Developmental trajectory of cingulate RSFC from childhood to adulthood

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**Background:** Characterization of normative age-related changes in fMRI-based brain activity and functional connectivity can inform the neural underpinnings of psychiatric diseases, now considered for the most part to be neuro-developmental. This study examines resting-state functional connectivity (RSFC) of the cingulate cortex (CC). This multicomponent structure mediates key behaviors altered in anxiety and mood disorders. Accordingly, the subgenual anterior CC (sACC) is linked to visceral integration; caudal ACC (pACC), emotion; anterior middle CC (aMCC), response selection and fear-avoidance; posterior MCC (pMCC), skeletomotor orientation; rostral posterior CC (dPCC), visuospatial orientation; and ventral PCC (vPCC), self-relevance assessment (Vogt 2016, 2005). The cingulate cortex is also a key node of two RSFC canonical networks, the default mode (DMN) and salience (SN) networks. To mitigate MRI artifacts, the innovative multi-echo (ME) acquisition was used.

**Methods:** 52 healthy volunteers (8-43 years) completed a 10min ME-RS fMRI scan, with instructions to fixate a central crosshair. Image preprocessing was completed using ME-ICA method (Kundu et al, 2013). Six seeds (3mm spheres) located across CC subregions were identified through literature on anxiety and mood disorders and corresponded to Vogt (2016, 2005) designations. Age-dependent RSFC seed-based correlational analyses were conducted using AFNI 3dGroupInCorr examining age as the main effect.

**Results:** The DMN and SN RSFC patterns replicated the literature. All seeds showed predominantly RSFC increases with age across the brain. Specifically, the sACC and pACC seeds showed age-related increased RSFC in prefrontal cortex, insula, amygdala, parahippocampal and precuneus regions. Dorsal and posterior CC seeds displayed age-related increased RSFC with many of these same regions with additional CC regions (sACC and pPCC).

**Conclusions:** The strengthening of CC RSFC with many brain regions may parallel increased demand in executive function, affective and sensorimotor integration, and self-agency from childhood to mid-life. Of note, the strengthening of DMN and SN iFC with age suggests mechanisms for dysregulation in anxiety and mood disorders. These data can provide a normative benchmark against which RSFC of patient populations can be contrasted.