Neonatal brain age models in preterm infants

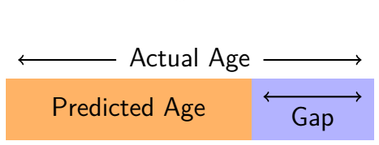
Howard Chiu [1] Adam Richie-Halford [2] Rocio Velasco Poblaciones [2] Melissa Scala [3] Molly Lazarus [4]
Virginia Marchman [2] Katherine Travis [4] Heidi Feldman [2] Jason Yeatman [1]

[1]Graduate School of Education, Stanford University, Stanford, CA, USA
[2]Division of Developmental Behavioral Pediatrics, Stanford University School of Medicine, Stanford, CA, USA
[3]Department of Pediatrics, Division of Neonatology, Stanford University, Stanford, CA, USA
[4]Burke-Cornell Medical Research Institute, Department of Pediatrics, Weill Medical College, Cornell University, New York, NY, USA

Introduction

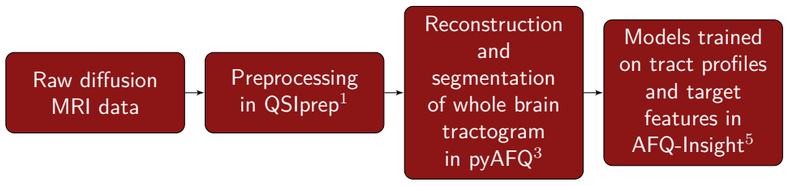
Preterm birth (<37 weeks of pregnancy) is an important public health issue affecting $> 10\%$ of children worldwide. Among children born very preterm, <32 weeks gestational age (GA), about $\frac{1}{2}$ have disrupted neurodevelopment, including abnormalities in the white matter (WM).

In this study, we aim to develop a brain age model that can be used as a summary statistic of infant neurodevelopment which can guide clinical decision-making.

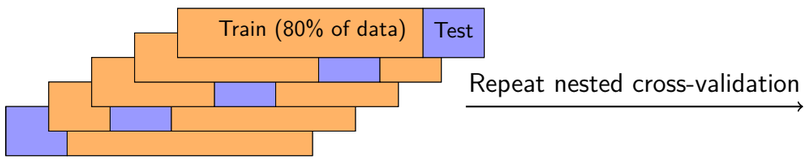


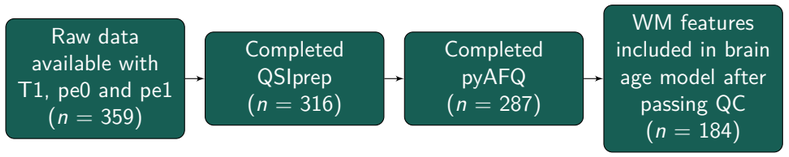
Can we conceptualize a positive brain age gap as a distal summary statistic for **poorer** infant health?

Methods



- 3 Models
  - Principal components regression (PCR) - No regularization
  - Lasso principal components regression (PCR-Lasso) - L1 regularization enforces sparsity
  - Bundle-wise principal components regression with sparse group lasso penalties (PCR-SGL) - L1 and L2 regularization
- 3 Targets
  - GA (age since conception)
  - Chronological age (CA; age since delivery)
  - Post-menstrual age (PMA) at scan (sum of GA + CA)

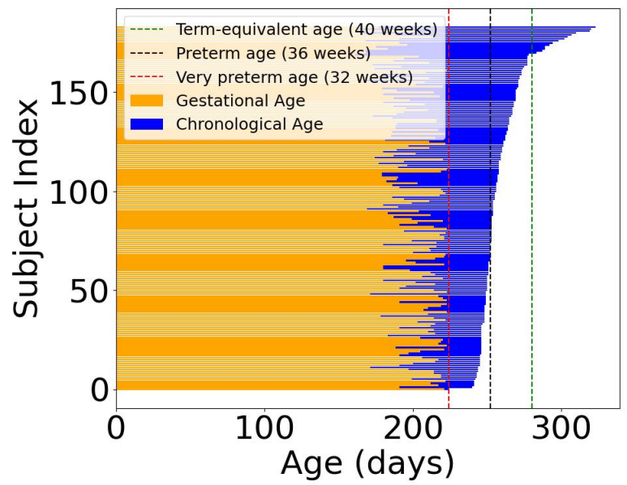




Their health acuity was evaluated based on a sum of binary indicators for 4 major comorbidities of prematurity (mean = 0.69, range: 0 – 4):

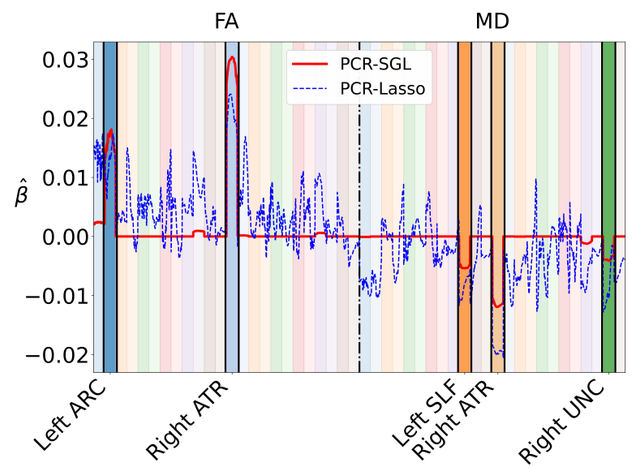
- Sepsis
- Necrotizing enterocolitis
- Intraventricular hemorrhages (IVH) of grade 1 and above
- Bronchopulmonary dysplasia of grade 2 and above

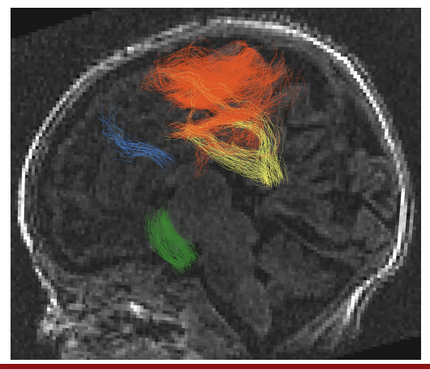
Participants (*n* = 184; males = 104) were infants born at <32 weeks GA. CA and GA were highly negatively correlated (*r* = -0.85).



Right anterior thalamic radiation (ATR) microstructure contributes the most to the prediction of brain age in this sample.

The brain age gaps from both PCR-Lasso and SGL models were highly correlated ($r = 0.872$). PCR-SGL produces a much sparser distribution of coefficients compared to PCR-Lasso.





- Left Arcuate (ARC)
- Left Anterior Thalamic Radiation (ATR)
- Left Superior Longitudinal Fasciculus (SLF)
- Left Uncinate (UNC)

Left hemisphere tracts plotted for illustrative purposes. Tract endpoints have been clipped in pyAFQ.

Infant WM features explain 21% of variance in PMA at scan. Including both FA and MD increases test R^2.

In general, the infants with the highest PMA at scan had higher FA and lower MD values.

When PMA at scan is decomposed into GA at birth and CA, diffusion properties explain 15% of variance in CA and 2% of variance in GA, respectively (not shown in table below).

Model	Target	Train R^2	Test R^2	Train MAE	Test MAE
PCR	PMA at scan	0.559	0.198	8.14	9.84
PCR-Lasso	PMA at scan	0.491	0.208	6.99	7.67
PCR-Lasso (FA only)	PMA at scan	0.428	0.144	6.75	7.43
PCR-Lasso (MD only)	PMA at scan	0.180	0.047	8.30	8.71
PCR-SGL	PMA at scan	0.264	0.104	8.05	8.19
PCR-SGL (FA only)	PMA at scan	0.220	0.054	8.14	8.25
PCR-SGL (MD only)	PMA at scan	0.170	0.041	8.47	8.82

Brain age gap explains additional 2% of variance in health acuity above and beyond CA and GA. Variance explained by brain age gap is greater than any WM feature alone (mean tract FA or MD).

Model 2: $\text{health\_acuity} \sim 1 + \text{CA} + \text{GA} + \text{brain\_age\_gap}$

Variables	Model 1	Model 2	Model 3
Intercept	-0.280	2.93	✓
CA	0.018***	0.005	✓
GA	0.001	-0.013	✓
PMA at Scan Gap	-	0.019**	-
Mean Tract FA or MD	-	-	✓
Likelihood Ratio (LR)	-	6.91**	

Asterisks denote level of significance: *** $p < .001$, ** $p < .01$, * $p < .05$

Conclusion

The brain age gap **shows promise** as a summary statistic for infant health, above and beyond information that can be gleaned from age and individual measures of WM microstructure.

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howardchiu@stanford.edu