Infant cerebellar microstructure influences motor and language performance in toddlers

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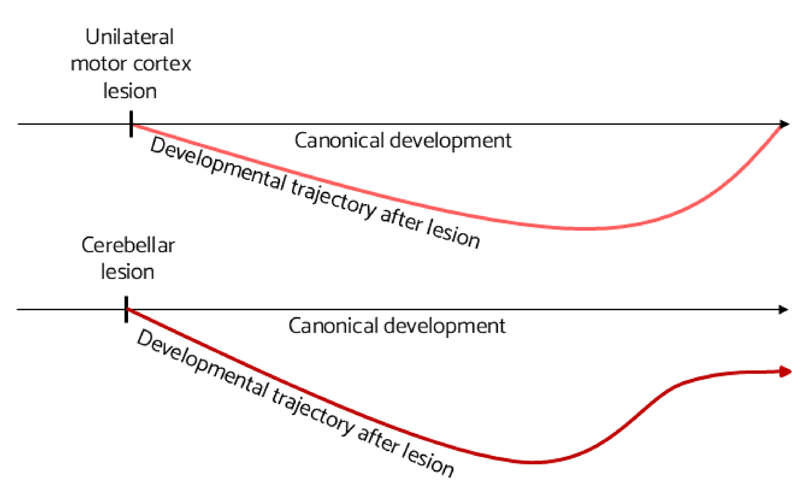
Background

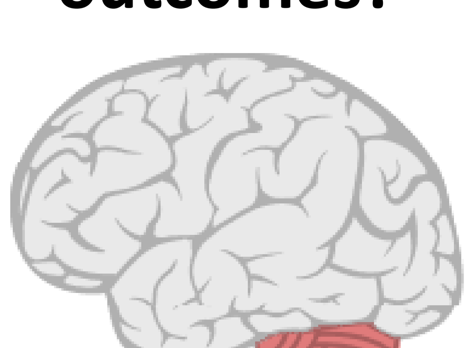
- Infants go through immense behavioral and brain development in the first year of life[1,2].
- The cerebellum sees some of the most dramatic changes during this period:
  - volume doubles in the first 90 days[3] and continues to increase - by 240% - in the first year of life[4]
  - it is much **less** plastic than the cerebrum during childhood[5,6]
- The cerebellum may play an essential role in building, language, motor, and social models of the world. Fetal and infant cerebellar damage is associated with very poor outcomes.



Motivating Question

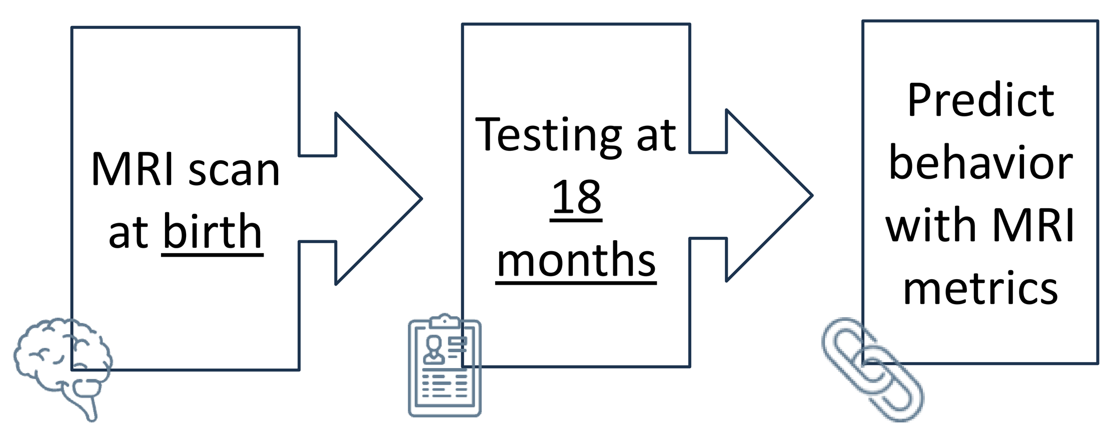
- The cerebellum seems to play an important role in behavioral development.
- Metrics of the brain can be used to predict later developmental outcomes[7-11].

Does cerebellar structural profile at birth predict later motor and cognitive outcomes?



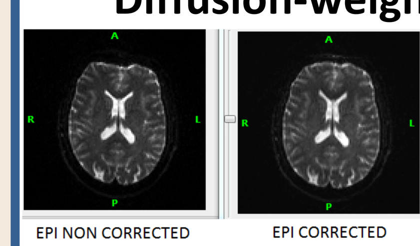
Methods

The developing Human Connectome Project (dHCP) dataset[12]

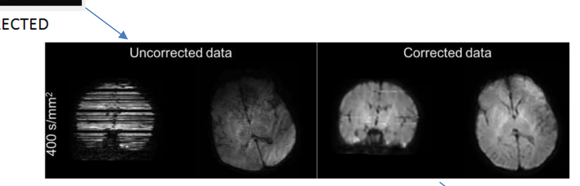


Exclusion criteria: Missing data (MRI and behavioral), preterm birth (< 37 weeks), and twin birth. **Final n = 253.**

Diffusion-weighted imaging pre-processing pipeline



Corrects for image bias from the direction of magnetic pulses in the scanner[13]



Advanced motion correction[14]

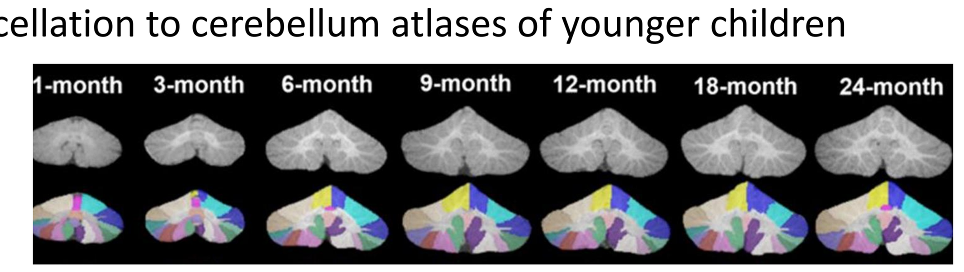
The AMICO package is available on GitHub to be used for NODDI analysis[15]

Neurite Orientation Dispersion and Density Imaging (NODDI) analysis[16]

- Accounts for free water, which is a concern in neonates.
- Histologically validated in mice, post-mortem brains, tissue samples from individuals with neurodegenerative diseases.
- Key metric: **orientation dispersion index** (ODI) - pattern of sprawling dendritic processes, speaks to grey matter complexity[17]

Cerebellum Lobule Parcellation

- Wang et al. (2023) created a neonatal cerebellar lobule parcellation
- Done by down-sampling the adult SUIT parcellation[19,20] the parcellation to cerebellum atlases of younger children



Behavioral Testing

Bayley Scales of Infant Development, 3rd Edition (BSID-III)[21]

- Screens for developmental delay and includes:
  - Receptive and expressive language subscales
  - Fine and gross motor subscales

Quantitative Checklist for Autism in Toddlers (Q-CHAT)[22]

- Early screening for autism
- Parent reported

Generalized Additive Model (GAM) regression analysis[23]

Predictor variables:
- ODI values extracted from 20 cerebellar lobules (regions)

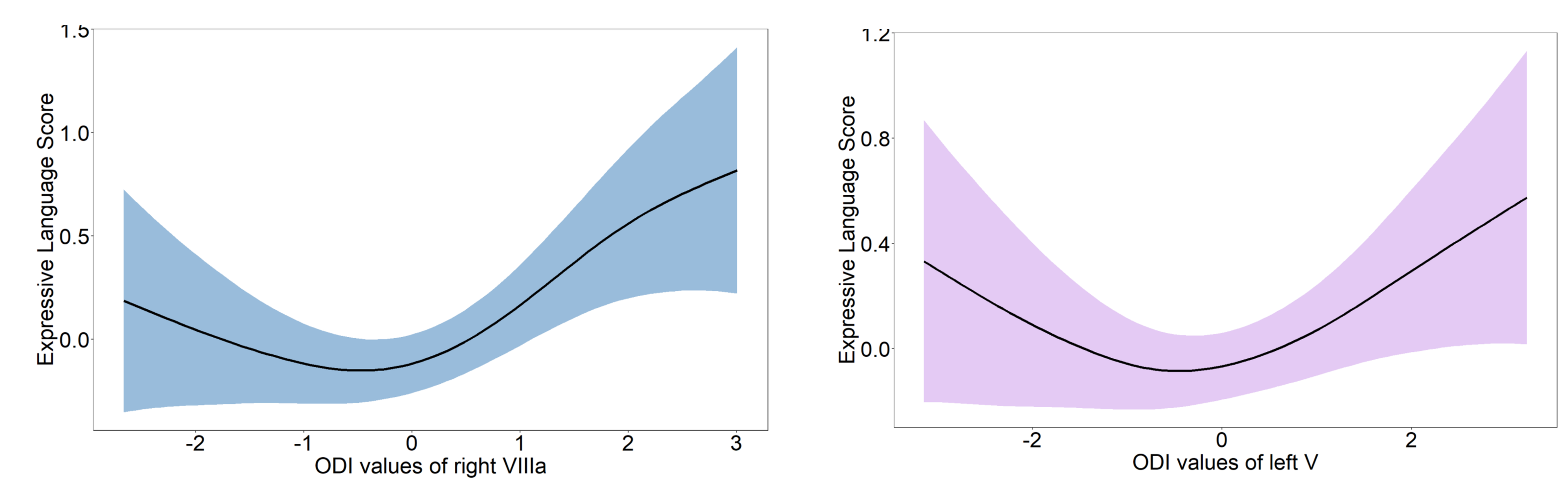
Control variables:
- Sex
- Mother's age
- Father's age
- Mother's education
- Postmenstrual age
- Age at behavioral interview

Outcome variables:
- Receptive language (BSID-III)
- Expressive language (BSID-III)
- Fine motor (BSID-III)
- Gross motor (BSID-III)
- Autism symptoms (Q-CHAT)

Results

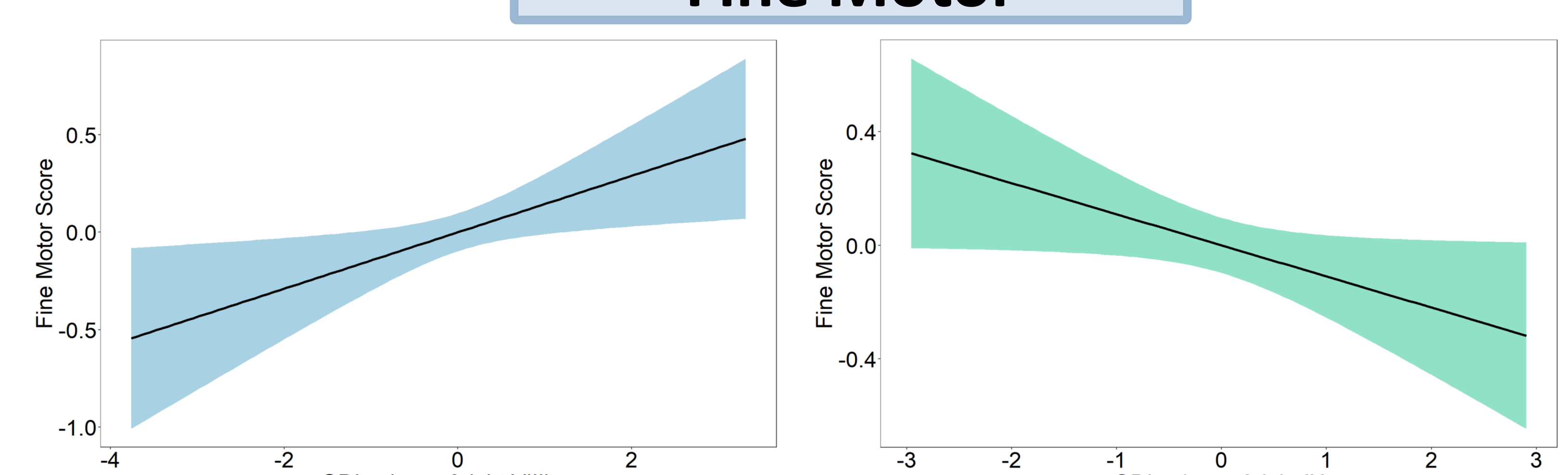
Partial residual graphs – graphs that represent the relationship between the predictor and outcome variable while accounting for all other variables in the regression model

Expressive Language



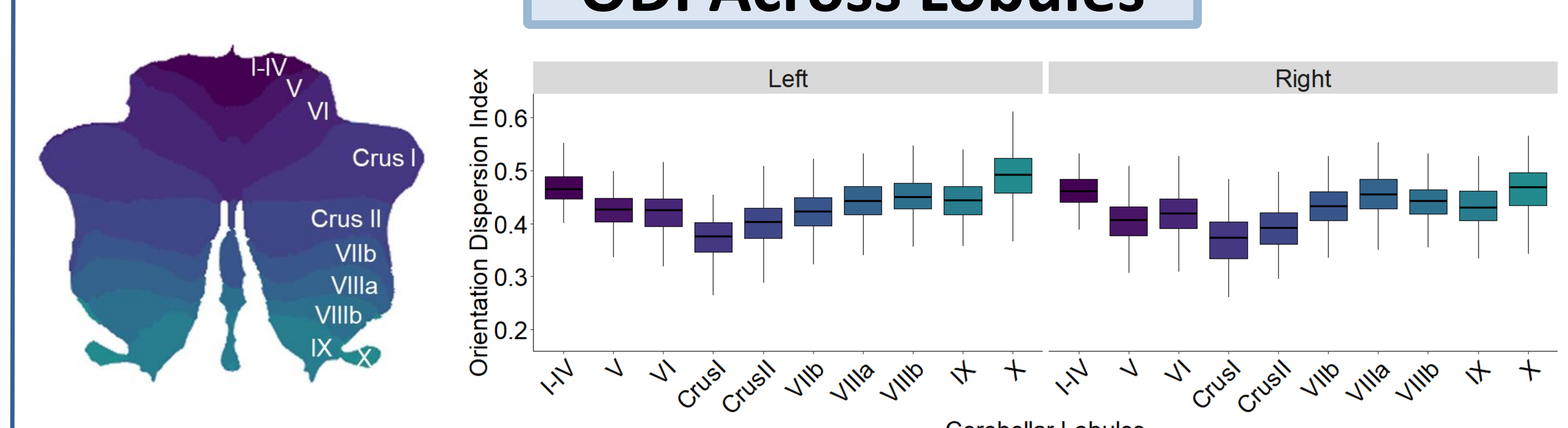
ODI in right VIIIa and left lobule V predicts **6% more variance** in the expressive language variable compared to the control model.

Fine Motor



ODI in right VIIIb and right IX predict **3% more variance** in the fine motor variable compared to the control model.

ODI Across Lobules



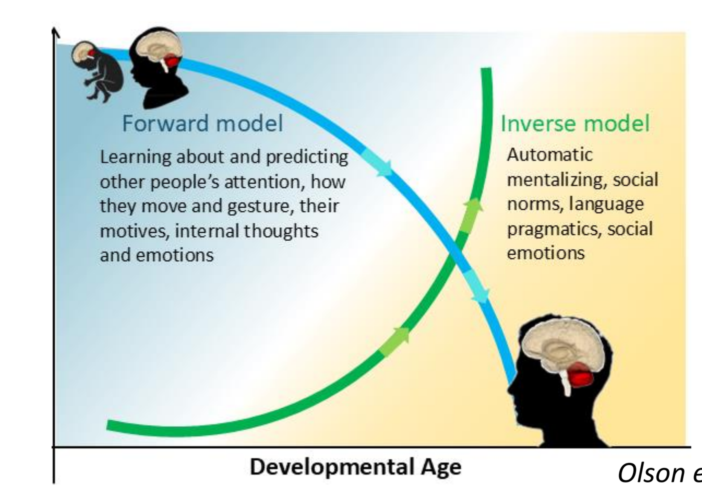
Higher ODI is motor regions (I-IV and X) reflects relatively earlier maturation of motor regions as compared to more cognitive regions, Crus I and II.

Conclusions

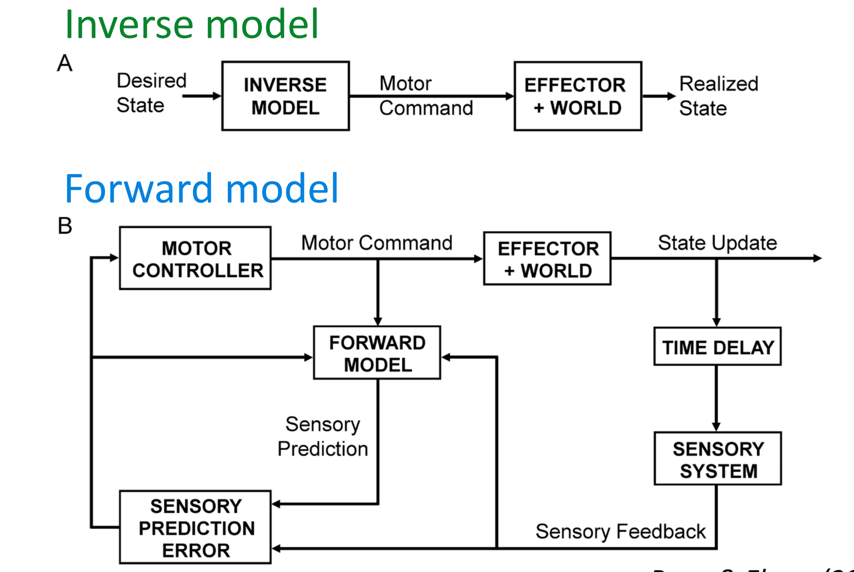
1. Cerebellar neurites at birth are predictive of expressive language and fine motor abilities at 18 months.
2. Neurites in a control region, the occipital lobe, did not explain any variance in these metrics.
3. Regions involved in verbal working memory (VIIIa and VIIIb)[24], tongue (VIIIa) and mouth movements (V)[25] and ocular-motor behavior/default mode network (IX)[26] were found to drive these relationships.

Theoretical Implications

The cerebellum might support the development of language and motor behavior through the creation and execution of internal models.



Olson et al. (2023)



Popa & Ebner (2022)

Citations & Author Info