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Functional network integration and attention skills in young children

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ABSTRACT

Children acquire attention skills rapidly during early childhood as their brains undergo vast neural development. Attention is well studied in the adult brain, yet due to the challenges associated with scanning young children, investigations in early childhood are sparse. Here, we examined the relationship between age, attention and functional connectivity (FC) during passive viewing in multiple intrinsic connectivity networks (ICNs) in 60 typically developing girls between 4 and 7 years whose sustained, selective and executive attention skills were assessed. Visual, auditory, sensorimotor, default mode (DMN), dorsal attention (DAN), ventral attention (VAN), salience, and frontoparietal ICNs were identified via Independent Component Analysis and subjected to a dual regression. Individual spatial maps were regressed against age and attention skills, controlling for age. All ICNs except the VAN showed regions of increasing FC with age. Attention skills were associated with FC in distinct networks after controlling for age: selective attention positively related to FC in the DAN; sustained attention positively related to FC in visual and auditory ICNs; and executive attention positively related to FC in the DMN and visual ICN. These findings suggest distributed network integration across this age range and highlight how multiple ICNs contribute to attention skills in early childhood.

1. Introduction

Early childhood is a particularly crucial period in a child's development when many cognitive skills, including top-down attention, are rapidly maturing (Brown and Jernigan, 2012). For many children, this is the beginning of formal reading instruction and attention skills appear to be foundational for reading acquisition (Franceschini et al., 2012). More generally, as children approach school age they are increasingly expected to attend to arbitrary symbols, such as numbers and letters (Sørensen and Kyllingsbaek, 2012). Thus, the pre- and early-school period represents a time when attentional demands placed on children not only increase, but also expand to include symbolic stimuli that require considerable perceptual expertise (Ristic and Enns, 2015). Relatively weak attention skills can place children at a disadvantage in school, which can have lifelong consequences on academic attainment, employment, and social skills (Rueda et al., 2010; Stevens and Bavelier, 2012). However, we have a limited understanding of the neural basis of inter-individual variability in early childhood attention skills.

Top-down, or deliberate, attention can be categorized into three component processes: (1) "selective attention" or "orienting" which refers to the ability to search for an object amongst other similar 'distracter' objects, (2) "sustained attention" or "alerting", the ability to maintain attention for longer periods of time, and (3) "executive attention" or "executive control", the ability to override pre-potent responses (Breckenridge et al., 2013; Petersen and Posner, 2012). Top-down attention skills show vast changes as children develop and are faced with differing demands (Breckenridge et al., 2013). These changes are associated with unique maturational trajectories (Dye and Bavelier, 2010; Hommel et al., 2004; Lobaugh et al., 1998; Zhan et al., 2011), with the most protracted changes occurring in executive attention (Zhan et al., 2011). These divergent cognitive developmental trajectories suggest that distinct attention components have at least partially distinct neural substrates.

Indeed, it has been proposed the three components of top-down attention may be facilitated by distinct brain networks (Petersen and Posner, 2012; Posner and Petersen, 1990). The top-down "orienting

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network" is centered on the intraparietal sulcus (IPS) and the frontal eye fields (FEF), and is otherwise known as the dorsal attention network (DAN) (Casey et al., 2005; Rohr et al., 2017). In adults, functional connectivity (FC) between the IPS and FEF is enhanced during selective attention (Szczepanski et al., 2013), and FC between the IPS and visual regions is increased during sustained visual attention (Greenberg et al., 2012; Lauritzen et al., 2009). The "alerting network" and "executive network" largely overlap; both contain the IPS as well as the dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex (ACC), anterior insula, and thalamus, and as such combine features of the frontoparietal (FPN) and cingulo-opercular networks (Petersen and Posner, 2012; Xuan et al., 2016). In adults, sustained and executive attention skills have been associated with FC of FPN nodes at rest (Markett et al., 2014).

Although data from adults suggests associations between functional network organization and attentional skills, few studies to date have linked intrinsic connectivity networks (ICNs) to specific attentional abilities in childhood. In infants and toddlers, significant positive associations between FC and joint attention were observed between the visual network, the DAN and the default mode network (DMN) (Innocenti and Price, 2005; Thompson et al., 2000). In children aged 7–9 years, an association between the synchronization of primary auditory network and attention skills was shown (Seither-Preisler et al., 2014). Children aged 10–14 were found to show greater functional activity in the anterior cingulate, precentral gyrus, amygdala and fusiform gyrus in relation to selective and executive attention (Cascio et al., 2007; Lebel et al., 2008). Data in early childhood are particularly limited. We previously investigated the link between attention and functional brain development in the dorsal attention network (DAN) using a hypothesis-driven seed-based FC approach (Rohr et al., 2017). In line with the established role of the DAN in attention (Corbetta and Shulman, 2002), we observed that stronger selective attention skills predicted greater connectivity strength between DAN nodes with increasing age (Rohr et al., 2017). However, in line with the studies on attention in childhood, recent work has shown that sustained attention in both children and adults relies on a multitude of regions outside the canonical attention networks, providing further evidence the DAN is not the only ICN involved in top-down attention processes (Rosenberg et al., 2016). It is therefore of interest to ask whether distributed functional networks are associated with attention skills in early childhood. In the present study, we therefore examined multiple well-known ICNs in relation to attention skills using Independent Component Analysis (ICA). Specifically, we examined the ICNs extracted from functional magnetic resonance imaging (fMRI) data, which was collected during a passive viewing paradigm in children aged 4–7 years who also completed assessments of sustained, selective and executive attention skills.

We reasoned that given the substantial positive association between age and attention skills in this age range, networks that are associated with attention are likely to be those that show functional integration with age. We therefore began by examining associations between age and FC in our sample. Although the literature shows that the functional networks found in adults are present in children, there appear to be ongoing changes in the degree of "integration" of some regions into functional brain networks (greater intra-network FC) and "segregation" of sets of regions into separate functional networks (less inter-network FC) as children get older (Gu et al., 2015; Kaufmann et al., 2017; Marek et al., 2015; Menon, 2013; Power et al., 2010) (for a comprehensive developmental review see (Grayson and Fair, 2017)). Few studies have specifically addressed changes in early childhood. In children aged 5–8 years, developing ICNs were found to be more diffuse and fragmented compared to adults (de Bie et al., 2012). Localized associations with local and global activity and connectivity measures were recently shown in 2–6 year old children (Long et al., 2017), with prominent age effects in dorsal frontal and parietal regions. Studies extending into later childhood and adolescence also suggest functionally dependent ICN maturation. For example, sensory ICNs (e.g. visual) appear to show a linear trajectory of integration from childhood to adulthood, whereas the maturation trajectory of cognitive ICNs appears to be non-linear, with integration followed by segregation phases sometime in adolescence (Jolles et al., 2011), and heterogeneity across networks (Muetzel et al., 2016). However, the details of ICN maturational trajectories are still being worked out (Grayson and Fair, 2017) and more studies are needed, particularly in early childhood.

Here we present findings using dual-regression ICA, a technique with high test-retest reliability (Chen et al., 2015; Zuo et al., 2010; Zuo and Xing, 2014), to assess associations between ICNs and age. We then report associations between FC in these ICNs and attention skills after controlling for age. We hypothesized that cognitive, as well as sensory, ICNs would show functional integration across this period, and that greater integration in these ICNs would be associated with greater sustained, selective and executive attention skills.

2. Methods

2.1. Participants

Eighty typically developing (TD) female children between the ages of 4 and 7 years were recruited to participate in this study as part of an ongoing study of genetic disorders affecting girls. This study was approved by the Conjoint Health Research Ethics Board at the University of Calgary and conducted at the Alberta Children's Hospital. Informed consent was obtained from the parents and informed assent from participating children. Potential participants were excluded if they had a history of neurodevelopmental or psychiatric disorders, neurological problems, were born earlier than 37 weeks gestation or had other medical problems that prevented participation. Participants' data were evaluated for outliers in behavioral scores and motion on the fMRI scans. For the behavioral measures, outliers were defined as > 3 SD from the mean. No participants were excluded because of outlier scores. A total of twenty participants were excluded: 3 were unable to successfully complete the practice session in the MR simulator, 15 had excessive head motion on their fMRI scan (as described below), one fell asleep during fMRI acquisition, and one received an exclusionary diagnosis within 12 months of data acquisition. The final sample consisted of 60 participants (mean age = 5.54 ± 0.79 SD years; IQ range 90–137; mean = 110.7 ± 9.7 SD). Six of these participants were described as non right-handed by their parents: 3 were described as left-handed, 3 as more left-handed than right-handed, and 1 was described as ambidextrous. Handedness was therefore included as a regressor of no interest in the fMRI analysis.

2.2. Data acquisition: procedure

Cognitive assessments and MR imaging were collected over two separate two-hour sessions that took place within two weeks of each other. The first session included a general cognitive assessment using the Wechsler Preschool and Primary Scale of Intelligence – 4th Edition[CDN] (WPPSI-IV [CDN]) (Wechsler, 2012), a first set of attention measures, and training in an MRI simulator to acquaint the children with the MR environment. During training in the simulator, children watched the same 18-min video that was played during the actual scan and practiced lying still while the sounds of MR scanning were played to them via headphones. If children were not comfortable in the simulator or not able to hold still, data collection was terminated; three children were excluded at this stage. The second visit consisted of the actual MR scanning and children completed the remainder of the attention measures. Attention measures were randomly ordered both across and within data collection days and were conducted in a testing room adjacent to the MR simulator.