



Efficiency of structural connectivity networks relates to intrinsic motivation in children born extremely preterm

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Abstract

Intrinsic motivation is essential for academic success and cognitive growth, but limited work has examined the neuroanatomical underpinnings of intrinsic motivation from a network perspective, particularly in early childhood. Using graph theoretical analysis, this study investigated global and local properties of structural connectivity networks in relation to intrinsic motivation within a vulnerable group of children at early school age. Fifty-three 7 year-old children born extremely preterm (<28 weeks' gestational age)/extremely low birth weight (<1000 g) underwent T1 and diffusion weighted imaging. Structural connectivity networks were generated using 162 cortical and subcortical nodes, and edges were created using constrained spherical deconvolution-based tractography. Global and node-specific network measures were analyzed in association with self-reported aspects of intrinsic motivation for school learning (Mastery, Challenge and Curiosity) using linear regression. Results indicated that increased information transfer across the network was associated with greater Mastery, while increased clustering and small-world topology related to greater Challenge. Increased efficiency and connection strength of the striatum in particular, related to greater intrinsic motivation. These findings suggest that both integrated and segregated network communication support aspects of intrinsic motivation in childhood, and shed new light on structural network properties important for intrinsic motivation orientations in extremely preterm children at early school age.

Keywords Intrinsic motivation · Diffusion weighted imaging · Graph theory · Preterm birth

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Introduction

Intrinsic motivation is the inherent propensity to engage in an activity due to interest and a desire to extend one's abilities and knowledge. It is essential for cognitive growth and development, particularly during childhood (Ryan and Deci 2000a, 2000b). Meta-analyses have suggested that intrinsic motivation is the most important form of motivation for school achievement, over extrinsic or incentive-based motivation (Taylor et al. 2014). Here we focus on three key aspects of intrinsic motivation: mastery, challenge and curiosity (Lepper et al. 2005). Mastery is the desire to develop abilities or accomplish something challenging through mostly independent work (Dweck 1986; Elliot 1999; Nicholls 1984). Challenge is centered on a preference for activities that require effort, while curiosity relates to enjoyment or interest for engaging in tasks (Lepper et al. 2005). There is a growing body of literature on potential cognitive processes that underlie intrinsic motivation (Deci and Ryan 1985; Dweck 1986; Nicholls 1984; Ryan and Deci 2000b), however limited work has

examined the biological underpinnings of intrinsic motivation or whole-brain anatomical variations in individuals with low or high intrinsic drive for learning. Identifying neural biomarkers of intrinsic motivation in childhood may allow for early identification of atypical motivation profiles, which may complement and enhance behavioral observations.

Emerging research investigating the neuroscience of intrinsic motivation acknowledges that, while multiple neural structures and networks support intrinsic motivation, the dopaminergic system is likely to be central (Di Domenico and Ryan 2017). To date, the majority of neuroimaging studies have relied on reward or feedback conditions to elicit brain activity in adults. Specifically, these studies have implicated the dopaminergic subsystem and brain regions, such as the ventral tegmental area, the ventral striatum, the orbitofrontal cortex (OFC), amygdala, insula, and anterior cingulate cortex (ACC) (Camara et al. 2009; Mizuno et al. 2008; Murayama et al. 2010; Satterthwaite et al. 2012; Shohamy 2011; Szatkowska et al. 2008; Szatkowska et al. 2011). While it is understood that extrinsic drives and rewards are not analogous to intrinsic motivation (Ryan and Deci 2000a), findings from these reward-based studies highlight a sub-network of brain regions that may relate to intrinsic motivation.

Functional MRI (fMRI) studies investigating hemodynamic responses associated with intrinsically-driven motivation (i.e., where participants engaged in, or imagined engaging in, an intrinsically motivating task) have observed increased activation in striatal and anterior insular regions, similar to the pattern of activation observed during reward processing (Lee and Reeve 2013, 2017). Given these initial findings, the striatum and anterior insular cortex may be particularly important for feelings of intrinsic task satisfaction. Further, the ACC is noted to have strong anatomical and functional connections with many other brain regions involved in decision-making and reward processing (Parvizi et al. 2013; Seeley et al. 2007), and may be another neural region involved in intrinsic motivational processes.

While previous neuroimaging studies have provided a useful framework for considering the *functional* representations of intrinsic motivation, little is understood about the *structural* pathways involved in supporting intrinsically-driven behavior, particularly from a network perspective. Graph theory is a useful approach for examining global and local brain network properties by quantifying anatomical patterns of brain connectivity (Bullmore and Sporns 2009; He and Evans 2010). Complex brain networks are described as *graphs* that are composed of *nodes*, which represent brain regions, linked together by *edges* that denote connections, such as axonal white matter projections (Sporns 2014). Useful network metrics can be obtained using graph theory, allowing for identification and quantification of network efficiency (i.e., local and global), organization (i.e., modularity) and key nodes or regions (i.e., hub nodes) within the network (Guye et al. 2010; Rubinov and Sporns 2010). The only research to date using

graph theory to investigate the association between motivational processing and functional network connectivity was an adult study, which found that global efficiency (i.e., integration within the brain's network) increased during reward conditions (Kinnison et al. 2012). While this study further implicated a role for the nucleus accumbens, caudate, and the ACC for reward processing (Kinnison et al. 2012), to date no study has applied graph theory to investigate structural connectivity networks associated with intrinsic motivation in childhood.

Some studies have applied graph theory metrics to understand patterns of network connectivity and their relationship with functional outcomes in children (Kim et al. 2016; Thompson et al. 2016), including vulnerable subgroups of children such as those born preterm. Reduced network connectivity strength and altered structural connections were found to be associated with poorer behavioral and functional outcomes in preterm children (Fischi-Gomez et al. 2014; Pandit et al. 2014; Thompson et al. 2016). These findings suggest that graph theory may be a potentially sensitive and useful approach for examining brain-behavior relationships, and may be a promising tool for quantifying structural networks of intrinsic motivation in at-risk groups of children.

Extremely preterm children (born <28 weeks' gestation) are known to be at greater risk of cognitive, academic and social difficulties compared with children born at term (Anderson and Doyle 2003; Hutchinson et al. 2013; Johnson et al. 2009). Further, intrinsic motivation for school learning is important for working memory abilities and academic performance in this population (Pascoe et al. 2018). Therefore, understanding the neural systems that support motivational behavior and perception may have the greatest implications for improving outcomes in vulnerable populations like extremely preterm children. Knowing the neural correlates associated with intrinsic motivation may assist with firstly understanding how motivational processes influence cognitive processes, and secondly, identifying neural features that may later allow us to better maximize intervention benefits for this vulnerable population.

Given the recent call for attention to the neuroscience of intrinsic motivation (Di Domenico and Ryan 2017), we propose an initial neurobiological account of intrinsic motivation by examining whole-brain structural connectivity networks in relation to mastery, challenge and curiosity, and exploring a priori regions of interest that may be important for intrinsic motivational processes. To the best of our knowledge, no study has explored the neuroanatomical basis of intrinsic motivation in extremely preterm children. Furthermore, no study has focused on key brain regions thought to be involved in motivation to ascertain the importance of their connectivity with the rest of the brain for intrinsic motivation orientations. We aimed to apply graph theoretical analysis to understand global and local features of whole-brain network properties associated with intrinsic motivation orientations in 7 year-

old children born extremely preterm. Early school age is a particularly pertinent development period to examine these associations given that intrinsic motivation for school learning is high compared with later schooling years (Lepper et al. 2005), and large changes in neural connectivity are occurring to support learning and cognitive development (Cao et al. 2017). It was hypothesized that 1) increased global and local efficiency of whole-brain structural networks and 2) greater small-world organization (integration-segregation of the network) would be associated with greater mastery, challenge and curiosity. It was further hypothesized that increased strength and efficiency of key network nodes (ACC, OFC, insula, amygdala, striatum) would be associated with greater intrinsic motivation.

Materials and methods

Participants

The study included 7-year-old children who were born extremely preterm (EP; <28 weeks' gestational age (GA)) or extremely low birth weight (ELBW; <1000 g) in the state of Victoria, Australia in 2005, and were part of a randomized controlled trial of a cognitive training intervention (Pascoe et al. 2013). The current study is focused on data collected at the baseline assessment prior to randomization into the trial. Exclusion criteria for the study included (1) severe intellectual, sensory or physical impairment that affected the child's capacity to complete training (IQ more than 3 SD below the mean, severe cerebral palsy (non-ambulant) or blindness in both eyes), and (2) families considered unable to comply with the cognitive training schedule. The study was approved by the Human Research Ethics Committee of the Royal Children's Hospital in Melbourne, Australia, and written informed consent was obtained from primary caregivers before participation. Ninety-one children were enrolled in the trial. Of these, 60 children consented to and completed baseline brain MRI scans. Structural connectivity analyses were performed for 53 children with available and usable MRI data. Loss of data was due to required MRI sequences not being completed ($n = 1$), severe movement artifact ($n = 3$), structural brain abnormalities that affected parcellation ($n = 2$) and tractography processing difficulties ($n = 1$).

Measures

Perinatal and demographic characteristics

Perinatal and neonatal characteristics were documented from medical records, including gestational age (GA), sex, birth weight, multiple birth, bronchopulmonary dysplasia (requirement for oxygen at or beyond 36 weeks' gestational age), and

severe brain injury on cranial ultrasound (grade 3 or 4 intraventricular hemorrhage or cystic periventricular leukomalacia). At 7 years, social risk was estimated based on a composite measure assessing family structure, education of the primary caregiver, occupation and employment status of the primary income earner, language spoken at home, and maternal age when the child was born (Roberts et al. 2008), with higher scores (range 0–12) indicating greater social risk. General intellectual functioning (IQ) was estimated using the General Conceptual Ability composite score from the Differential Ability Scales- 2nd edition (DAS-II), with a mean of 100 and standard deviation of 15 (Elliott 2007).

Intrinsic motivation

Intrinsic motivation was assessed using the Intrinsic Motivational Scale (IMS). This scale evaluates intrinsic motivation towards learning and academic achievement, and has been previously administered as a self-report measure to children aged 8 to 14 years (Lepper et al. 2005; Lepper et al. 1997). This measure, adapted from Harter's (1981) scale of intrinsic versus extrinsic orientation, has been widely used with elementary (primary and middle) school children. It consists of 17 items estimating preference for mastery (e.g., "I like to try to figure things out at school on my own"; "I like to do my school work without help"), challenge (e.g., "I like hard work because it's difficult"; "I like difficult problems because I enjoy trying to figure them out"), and curiosity (e.g., "I work on problems to learn how to solve them"; "I ask questions in class because I want to learn new things"). Although the response items are originally based on a 5-point scale (ranging from *Not like me at all* to *Exactly like me*), for this study the children responded on a 3-point scale: *yes* (3), *sometimes* (2), and *no* (1), to ensure their understanding of response options and increase the reliability of responses given by young children. A member of the study team administered the measure to children individually in a face-to-face interview. Total scores were calculated for the three subscales (Harter 1981; Lepper et al. 2005): Challenge (6 items; range 6–18), Curiosity (6 items; range 6–18) and Independent Mastery (5 items; range 5–15). For each subscale, higher scores reflected higher levels of intrinsic motivation.

Neuroimaging

MRI acquisition

MRI was undertaken without sedation using a Siemens 3 Tesla Magnetom Trio scanner and a 32-channel head coil at the Royal Children's Hospital in Melbourne, Victoria. Children underwent 3-D T₁ weighted (0.85 mm sagittal slices, in-plane resolution 0.82 mm², flip angle = 9°, repetition time = 1900 ms, echo time = 2.27 ms, field of view = 210 × 210 mm,

matrix = 256×256), 3-D T_2 weighted (0.9 mm sagittal slices, in-plane resolution 0.9 mm^2 , repetition time = 3200 ms, echo time = 540 ms, field of view = $240 \times 215 \text{ mm}$, matrix = 256×256) and spin-echo diffusion weighted imaging (45 gradient directions, $b = 3000 \text{ s/mm}^2$, 5 $b = 0 \text{ s/mm}^2$ images, repetition time = 8500 ms, echo time = 112 ms, matrix = 98×98 , field of view = $225 \times 225 \text{ mm}$, voxel size = 2.3 mm^3 isotropic). Reversed phase-encoded images were collected to correct for susceptibility distortions in the diffusion images (Andersson et al. 2003).

Neuroimaging preprocessing

Each of the preprocessing steps was executed using an in-house processing pipeline created by the Developmental Imaging Group at the Murdoch Children's Research Institute (Thompson et al. 2016). To generate nodes (grey matter regions), T_1 weighted scans underwent skull stripping, tissue classification and segmentation using FreeSurfer software, with T_2 weighted scans used to improve the pial surface reconstruction (version 5.3; <http://surfer.nmr.mgh.harvard.edu/>). The structural brain images were parcellated into 74 cortical regions per hemisphere based on the Destrieux parcellation scheme (Destrieux et al. 2010), and 7 subcortical regions per hemisphere (Fischl et al. 2002), providing a total of 162 regions across the brain. For our node strength and efficiency analyses, we focused on five cortical and subcortical regions of interest (left and right regions examined independently) as delineated by the Destrieux atlas: anterior cingulate cortex (ACC), orbitofrontal cortex (OFC), insula cortex (short and long gyri, and anterior and superior regions), amygdala and the striatum (caudate, putamen and the nucleus accumbens). Whole-brain intracranial volume (ICV) was also obtained using FreeSurfer to enable us to adjust for total ICV differences between participants. For the diffusion-weighted scans, eddy-current-induced distortions and head movements, and susceptibility-induced distortions, were corrected using the FMRIB Software Library (Andersson et al. 2003; Andersson and Sotiropoulos 2016; Jenkinson et al. 2012). Diffusion-weighted images were registered to the T_1 structural images using linear and non-linear registration with FMRIB's Linear Image Registration Tool (FLIRT) and Advanced Normalization Tools (ANTs; (Avants et al. 2008) respectively, to allow for accurate alignment of nodes and edges in native space. Diffusion-weighted data underwent constrained spherical deconvolution (CSD) in order to identify fiber orientations for tractography of white matter connections (representing the edges) in a manner robust to crossing fibers, using the MRtrix software package (Tournier et al. 2007, 2012). The white matter fiber tracts were modeled using probabilistic tractography in MRtrix, with white matter masks used as the seeds, and the node masks as the endpoints. Streamlines were terminated upon intersection with seed masks, exceeding

a curvature threshold of 30° per mm or entering an exclusion region. Both ends of a streamline were required to intersect with a seed mask for inclusion. Streamlines that connected sub-cortical grey seeds to any contralateral seed were discarded as they were assumed to be spurious.

Connectivity network construction

Raw connectivity matrices (162×162) were constructed where cells within the matrix represent edges (i.e., estimated edge strength value), and columns and rows represent nodes using MATLAB (The MathWorks 2000). Analyses were based on undirected, weighted connectivity graphs, where edges in the graph were weighted according to streamline counts within fiber tracts (i.e., number of streamlines per unit of volume of gray matter node) and normalized by streamline length and average node volume to reflect their relative strength within the network (Hagmann et al. 2008). This edge weighting approach allows for bias correction of longer streamlines and larger node volumes. In order to compare network measures across individuals, a uniform density across individuals was achieved by applying a density threshold to networks where the top 30% of the maximum number of possible edges in the graph were retained, which has been successfully performed in previous studies examining structural connectivity in preterm children (Thompson et al. 2016).

Graph theory metrics

A range of metrics have been developed that are designed to capture different organizational properties of a network (Bullmore and Sporns 2009). In this study, we explored whole-brain as well as nodal structural connectivity using standard graph theory metrics of weighted-edge graphs (Beare et al. 2017; Thompson et al. 2016). In particular we consider the following: *raw density* which represents the fraction of present connections to all possible connections within that network; *characteristic path length* which is a measure of serial information transfer between nodes and is defined as the average shortest path length between all pairs of nodes in a network; *average clustering coefficient* which is a measure of clustering based on a ratio of the number of triangular connections between groups of three closely connected nodes (i.e., neighborhood) to the number of possible triangles of edges; *modularity* which is a measure of network structure, and is the difference between the fraction of edges within communities and the expected fraction of edges between communities; *global efficiency* which is a measure of the network's capacity for parallel information transfer between nodes and refers to the average inverse shortest path length in the network, where the shortest path between every pair of nodes in the network is determined, and the average of these shortest paths is calculated; *local efficiency* which refers to

efficiency at the level of local neighborhoods of nodes and relates to the *average clustering coefficient*; *small worldness* which is a measure of the simultaneous integration and segregation of a network, and defined as a ratio of global and local efficiency to those in the random or regular network (Watts and Strogatz 1998); and *node strength* defined as the sum of weights of links connected to the node, and *node efficiency* was the inverse of the harmonic mean of the shortest path length between an index node and all other nodes in the network (Achard and Bullmore 2007).

Data analysis

Data were analyzed using Stata 13.0 (StataCorp 2013). Associations between whole-brain connectivity metrics (predictor) and intrinsic motivation components (outcome) were examined using linear regression. Primary analyses included total ICV and corrected age at scan to account for variation in brain size and maturation. Secondary analyses further adjusted for sex, IQ and social risk, as there is evidence of sex differences in the brain, and general intelligence and socioeconomic factors have been associated with structural brain development (Brito and Noble 2014; Ruigrok et al. 2014; Shaw et al. 2006). Gestational age at birth was also included as a covariate to account for the impact of prematurity on network organization (Batalle et al. 2017). Additionally, sex and IQ have also been shown to vary in accordance with achievement (or academic) motivation constructs (Garon-Carrier et al. 2015; Gottfried 1990). Linear regression models were also applied to examine the efficiency and strength of selected nodes of interest (predictor) in association with intrinsic motivation components (outcome), with similar primary and secondary models. All regression models were fitted using Generalized Estimating Equations (GEEs) with an exchangeable correlations structure and are reported with robust standard errors to allow for correlations between twins/triplets in the sample (Carlin et al. 2005). When regression models could not be fitted using GEEs due to convergence issues, results are reported from standard regression models reported with robust (sandwich) estimates of standard errors to allow for correlations between twins/triplets. No correction for multiple comparisons were made for whole-brain or nodal analyses (Rothman 1990), consistent with previous studies (Achard and Bullmore 2007). Results were interpreted based on the profile and pattern of associations, which included measurement of effect size for significant associations using Cohen's f^2 (Cohen 1988). Cohen's f^2 is appropriate for calculating effect size within multiple regression models where independent and dependent variables are continuous; its global effect is commonly calculated in the following form (Selya et al. 2012): $f^2 = \frac{R^2}{1-R^2}$. Cohen's f^2 for small, medium

and large effects were interpreted based on values of .10, .25 and .40 respectively (Kotrlík and Williams 2003).

Results

Sample characteristics

The clinical characteristics of the study sample ($n = 53$) are presented in Table 1. Characteristics of the study sample were similar to non-participants ($n = 38$, data not shown).

Intrinsic motivation and whole-brain network connectivity

There was evidence that greater Mastery was associated with a higher density of connections ($f^2 = 0.15$), but this weakened after adjustment for gestational age, sex, IQ, and social risk; although a similar relationship was not evident for Challenge and Curiosity (Table 2). Greater Mastery was also associated with shorter characteristic path length ($f^2 = 0.15$), which persisted after adjustment for gestational age, sex, IQ, and social risk. There was also some evidence that greater Mastery and Challenge were associated with higher average clustering coefficient (Mastery: $f^2 = 0.14$; Challenge: $f^2 = 0.12$), although these associations weakened in the secondary analysis. There was evidence that greater Curiosity was associated with a more modular network organization, particularly

Table 1 Perinatal and demographic characteristics of the study sample

	Extremely Preterm/Extremely Low birth weight sample n = 53
Gestational age at birth in weeks, <i>M (SD)</i>	26.8 (2.0)
Birth weight (g), <i>M (SD)</i>	868.8 (186.9)
Male, <i>n (%)</i>	24 (45.3)
Multiple birth, <i>n (%)</i>	14 (26.4)
Bronchopulmonary dysplasia, <i>n (%)</i>	26 (49.0)
Intraventricular hemorrhage grade 3/4, <i>n (%)</i>	5 (9.4)
Cystic Periventricular Leukomalacia, <i>n (%)</i>	1 (2.0)
Corrected age at scan in years, <i>M (SD)</i>	7.8 (.43)
Social risk score, <i>M (SD)</i>	2.6 (2.1)
Total ICV (mm ³), <i>M (SD)</i>	1, 375, 527 (146, 989)
General Intellectual functioning, <i>M (SD)</i>	99.9 (12.4)
Motivation components, <i>M (SD)</i>	
Mastery	10.4 (2.76)
Challenge	13 (3.27)
Curiosity	14.5 (3.0)

M mean, *SD* standard deviation, *ICV* intracranial volume

Table 2 Associations between global network connectivity metrics and intrinsic motivation components

	Mastery			Challenge			Curiosity											
	Secondary analysis ^b			Primary analysis ^a			Secondary analysis ^b			Primary analysis ^a								
	β	(95% CI)	<i>p</i>	β	(95% CI)	<i>p</i>	β	(95% CI)	<i>p</i>	β	(95% CI)	<i>p</i>						
Raw density	40.7	(7.7, 73.7)	.02	23.5	(-11.6, 58.6)	.19	24.6	(-8.8, 58.1)	.15	10.2	(-22.2, 42.6)	.54	-4.69	(-40.5, 31.2)	.80	-18.2	(-51.3, 14.9)	.28
Characteristic path length	-0.06	(-0.1, -0.01)	.01	-0.05	(-0.09, -0.02)	<.01	-0.02	(-0.08, .04)	.52	-0.03	(-0.09, .02)	.26	.02	(-0.02, .07)	.32	.02	(-0.02, .06)	.24
Average clustering coefficient	251.2	(13.3, 489.1)	.04	203	(-50.9, 456.9)	.11	264.6	(-11.2, 540.5)	.06	242.7	(-84.3, 569.7)	.15	87.9	(-166.7, 342.5)	.50	134.8	(-170, 439.6)	.39
Modularity	-39.9	(-85.1, 5.4)	.08	-25.5	(-82, 31)	.37	-9.49	(-64.8, 45.9)	.74	-6.12	(-70.2, 57.9)	.85	36.96	(-15.8, 89.7)	.17	53.4	(1.42, 105.3)	<.05
Local efficiency	259.4	(-471.9, 990.7)	.49	187	(-396.9, 771)	.52	-613.8	(-1503.3, 275.7)	.18	-369.6	(-1269, 529.8)	.42	-887	(-1476.7, -297.3)	<.01	-594.5	(-1450.2, 261.2)	.17
Global efficiency	790.5	(-374.8, 1955.9)	.18	705.1	(-188.7, 1599)	.12	-479.9	(-1879.6, 919.8)	.50	-210.6	(-1488.5, 1067.2)	.74	-792.65	(-1991.8, 406.5)	.19	-840	(-2034.9, 354.8)	.16
Small worldness	6.42	(-5.66, 18.5)	.29	7.99	(-2.2, 18.2)	.12	8.62	(.9, 16.3)	.03	7.79	(-.73, 16.3)	0.07	-1.5	(-10.7, 7.7)	.75	1.16	(-9.27, 11.6)	.83

^a adjusted for ICV and age at scan; ^b adjusted for ICV, age at scan, gestational age, sex, IQ and social risk. β = regression coefficient, CI = confidence intervals

after adjustment in the secondary analysis (Table 2; $f^2 = 0.18$). In terms of local efficiency, greater Curiosity was associated with reduced local efficiency ($f^2 = 0.06$), although the association weakened considerably in the secondary analysis, and was not evident for Mastery or Challenge. There was weak evidence that greater Mastery was associated with higher global efficiency, which strengthened in the secondary analysis ($f^2 = 0.30$), although a similar association was not evident for Challenge or Curiosity. There was evidence that greater Challenge was associated with higher small worldness ($f^2 = 0.10$), although this association weakened slightly in the secondary analyses, and was not evident for Mastery or Curiosity.

Intrinsic motivation and node strength

As illustrated in Fig. 1, greater connection strength of the ACC, OFC and nucleus accumbens were associated with greater Mastery, but these relationships were often stronger in the left than in the right regions (Fig. 1). Associations between Mastery and the left regions of the ACC and OFC persisted after adjustment for sex, gestational age, IQ and social risk (ACC: $f^2 = 0.32$; OFC: $f^2 = 0.43$). There was evidence that increased connection strength of the right nucleus accumbens region was associated with greater Challenge, though this weakened slightly in the secondary analysis ($f^2 = 0.26$). There was weak evidence that greater Curiosity was associated increased connection strength of the anterior insula (left more so than right region), which weakened after adjustment for covariates (left region: $f^2 = 0.13$).

Intrinsic motivation and node efficiency

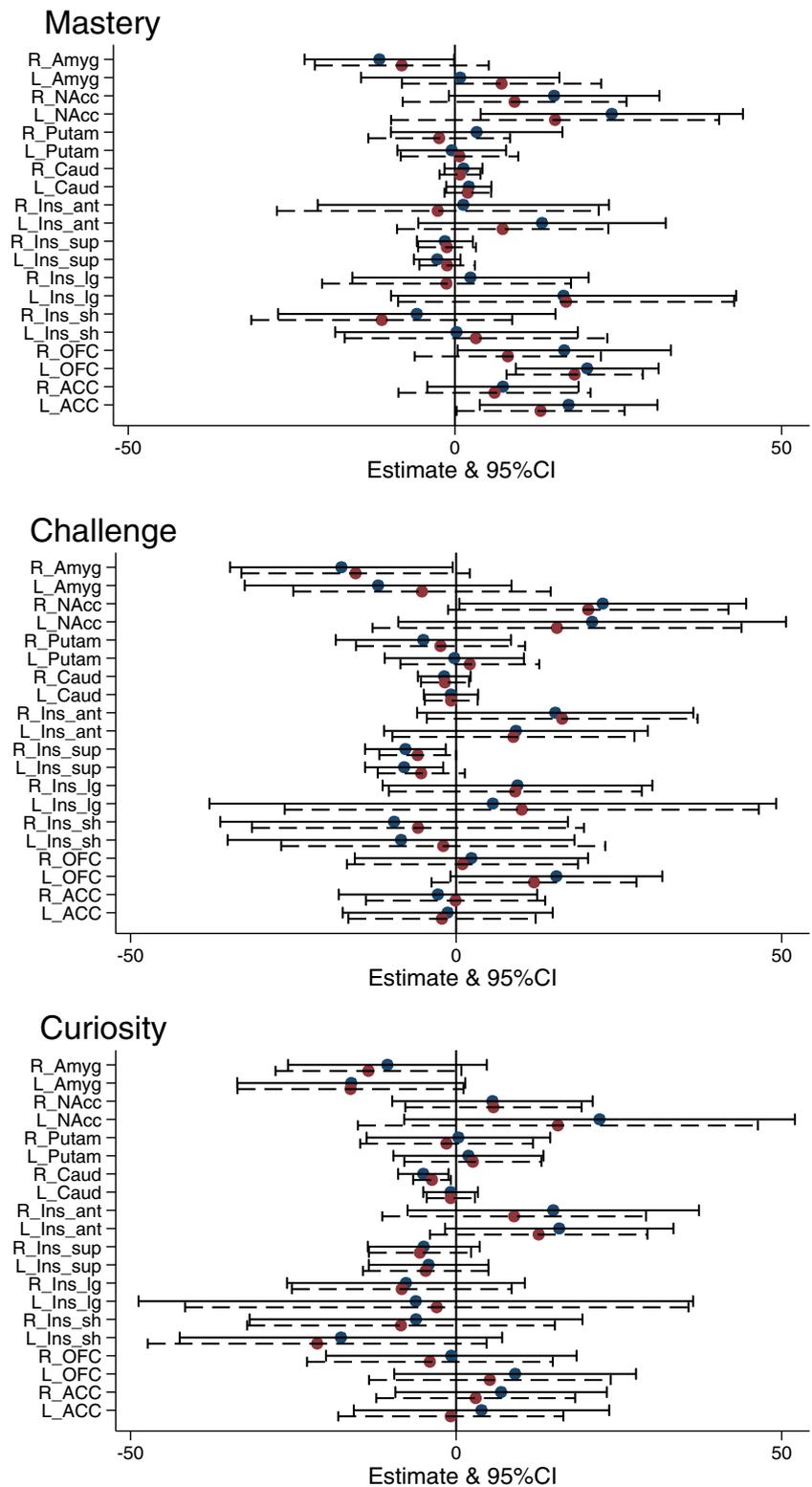
There was some evidence that greater Mastery was associated with higher nodal efficiency of the caudate (particularly the right), which strengthened after adjustment for sex, IQ, and social risk (Fig. 2; $f^2 = 0.33$). Conversely, greater Curiosity was associated with reduced nodal efficiency of the putamen and superior insula, however evidence for these associations were negligible in the secondary analysis (Fig. 2). There was little evidence that Challenge was associated with the efficiency of any of the node regions examined (Fig. 2).

Discussion

Intrinsic motivation and whole-brain connectivity

This is the first study to examine the association between whole-brain structural networks and intrinsic motivation in EP/ELBW children. We demonstrated that greater information transfer and small-world organization of whole-brain structural networks, alongside greater connectivity of key brain nodes, are associated with greater desire for mastery,

Fig. 1 Associations between nodal strength of key cortical and subcortical regions and intrinsic motivation components: Mastery, Challenge and Curiosity. Estimates are regression coefficients indicating the change in the dependent variable (intrinsic motivation component score) for each unit change in the independent variable (nodal strength) with 95% confidence intervals (CI) from separate regression models for each predictor/outcome combination. Solid lines (with blue point estimates) are based on results adjusted for ICV and age at scan; dashed lines (with red point estimates) are based on results adjusted for ICV, age at scan, gestational age, sex, IQ and social risk. R_ = right, L_ = left; Amyg = Amygdala, Ins_ = Insular cortex (lg = long gyrus, sh = short gyri, ant = anterior, sup = superior), NAcc = Nucleus accumbens, Putam = Putamen, Caud = Caudate, OFC = Orbitofrontal cortex, ACC = Anterior cingulate cortex



challenge and curiosity in school learning at age 7 years. Our finding that greater mastery in school learning is associated with shorter path length and increased global efficiency, indicative of greater information transfer across the network, is consistent with our understanding that intrinsic motivation is

a complex cognitive and affective state important for goal-directed behavior, and likely supported by multiple neural structures and processes (Di Domenico and Ryan 2017).

While there are no previous structural connectivity studies investigating intrinsic motivation, results from a functional

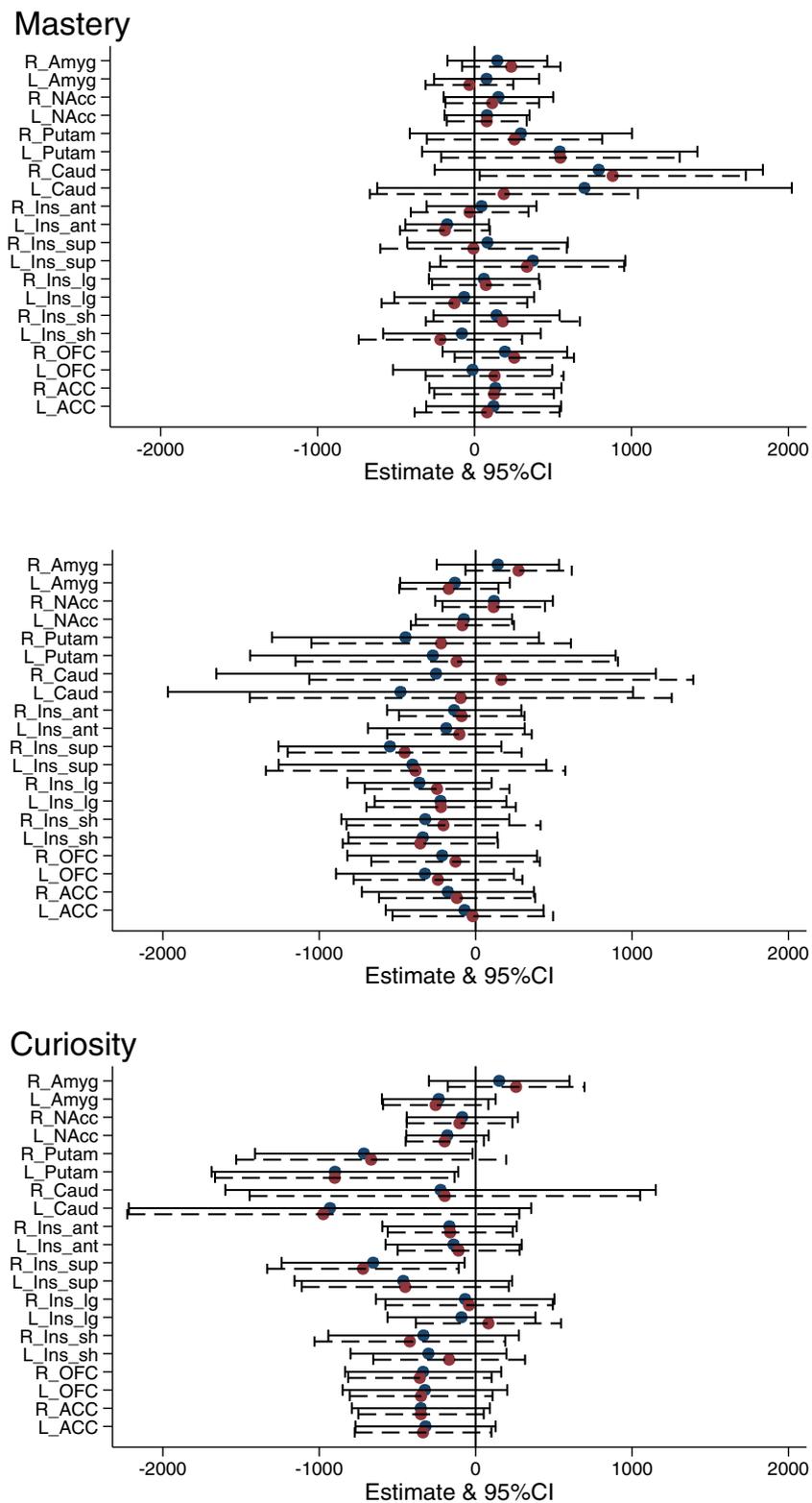


Fig. 2 Associations between nodal efficiency of key cortical and subcortical regions and intrinsic motivation components: Mastery, Challenge and Curiosity. Estimates are regression coefficients indicating the change in the dependent variable (intrinsic motivation component score) for each unit change in the independent variable (nodal strength) with 95% confidence intervals (CI) from separate regression models for each predictor/outcome combination. Solid lines (with blue point

estimates) are based on results adjusted for ICV and age at scan; dashed lines (with red point estimates) are based on results adjusted for ICV, age at scan, gestational age, sex, IQ and social risk. R_ = right, L_ = left; Amyg = Amygdala, Ins_ = Insular cortex (lg = long gyrus, sh = short gyri, ant = anterior, sup = superior), NAcc = Nucleus accumbens, Putam = Putamen, Caud = Caudate, OFC = Orbitofrontal cortex, ACC = Anterior cingulate cortex

connectivity study examining graph theory network properties during motivational processing in young adults (M (SD): 21(2.4) years), demonstrated increased global efficiency and reduced modularity across a network that exhibited greater activation to reward than the control cues (Kinnison et al. 2012). Indeed there is growing suggestion that the brain undergoes structural reorganization following preterm birth in an attempt to prioritize global connectivity (through the preservation of highly connected modules of nodes known as ‘rich-clubs’) over peripheral connectivity of less connected modules (Karolis et al. 2016). Further, the regions identified within the functional network by Kinnison et al. (2012), were similar to those found to be associated with intrinsic motivation in the current study, namely the ACC, putamen, caudate and nucleus accumbens.

While our evidence was weak, we also found some indication that greater desire for mastery in school learning was associated with a reduced modular network organization and clustering. This difference may reflect continuing maturation of structural networks in childhood, where gradually increasing integration and decreasing segregation continues to occur well into late childhood and adolescence (Huang et al. 2013; Batalle et al. 2017). Similarly, there is a suggestion that long-range connections develop at a faster rate than local, short-range connections, which enables greater global efficiency with increasing maturity of the structural network compared with local efficiency (Batalle et al. 2017). It is therefore reasonable to expect the strength of associations between structural network properties and intrinsic motivation to be weaker earlier in development compared with later life when the network is stronger and more efficiently organized to support intrinsically-driven processes.

We found that a desire for challenge and curiosity in school learning were associated with network measures reflective of segregation and small-world organization. These findings may suggest that relatively greater information transfer at the community (i.e., neighborhood) than global level facilitates a stronger desire for challenge and curiosity in school learning. Evidence for increased clustering to be associated with a desire for challenge is in line with our understanding of a small-world network, which typically reflects more short-range connections and greater clustering compared with a random network. These preliminary findings may indicate that greater information processing occurring ‘within’ network communities plays a more vital role for a desire for challenge and curiosity in school learning in extremely preterm children than communications ‘between’ communities of the whole-brain network. However clarification from future studies is warranted regarding whether challenge and curiosity in school learning in these children are strengthened by a modular, segregated network structure. Understanding these associations within a longitudinal, developmental framework will be important given there is no clear monotonic relationship with modular organization across development. Some studies report

decreased connectivity within modules (likely reflecting the pruning process) with increasing connectivity between modules (Huang et al. 2013), and others note increased connectivity within modules (likely reflecting functional specialization that takes place) with declining between-module connectivity in childhood and adolescence (Baum et al. 2017).

Intrinsic motivation and nodal connectivity

We found increased connectivity strength of the OFC, ACC, and the nucleus accumbens to be associated with intrinsic motivation orientations, particularly mastery and challenge. These findings provide initial support for the contribution of the mesocorticolimbic dopaminergic system to intrinsic motivational processes that are important for school learning. It has previously been acknowledged that the dopaminergic system is important for motivation and learning, with evidence of the functional and neuroanatomical importance of its regions for both reward processing (Haber and Knutson 2009; Kinnison et al. 2012; Seeley et al. 2007) and intrinsically-motivating activities (Lee and Reeve 2013, 2017). Similar to the work of Lee and Reeve (2013, 2017) who found the anterior insula was uniquely activated when adults answered curiosity-inducing questions, solved competence-enabling anagrams, and imagined self-determined action, we found weak evidence for the connectivity strength of the anterior insula to be important for curiosity in school learning in EP/ELBW children. It is thought that the anterior insula is closely associated with processing socio-emotional and cognitive input, as well as integrating internal, biological needs into subjective feelings (Flynn 1999; Lee and Reeve 2017). While weak, our preliminary findings provide further support for the anterior insular cortex to be an important component for intrinsic motivational processes, even early in development. Our results allude to the importance of both subjective feelings, and past cognitive experiences, for shaping curiosity towards school learning in early childhood.

Further, our findings indicated stronger relationships between the connectivity strength of the left side of node regions with intrinsic motivation, compared with the right side. This result may indicate potential laterality effects of node connectivity for intrinsic motivation. It is suggested that certain emotional and motivational behavior is governed by the left, rather than right hemisphere; with the left hemisphere guided by internal predictions and thought to be involved in anticipating future scenarios, and the right hemisphere controlled by responses to unpredicted, novel events or stimuli in the environment (Dien 2008). This view has been supported by the electroencephalogram (EEG) literature in adults, where left frontal activity has been associated with approach motivation and drive for reward, while right frontal activity has been associated with avoidance motivation, submission, and inhibition (Tops et al. 2017). Conversely, others have shown a rightward

asymmetry of dopaminergic response to reward in the striatum, whereby the ventral striatum appears to be right lateralized in right-handed adults (Martin-Soelch et al. 2011). Given that little is understood about lateralization of intrinsically-driven learning, particularly in childhood, our findings are the first to suggest a potential leftward asymmetry of node connectivity strength for intrinsic drives of school learning in a vulnerable group of children.

In contrast to a previous study in adults demonstrating that increased activity in caudate regions is correlated with increasing curiosity for knowledge (anticipation of information; Kang et al. 2009), we found decreased nodal efficiency of putamen was associated with greater curiosity in school learning. While it is uncertain why there was a negative association, it is important to highlight that the context and nature in which curiosity was examined varied across studies, e.g. past research has focused on measuring curiosity for semantic knowledge (i.e., trivia) as opposed to curiosity for school-based learning in the current study. Additionally, our result was not robust, as the association diminished considerably after adjustment for sex, IQ and social risk. Instead, we found strong evidence for increased connectivity (strength and efficiency) of the nucleus accumbens to be important for a desire for mastery and challenge in school learning. While the caudate and putamen (dorsal striatum) are known to be involved in reward anticipation, value and expectation, the nucleus accumbens (ventral striatum) is thought to be a core structure of an active ‘seeking’ system, that supports exploration and an individual’s feelings of interest, curiosity and sensation seeking (Di Domenico and Ryan 2017; Panksepp 1998), as well as changes in affective states and goal-directed behaviors (Haber 2011). Animal model studies have also highlighted the importance of nucleus accumbens dopamine for effort-related behavior and decision-making (Salamone et al. 2007). This subtle functional distinction between striatal subdivisions may indicate stronger involvement of the ventral striatum regions, such as the nucleus accumbens, when individuals reflect on their achievement goals and engagement in effortful activities, like school learning.

The identification of the striatum (caudate, putamen, nucleus accumbens) as an important node within the whole-brain network in relation to a desire for mastery and challenge in school learning is in line with evidence of its extensive functional and neuroanatomical connections (Cauda et al. 2011; Haber 2011). The striatum likely serves as a key hub node within the brain’s network, receiving and integrating information from multiple brain regions (including the OFC and ACC) and facilitating increased information transfer and network efficiency needed to support a desire for mastery and challenge in school learning. Even following preterm birth, where the basal ganglia are often most vulnerable to connectivity alterations, this subcortical structure is thought to support global information transfer and preserve structural network integrity in the preterm brain as a result of reorganization

and restructuring (Karolis et al. 2016). This has been demonstrated using simulated models of ‘lesioned’ white matter connections, where lesioning white matter connections of the basal ganglia best differentiated rich-club organization in preterm and term-born individuals (Karolis et al. 2016).

Evidence of increased connectivity strength of the ACC and OFC for a desire for mastery in school learning, is consistent with previous knowledge of their involvement in the brain’s reward circuitry (Haber and Knutson 2009), with the ACC thought to be involved in guiding the choices of actions based on reward value (Chudasama et al. 2013), and the OFC being more involved in evaluating reward value and outcome (Stalnaker et al. 2015). Potential preservation, or relative ‘sparing’, of these core connections and regions in the preterm brain (Ball et al. 2014) may enable these nodes to facilitate information transfer across the structural connectome despite the identified changes in structural network topology in preterm children (Pandit et al. 2014; Fisci-Gomez et al. 2014). While future research is needed to understand whether different components or sub-regions of the striatum, ACC and OFC have varying roles for these motivational orientations, our findings provide some suggestion about the importance of the connectivity these regions for intrinsically-driven school learning at early school age.

Strengths and limitations

This study was the first to investigate whole-brain structural connectivity networks in relation to intrinsic motivation, using cutting-edge network science and examining three key components of intrinsic motivation important for school learning in childhood. However, our study has some inherent limitations common to studies involving tractography and pediatric cohorts. Namely, there are a number of factors that may have affected the calculation of network measures, including motion artifact from head movement, and sub-optimal image registration. Further, tractography-based connectomes have recently been suggested to lead to a significant proportion of systematically invalid white matter connections (Maier-Hein et al. 2016). However, these limitations are known challenges of tract reconstruction methods, and as the fields of connectomics and tractography continue to grow, practices will evolve and improve, enhancing our ability to more accurately map and quantify neural networks. An additional limitation is that our definition of intrinsic motivation was based on a single motivation theory, i.e., self-determination theory. While this theory has received growing attention in neuroscience (Di Domenico and Ryan 2017), it still lacks sufficient empirical evidence to support it.

Another potential limitation relates to measurement insufficiencies. Limited comprehension and metacognitive abilities in children make self-report measurement challenging, as children often lack the skills and knowledge needed to make self-

evaluations on abstract states and attributes, like intrinsic motivation. This may be particularly apparent for preterm cohorts, given young preterm children are reported to have poorer insight and metacognitive skills, as well as reduced curiosity and interest, compared with healthy controls (Anderson and Doyle 2004; Bohm et al. 2004; Scott et al. 2012). While self-reported intrinsic motivation for school learning likely decreases as children progress through school (Lepper et al. 2005), little is understood about the developmental trajectories of specific intrinsic motivation components across childhood. We therefore acknowledge the limitation in our use of self-report measurement for intrinsic motivation. While assessment of intrinsic motivation for specific academic subjects may be helpful in determining the subject areas preterm children are most motivated in, existing measures, such as the Children's Academic Intrinsic Motivation Inventory, are currently not appropriate for administration with young school-age children at age 7 years (Gottfried 1986).

We accept that this study was further limited by the lack of a healthy, full-term comparison group to examine whether these associations vary in typically developing children, and did not include intrinsic motivation ratings from multiple observers (i.e. primary caregivers or teachers), hence it was not possible to validate the children's record of their intrinsic motivation. Lastly, we recognize our modest sample size, which limits the statistical power to identify relationships, and acknowledge the potential bias of our sample resulting from being part of a randomized trial and non-consent to MRI.

Future directions

Further research is required to confirm our findings and extend investigations to larger samples and developmental ages, to multi-faceted assessment of intrinsic motivation, and to include term controls to allow comparison of brain-behavior associations between populations. Examining mechanisms of motivation-cognition interactions from a network perspective would be advantageous, considering the growing importance on the interplay between motivational orientation, cognitive effort and goal-directed behavior (Braver et al. 2014). Given neuroimaging work is beginning to support behavioral and theoretical studies outlining the impact of extrinsic incentives on intrinsic motivation (Marsden et al. 2015; Murayama et al. 2010), future studies should explore the connectivity 'overlap' between intrinsic and extrinsic motivation, particularly early in development when large changes in neural structural connectivity and topology occur to support functional specialization and increasing social and cognitive demands (Cao et al. 2017; Khundrakpam et al. 2013).

Conclusions

The current study sheds new light on structural network properties that are associated with intrinsic motivation orientations

in EP/ELBW children at early school age. Specifically, we have demonstrated that intrinsic motivation for school learning is supported by increased network communication at both the global and regional level. Such knowledge may assist with detecting brain network properties robust to the consequences of preterm birth, which could subsequently be used to inform and identify resilience factors in children born preterm. Promoting and fostering such positive attitudes could serve as a useful avenue for improving and boosting learning and educational outcomes in children born preterm.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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