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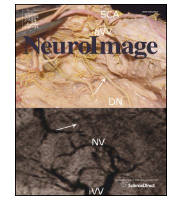

Children's intellectual ability is associated with structural network integrity

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Recent structural and functional neuroimaging studies of adults suggest that efficient patterns of brain connectivity are fundamental to human intelligence. Specifically, whole brain networks with an efficient small-world organization, along with specific brain regions (i.e., Parieto-Frontal Integration Theory, P-FIT) appear related to intellectual ability. However, these relationships have not been studied in children using structural network measures. This cross-sectional study examined the relation between non-verbal intellectual ability and structural network organization in 99 typically developing healthy preadolescent children. We showed a strong positive association between the network's global efficiency and intelligence, in which a subtest for visuo-spatial motor processing (Block Design, BD) was prominent in both global brain structure and local regions included within P-FIT as well as temporal regions involved with pattern and form processing. BD was also associated with rich club organization, which encompassed frontal, occipital, temporal, hippocampal, and neostriatal regions. This suggests that children's visual construction ability is significantly related to how efficiently children's brains are globally and locally integrated. Our findings indicate that visual construction and reasoning may make general demands on globally integrated processing by the brain.

Introduction

The inter-relationship among localized and distributed brain regions has been conceptualized as an integrated network organized into many segregated subregions linked by axonal white matter tracts (Sporns et al., 2005). A robust finding from the network perspective is that the human brain is organized in a highly efficient way for integrated information transfer, in so called *small-world* topology (for a review, see Bullmore and Sporns, 2009). Moreover, recent neuroimaging studies have suggested that some brain regions including the precuneus, posterior cingulate, and medial prefrontal cortex play a pivotal role as *hubs* or part of a structural *core* in the brain (Hagmann et al., 2008; Sporns et al., 2007) supporting fast communication between distributed regions. These key cortical hubs also are likely to be preferentially connected to each other forming a *rich club* (van den Heuvel and Sporns, 2011). Network organization undergoes rapid alterations in development with changes in axonal synaptic connectivity, white matter volume, and the thickness of corresponding cortical regions; see Vertes and Bullmore (2015) for a summary of developmental changes in network organization. In particular, structural maturation of white matter as well as cortical and subcortical areas is strongly associated with intellectual abilities from early childhood throughout adolescence (Shaw et al., 2006; Tamnes et al., 2010). However, the relationship of network properties derived from axonal white matter tracts such as network efficiency with intelligence during childhood has received little investigation.

Intelligence can be defined as the individual's capacity for mental functioning across a variety of domains including reasoning, executive function, information processing speed, memory and spatial manipulation — so called, general intelligence (*g*). Efficient and economical information processing among the distributed brain regions along white matter fibers is thought to contribute to general intelligence capacity (Deary et al., 2010; Gray and Thompson, 2004). The parieto-frontal integration theory (P-FIT) postulates that the dorsolateral prefrontal cortex and the parietal cortex, including the arcuate fasciculus connecting those two regions, comprise an important neuronal network associated with efficient intellectual functioning (Jung and Haier, 2007). The P-FIT of intelligence has been supported by neuroimaging findings including studies of gray matter volumes (Colom et al., 2009), cortical thickness

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(Narr et al., 2007) and white matter tracts (Van Beek et al., 2014). A brain network perspective provides a quantitative model for elucidating the association between the efficiency of brain networks and intelligence (Cole et al., 2012; van den Heuvel et al., 2009). Network approaches to understanding adult intelligence reveal consistent positive associations between intellectual performance and network integrity characterized by diffusion tensor imaging (DTI; Fischer et al., 2014; Li et al., 2009), resting-state functional MRI (van den Heuvel et al., 2009), and the electroencephalogram (EEG; Langer et al., 2012). Since brain development in childhood is associated with large-scale changes in synaptic connectivity, gray matter thickness and myelination, these relationships could be quite different than those observed in the adult brain. For example, there is evidence that the association between cortical regions and intelligence must include consideration of the trajectory of brain development, in which the relations between brain systems and function are dynamic and are altered as a function of age (Shaw et al., 2006). While one imaging study for children showed no relation of functional brain networks with IQ (Wu et al., 2013), no neuroimaging studies have been performed to date to investigate the relations between children's intellectual ability and whole-brain structural network properties.

In this study, we applied a graph theoretic network analysis to structural neuroimaging data acquired in typically developing children. This approach enabled characterization of global network associations with children's intelligence scores, including the role of hub regions and specific local regions in brain network architecture. We tested the hypothesis that the perceptual reasoning index (PRI), representing individual's nonverbal fluid reasoning skills, was associated with individual's structural network organization. Based on network studies on adults, higher structural network integration was predicted to be significantly associated with higher perceptual reasoning abilities. In addition to this, we particularly focused on domain-specific associations derived from three PRI subtests (Block Design, Picture Concepts, and Matrix Reasoning), and examined the association between cortical network architecture and specific intellectual performance of preadolescent children.

Materials and methods

Participants

The dataset of 99 typically developing healthy preadolescent children was collected from a subset of children participating in longitudinal developmental studies who were born at one of two hospitals in the greater Los Angeles area (UC Irvine Medical Center or Long Beach Memorial Medical Center) — Table 1. All children were between 6 and 11 years old (mean ± SD: 7.80 ± 1.22 years), right-handed (defined by the modified version of the Edinburgh Handedness Inventory; Oldfield, 1971), and were the result of a singleton pregnancy. This low risk sample of children was full-term at birth, had a stable neonatal course (median Apgar score = 9, range 7–10) and did not have congenital, chromosomal, or genetic anomalies. Further there was no evidence of intraventricular hemorrhage (determined by ultrasound), periventricular leukomalacia, and/or low-pressure ventriculomegaly in the newborn period. At the study entry, all children had normal neurological findings based on review of MRI scans by a neuroradiologist. All children were typically developing and in the appropriate grade for their age. Further, no emotional or physical problems were reported in a structured interview using the MacArthur Health and Behavior Questionnaire (HBQ; Armstrong and Goldstein, 2003). After providing a complete description of the study to all participants, written and verbal informed consent was obtained from a parent and affirmed assent was obtained from the children. The research protocol was approved by the Institutional Review Board for protection of human subjects.

Table 1
Demographic data of the study sample.

Number of children	99
Sex (% male)	54
Handedness (% right handed)	100
Gestational age at birth (weeks)	39.4 ± 1.3 (37–42.6)
Age at assessment (years)	7.80 ± 1.22 (6.1–10.6)
Birth weight (gram)	3395.1 ± 449.3 (2020–4561)
Maternal age (years)	29.4 ± 6.6 (16.2–43.2)
Maternal education (%)	
Elementary or middle school	7.1
High school or equivalent	33.3
Associates or vocational	19.2
Bachelors degree	28.3
Graduate degree	12.1
Annual household income (%)	
$0–$30,000	14.1
$30,001–$60,000	27.2
$60,001–$100,000	25.4
Over $100,000	33.3
Child race/ethnicity (%)	
Hispanic	33.3
Non-Hispanic White	32.3
Asian	5.1
African American or Black	4.0
Multi-ethnic	25.3
Bilingual households (%)	49.5
Performance IQ (PRI[a])	105.67 ± 15.8 (73–139)
Block design (BD)	9.9 ± 3.1 (3–16)
Picture concepts (PC)	11.6 ± 2.9 (3–18)
Matrix reasoning (MR)	11.3 ± 3.5 (4–19)

[a] PRI — perceptual reasoning index.

Standardized intelligence assessment

To eliminate a possible bias associated with language in our diverse sample, children's *intelligence* was assessed using the Perceptual Reasoning Index (PRI) of the Wechsler Intelligence Scale for Children (WISC-IV). The PRI does not require expressive language responses from the children and is relatively culturally-fair (Baron, 2004). Two of the three subscales (Matrix Reasoning and Block Design) have been shown to be excellent indicators of general intelligence (Baron, 2004; Wechsler, 2002). In this study, three subtests – Block Design, Picture Concepts, and Matrix Reasoning – were administered. Table 2 shows the correlations among these measures.

Block design (BD)

Children were asked to re-create designs using several red-and-white blocks within a specified time limit. This task assesses visual perception and organization, the ability to process abstract visual stimuli (i.e., visual–spatial reasoning) and motor manipulation.

Picture concepts (PC)

Two or three rows of pictures were presented and the child was instructed to choose one picture from each row that shared a common characteristic. This subtest measures abstract, categorical reasoning ability and the ability to recognize common features within nonverbal stimuli.

Table 2
Correlations between IQ scores.

	BD	PC	MR
PRI	0.81	0.73	0.89
BD		0.33	0.64
PC			0.50

Abbreviations. PRI, perceptual reasoning index; BD, block design; PC, picture concepts; MR, matrix reasoning.