# Measuring cortical neurite-dispersion and perfusion in preterm-born adolescents using multi-modal MRI

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## 1) Extreme Prematurity at Adolescence (the EPICure@19 Project)

Extremely preterm birth coincides with a period of rapid brain growth and development.

Cohorts of extremely preterm born subjects studied in the 1990s are now beginning to reach adulthood and can now be studied

Disruption to normal development as a result of preterm birth is likely to result in both cerebrovascular and microstructural differences compared to term-born controls.

We investigate a cohort of 19 year-old adolescents consisting of **43 extremely-preterm** (born at less than 26 weeks completed gestation) and **21 term-born** individuals

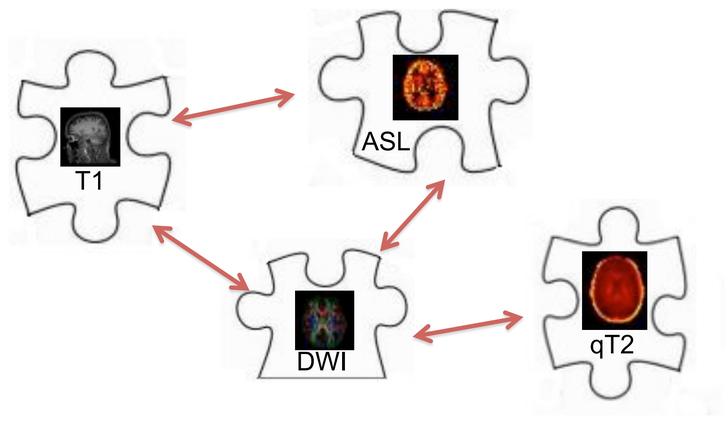



**Fig 1. Multi-modal model fitting elucidates the metaphorical puzzle of neurodevelopmental synchrony**

## 2) Imaging data and coupled model-fitting

**2.1) PCASL** data can be used to estimate a cerebral blood flow (CBF) map (CBF) [2]:

Plasma/tissue partition coefficient (0.9ml/g)
Post-label delay (1650ms)
Blood T1 (1650ms)

$$\mathrm{CBF} = \frac{6000\lambda}{2\alpha} \frac{e^{\mathrm{PLD}/\mathrm{T1}_{\mathrm{blood}}}}{\mathrm{T1}_{\mathrm{blood}}(1 - e^{-\tau/\mathrm{T1}_{\mathrm{blood}}})} \frac{(S_C - S_L)}{S_{PD}} [\mathrm{ml}/100g/\mathrm{min}]$$

Labelling efficiency (0.85)
Labelling duration (1650ms)

**2.2) DWI** and **multi-echo T2** data can be used to estimate cortical neuronal density and neuronal dispersion:

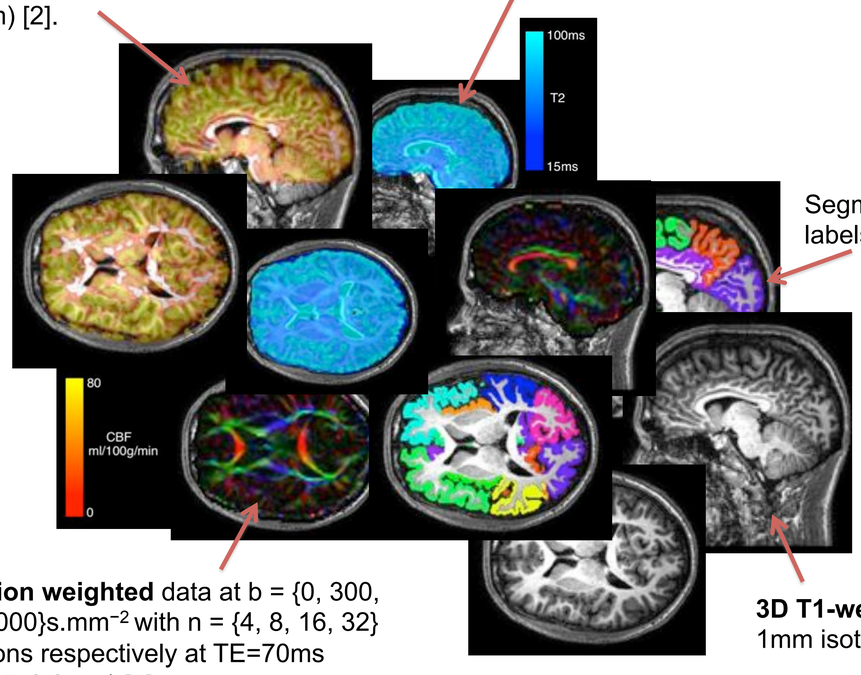
400ms
100ms

$$S(b, \mathbf{x}) = S_0 \left[ v_{iso} e^{-bd_{iso}} e^{-\mathrm{TE}/\mathrm{T2}_{iso}} + (v_{in} A_{in} + v_{ex} A_{ex}) e^{-\mathrm{TE}/\mathrm{T2}_{tis}} \right]$$

Free-water isotropic signal
Intra-neurite density
Extra-neurite density

Pseudo-Continuous ASL (**PCASL**) for 30 pairs with PLD=1800ms, label duration (τ)=1650ms (3x3x5mm) [2].

**T2 weighted** data with five echo times at TE={40,50,85,100,150}ms.




Segmentation and region labels [4].

**Diffusion weighted** data at b = {0, 300, 700, 2000}s.mm$^{-2}$ with n = {4, 8, 16, 32} directions respectively at TE=70ms (2.5x2.5x3.0mm) [5].

**3D T1-weighted** volume at 1mm isotropic resolution

## 3.1) Cortical Blood Flow

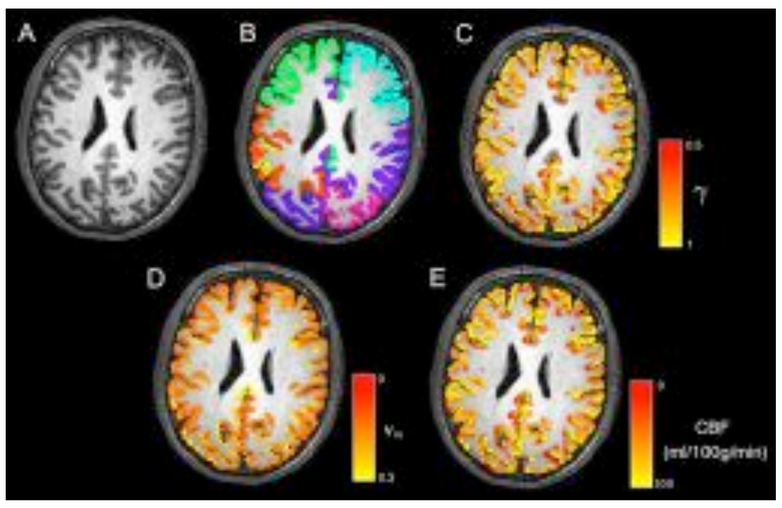



**Fig 2**. Single subject example: A) T1-weighted imaging, B) cortical parcellation, C) neurite orientation dispersion, D) intra-axonal volume fraction and E) cerebral blood flow.

- **GM volume is reduced in the EP group (0.578±0.06l vs. 0.621 0.05l)**
- **CBF values are lower in the EP group (48.67±5.6 vs 53.9±7.7 ml/100g/min)**
- **Correlation between CBF and Cortical Dispersion is reduced in the EP group (0.03<Δr<0.17, p=0.005), and when correcting for brain volume (p=0.006).**

## 3.2) Cortical Diffusion Imaging

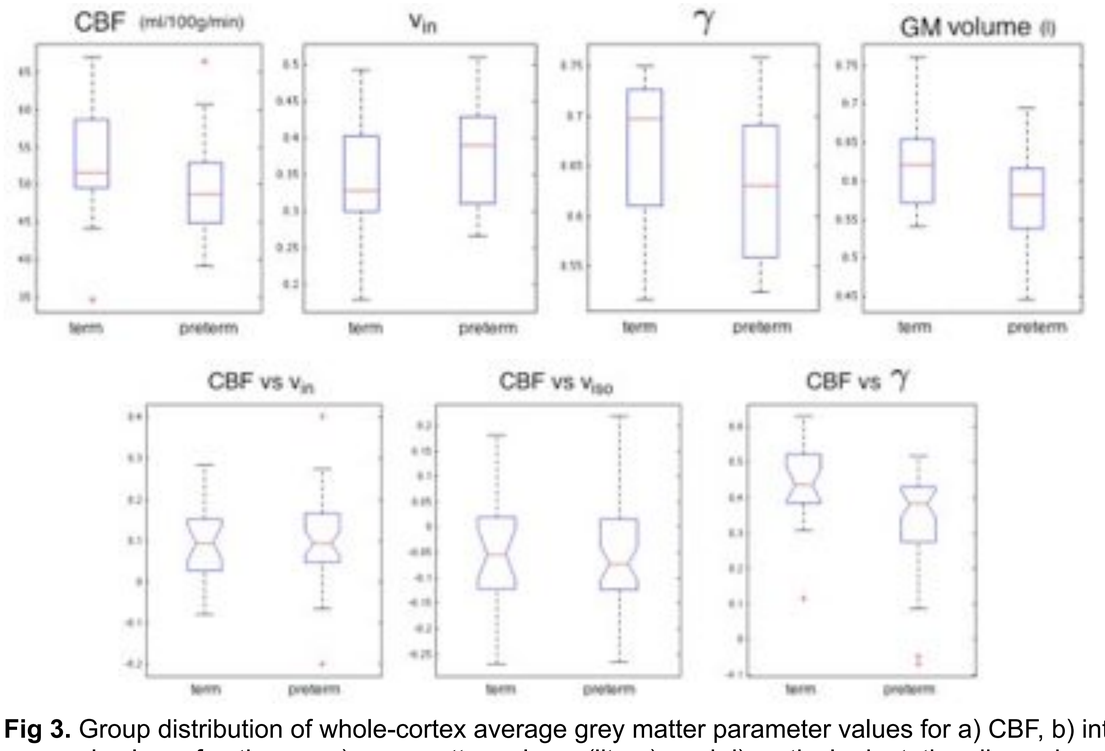



**Fig 3.** Group distribution of whole-cortex average grey matter parameter values for a) CBF, b) intra-axonal volume fraction $v_{in}$, c) grey matter volume (litres), and d) cortical orientation dispersion γ. Group distributions of the single-subject image correlation coefficients between CBF and grey matter parameter values for e) $v_{in}$, f) $v_{iso}$ and g) γ.

## 4) Conclusion

Coupled fitting of diffusion weighted, T2 relaxometry and Arterial Spin Labeled MRI is possible.

Early results suggest changes in the relationship between cortical orientation dispersion and CBF in preterm adolescents compared to controls independent of GM volume.

Revealing the long-term structural and functional differences in preterm cohorts, can help better inform on the likely outcomes of contemporary newborns

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