Functional network interactions during typical development in infancy and early childhood

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Target Audience: MR Image Analysts, Pediatric Imaging Neuroscientists, Neuroimaging Scientists

Purpose Functional networks derived from resting-state fMRI are presumed to reflect the specific cognitive and sensory networks of the brain. Developmental changes in both integration and segregation of these networks have been demonstrated in infants[1] and older children[2]. Using a large cohort of typically developing infants and toddlers in an under-sampled cross-sectional age range (3 months to 5 years) we investigate the effect of maturation on inter-network coupling.

Methods _Sample_ 80 infants, toddlers and young children aged between 84 and 1619 days (mean (SD) age of 688d (477d), 34 female) were scanned during natural sleep[3]. *Imaging* Resting state fMRI data were collected using a gradient echo-planar imaging sequence (TR=2.5, TE=34, FA=80^o) with resulting resolution of 3mm in-plane over 32 3.6mm slices. A high flip angle T_1–weighted SPGR image collected as part of a multicomponent relaxometry sequence (mcDESPOT[4]) was used for registration purposes (TR/TE=5/10ms, FA=14°, 1.7mm isotropic resolution). _Analysis_ After standard fMRI preprocessing (motion and slice timing correction), functional images were transformed to a common space in 2 stages. Initially, an example functional image was registered to the anatomical T_1 image using boundary-based registration and this T_1 image was then registered non-linearly to an age-appropriate template[5]. Finally spatially normalised data were smoothed to a global 5mm FWHM using 3dBlurToFWHM, ensuring that the effective spatial resolution was the same for all subjects[6]. fMRI data were analysed using independent component analysis (ICA[7]) and the dual regression and FSLNets packages[8]. Motion parameters and motion spikes (>0.2mm interscan motion) were included as confounds. In this *exploratory* analysis, we tested the relationship between functional coupling between ICA-derived networks and both age and cognitive ability in the same children (measured using the Mullen Scale). To account for multiple testing and comparisons, false discovery rate was applied across all contrasts at q<0.05.

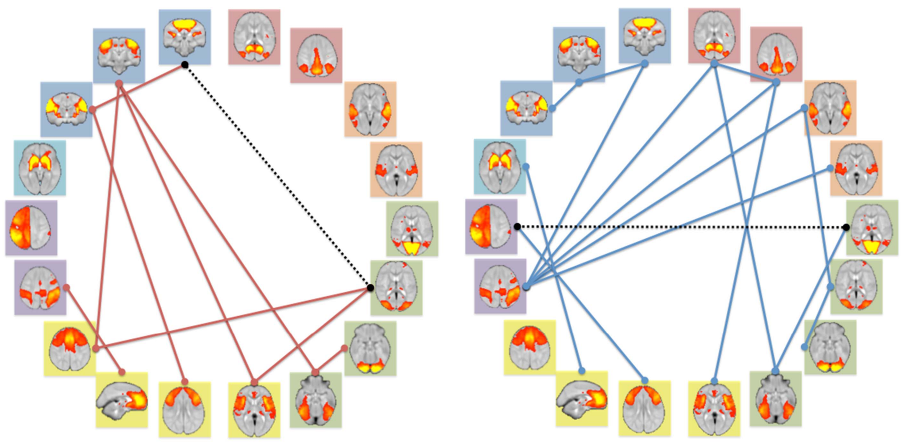

Figure 1: Functional networks from ICA decomposition shown colour coded according to gross functional system (motor blue, striatal aqua-marine, fronto-parietal purple, frontal yellow, visual green, auditory orange, and default red). Red lines (left) and blue lines (right) indicate networks demonstrating increasing and decreasing coupling with age respectively (p<0.05 corrected).

Results Age showed no significant or trend relationship with either (a) mean motion (b) number of interscan spikes or (c) image smoothness. ICA decomposed the group fMRI data into 25 components, with 18 showing correspondence to previously reported resting state networks. Coupling between networks changed as a function of age (figure 1) and specific systems showed more age-related changes than others. Frontal networks especially showed increased coupling with motor and visual networks with maturity (frontal networks were involved in 6 of 9 significant positive relationships). Networks showing decreased coupling tended to be spatially adjacent to each other (especially clear for sensory networks), though the left-dominant fronto-parietal especially and default mode networks showed decreased coupling with spatially disparate regions. We hypothesized that there would be a relationship between coupling in resting state networks and cognitive scores, but only one positive (figure 1, left, dashed line) and negative (figure 1, right, dashed line) relationship was detected.

Conclusions: Our results demonstrate age-varying interactions between functional networks, replicating trends seen in younger[1] and older[2] cohorts, though with differing patterns. This indicates distinct functional network changes during this important stage of development. Individual differences in network coupling do not show *strong* relationships with cognition in this typically developing cohort.

References: 1 Gao et al, Brain Structure & Function, 2014 | 2 Fair et al, PLoS Comp Biol, 5, e1000381 | 3 Manning et al, Neuroimage; 83, 288-293 2013 | 4 Deoni et al, Neuroimage; 63, 1038-1053, 2012 | 5 Avants et al, Neuroimage, 49, 2457-2466, 2010 | 6 Scheinost et al, Neuroimage; 95, 13-21 | 7 Beckmann & Smith Neuroimage, 25, 294–311, 2005 | 8 http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLNets