Whole-brain connectivity mapping in infants reveals widespread areas of white matter damage associated with prematurity

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Background: New approaches using diffusion magnetic resonance imaging (MRI) *in vivo* make it possible to characterise changes in whole-brain structural connectivity during early development. Here we explore the influence of two factors predicted to affect connectivity in early infancy: the age at scan and the degree of prematurity at birth.

Methods: T1, T2 weighted and diffusion MRI was obtained in fifty-six infants born between 25 and 35 weeks post-conceptional age with a corrected scanning age between 11 and 31 months. Subjects were excluded if major pathology was present. Diffusion imaging was carried out using a Philips 3T MRI scanner as described previously[1] . An optimised processing pipeline combining anatomical[2] and tissue segmentations with diffusion tractography[3] was used to map a coarse whole-brain structural connectome for each infant and mean tract anisotropy was obtained as a measure of connection strength (Fig 1). Sparse penalised Lasso regression[4] and stability selection[5] were then employed to identify tracts in which connection strength was most related to gestational age at birth or imaging. By performing repeated subsampling from the data: a Lasso model was fitted for each random sub-sample across a range of *lambda* regularisation values and an estimate of the regression coefficients from each model was taken. The selection probability for each connection was calculated by taking the ratio between the number of times the variable was selected and the total model fits.

Figure 1

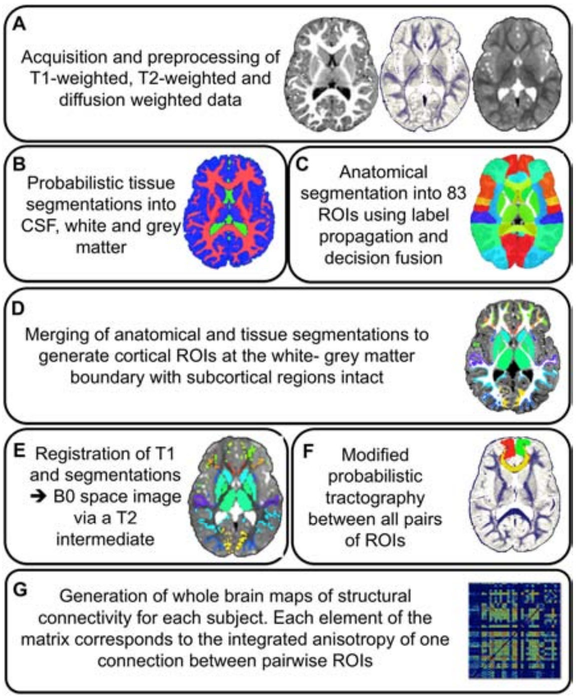


Figure 3

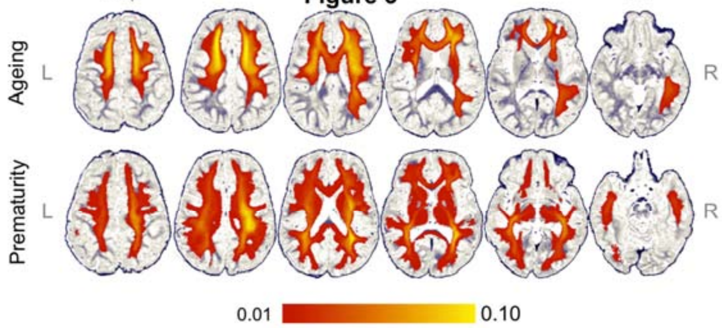
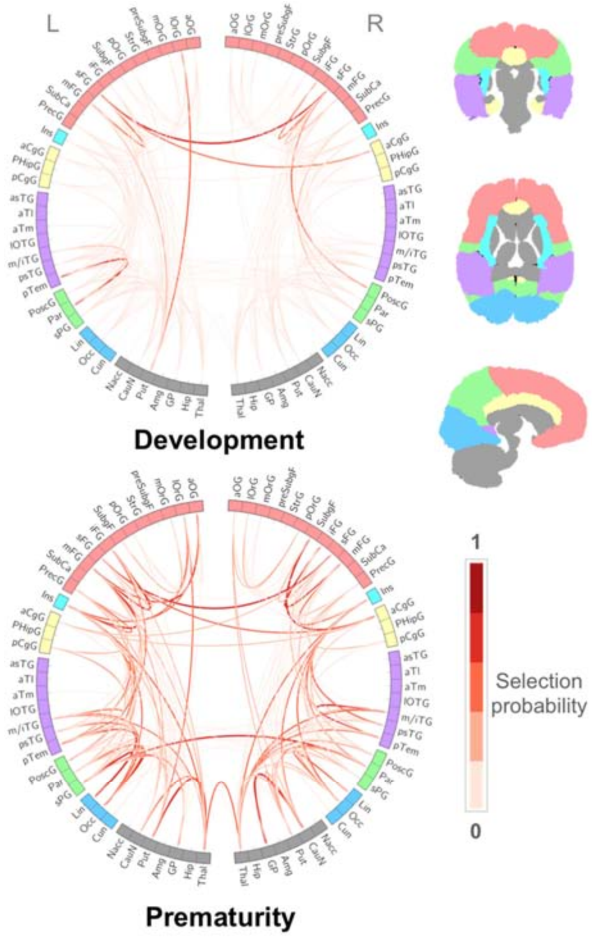


Figure 2



Results: Figure 2 highlights the group-wise connectivity in topographical space[6] weighted by selection probability using corrected age-at-scan (development) or post-conceptional age at birth (prematurity) as the response variable, whilst Figure 3 merges the set of connections to create a *voxel-wise* selection probability map for each response variable in anatomical space. Selected tracts joining anterior or fronto-temporal structures were positively associated with postnatal age, while more extreme prematurity at birth was related to widespread reductions in the connection strength in tracts involving all cortical lobes and several subcortical structures.

Conclusion: We present a non-subjective approach to mapping whole-brain connectivity in the developing brain, which detected changes in the strength of intra-cerebral connections during development and suggests that premature birth is associated with widespread reductions in connectivity strength.

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