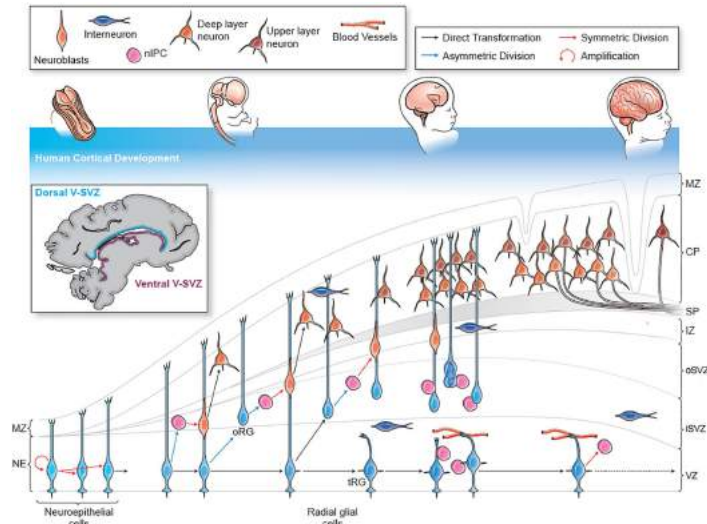


# Differential Patterns of Cortical Expansion in Fetal and Preterm Brain Development

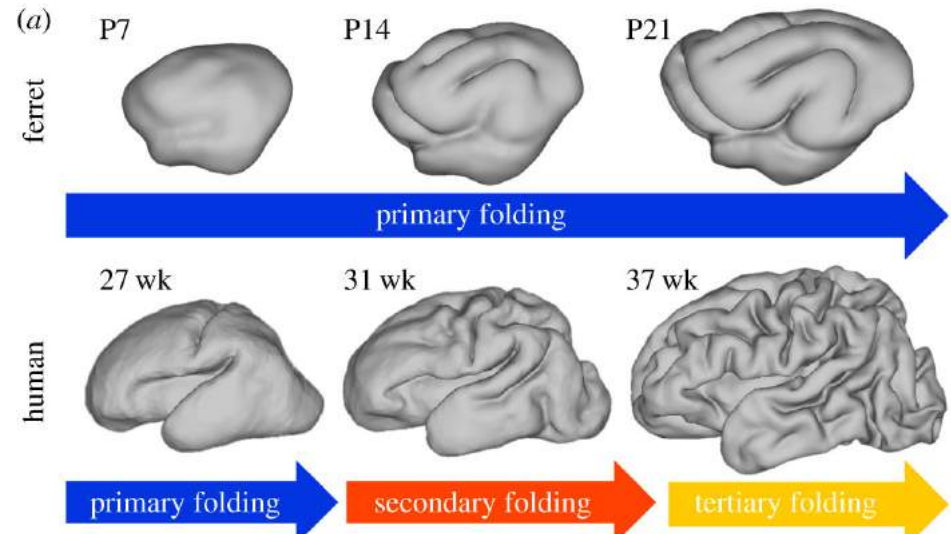


# CORTICAL FOLDING

- Cortical folding is a critical process in brain development. In normal human fetal development, it occurs between the 15th and 40th weeks of gestation.



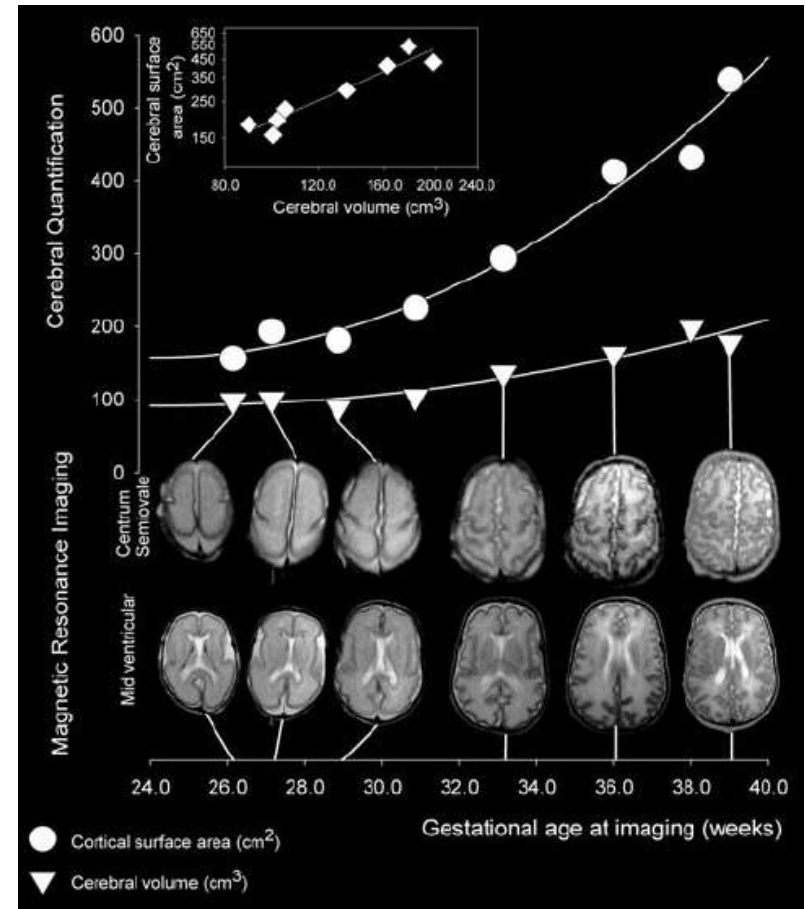
Subramanian, L., Calcagnotto, M.E., Paredes, M.F., 2020. Cortical Malformations: Lessons in Human Brain Development. *Frontiers in Cellular Neuroscience* 13.



Garcia, K.E. et al, 2018. Dynamic patterns of cortical expansion during folding of the preterm human brain. *Proceedings of the National Academy of Sciences* 115, 3156–3161.

# CORTICAL FOLDING

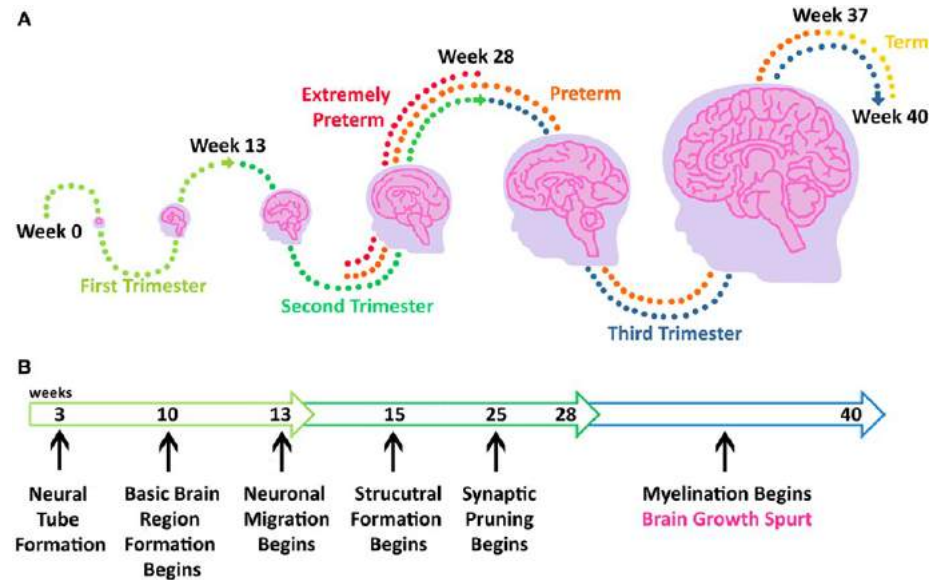
- The folded shape of the human brain allows the cerebral cortex to attain a large surface area relative to brain volume.
- From around the 25<sup>th</sup> week, the cortical surface area begins to grow much faster than the total brain volume, as the gyrification process occurs.



Kapellou, O., et al, 2006. Abnormal Cortical Development after Premature Birth Shown by Altered Allometric Scaling of Brain Growth. PLOS Medicine 3, e265.

# PRETERM BIRTH

- Preterm birth is defined as being born before 37 weeks gestational age (GA).
- Magnetic Resonance Imaging (MRI) studies have shown that preterm infants have altered cortical growth, expansion, folding and microstructure at term-equivalent age.
- The truncation of gestation due to preterm birth is associated with widespread alterations in cortical morphometry.



Newville J, Ortega M and Maxwell J (2018) Babies Born Early Can Have Brain Injury. Front. Young Minds. 6:20. doi: 10.3389/frym.2018.00020

# STUDIES ON FETAL CORTICAL EXPANSION

Preterm Data

Cross-sectional Fetal Data

Longitudinal Fetal Data

**a**

24w 26w 28w 30w 32w 34w 36w 38w

**b**

Whole Brain

$Y = Y_0 e^{kx}$

Surface Area (mm<sup>2</sup>)

GA/week

Hemisphere

• left

• right

Surface Area (mm<sup>2</sup>)

GA/week

Parietal

Surface Area (mm<sup>2</sup>)

GA/week

Temporal

Surface Area (mm<sup>2</sup>)

GA/week

Frontal

Surface Area (mm<sup>2</sup>)

GA/week

Occipital

Surface Area (mm<sup>2</sup>)

GA/week

Sup\_Temp\_pos

Surface Area (mm<sup>2</sup>)

GA/week

Med\_Inf\_Temp

Surface Area (mm<sup>2</sup>)

GA/week

Lat\_Occipitaltemporal

Surface Area (mm<sup>2</sup>)

GA/week

Parahippocampal

Surface Area (mm<sup>2</sup>)

GA/week

Med\_Inf\_Temp\_pos

Surface Area (mm<sup>2</sup>)

GA/week

Med\_Inf\_Temp\_ant

Surface Area (mm<sup>2</sup>)

GA/week

Lat\_Occipitaltemporal\_pos

Surface Area (mm<sup>2</sup>)

GA/week

Lat\_Occipitaltemporal\_ant

Surface Area (mm<sup>2</sup>)

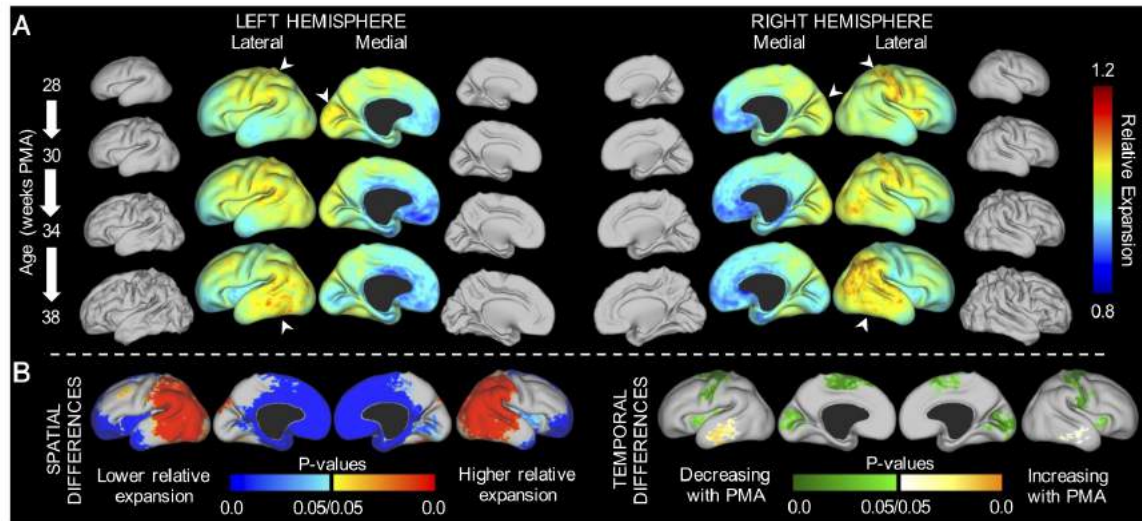
GA/week

## Patterns of Cortical Expansion in Fetal and Preterm Brain Development



# DYNAMIC PATTERNS OF CORTICAL EXPANSION DURING FOLDING OF THE PRETERM HUMAN BRAIN (GARCIA ET AL, 2018)

- Continuous patterns of surface expansion following preterm birth were computed using longitudinal surface registration with biomechanical constraints.
- Patterns were shown to differ to some ROI-based analysis, due to the use of very large regions in previous studies.
- In ROI analysis, finer differential patterns can be incorrectly averaged-out.



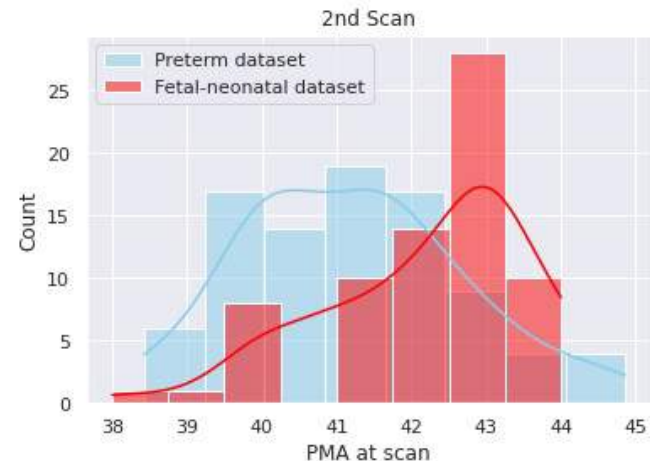
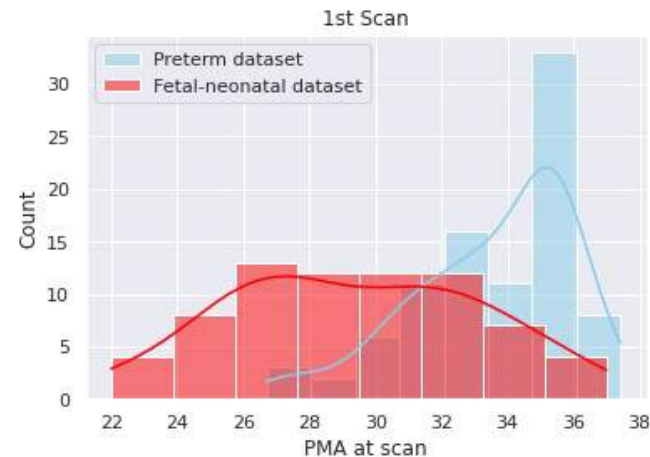
# DATASET - dHCP

- **72 subjects born at term (38 to 42 weeks)**

1. scanned in utero
2. and shortly after birth

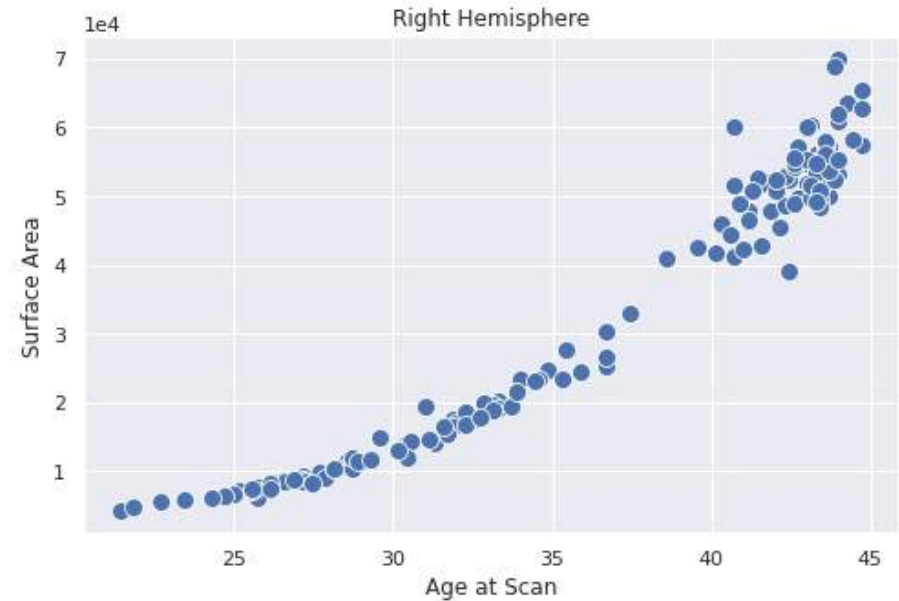
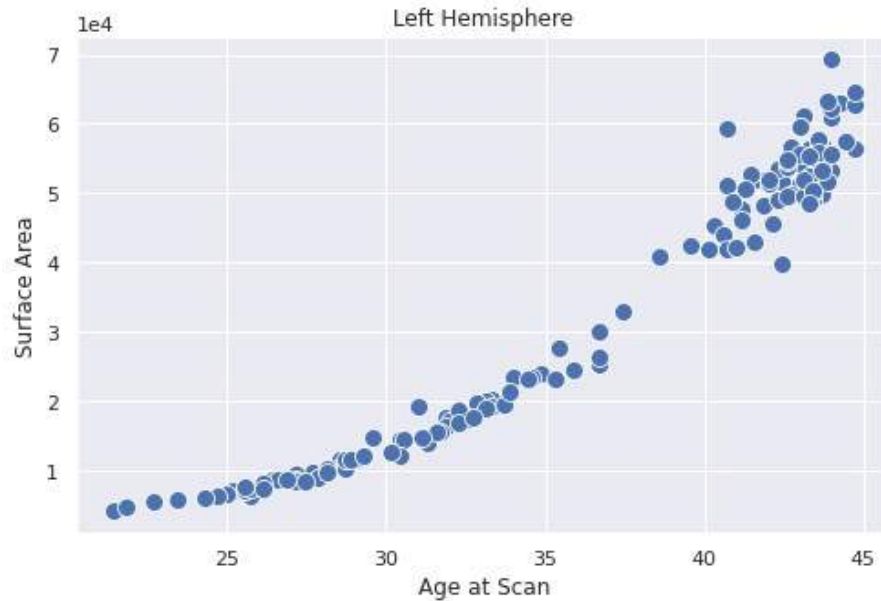
- **90 subjects born preterm (26 to 37 weeks)**

1. scanned shortly after birth
2. and at term-equivalent age





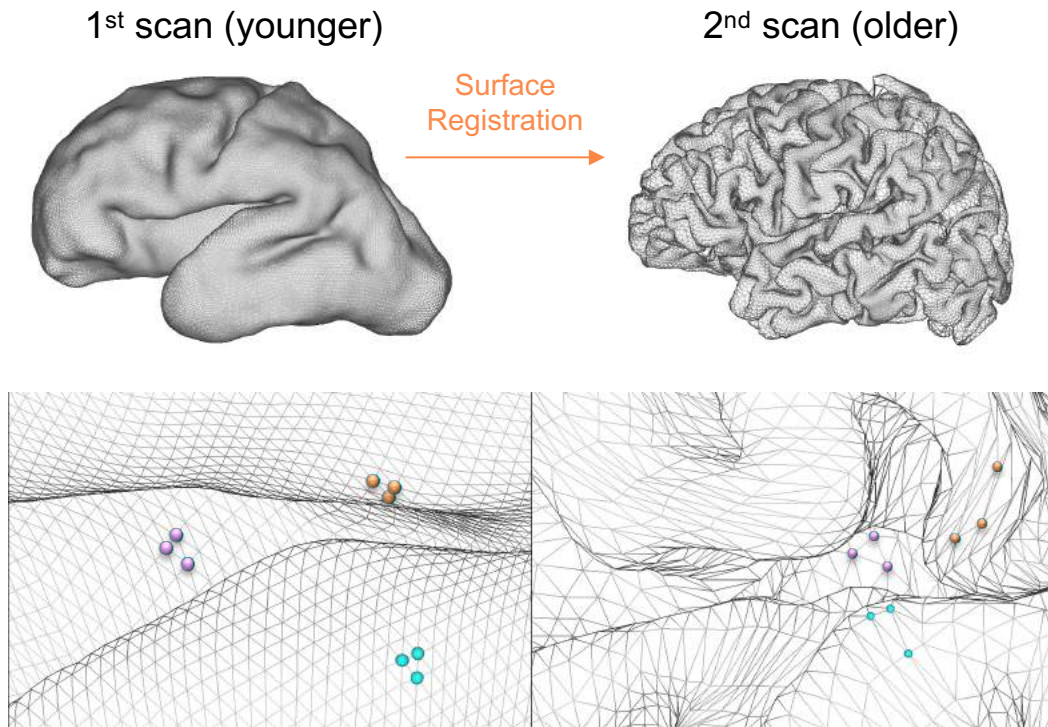
# INITIAL ANALYSIS: SURFACE AREA



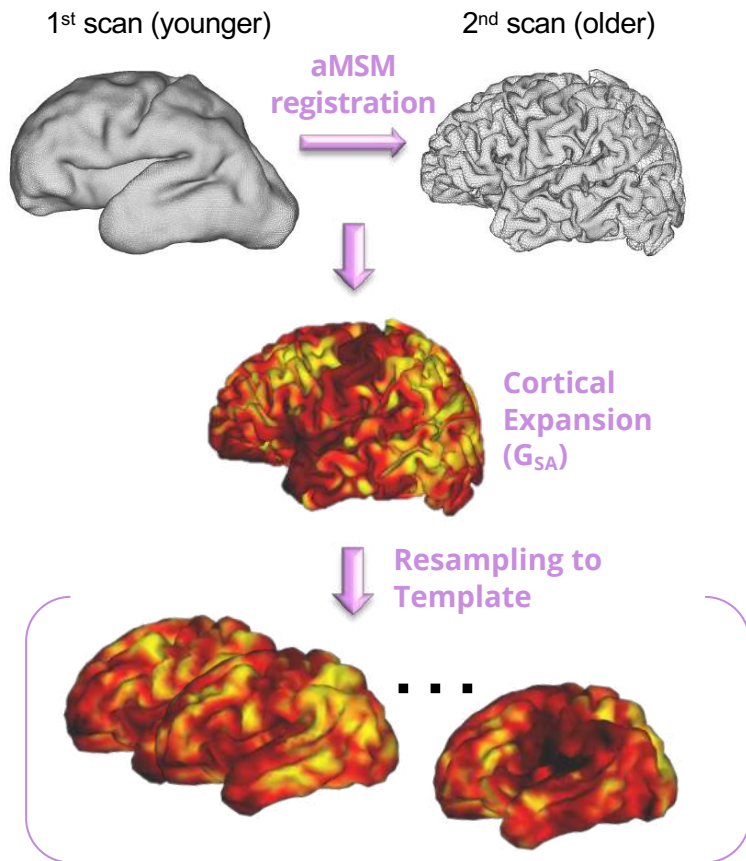
- Cross-sectional analysis of Surface Area vs Age at scan using all datapoints from fetal and neonatal scans (full-term only)

# SURFACE REGISTRATION WITH aMSM

- Longitudinal registration of the 1<sup>st</sup> to 2<sup>nd</sup> scan was performed using anatomically Constrained Multimodal Surface Matching
- Cortical expansion corresponds to  $J$  between input surface and registered surface, i.e. local area difference for each mesh element, between input and registered scan



# ESTIMATION AND ANALYSIS OF CORTICAL EXPANSION



## Exponential model of growth

$$G_{SA} = e^{k_0 - k_1 age_{fetal} + k_2 age_{neonatal}}$$

Rate of growth      Fixed  $age_{neonatal}$

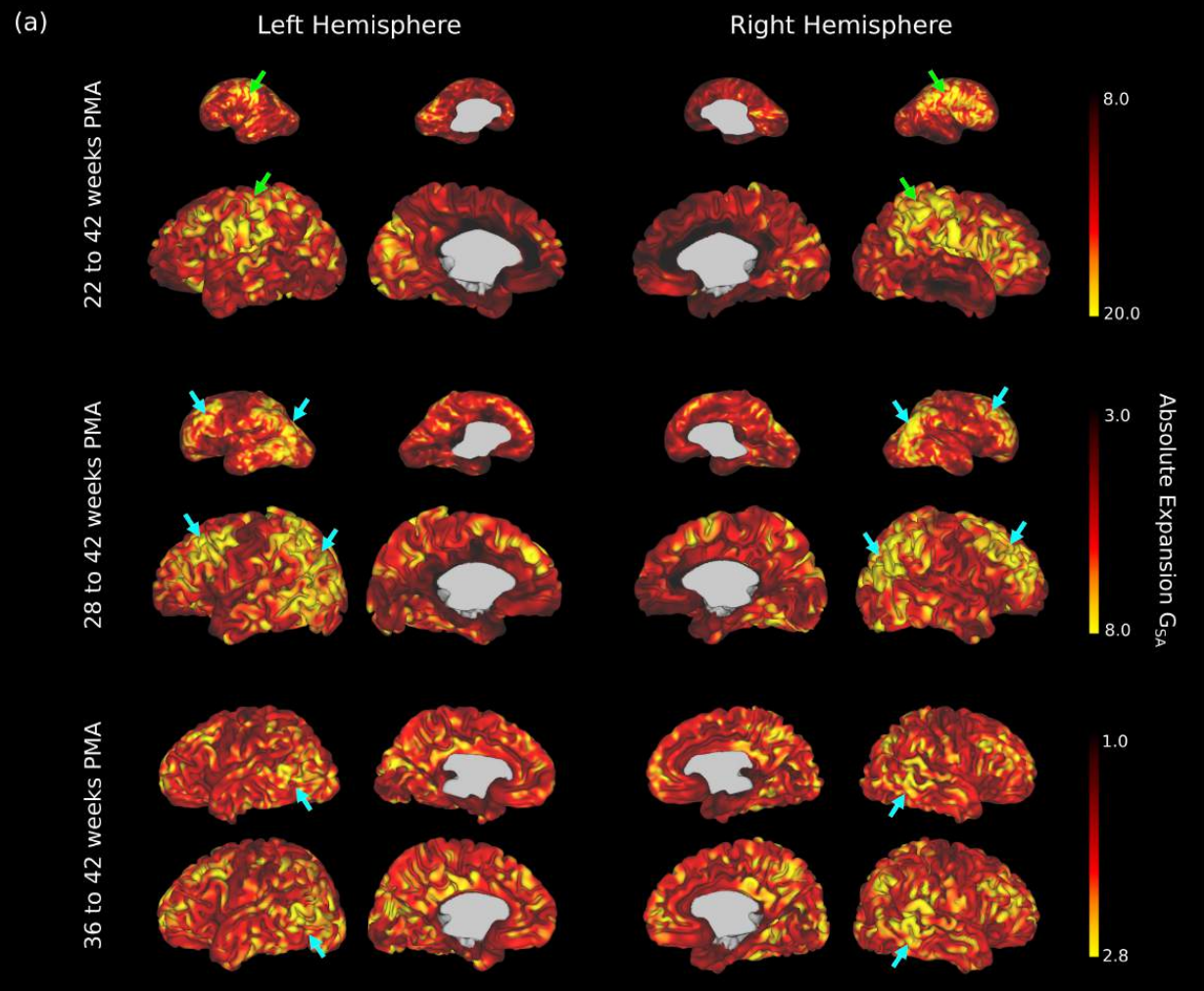
$$\log(G_{SA}) = \log(k_0) - k_1 age_{fetal} + k_2 age_{neonatal}$$



$$\log(G_{SA} \text{ 22} \rightarrow \text{23}) = \log(G_{SA} \text{ 22} \rightarrow \text{40}) - \log(G_{SA} \text{ 23} \rightarrow \text{40})$$

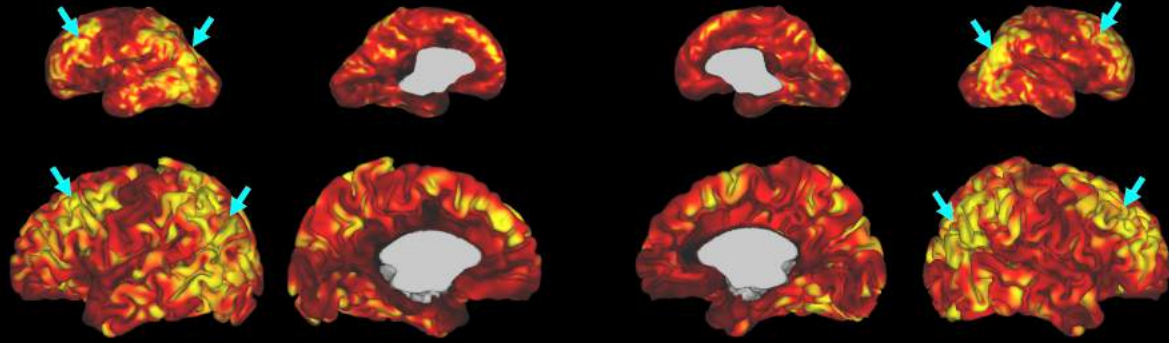
# RESULTS

- Absolute cortical surface expansion maps ( $G_{SA}$ ) for 3 individual pairs of surfaces, visualized in both the first and second scan.



## Fetal-neonatal

28 to 42 weeks PMA



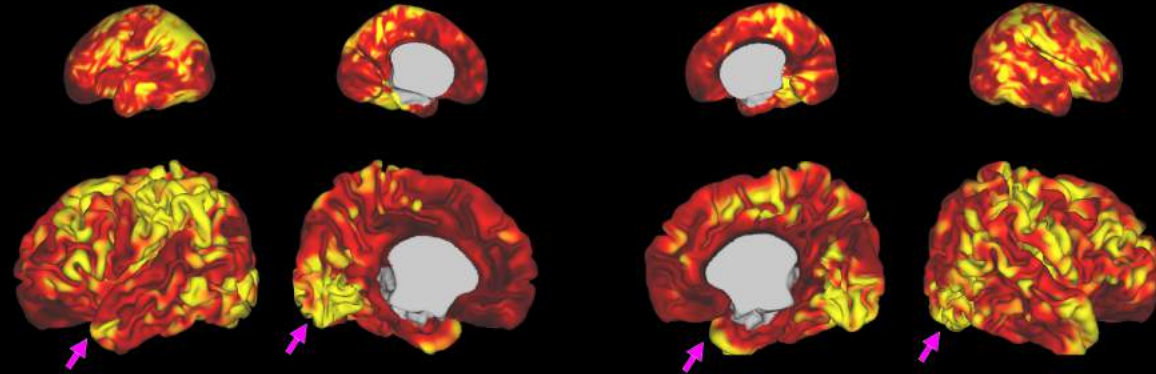
Absolute Expansion  $G_{SA}$

3.0

8.0

## Preterm

28 to 42 weeks PMA



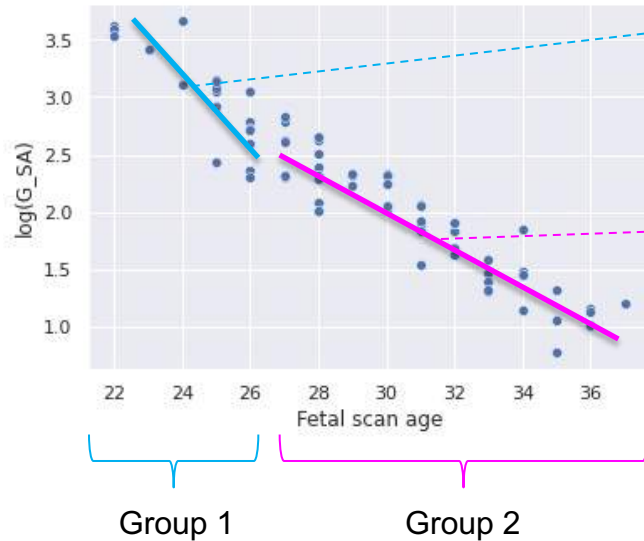
3.0

8.0

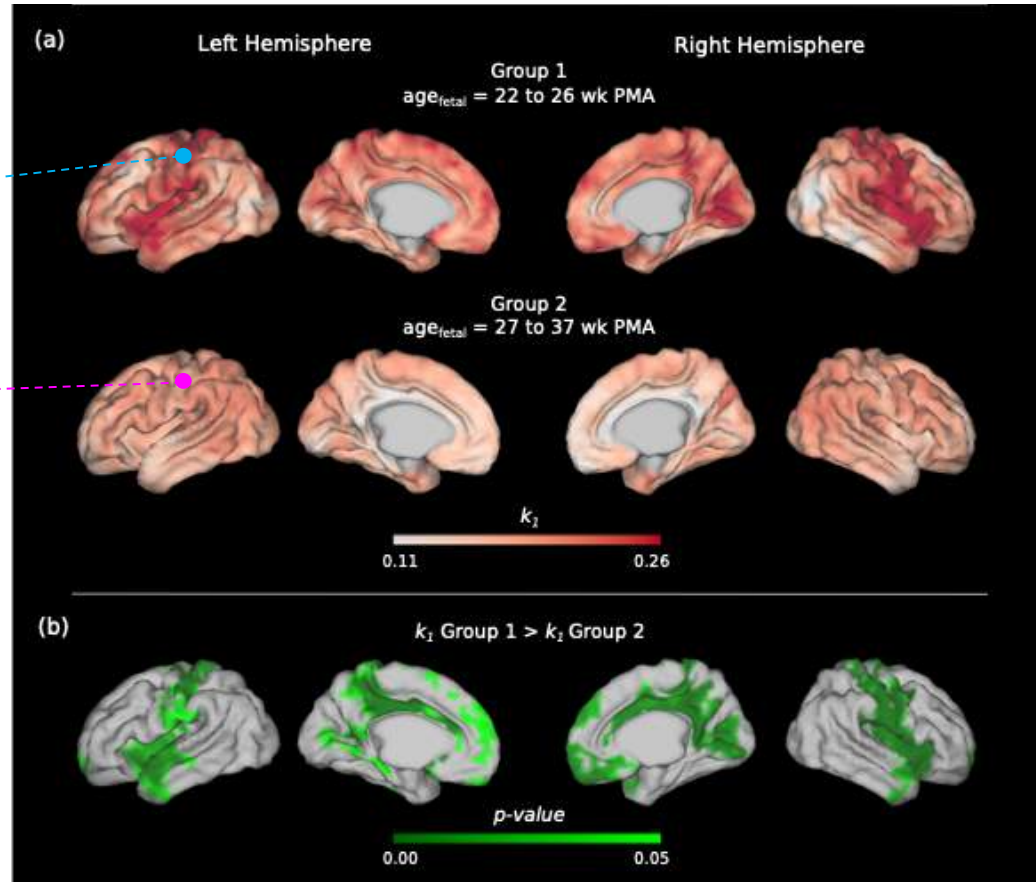


# CORTICAL EXPANSION RATES

$$\log(G_{SA}) = \log(k_0) - k_1 \text{age}_{fetal}$$



**t-test:**  $k_1 \text{ Group 1} > k_1 \text{ Group 2}$





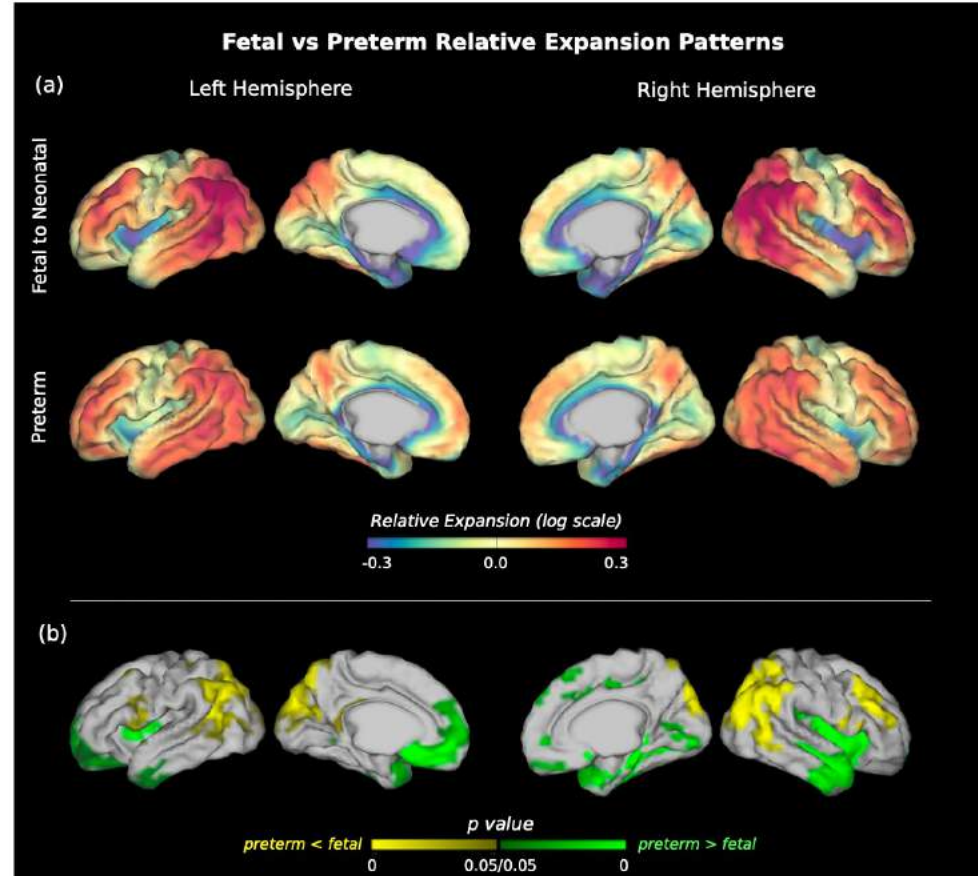
# COMPARISSION WITH PRETERM DATASET

- Relative expansion maps (normalised by global growth) reveal different regional patterns between fetal and preterm development, for the same scan ages.
- Preterm neonates exhibit higher relative expansion in the temporal and frontal poles and insula, while fetal relative expansion was higher for the posterolateral parietal cortex.



**t-test:** Relative  $G_{SA}$  Preterm > Relative  $G_{SA}$  Fetal

**t-test:** Relative  $G_{SA}$  Preterm < Relative  $G_{SA}$  Fetal



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...and the entire MeTrICS Lab!

