Developmental Cognitive Neuroscience 13 (2015) 32–42

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn

# Variation in functional connectivity along anterior-to-posterior intraparietal sulcus, and relationship with age across late childhood and adolescence

Sarah A. Vinette[a,b,d], Signe Bray[a,b,c,d,*]

[a] Alberta Children's Hospital Research Institute, Room 293, Heritage Medical Research Building, 3330 Hospital Drive, NW, Calgary, AB, Canada T2N 4N1
[b] Department of Radiology, Cumming School of Medicine, University of Calgary, Room 812, North Tower, Foothills Medical Centre, 1403 – 29th Street NW, Calgary, AB, Canada T2N 2T9
[c] Department of Paediatrics, Cumming School of Medicine, University of Calgary, 2888 Shaganappi Trail NW, Calgary, AB, Canada T3B 6A8
[d] Child and Adolescent Imaging Research Program, Alberta Children's Hospital, 2888 Shaganappi Trail NW, Calgary, AB, Canada T3B 6A8

ARTICLE INFO

*Article history:*
Received 29 September 2014
Received in revised form 12 April 2015
Accepted 13 April 2015
Available online 21 April 2015

*Keywords:*
Functional connectivity
Resting-state fMRI
IPS
Visual-spatial
Attention
Visuotopic

ABSTRACT

The intraparietal sulcus (IPS), a region in the dorsal attention network (DAN), has been implicated in multi-sensory attention and working memory. Working memory and attention develop across childhood; changes in functional connectivity within the DAN may relate to this maturation. Previous findings regarding fronto-parietal intrinsic functional connectivity age-effects were mixed. Our study aimed to circumvent limitations of previous work using a large cross-sectional sample, 183 typically developing participants 6.5–20 years, from the Autism Brain Imaging Data Exchange, and seed regions along the anterior-to-posterior axis of the IPS. These seeds, IPS0-4, were entered into functional connectivity models. Group-level models investigated differential connectivity along the IPS and relationships with age. Anterior IPS3/4 exhibited greater connectivity with sensorimotor/pre-motor regions. Posterior IPS0/1 demonstrated greater connectivity with dorsal and ventral visual regions. Positive age-effects were found between IPS3-4 and visual regions. Negative age-effects were found between IPS and superior parietal and medial orbitofrontal cortices. Follow-up region of interest analyses were used to estimate age-effects for DAN and anticorrelated default mode network regions. Results suggest age-effects on IPS functional connectivity are relatively modest, and may differ pre- and across-adolescence. Studying typical age-related connectivity variability within this network may help to understand neurodevelopmental disorders marked by impaired attention.



*Abbreviations:* IPS, intraparietal sulcus; hFEF, putative human frontal eye fields; hSMA, human supplementary motor area; DLPFC, dorsolateral prefrontal cortex; MT, middle temporal; fMRI, functional magnetic resonance imaging; TD, typically developing; ABIDE, Autism Brain Imaging Data Exchange; IRB, institutional review board; FWHM, full width at half maximum; WM, white matter; CSF, cerebrospinal fluid; FWE, family wise error; DAN, dorsal attention network; FPN, fronto-parietal network; DMN, default mode network; ROI, region-of-interest; TPJ, temporoparietal junction; ASD, autism spectrum disorders; TR, repetition time; TE, echo time; FOV, field of view; MNI, Montreal Neurological Institute; VLPFC, ventrolateral prefrontal cortex; SM, sensorimotor; FG, fusiform gyrus; Calc, peri-calcarine cortex; OT, occipto-temporal; MO, mid occipital; PT, posterior thalamus; VMPFC, ventromedial prefrontal cortex; IPL, inferior parietal lobule; PCUN, precuneus; Mid Temp, middle temporal; CN, caudate nucleus; WASI, Wechsler Abbreviated Scale of Intelligence; DAS, Differential Ability Scales; PPVT, Peabody Picture Vocabulary Test; FIQ, Full Scale IQ; VIQ, Verbal IQ; PIQ, Performance IQ; BA, Brodmann area; BOLD, blood oxygenation level-dependent.

* Corresponding author at: 2888 Shaganappi Trail NW, Calgary, AB, Canada T3B 6A8. Tel.: +1 403 955 7389.
*E-mail addresses:* savinett@ucalgary.ca (S.A. Vinette), slbray@ucalgary.ca (S. Bray).

http://dx.doi.org/10.1016/j.dcn.2015.04.004

## 1. Introduction

The intraparietal sulcus (IPS) is located along the dorsal visual pathway and is a key node in the network underlying spatial attention (Astafiev et al., 2003; Corbetta et al., 2000; Goodale and Milner, 1992; Silver and Kastner, 2009). This functionally heterogeneous brain region has also been implicated in multisensory attention (Anderson et al., 2010), working memory (Champod and Petrides, 2007; Pessoa et al., 2002), and numerical cognition (Cantlon and Li, 2013; Dehaene et al., 2003; Pinel et al., 2001; Rosenberg-Lee et al., 2011). The IPS is a core node of the dorsal attention (Power et al., 2011) or task-positive network (Fox et al., 2005; Toro et al., 2008), which includes putative human frontal eye fields (hFEF) and supplementary motor area (hSMA) as well as dorsolateral prefrontal cortex (DLPFC) and occipito-temporal regions (near human middle temporal (MT)+).

The IPS can be divided into a set of regions spanning the anterior-to-posterior axis, on the basis of phase reversals in topographic organization, similar to retinotopic visual cortex (Sereno et al., 2001). These regions show differences in functional responses across tasks (Bray et al., 2013a; Sheremata et al., 2010; Silver and Kastner, 2009; Swisher et al., 2007; Szczepanski et al., 2013), and differential white matter structural connectivity to visual regions and parts of the dorsal attention network (Bray et al., 2013b; Greenberg et al., 2012; Szczepanski et al., 2013). In these studies, structural connectivity is defined using probabilistic tractography to determine the likelihood that two regions are joined by a direct white matter pathway. With regards to the IPS, posterior regions show preferential connectivity with dorsal and ventral visual regions (Bray et al., 2013b; Greenberg et al., 2012), while anterior regions show more probable connections to prefrontal and pre-motor regions (Bray et al., 2013b; Mars et al., 2011; Szczepanski et al., 2013). Lesion studies (Vandenberghe et al., 2012) and task activation and connectivity studies (Hutchinson et al., 2015) further support functional sub-divisions along the IPS.

Visual-spatial attention and working memory mature across late childhood and adolescence (Westerberg et al., 2004; Zhan et al., 2011). Functional connectivity is a measure believed to reflect the synchrony between brain regions (Friston, 1994), and is often calculated as the temporal correlation between pairs of time-series. Changes in functional and structural/white matter connectivity with age are hypothesized to be a key driver of cognitive maturation (Blakemore, 2012; Fair et al., 2007; Rubia, 2013; Supekar et al., 2009; Uddin et al., 2011). In support of this view, protracted development of white matter structure has been observed through early adulthood (Lebel et al., 2008). Age-related variation in fronto-parietal white matter properties across childhood has been linked to increased working memory capacity (Nagy et al., 2004; Østby et al., 2011), and visual-spatial attention (Klarborg et al., 2013).

Findings regarding age-effects on fronto-parietal functional connectivity have been mixed. Several developmental neuroimaging studies have shown increased functional magnetic resonance imaging (fMRI) blood oxygenation level-dependent (BOLD) signal during working memory tasks, relative to baseline, in frontal and parietal regions with age-related increases in working memory capacity (Crone et al., 2006; Klingberg et al., 2002; Scherf et al., 2006). Computational modeling has further suggested that fronto-parietal connectivity underlies inter-individual differences in working memory capacity (Edin et al., 2007). In resting-state connectivity studies, although somewhat controversial due to inconsistencies in handling motion artifacts (Power et al., 2012), a general pattern of increasing long-range connectivity with age has been described (Dosenbach et al., 2010; Fair et al., 2007). The spatial pattern of attention networks in children 5–8 years of age has been reported to be fragmented and incomplete compared to the same networks seen in adults (de Bie et al., 2012). In older children, while differences compared to adults in IPS-to-DPLFC connectivity have been observed (Barber et al., 2013), other work has found no difference in fronto-parietal functional connectivity (Jolles et al., 2011; Uddin et al., 2011).

Several factors may contribute to variability in findings regarding developmental changes, or age-related variability, in fronto-parietal functional connectivity, including differential sensitivity of task compared resting scans, analysis approach, and small sample size. Among studies that have used region-of-interest (ROI) approaches, choice of seed region may also impact findings, as there is considerable heterogeneity of function and connectivity within both prefrontal (Kahnt et al., 2012; Liu et al., 2013; Moayedi et al., 2014) and parietal (Anderson et al., 2011; Mars et al., 2011; Nelson et al., 2010) cortices.

Developmental abnormalities in the IPS have been linked with aberrant numerical and visuospatial cognition (Auzias et al., 2014; Bray et al., 2011; Kesler et al., 2004, 2006; Molko et al., 2003; Nordahl et al., 2007). Therefore, characterizing age-related variability in fronto-parietal functional connectivity is important, both for understanding the neural basis of typical cognitive maturation, and as a baseline for comparing atypical development. The present study investigated age-related variability in IPS functional connectivity across childhood and adolescence, and aimed to circumvent limitations of previous work by (1) using a large database of resting-state fMRI data, and (2) using multiple seeds along the anterior-to-posterior axis of the IPS, in locations corresponding to previously defined IPS0-4 (Swisher et al., 2007) with well characterized patterns of structural connectivity (Bray et al., 2013b; Greenberg et al., 2012; Szczepanski et al., 2013).

We hypothesized that IPS sub-regions would show varying functional connectivity with visual and prefrontal regions along the anterior-to-posterior axis, consistent with previous work (Mars et al., 2011). Specifically, we hypothesized that anterior regions of the IPS would be more strongly functionally connected with frontal regions of the network including hFEF, whereas posterior IPS regions would have greater functional connectivity with visual regions. We further hypothesized differential age-related variability in functional connectivity. Specifically, we hypothesized that as primary sensory brain systems have been shown to mature relatively early (Gogtay et al., 2004; Shaw et al., 2008; de Bie et al., 2010), posterior IPS-to-occipital connectivity patterns would be relatively stable, while anterior IPS-to-prefrontal (e.g. DLPFC Barber et al., 2013) connectivity would show a positive association with age.

## 2. Materials and methods

### 2.1. Participants

Typically developing (TD) participants less than 20 years of age were included the analyses from four sites from the Autism Brain Imaging Data Exchange (ABIDE; http://fcon_1000.projects.nitrc.org/indi/abide/) database (Di Martino et al., 2014). These four sites included the New York University Langone Medical Centre, University of Michigan (samples one and two), University of Utah School of Medicine, and the Yale Child Study Centre. These sites were chosen as they had more than 20 TD participants younger than 20 years of age, with an age span greater than 10 years across participants. The research protocols were approved by the institutional review board (IRB) at each site. While inclusion and exclusion criteria differed across the sites, TD participants were generally excluded if they had a history of neurodevelopmental or psychiatric diagnosis, neurological disorder or any contraindications for MRI (Supplementary Table 1). Written consent and assent were obtained as appropriate from all participants at each of the sites.