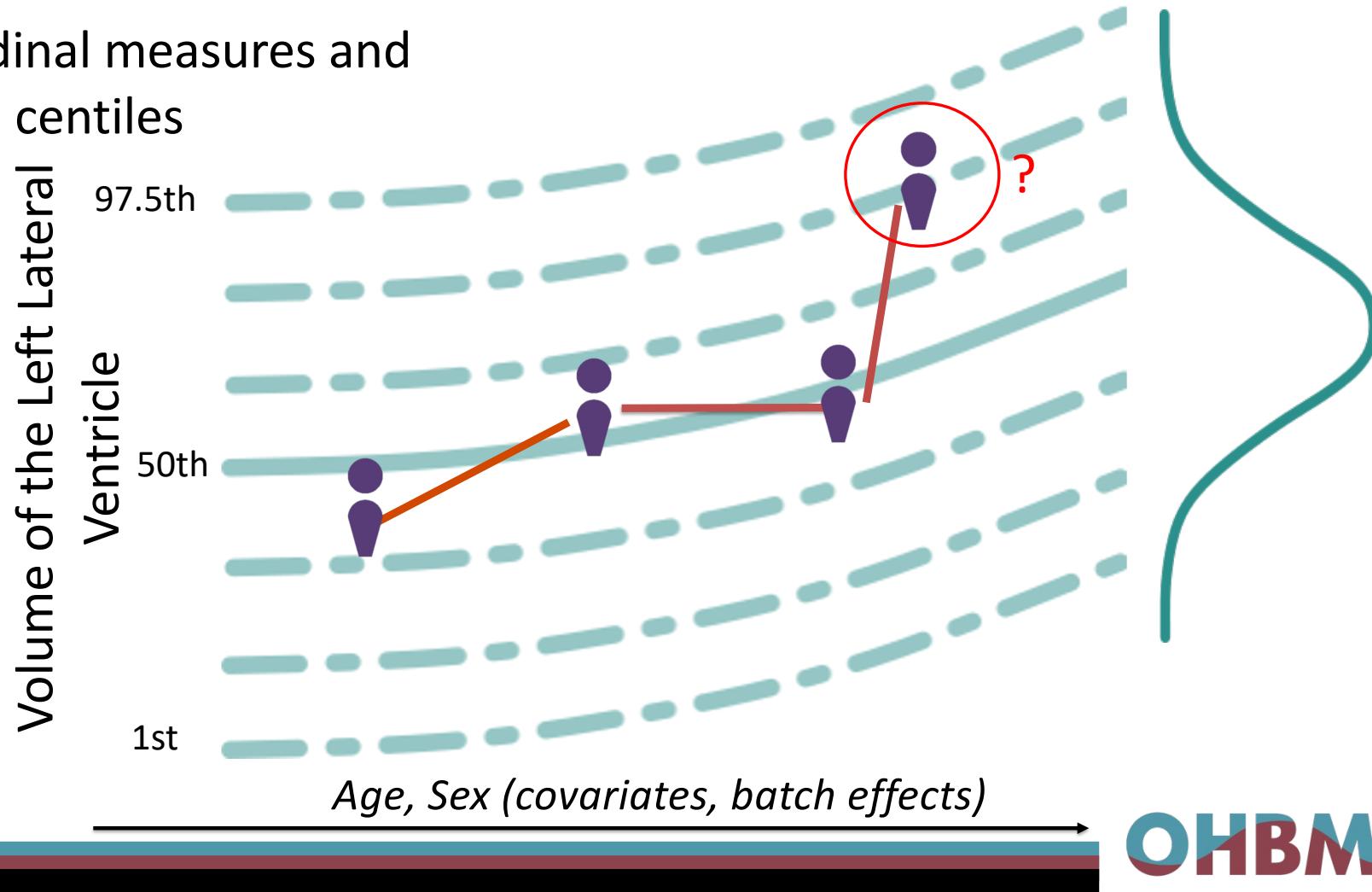
Cross-sectional normative models

(Distance) Centile



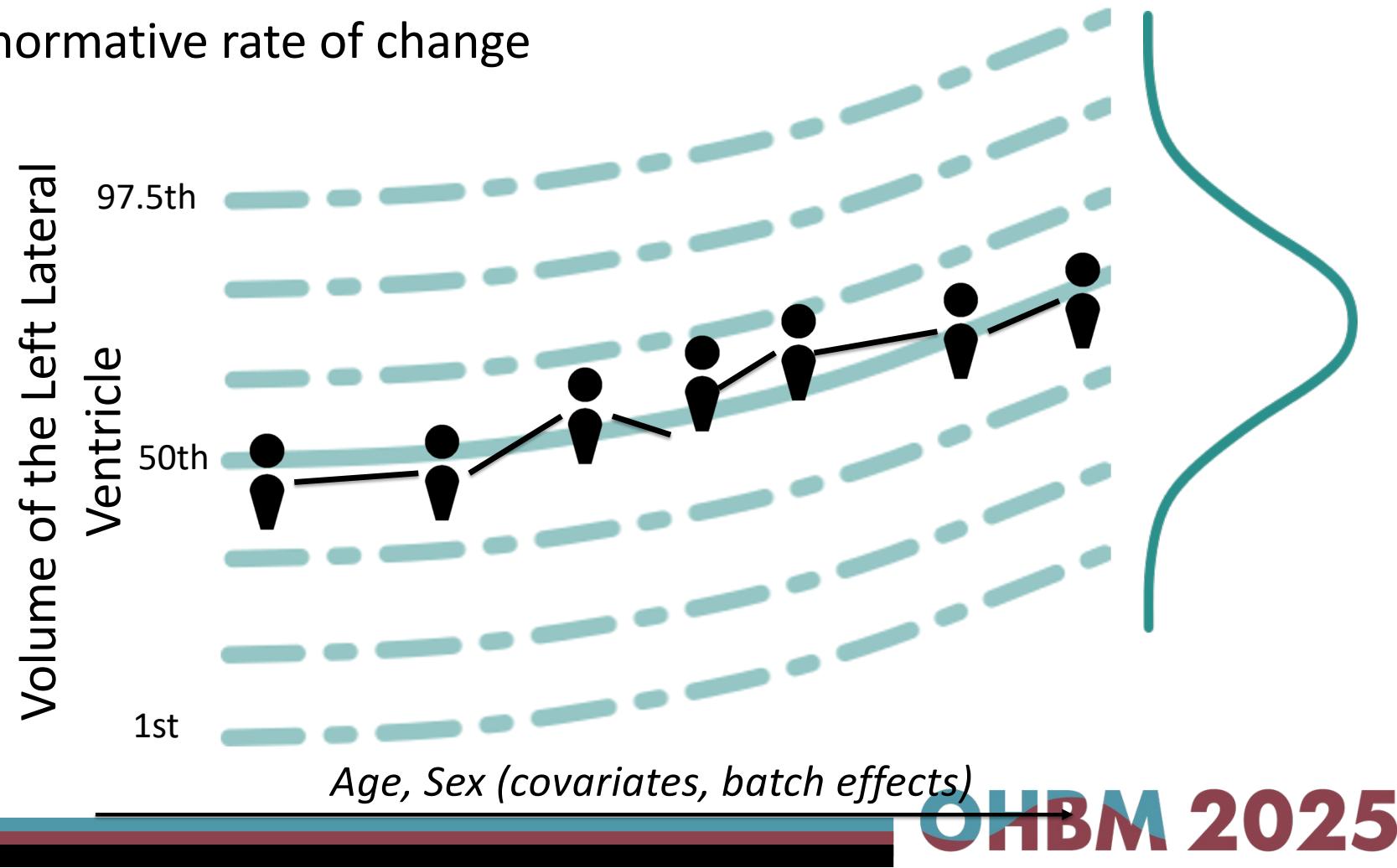
Cross-sectional normative models

Longitudinal measures and
distance centiles



Longitudinal normative models

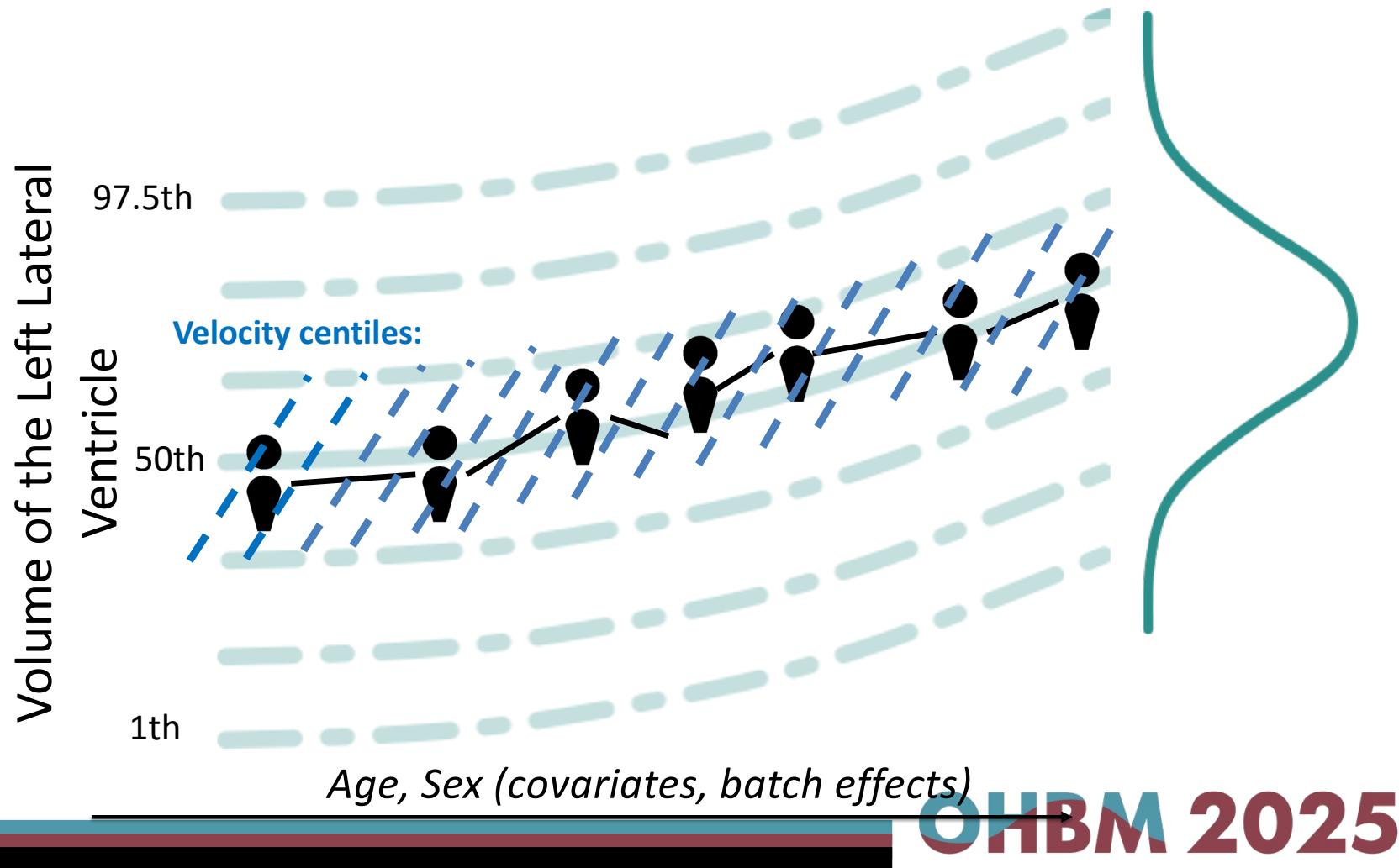
Quantifying the normative rate of change



Longitudinal normative models

Velocity centiles:

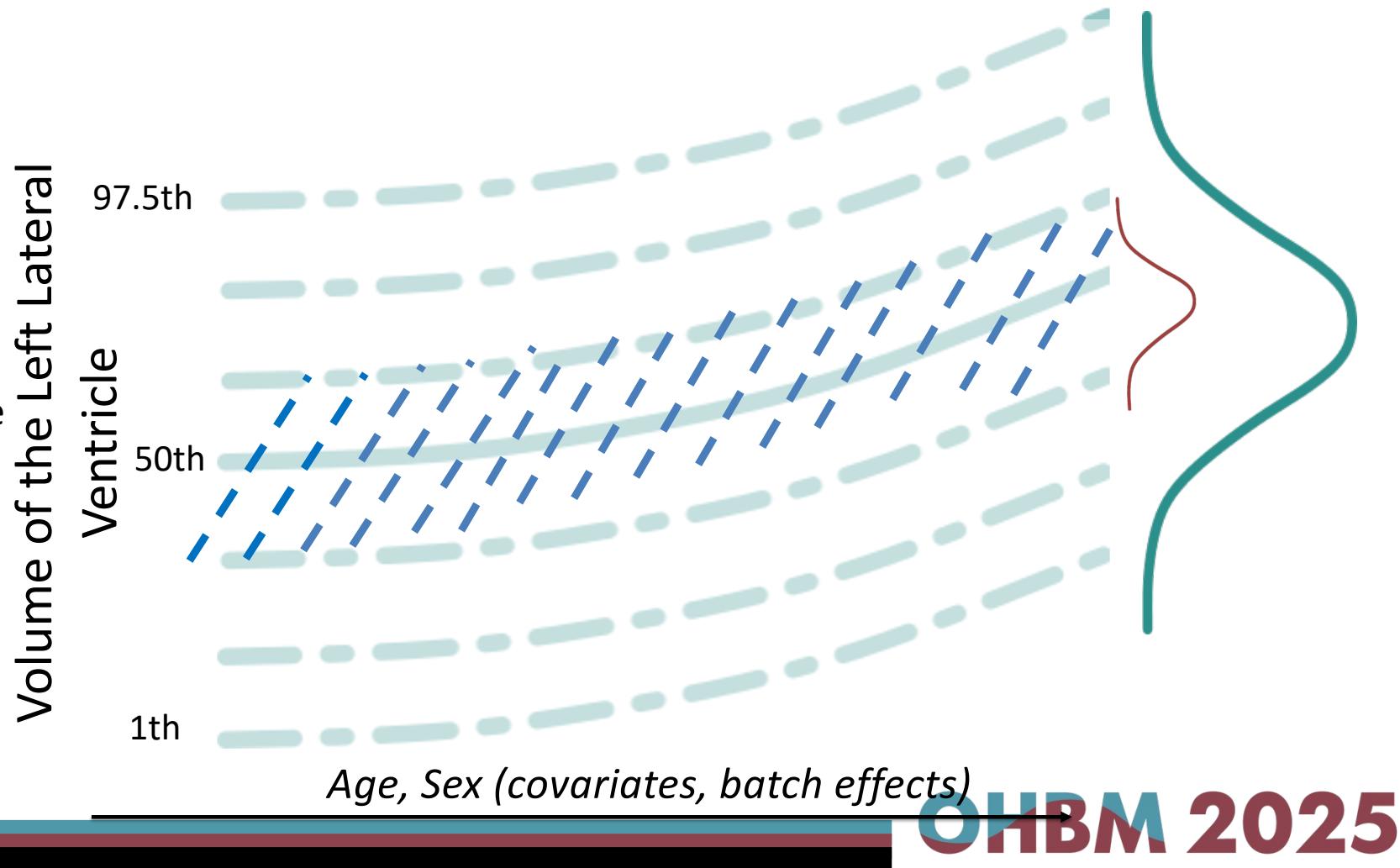
- Quantify the normative rate of change across the life span
- $D(t) = V$



Longitudinal normative models

Thrive lines:

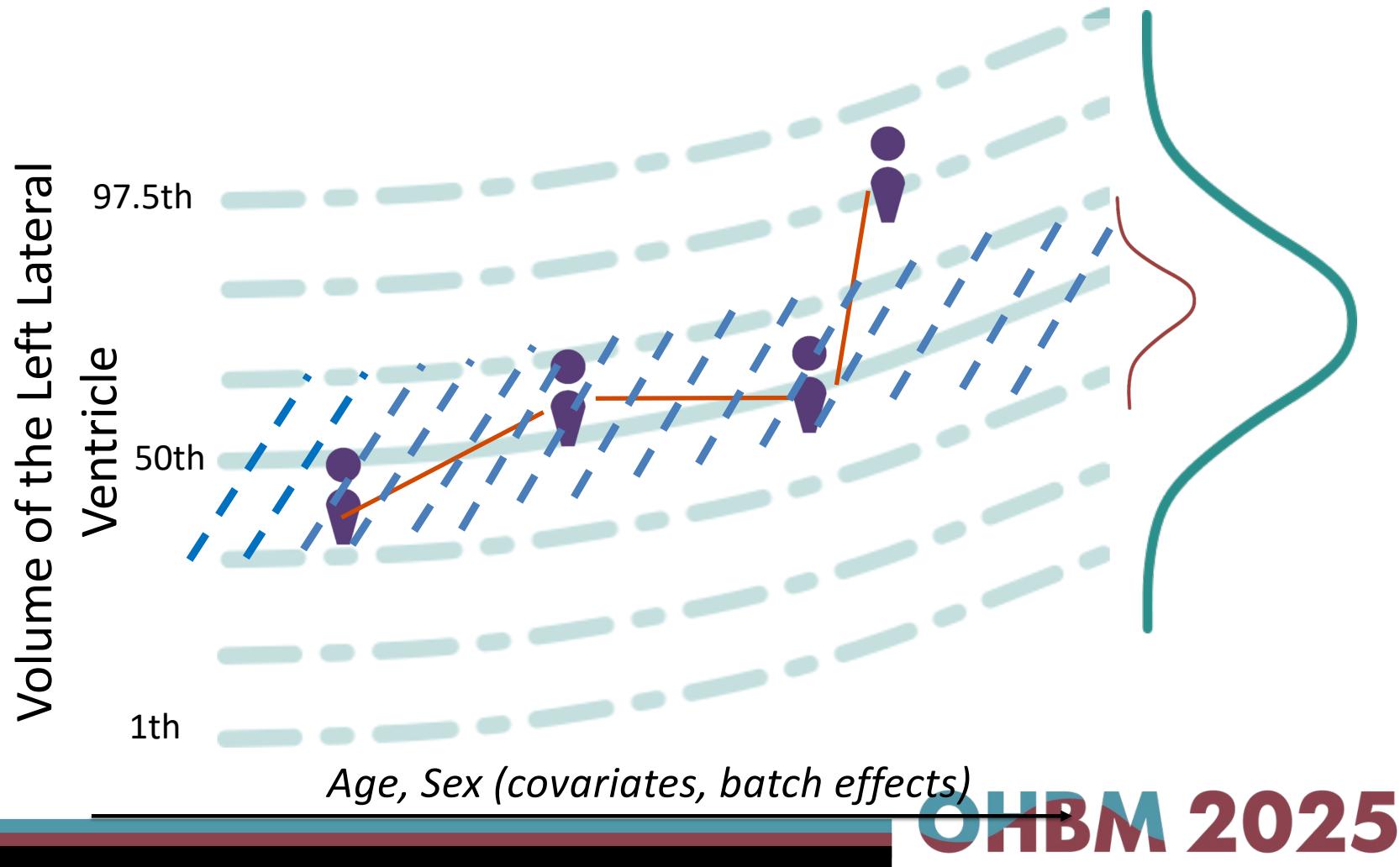
- significant length of velocity centile ($z = +/-1.96$)
- Change that is in the 5% of extreme changes



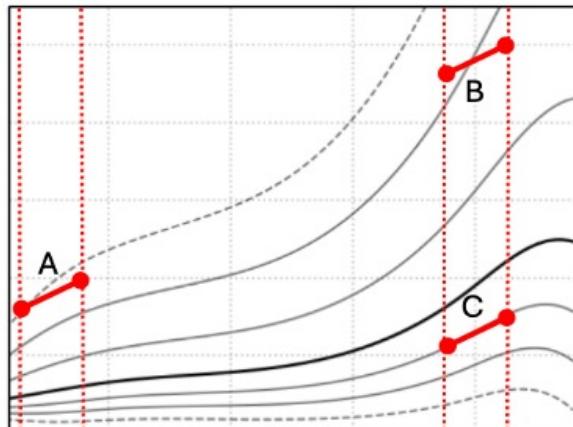
Cross-sectional normative models

Thrive lines:

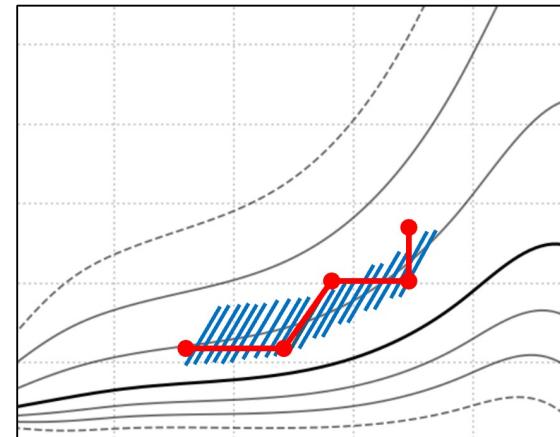
- significant length of velocity centile ($z = +/-1.96$)
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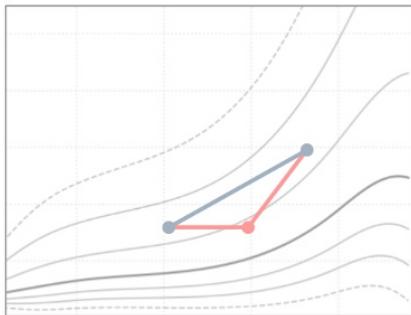
TO CONSIDER: DISTANCE VS VELOCITY



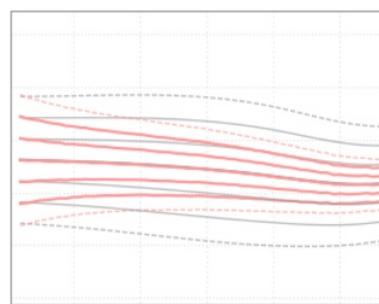
CONDITIONAL REFERENCE



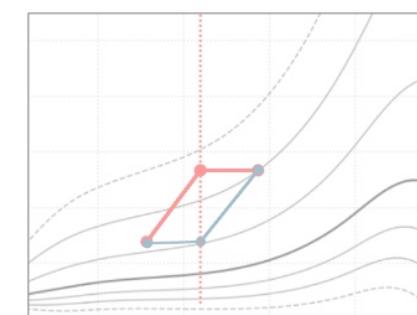
CENTILE CROSSING



MEASUREMENT DEPENDENCE



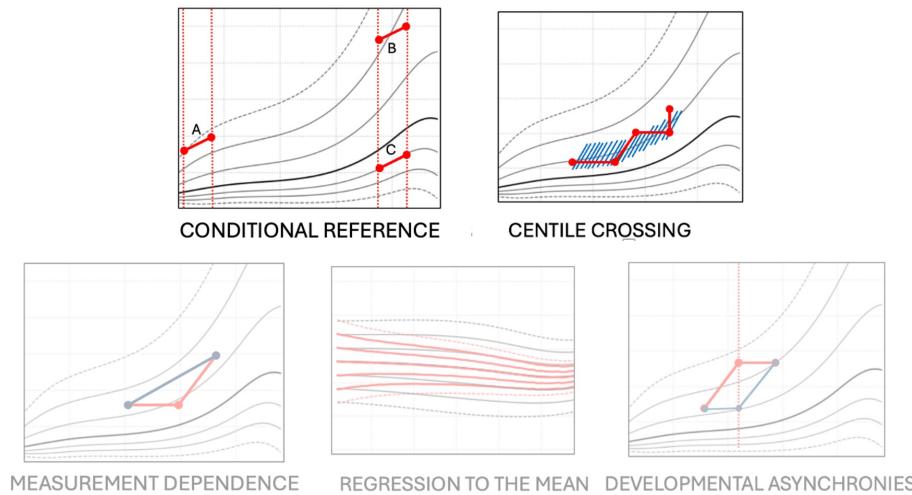
REGRESSION TO THE MEAN



DEVELOPMENTAL ASYNCHRONIES

Normative modeling

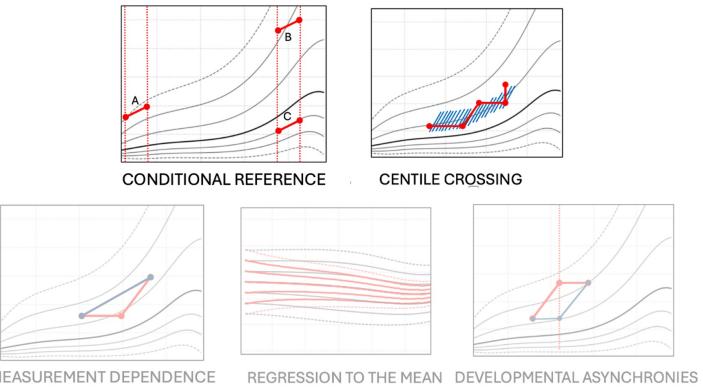
conditional, standardized velocity:



Normative modeling

conditional, standardized velocity:

- Velocity centiles need to be calculated from z-scores
- Z-Standardisation was obtained using a normative model based on the hierarchical Bayesian Regression framework with a SHASH S_{b1} likelihood (de Boer et al., 2023).



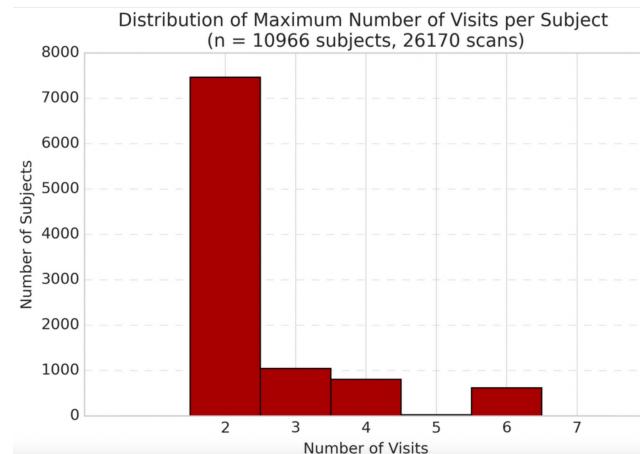
de Boer, A. A. A., Bayer, J. M. M., Kia, S. M., Rutherford, S., Zabihi, M., Fraza, C., Barkema, P., Westlye, L. T., Andreassen, O. A., Hinne, M., Beckmann, C. F., & Marquand, A. (2024). Non-Gaussian normative modelling with hierarchical Bayesian regression. *Imaging Neuroscience*, 2, 1–36.

Data

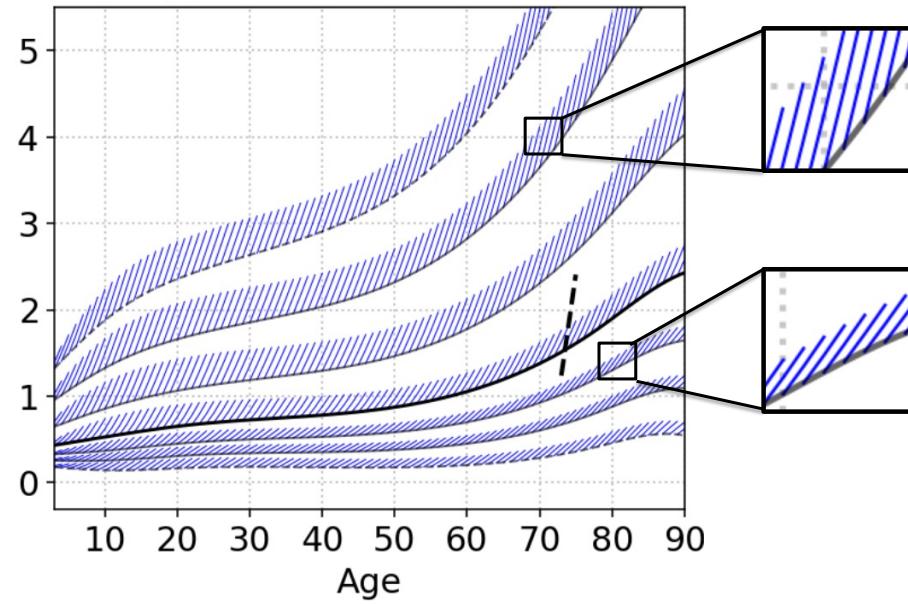
Velocity centiles can only be derived from longitudinal data

TRAINING SET			
Type	N scans	N subjects	N sites
Cross-sectional	29181	29181	85

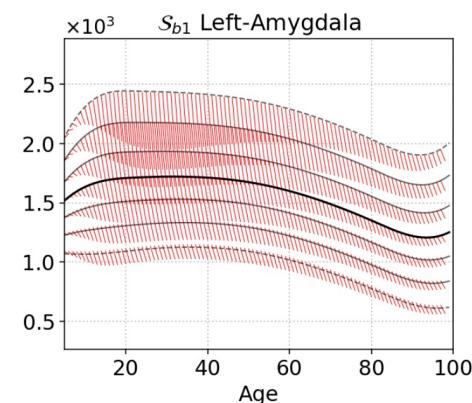
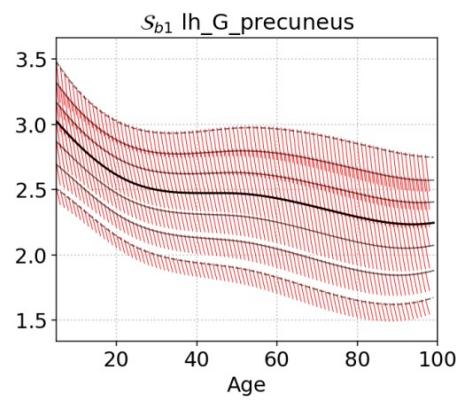
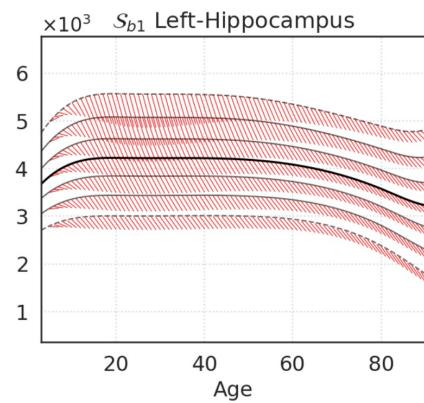
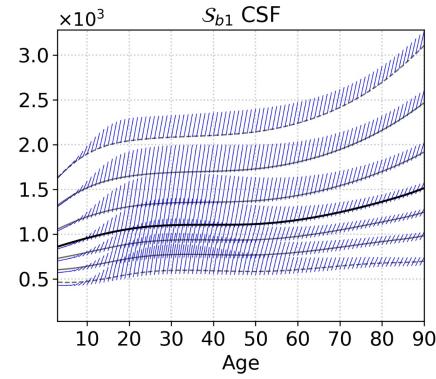
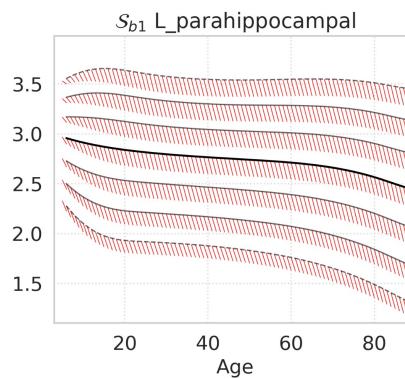
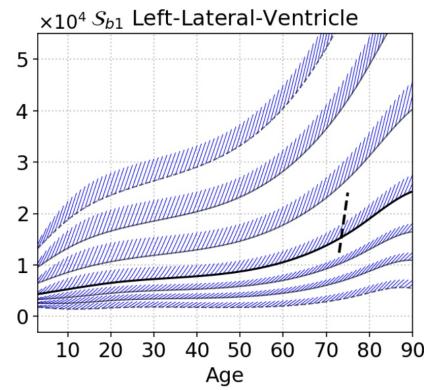
TEST SET			
Type	N scans	N subjects	N sites
Cross-sectional	18340	18340	85
Longitudinal	26170	10966	39
ADNI (clinical)	4595	996	67
ADNI (healthy controls)	1360	336	67
OASIS (clinical)	362	169	5



$\times 10^4 S_{b1}$ Left-Lateral-Ventrie



Thrive lines, examples:

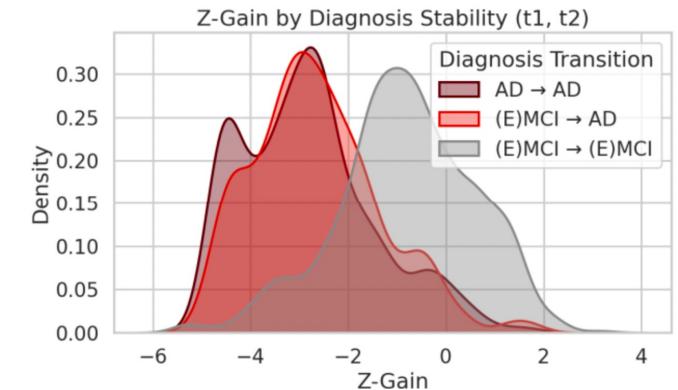
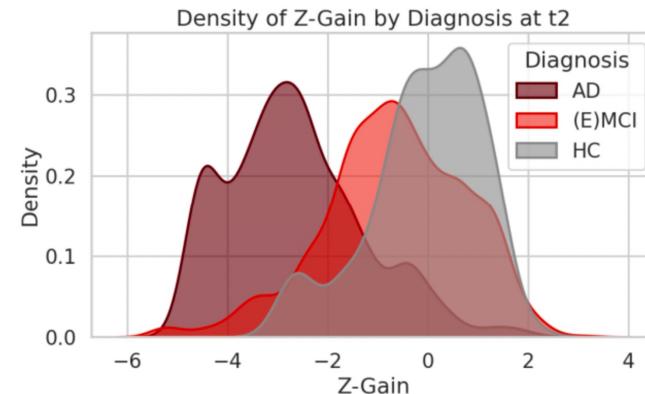
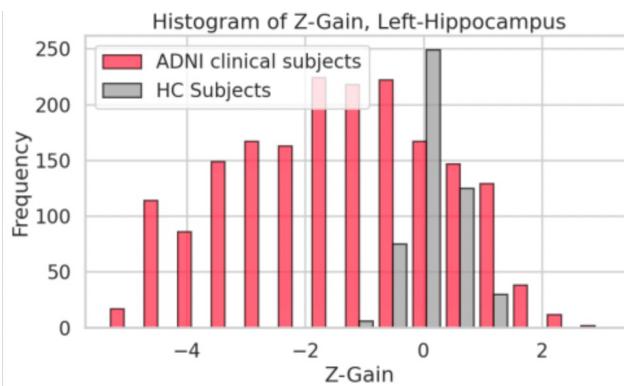


Results

Z-gain: quantification of significance of a change

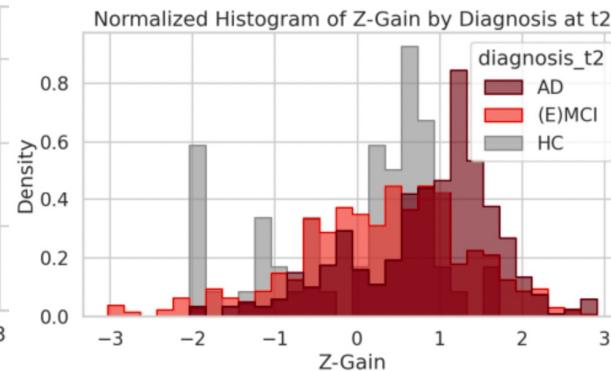
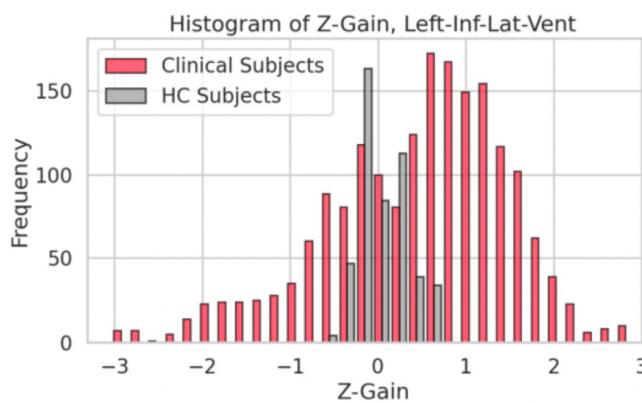
HC: Healthy controls
(E)MCI: (early) mild cognitive impairment
AD: Alzheimer's disease

Left Hippocampus

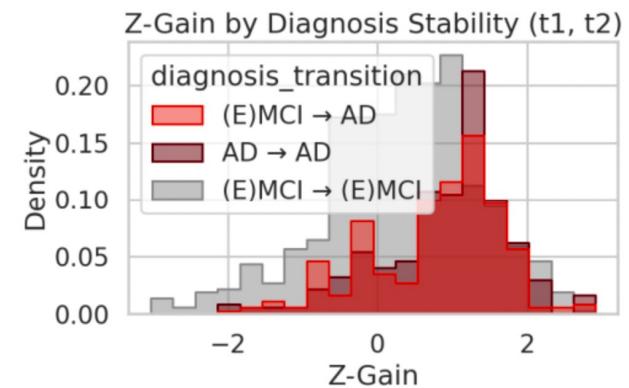


Results

Left Lateral Ventricle:



HC: Healthy controls
(E)MCI: (early) mild cognitive impairment
AD: Alzheimer's disease



Conclusion

- Information derived from longitudinal normative models, such as **thrive lines** and **z-gains**, are sensitive to detecting clinical change over time.
- Healthy individuals exhibit variability around normative centiles, but in clinical subjects this variability is much more widespread.
- Classical distance centiles **can not** provide information about change over time, rather it is essential to base these inferences on **velocity centiles** derived from **normed longitudinal data**.

THANK YOU

Special thanks to:

Augustijn de Boer
Hannah Savage



Predictive
Clinical
Neuroscience Lab

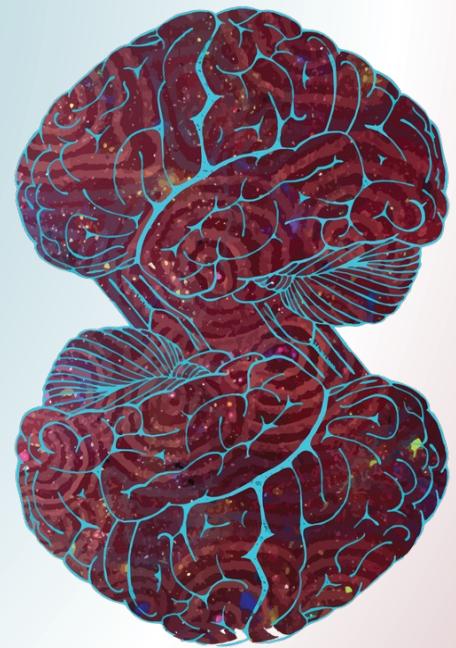
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