Identifying spatiotemporal changes in cortical neurodevelopment using post-mortem and in vivo data

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Background

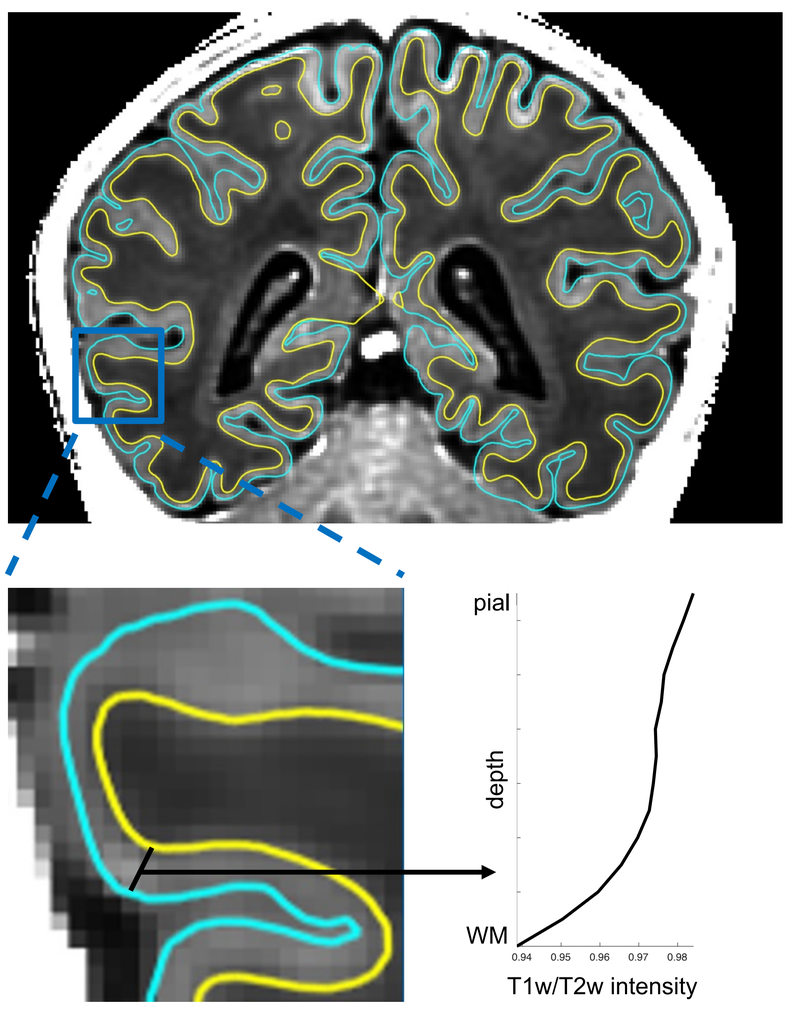
- **Neurodevelopment** is a multifaceted process, comprising the molecular, structural and functional maturation of the brain
- The human **cortex** undergoes continuous structural reorganization during early stages of development (Vasung et al., 2019)
- The temporal and spatial progression of cortical development is still insufficiently described on a **multi-scale level**

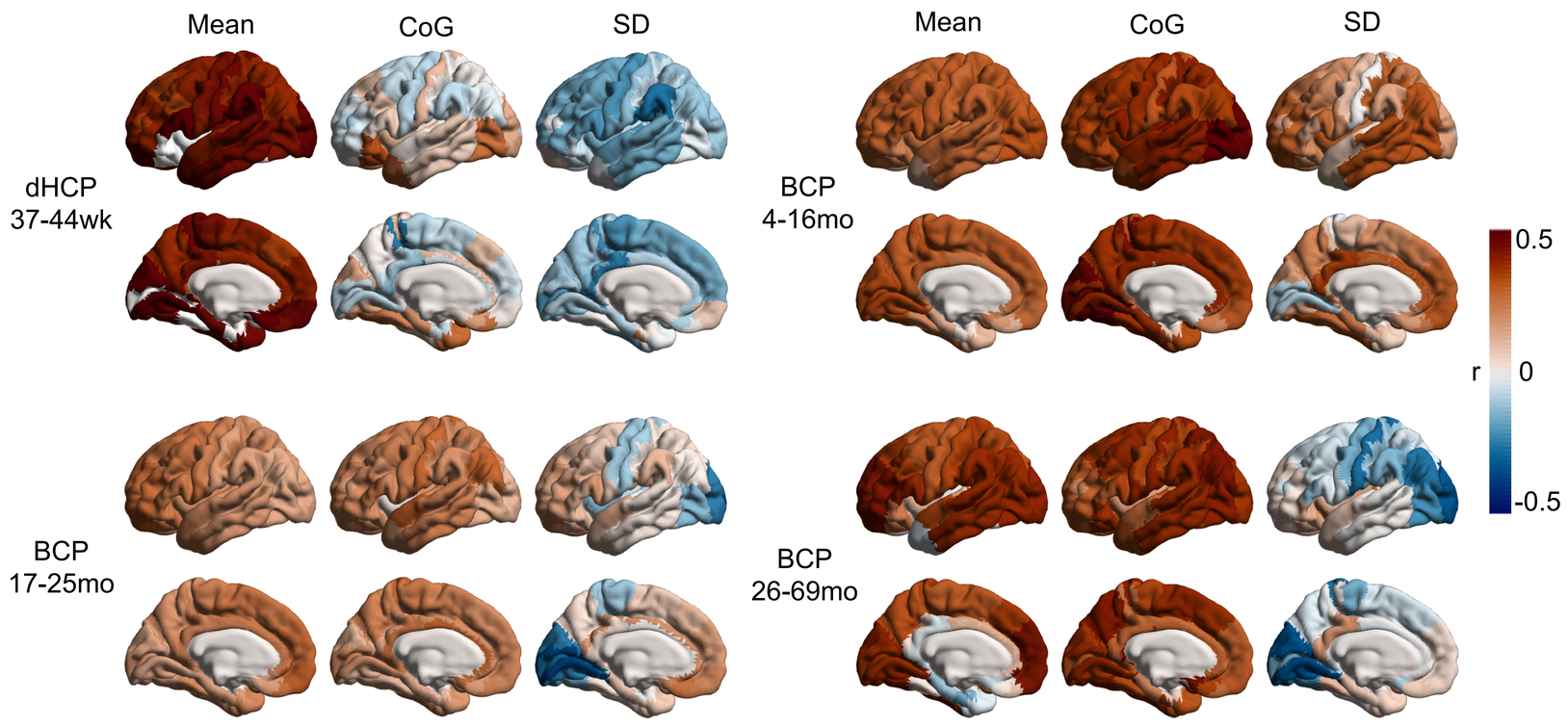
Materials & Methods

- **MRI analysis**: Characterisation of cortical mictostructure in the developing Human Connectome Project (dHCP, n=328, 37-44 post-menstrual weeks; Makropoulos et al., 2018) and Baby Connectome Project (BCP, n=216, 4-69 months; Howell et al., 2019). Intensities were sampled at 14 intracortical depths (Paquola et al., 2019) at each vertex of T1w/T2w images and the intensity profiles were synopsised using central moments (CMs; mean, centre of gravity and standard deviation). Area-specific, age-related changes in CMs were assessed via product-moment correlations.
- **Histological analysis**: Extraction of cytoarchitecture measurements (number of cells and area occupied by cells) in photomicrographs of *post-mortem* human tissue (254 cortical patches; 0, 1, 3, 15, 24 and 48 months; Conel J. L., 1939; 1942; 1947; 1955; 1959; 1963) via a sliding-window approach. Measurements were averaged across matching depths and product-moment correlation coefficients were calculated between age and cytoarchitecture.

Results

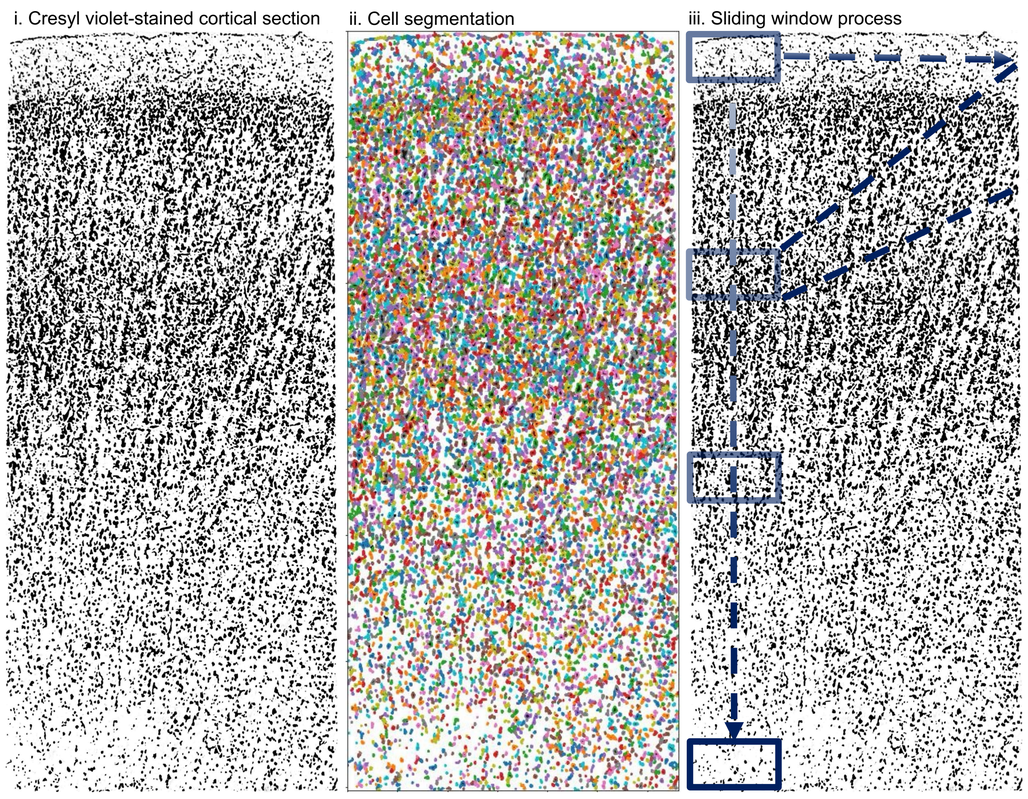
A. *In vivo* microstructure profiling & correlation with age

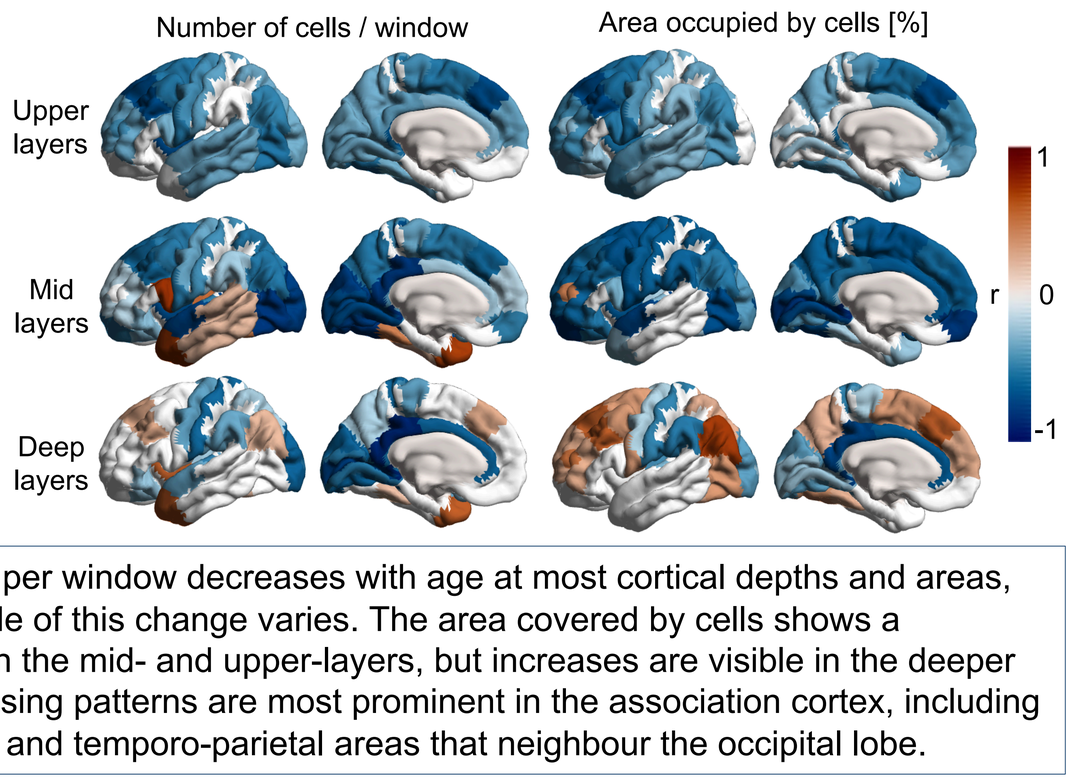




The mean intensity of T1w/T2w-intensity profiles increases throughout development. The changes in the centre of gravity (CoG) of these profiles vary across regions in early postnatal development, but follow an increasing pattern across the whole cortex in later development, suggesting microstructural increases deeper in the cortex. In contrast, the standard deviation (SD) decreases globally in early postnatal development, increases in late infancy and shows region-specific changes in early childhood.

B. *Post mortem* cytoarchitectural characterisation of cortical sections & depth-specific correlation with age





The number of cells per window decreases with age at most cortical depths and areas, though the magnitude of this change varies. The area covered by cells shows a decreasing pattern in the mid- and upper-layers, but increases are visible in the deeper layers. These increasing patterns are most prominent in the association cortex, including the prefrontal cortex and temporo-parietal areas that neighbour the occipital lobe.

Conclusions

- Rapid changes in intracortical microstructure occur across the entire cortex during infancy
- The area- and depth-specific nature of microstructural changes produces large-scale cortical differentiation, which is likely linked to functional specialisation and cognitive maturation

Outlook

- Implement more sophisticated statistical models to analyse the velocity and peak of changes across age
- Test how microstructural changes interact with macrostructural maturation, such as thickness and gyrification
- Generate a normative model of intracortical development to enable better characterisation of brain maturation in individuals with neurodevelopmental disorders

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