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## Imaging structural covariance in the development of intelligence

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### ABSTRACT

Verbal and non-verbal intelligence in children is highly correlated, and thus, it has been difficult to differentiate their neural substrates. Nevertheless, recent studies have shown that verbal and non-verbal intelligence can be dissociated and focal cortical regions corresponding to each have been demonstrated. However, the pattern of structural covariance corresponding to verbal and non-verbal intelligence remains unexplored. In this study, we used 586 longitudinal anatomical MRI scans of subjects aged 6–18 years, who had concurrent intelligence quotient (IQ) testing on the Wechsler Abbreviated Scale of Intelligence. Structural covariance networks (SCNs) were constructed using interregional correlations in cortical thickness for low-IQ (Performance IQ =  $100 \pm 8$ , Verbal IQ =  $100 \pm 7$ ) and high-IQ (PIQ =  $121 \pm 8$ , VIQ =  $120 \pm 9$ ) groups. From low- to high-PIQ group, we observed constrained patterns of anatomical coupling among cortical regions, complemented by observations of higher global efficiency and modularity, and lower local efficiency in high-PIQ group, suggesting a shift towards a more optimal topological organization. Analysis of nodal topological properties (regional efficiency and participation coefficient) revealed greater involvement of left-hemispheric language related regions including inferior frontal and superior temporal gyri for high-PIQ group. From low- to high-PIQ group, we did not observe significant differences in anatomical coupling patterns, global and nodal topological properties. Our findings indicate that people with higher verbal intelligence have structural brain differences from people with lower verbal intelligence – not only in localized cortical regions, but also in the patterns of anatomical coupling among widely distributed cortical regions, possibly resulting to a system-level reorganization that might lead to a more efficient organization in high-PIQ group.

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### Introduction

One of the most thought-provoking questions we face is why some people are more proficient in several cognitive skills than others. Understanding the biological bases of these differences is of utmost importance to basic and applied neuroscience. Initial insights to the biological bases came from studies based on post mortem data that revealed positive association between cerebral volume and intelligence (Witelson et al., 2006). However, the advent of advanced MRI techniques which enabled scientists to investigate highly-localized (voxel-level) relationships of brain measurements (e.g. gray matter density, cortical thickness) with intelligence, provided a different perspective. Several such studies at the voxel and regional levels demonstrated positive correlation

of morphometry with intelligence in brain regions that are especially relevant to higher cognitive functions including frontal, temporal, parietal, hippocampus and cerebellum (Andreasen et al., 1993; MacLulich et al., 2002; Shaw et al., 2006; Narr et al., 2007; Colom et al., 2009; Karama et al., 2011; Burgaleta et al., 2014). Thus, came the proposition that increased volume in specific brain regions may account for the association between intelligence and global brain volume.

General intelligence is considered to be broadly dissociable into fluid and crystallized intelligence (Cattell, 1943), and brain areas corresponding to each have been shown in several studies (Choi et al., 2008; Karama et al., 2011; Ramsden et al., 2011; Colom et al., 2013; Burgaleta et al., 2014). Fluid intelligence, alternatively described as reasoning (non-verbal) ability, involves reasoning and novel problem-solving ability (Cattell, 1943), and has been shown to depend on working memory (Kyllonen and Christal, 1990; Kane and Engle, 2002). Crystallized intelligence, on the other hand, refers to verbal ability; this includes the ability of using language in analysing, remembering and understanding information, and is

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assumed to depend on acquired and accumulated knowledge including semantic memory (Naglieri and Bornstein, 2003). Apart from the conceptual difference, verbal and non-verbal intelligence have also been shown to be empirically separable. For example, patients with lesions specifically in prefrontal cortex have lower non-verbal intelligence while verbal intelligence is compromised in patients with lesions specifically in anterior temporal regions (Duncan et al., 1996; Waltz et al., 1999). The Wechsler Abbreviated Scale of Intelligence (WASI) is used as a screener of verbal and non-verbal abilities, and give verbal and performance IQ scores (Wechsler, 1999). Using the VIQ and PIQ scores, several neuroimaging studies have also noted a dissociation of verbal and non-verbal intelligence: positive associations of GM density in temporal regions with verbal intelligence (Choi et al., 2008; Lee et al., 2014) and in prefrontal regions with non-verbal intelligence (Gray et al., 2003). It may be noted that VIQ and PIQ scores are partial estimates and may not fully describe the verbal and non-verbal abilities.

Although the above findings demonstrate dissociation of cortical regions for verbal and non-verbal intelligence, the possibility that the relationships between different cortical regions vary in distinct patterns for verbal and non-verbal intelligence remains unexplored. Such a motivation arises in light of recent studies that have revealed distinct patterns in anatomical coupling among cortical regions associated with greater general intelligence (Lerch et al., 2006) and vocabulary abilities (Lee et al., 2014). Lerch et al. (2006) found stronger anatomical coupling between a seed region at BA 44 (part of Broca's area) with several frontal and parietal regions for individuals with higher general intelligence; while Lee et al. (2014) observed stronger anatomical coupling in multiple regions involved in language in people who possess greater vocabulary skills. Although these two studies have shown modifications in anatomical coupling with greater general intelligence and vocabulary, there has not been any study that explored the dissociation of verbal and non-verbal intelligence in terms of differences in the patterns of anatomical coupling among cortical regions. Given the distinct focal differences in cortical thickness with greater verbal and non-verbal intelligence, we postulate that there will be distinct variations in the patterns of anatomical coupling with greater verbal and non-verbal intelligence.

A recently introduced methodology to examine anatomical coupling among broadly distributed cortical regions instead of focussing on each cortical region in statistical isolation from all others, is the study of structural covariance networks (SCNs) (He et al., 2007; Khundrakpam et al., 2013; for detail reviews, see Alexander-Bloch et al., 2013; Evans, 2013). Several studies have replicated patterns of SCNs in normal brains (Zielinski et al., 2010; Raznahan et al., 2011; Khundrakpam et al., 2013), and alterations in the SCN patterns have been shown in several diseases including Alzheimer's disease, schizophrenia, multiple sclerosis, autism etc. (Bassett and Bullmore, 2009; He et al., 2009; Sharda et al., 2014).

Additionally, accumulating evidence have also shown anatomical (white matter connectivity) and functional (resting state fMRI connectivity) correspondence with SCNs suggesting that SCN patterns might capture some aspects of brain connectivity (Gong et al., 2012; Kelly et al., 2012).

Given that SCNs provide a good framework for investigating anatomical coupling among cortical regions, we hypothesize that they will provide information about differences in the patterns of anatomical coupling among cortical regions associated with greater verbal and performance intelligence. Additionally, we aim to explore differences in topological organization corresponding to greater verbal and performance intelligence.

## Materials and methods

### Participants

Data for the study were taken from the NIH MRI Study of Normal Brain Development (Evans and Brain Development Cooperative, 2006); a multi-site project undertaken to offer a normative database for normal brain and cognitive development. 586 MRI scans of subjects aged 6–18 years scanned up to 3 times at 2 year intervals that had concurrent intelligence quotient (IQ) testing on the Wechsler Abbreviated Scale of Intelligence (WASI) were used. Detailed demographics of the subjects are given in Table 1.

### Psychometric measures

Several batteries of behavioral measures were acquired from the subjects on or within few days of brain imaging (for details, see Evans and Brain Development Cooperative, 2006; Waber et al., 2007). Cognitive measures used in the study were the Wechsler Abbreviated Scale of Intelligence (WASI); (Wechsler, 1999) from the NIH MRI Study of Normal Brain Development. The WASI consisted of vocabulary, similarities, matrix reasoning, and block design subtests. Verbal IQ (VIQ) and performance IQ (PIQ) measures were computed by normalizing the scores on individual subtests (vocabulary and similarities for VIQ, and matrix reasoning and block design for PIQ) against age-specific norms. Thus, VIQ comprised those tests more related to verbal skills while PIQ involved tests more independent of verbal skills.

### MRI acquisition and processing

For each subject, a 3D T1-weighted (T1W) Spoiled Gradient Recalled (SPGR) echo sequence with 1.5 T scanners was acquired, with 1mm isotropic data obtained sagittally from the whole head. For GE scanners, slice thickness of ~1.5 mm was obtained due to their limit of 124 slices. Additionally using a two-dimensional (2D)

**Table 1**  
Demographics of the subjects used in the study. Means with standard deviation, and range given in parentheses. The last column shows the overlap/statistical dependency between PIQ and VIQ scores. PIQ, performance IQ; VIQ, verbal IQ.

PIQ					VIQ			
Group	Scans	Subjects (M/F)	Age	PIQ score	Subjects (M/F)	Age	VIQ score	t test (PIQ/VIQ)
Low-IQ	293	187 (88/99)	12.8 ± 3.	100 ± 8 (72–110)	189 (93/96)	13.0 ± 3.7	100 ± 7 (74–109)	p=0.55
High-IQ	293	180 (86/94)	12.9 ± 3.8	121 ± 8 (111–157)	185 (88/97)	12.7 ± 3.7	120 ± 9 (110–156)	p=0.21

Total number of subjects, n=306 (scanned up to 3 times).

Total number of scans, N=586.

Males/females=141/165.

Age=6–18 years.

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