Anatomical Coupling Among Distributed Cortical Regions in Youth Varies as a Function of Individual Differences in Vocabulary Abilities

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Abstract: Patient lesion and functional magnetic resonance imaging (fMRI) studies have provided convincing evidence that a distributed brain network subserves word knowledge. However, little is known about the structural correlates of this network within the context of typical development and whether anatomical coupling in linguistically relevant regions of cortex varies as a function of vocabulary skill. Here we investigate the association between vocabulary and anatomical coupling in 235 typically developing youth (ages 6–19 years) using structural MRI. The study's primary aim was to evaluate whether higher vocabulary performance was associated with greater vertex-level cortical thickness covariation in distributed regions of cortex known to be associated with word knowledge. Results indicate that better vocabulary skills are associated with greater anatomical coupling in several linguistically relevant regions of cortex, including the left inferior parietal (temporal-parietal junction), inferior temporal, middle frontal, and superior frontal gyri and the right inferior frontal and precentral gyri. Furthermore, in high vocabulary scorers, stronger coupling is found among these regions. Thus, complementing patient and fMRI studies, this is the first investigation to highlight the relevance of anatomical covariance within the cortex to vocabulary skills in typically developing youth, further elucidating the distributed nature of neural systems subserving word knowledge. *Hum Brain Mapp 35:1885–1895, 2014.* © 2013 Wiley Periodicals, Inc.

Key words: brain; cerebral cortex; magnetic resonance imaging; semantics; language; cognition; child; adolescent

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INTRODUCTION

The neuroanatomical correlates of language have been the focus of scientific investigation for approximately 150 years, most notably dating back to the work of Broca [1861] and Wernicke [1874]. However, surprisingly little is known about these correlates in typically developing youth, despite the fact that linguistic and conceptual abilities blossom during childhood and adolescence. Here we use a novel analytic technique to link individual differences in vocabulary skill (as measured by the Wechsler scales Vocabulary subtest) to the strength of anatomical coupling (i.e., the covariance of cortical thickness [CT] in

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distributed brain regions) in a large sample of typically developing youth.

Vocabulary tests evaluate lexical knowledge—that is, knowledge of the meanings of words in a given language. Thus, they tap not only semantic representations (i.e., representations of meaning or concepts) but also phonological representations (i.e., representations of the speech sounds that comprise words; Cutting and Ferreira, 1999]. In addition, these tasks call upon higher-level executive function skills [Ye and Zhou, 2009] such as focused attention, as they require participants to search the mental lexicon for word meanings and their corresponding phonological representations and to formulate and articulate a precise response.

Given the multifaceted nature of vocabulary tests, they are likely to tap the workings of multiple neural regions rather than one discrete region of cortex. Thus, to investigate the neural correlates of individual differences in vocabulary skill using structural magnetic resonance imaging (sMRI), it may be beneficial to examine how different regions of cortex relate to one another (i.e., how volume or CT estimates from one region of cortex correlate with other regions of cortex, analogous to examining correlations in activations using functional MRI) rather than limiting investigations to estimating the size of a single anatomical region or group of regions. Existing sMRI investigations of gray matter correlates of vocabulary skill have largely been characterized by the latter approach—that is, they often relate regional brain volume or CT estimates to individual vocabulary scores. In the sections that follow, we will review the few published studies focused on gray matter correlates of vocabulary skill, then briefly turn to diffusion tensor imaging (DTI) investigations of vocabulary and new word learning. Finally, we will conclude with a summary of the fMRI literature on the physiological correlates of semantic skill in which the distributed nature of semantic brain networks has been emphasized.

Three cross-sectional quantitative morphometric studies of vocabulary skill/new word learning in typical children and adults have reported a positive correlation between vocabulary performance and gray matter density of the posterior supramarginal gyrus [Lee et al., 2007; Mechelli et al., 2004; Richardson et al., 2010]. These investigators have suggested that this region of cortex may be particularly relevant to vocabulary skills and new word learning because of its connections with regions of the inferior parietal lobe that are thought to subserve the processing of either the sounds or meanings of words. Complementing these posterior findings, Konrad et al. [2012] reported a positive association between gray matter density in the inferior frontal gyrus, roughly corresponding to Broca's area, and verbal intellectual abilities in a young sample of typically developing individuals. Sowell et al. [2004] investigated the CT correlates of vocabulary skill in a pediatric sample followed longitudinally and reported that greater cortical thinning of several bilateral and spatially distributed regions of cortex (including temporal-parietal and to a lesser extent inferior frontal) was associated with larger increases in vocabulary knowledge over time.

Complementing, these gray matter studies are a few studies that have examined the relations between individual differences in white matter and vocabulary/new word learning skill in typically developing individuals using DTI. Wong et al. [2011] reported a positive correlation between the degree of fractional anisotropy in a temporal-parietal region and the mapping of sound-meaning correspondences using a foreign phonetic contrast, suggesting that greater white matter density in this region was related to greater performance on a task with demands very similar to those required in new word learning. Contrasting these findings of greater fractional anisotropy being related to stronger performance, Konrad et al. [2012] reported a negative relationship between fractional anisotropy and verbal intellectual abilities in the left inferior frontal gyrus, corresponding to Broca's area. Finally, a study by Lebel and Beaullieu [2009] focused on arcuate fasciculus lateralization and its relation to verbal abilities in a pediatric sample. They reported that those children who had an entirely left-lateralized arcuate fasciculus demonstrated stronger performance on tasks of semantic and phonological processing than those with a right-lateralized arcuate fasciculus.

In contrast to the limited sMRI literature, the fMRI literature on word knowledge or semantic processing is prolific. Several reviews of this literature have been completed in the past 15 years [see Bookheimer, 2002; Martin, 2007; Price, 2010]. These reviews highlight the fact that a highly distributed network of regions are activated during the completion of tasks thought to tap semantic knowledge. In a meta-analysis of 120 fMRI studies that included at least one experiment evaluating semantic knowledge, Binder et al. [2009] reported that semantic task performance tended to be associated with activations in seven left-lateralized brain regions. These included the dorso- and ventro-medial prefrontal cortex, inferior frontal gyrus, posterior cingulate gyrus, posterior inferior parietal lobe, middle temporal gyrus, and the fusiform and parahippocampal gyri.

Thus, various lines of evidence suggest that vocabulary skills are likely to rely on the functioning of several distributed brain regions. Despite this, no studies explicitly describe how covariance of cortical gray matter relates to vocabulary skills in typical youth. Thus, this was the goal of this study. Specifically, we use a recently developed index of anatomical covariance [Lerch et al., 2006] to probe CT correlates of individual differences in vocabulary performance in 235 typically developing youth (ages 6–19 years). This approach has proven useful in prior studies of individual differences in higher-level cognitive functioning [He et al., 2007, 2008; Lerch et al., 2006] as well as in a developmental investigation of the coordinated maturation of CT in adolescents [Raznahan et al., 2011].

We reasoned that examining anatomical coupling (as opposed to absolute measurements of cortical gray or white matter) may be an effective way to characterize individual differences in vocabulary skills, because the literature on semantic knowledge, such as object concepts, suggests that these concepts are represented in distributed brain regions across the cortex that are thought to be active when information about the object is initially obtained (e.g., sensory and motor systems). Thus, it may be the case that children who are more adept at acquiring semantic knowledge have more coordinated development in distributed cortical networks that represent properties of objects or other concepts [see Martin, 2007 for a review]. To draw upon the Hebbian notion of "regions that fire together wire together" [Hebb, 1949], it could be that regions that fire together during the acquisition of semantic knowledge also grow (and prune) in a more coordinated fashion in children who have better semantic abilities. Consequently, this may be represented at the anatomic level by stronger CT covariance among these regions.

Based on this reasoning, the following questions guided the manuscript. Are stronger vocabulary skills associated with greater cross-cortical covariance in linguistically relevant brain regions? Specifically, is mean CT related more strongly to linguistically relevant areas in those who are more adept at a vocabulary test? Furthermore, is there stronger coupling among semantically relevant brain regions (which could be thought of as "nodes") in higher vocabulary scorers, suggesting greater anatomical coupling in neural networks that underlie semantic representations in the brain? We hypothesized that higher vocabulary scores would be associated with stronger correlations between distributed regions of cortex previously found to be related to semantic processing or word knowledge, including the inferior frontal gyrus, the middle temporal gyrus, and regions of the inferior parietal lobe.

MATERIALS AND METHODS

Participants

The study's cross-sectional sample was composed of 235 unrelated typically developing right-handed youth (112 females, 123 males) participating in an ongoing longitudinal brain imaging study of single and twin births being conducted in the Child Psychiatry Branch of the National Institute of Mental Health [NIMH; Giedd et al., 2009]. Table I summarizes demographic characteristics of the sample.

Participants were screened to confirm normative development, and thus, those participants who had ever required special services in school, taken psychiatric medications, received mental health treatment, or had any condition known to affect gross brain development were excluded. Verbal or written assent was obtained from minors along with written consent from the parents. Written consent was obtained for participants over the legal age of majority. The NIMH Institutional Review Board approved the protocol.

TABLE I. Demographic information about the sample ($n = 235$)

	N	*M*	SD	Range
Female	112			
Caucasian	196			
Age		11.65	3.63	6–19
Vocabulary[a]		55.15	9.75	32–78
Intelligence quotient (IQ)[b]		111.43	13.21	78–147

[a] Age-referenced *T*-scores are provided. They have a mean of 50 and SD of 10.

[b] Age-referenced standard scores are provided. They have a mean of 100 and SD of 15.

Cognitive Measures

The Wechsler Abbreviated Intelligence Test (WASI) [Wechsler, 1999] was administered to all participants. It is composed of four subtests—two in the verbal (Vocabulary and Similarities) and two in the nonverbal (Block Design and Matrix Reasoning) domains. The focus of this research study was on the Vocabulary subtest, a task during which participants must provide the meanings of increasingly challenging words stated by the examiner. For younger and less-able participants, oral vocabulary items may be preceded by several picture vocabulary items (items in which participants must point to the picture that matches the word the examiner stated).

Age-referenced standardized *T*-scores were used to quantify individual differences in vocabulary skill. These scores offer a common metric that can be used across age groups, as standard scores provide information about how an individual's performance compares to same age peers. The WASI subtest *T*-scores have a mean of 50 and a standard deviation of 10. So a 6-year-old and a 20-year-old who both received a *T*-score of 50 on the Vocabulary subtest would both have vocabulary skills that are at the 50th percentile compared to same age peers even though the absolute (raw) number of vocabulary words they can define on the subtest will be very different.

Because we were interested in vocabulary skills and not intellectual ability more generally, we regressed scores from the two WASI nonverbal subtests, Block Design and Matrix Reasoning, out of the Wechsler Vocabulary age-referenced *T*-score. Residuals from these analyses were used in all primary analyses. We chose to regress nonverbal IQ performance out of participant Vocabulary scores for two reasons. First, we wanted to avoid redundancy with Lerch et al.'s [2006] prior investigation of variation in structural covariance as a function of general intelligence. Second, because research suggests that all cognitive tests are correlated to a certain extent [Carroll, 1993; Spearman, 1904] and the focus of this manuscript is on vocabulary or lexical knowledge specifically, we sought to reduce some of the variance associated with general intelligence from our measure lexical knowledge. Furthermore, because we wanted to avoid throwing the proverbial "baby out with the bath water," we elected to regress variance from the two nonverbal IQ subtests out of Vocabulary scores rather than regress full scale IQ out of this score.

MRI Scan Acquisition and Processing Methods

All MRI scans were acquired at the National Institutes of Health Clinical Center in Bethesda, MD using the same General Electric 1.5 Tesla Signa Scanner. Each participant contributed one scan. Scans were completed during the same month as cognitive testing in the vast majority of cases ($n = 222$). A small subset ($n = 13$) of scans was acquired between 2 and 6 months of cognitive testing.

A three-dimensional spoiled gradient recalled echo sequence in the steady state, designed to optimize discrimination between gray matter, white matter, and cerebrospinal fluid, was used to acquire 124 contiguous 1.5-mm thick slices in the axial plane (Echo Time [TE]/Repetition Time [TR] = 5/24 ms; flip angle = 45°, matrix = 256 × 192, Number of Excitations [NEX] = 1, Field of View [FOV] = 24 cm, acquisition time = 9.9 min). Using a linear transformation [Collins et al., 1994], the native MRI scans were registered into standardized stereotaxic space and were corrected for nonuniformity artifacts [Sled et al., 1998]. Cerebral tissue was classified into gray matter, white matter, spinal fluid, and background with a neural net classifier [Zijdenbos et al., 2002]. Then the inner and outer cortical surfaces were extracted using deformable surface-mesh models [Kim et al., 2005; MacDonald et al., 2000]. They are aligned nonlinearly toward a standard template surface [Robbins et al., 2004]. CT was measured using the linked distance between the white and pial surfaces [t-link metric; Lerch and Evans, 2005; MacDonald et al., 2000] as measured in native space. Finally, a 30-mm surface-based diffusion smoothing kernel [Chung et al., 2003] was applied. These methods have been validated several ways, including manual measurements [Kabani et al., 2001], population simulation [Lerch and Evans, 2005], and validation within an Alzheimer's Disease study [Lerch et al., 2005]. Prior to data analyses, all scans were evaluated for motion and the quality of surface reconstruction by two or more raters. Only scans that were deemed acceptable by raters were included in analyses.

Statistical Analyses

Because this study's focus was on the effects of individual differences in vocabulary ability on anatomical coupling and not the effects of age or sex like many of our group's prior investigations (see Lerch et al., 2006 for an examination of these factors), we regressed age and sex terms out of vertex-level CT measurements and saved the residualized values so that they could be used in primary analyses. This approach allowed us to avoid confounding variations in cross-cortical correlations that relate to individual differences in vocabulary skill, our focus, with variations in cross-cortical correlations that relate to individual differences in age or sex. Age terms that were removed from CT measurements included the age at MRI scan as well as age-squared, consistent with the findings from our laboratory on the longitudinal trajectory of cortical gray matter development from childhood to young adulthood [Giedd et al., 1999].

To evaluate if children with higher vocabulary abilities demonstrate a greater degree of structural covariance (particularly in regions that have been implicated previously in neural investigations of semantic knowledge and other linguistic skills), an estimate of the relatedness of cross-cortical vertex-based CT was needed. One approach to evaluating this is to run the correlations of each vertex with every other vertex and average the mean correlation as an estimate of overall relatedness. We will refer to this as the "mean vertex-based correlation approach." To evaluate the effects of individual vocabulary differences on mean vertex-based correlation strength, groups of high and low performing participants would need to be created and the strength of the correlations compared. However, prior research by Lerch et al. [2006] has provided convincing evidence that correlating mean CT (MCT) with each vertex in the cortex yields remarkably similar correlation maps to the much more computationally expensive approach of averaging the correlation of each vertex with every other vertex. To demonstrate this similarity, we ran both the computationally expensive (the "mean vertex-based correlation") and inexpensive (MCT with all vertices) approaches with the complete sample of 235 participants. These findings are presented in Supporting Information Figure 1, panels (a) and (b), respectively. To compare the two approaches directly, we divided all vertices in a particular hemisphere (40,962) into deciles based on the strength of the correlation. We then compared the two approaches and identified which vertices fell within 1 decile of each other (presented in purple) or greater than 1 decile of each other (presented in turquoise). As can be seen in panel (c), the two approaches yielded very similar results. In fact, greater than 99% of the vertices had correlation strengths that were within one decile of each other (81% were in the same decile and an additional 18% were one decile apart) when the two approaches were compared. In contrast, less than 1% of vertices (a rate lower than chance) were identified to be two or three deciles apart by the two approaches.

Because these two methods converged, we chose to use MCT as a proxy for the relatedness of each vertex with all other vertices in subsequent analyses. This approach was preferred, as it allowed us to examine the interaction between MCT and vocabulary score continuously using regression in the complete sample of 235 participants. Use of the more computationally expensive approach would have necessitated the creation of (at least) two arbitrarily defined groups of participants who were categorized based on vocabulary performance to complete separate sets of correlational analyses within each group. Thus, using MCT permitted the use of continuous vocabulary scores across the entire sample of participants without assigning arbitrary categories for high versus low performance.

Two sets of analyses were completed to answer the study's primary research questions. First, a series of regression analyses were completed in which vertex thickness at 40,962 points in each hemisphere was predicted by the interaction of MCT and vocabulary performance. The regression equation was as follows: CT_i = Intercept + $ß_1$(MCT-residualized) + $ß_2$(Vocabulary-residualized) + $ß_3$(MCT-residualized × Vocabulary-residualized). This approach permitted the identification of seed regions relevant to individual differences in vocabulary task performance agnostically (rather than choosing seed regions a priori). As will be described in more detail in the Results section, four statistically significant regions in the left hemisphere and four in the right hemisphere were identified from the aforementioned regression analyses. These seed regions were a cluster of vertices in which the *T*-score associated with the MCT × Vocabulary regression term from the regression equation provided above exceeded statistical significance (after controlling for multiple comparisons using the false discovery rate or FDR adjustment; Benjamini and Hochberg, 1995). Next, the peak vertex (i.e., the vertex with the highest *T*-score for the interaction term) was selected from within these seed regions. The thickness of this vertex was used to predict the thickness of all other vertices as a function of vocabulary performance. Specifically, the regression equation for these analyses was as follows: CT_i = Intercept + $ß_1$(CT of seed region vertex$_j$-residualized) + $ß_2$(Vocabulary-residualized) + $ß_3$(CT of seed region vertex$_j$-residualized × Vocabulary-residualized).

To complement these analyses and provide additional evidence that our regression analyses yielded similar findings to a correlation-based approach in which high and low performing groups were compared, we dichotomized our sample into two age-matched subgroups taken from the upper ($n = 71$) and lower third ($n = 78$) of vocabulary scorers and compared the strength of the correlations for the two groups. See Supporting Information Table I for demographic information about these two subgroups.

RESULTS

Question 1: Are stronger vocabulary skills associated with greater cross-cortical covariance in linguistically-relevant brain regions? Stated another way, is the thickness of language-related cortical regions more highly correlated with the thickness of the rest of cortex (as estimated by MCT) in those with higher vocabulary abilities?

This question was evaluated separately at every vertex in each hemisphere in the complete sample of 235 participants using the following regression equation: CT_i = Intercept + $ß_1$(MCT[1]) + $ß_2$(Vocabulary[2]) + $ß_3$(MCT × Vocabulary). The resulting *t*-statistics associated with the MCT × Vocabulary interaction term was projected onto the cortical sheet. See Figure 1, panel (a). As displayed in panel (b) of Figure 1, statistically significant interactions (adjusted for multiple comparisons using the FDR; $q < 0.05$; Benjamini and Hochberg, 1995) were found in four regions on the left—[1] the superior frontal and [2] middle frontal gyri, [3] a posterior region of the inferior temporal gyrus and [4] the inferior parietal lobe/temporal-parietal junction—such that a steeper slope between these regions and MCT was associated with better vocabulary scores. Statistically significant interactions between vocabulary and MCT were also found on the right in two regions, [5] the inferior frontal gyrus and [6] the precentral gyrus. Again, these interactions reflected the fact that steeper regression line slopes were found for higher performers. Additionally, there were two regions on the right in which steeper regression line slopes between the vertices and MCT were associated with *lower* scores. These regions were in the superior temporal gyrus and inferior occipital gyrus. They can be viewed in Supporting Information Figure 3.

To complement these analyses and provide additional evidence that our regression analyses yielded similar findings to a correlation-based approach in which high and low performing groups were compared, we dichotomized our sample into two age-matched subgroups taken from the upper ($n = 71$) and lower third ($n = 78$) of vocabulary scorers and compared the strength of the correlations for the two groups. Correlations are presented in Supporting Information Figure 4, panels (a) and (b), for the high and low scorers, respectively. To contrast the correlation strength differences, coefficients for the high and low performing groups were compared using a Fisher's *R*-to-*Z* transformation. As can be seen in panel (c), the regions in which mean correlation strength was stronger in the high performers (shown in red) are very similar to those identified in regression analyses in which the interaction between MCT and vocabulary scores was used to predict vertex thickness. To present the similarity between these two approaches, we ranked the *z*-scores from the Fisher's *Z* transformation (panel c) and *t*-scores that resulted from the mean CT by vocabulary interaction (from panel d) and identified the top 2.5% ($P < 0.05/2$ for two-tailed tests) of vertices using both approaches. As can be seen in panel (e), there was a large degree of overlap for the two approaches—that is, the vertices falling into the top 2.5% for both approaches fell roughly in the same regions.

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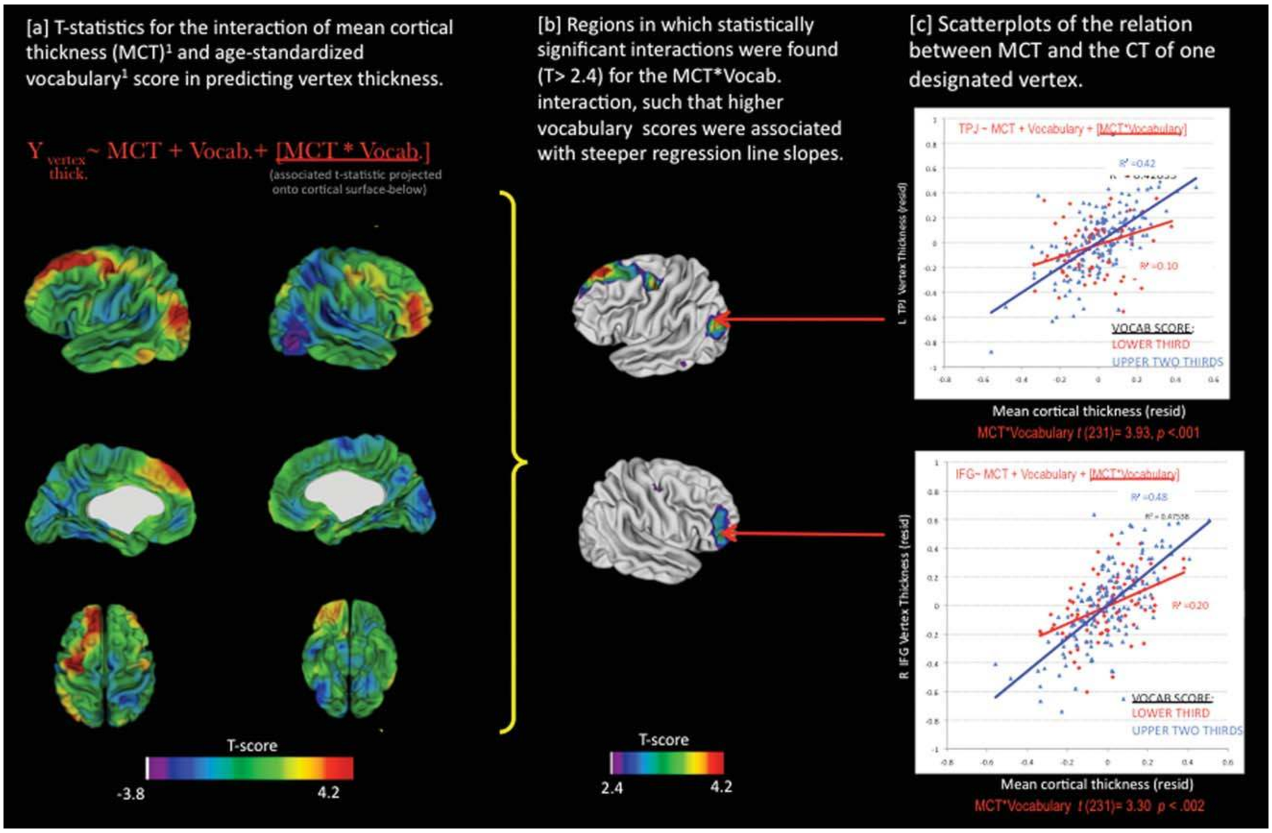
[1] The MCT measure used here was residualized, with the variance associated with age, age^2, and sex removed.

[2] The Vocabulary measure used here was residualized, with the variance associated with the Block Design and Matrix Reasoning subtests removed. To see results for unadjusted vocabulary performance, please refer to the Supporting Information Figure 2.



[a] T-statistics for the interaction of mean cortical thickness (MCT)[1] and age-standardized vocabulary[1] score in predicting vertex thickness.

[b] Regions in which statistically significant interactions were found (T> 2.4) for the MCT*Vocab. interaction, such that higher vocabulary scores were associated with steeper regression line slopes.

[c] Scatterplots of the relation between MCT and the CT of one designated vertex.

Figure 1.

Regions in which mean cross-cortical coupling varies as a function of vocabulary performance in the complete sample (n = 235). A series of linear regression analyses predicting CT at each vertex in both hemispheres was run in the complete sample (n = 235) using the following equation: $\text{CT}_i = \text{Intercept} + ß_1(\text{MCT}) + ß_2(\text{Vocabulary}) + ß_3(\text{MCT} \times \text{Vocabulary})$. (Note that MCT is a residualized score with variance associated with age, age squared, and sex removed, and vocabulary is a residualized score with variance associated with the two WASI nonverbal subtests [Block Design and Matrix Reasoning] removed). *T*-statistics associated with the MCT × Vocabulary interaction were projected onto the cortical surface in panel **a**. Then statistically significant *t*-values (with FDR adjustment for multiple comparisons; $q < 0.05$) were identified and are displayed in panel **b**. Panel **c** shows scatter plots of the relation between MCT and the CT of one designated vertex (the vertex with the highest *t*-score) in the left and right hemispheres. Steeper regression line slopes were associated with higher vocabulary scores, suggesting greater coupling between these regions and the rest of cortex in high performers. (See Supporting Information Fig. 3 for the two additional right hemisphere regions in which a steeper regression line slope was associated with poorer performance.) Finally, please note that the *t*-statistics reported below the scatter plots are for the MCT × continuous vocabulary score interaction in the whole sample of 235 participants. However, the figure includes two regression lines for high and low performing groups. These regression lines and associated r^2 values were included for illustrative purposes only. These two groups were not directly compared in the analyses presented here. Abbreviations: MCT, mean cortical thickness; TPJ, temporal-parietal junction; IFG, inferior frontal gyrus; resid, residualized; Vocab, Vocabulary; L, left; R, right.

Question 2: In individuals with stronger vocabulary skills, is there tighter coupling among the seed regions identified in Question 1?

To answer this question, the peak vertex from each of the seed regions on the left and right was used as an independent variable in lieu of MCT in the following regression equation: $\text{CT}_i = \text{Intercept} + ß_1(\text{CT of seed region vertex}_j\text{-residualized}) + ß_2(\text{Vocabulary-residualized}) + ß_3(\text{CT of seed region vertex}_j\text{-residualized} \times \text{Vocabulary-residualized})$. See Figures 2 and 3 for the findings in the left and right[3] hemispheres, respectively. Overall, greater coupling between these seed regions was associated with higher vocabulary scores (i.e., higher *t*-statistics,

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[3] See Supporting Information Figure 3 for seed region coupling in seeds that were more coupled with MCT in children with poorer vocabulary performance.

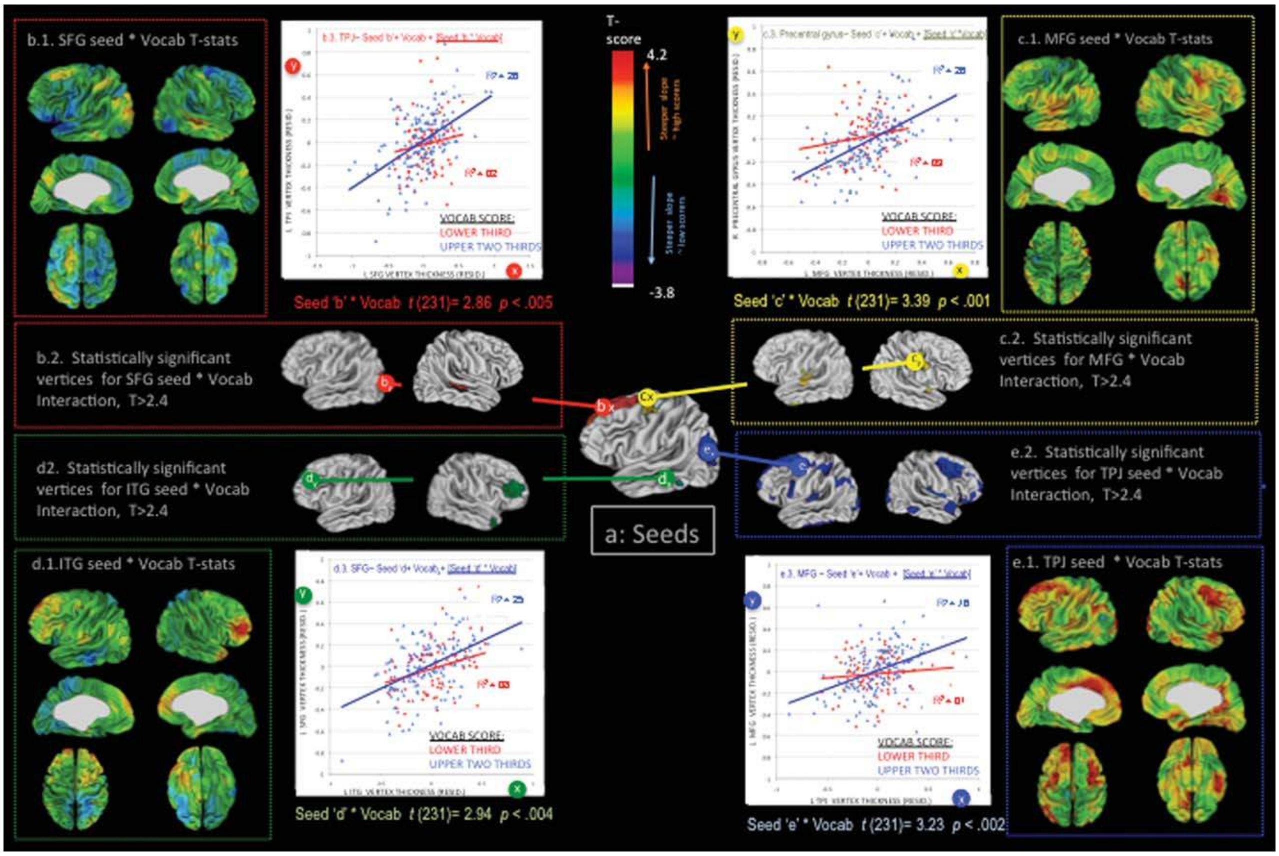

Figure 2.

Vertex coupling for left-hemisphere seed regions that were found to be more strongly related to MCT in those with better vocabulary skills ($n = 235$). Left-hemisphere seed regions identified from the prior analyses (Fig. 1) for which cross-cortical coupling varied as a function of vocabulary skill were used as an independent variables in the analyses presented in this figure. Panel **a** (center of the figure) displays the four left-hemisphere seed regions—superior frontal gyrus (panel **b**; red), middle frontal gyrus (panel **c**; yellow), inferior temporal gyrus (panel **d**; green), and the inferior parietal lobe/temporal-parietal junction (panel **e**; blue). The peak vertex from each seed region (i.e., the vertex with highest *t*-statistic for the seed × vocabulary interaction) was used in a series of regression analyses with the following equation: $\mathrm{CT}_i = \mathrm{Intercept} + \beta_1(\text{Seed vertex thickness}) + \beta_2(\text{Vocabulary}) + \beta_3(\text{Seed vertex thickness} \times \text{Vocabulary})$. (Note that seed vertex thickness is a residualized score with variance associated with age, age squared, and sex removed, and vocabulary is a residualized score with variance associated with the two WASI nonverbal subtests [Block Design and Matrix Reasoning] removed). Panels b.1.–e.1. display the *T*-statistics associated with the seed × vocabulary interaction term. Panels b.2.–e.2. display the statistically significant *t*-values (with FDR adjustment for multiple comparisons; $q < 0.05$) that were identified for each of these analyses. Finally, panels b.3.–e.3. display the scatter plots of the relation between the peak vertex in the seed and the designated vertex. In all instances displayed here, steeper regression line slopes were associated with higher vocabulary scores, suggesting greater coupling between these regions and the seed region in those more adept at the vocabulary test. Finally, please note that the *t*-statistics reported below the scatter plots are for the seed × continuous vocabulary score interaction in the whole sample of 235 participants. However, the figure includes two regression lines for high and low performing groups. These regression lines and associated r^2 values were included for illustrative purposes only. These two groups were not directly compared in the analyses presented here. Montreal Neurological Institute (MNI) coordinates for the peak vertex in the four seeds were as follows: superior frontal: −12, 48, 43; middle frontal gyrus: −34, −7, 50; inferior temporal gyrus: −59, −47, −11; inferior parietal/temporal-parietal junction: −48, −67, 34. Abbreviations: MCT, mean cortical thickness; TPJ, temporal-parietal junction; ITG, inferior temporal gyrus; MFG, middle frontal gyrus; SFG, superior frontal gyrus; resid, residualized; Vocab, Vocabulary; L, left; R, right.

represented by warmer colors, were found in similar regions of cortex to those identified when MCT was used as an independent variable). However, the extent of coupling between different seeds varied. Furthermore, a few additional regions were identified as being more coupled with these seeds in children with higher

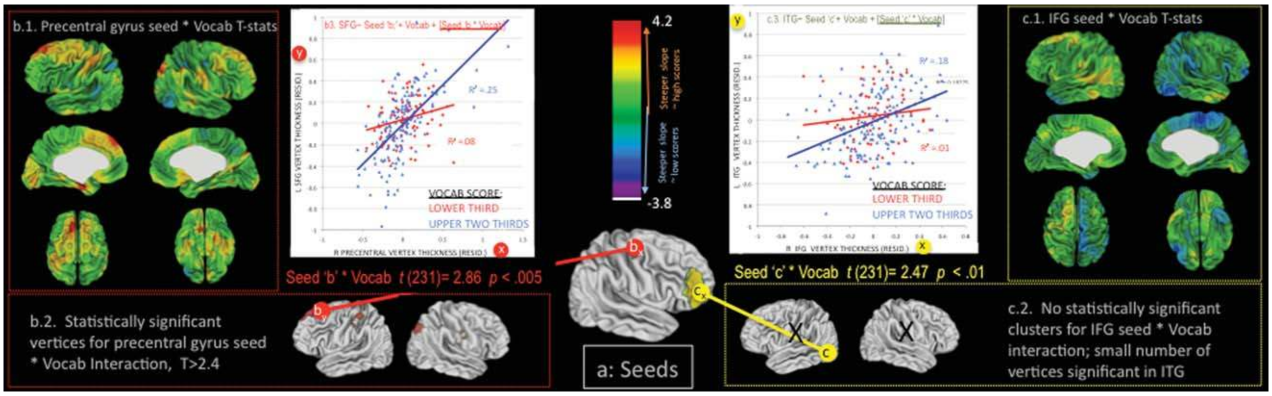

Figure 3.

Vertex coupling for right-hemisphere seed regions that were found to be more strongly related to MCT in those with better vocabulary skills ($n = 235$). Right-hemisphere seed regions for which stronger coupling was associated with better vocabulary skills were used as independent variables in the analyses presented in this figure. Panel **a** (center bottom of the figure) displays the two seed regions. Coupling between these seed regions and the rest of cortex can be seen in panel **b** (red) for the precentral gyrus and panel **c** (yellow) for the inferior frontal gyrus. The peak vertex from each seed region (i.e., the vertex with highest t-statistic for the seed × vocabulary interaction) was used in a series of regression analyses with the following equation: $CT_i = \text{Intercept} + \beta_1(\text{Seed vertex thickness}) + \beta_2(\text{Vocabulary}) + \beta_3(\text{Seed vertex thickness} \times \text{Vocabulary})$. (Note that seed vertex thickness is a residualized score with variance associated with age, age squared, and sex removed, and vocabulary is a residualized score with variance associated with the two WASI nonverbal subtests [Block Design and Matrix Reasoning] removed). Panels b.1. and c.1. display the T-statistics associated with the seed × vocabulary interaction term. Panels b.2. and c.2. display the statistically significant t-values (with FDR adjustment for multiple comparisons; $q < 0.05$) that were identified for each of these analyses. Finally, panels b.3. and c.3. display the scatter plots of the relation between the peak vertex in the seed and the designated vertex. For both of these seeds, steeper regression line slopes were associated with higher vocabulary scores, suggesting greater coupling between these regions and the seed region in those who were more adept at a vocabulary test. Please note that the t-statistics reported below the scatter plots are for the seed × continuous vocabulary score interaction in the whole sample of 235 participants. However, the figure includes two regression lines for high and low performing groups. These regression lines and associated r^2 values were included for illustrative purposes only. These two groups were not directly compared in the analyses presented here. MNI coordinates for the peak vertex in the two seeds were as follows: precentral gyrus: 47, −4, 52; inferior frontal gyrus: 42, 44, −6. Abbreviations: MCT, mean cortical thickness; IFG, inferior frontal gyrus; ITG, inferior temporal gyrus; resid, residualized; Vocab, Vocabulary; L, left; R, right.

vocabulary scores. This was particularly the case for the inferior parietal/temporal-parietal junction seed (see Fig. 3, panel e).

Finally, we have summarized coupling among these seed regions or nodes in Figure 4. Specifically, we have connected pairs of nodes for which coupling is modified as a function of vocabulary performance (i.e., the P-value associated with the peak vertex seed × vocabulary interaction was less than 0.05). As can be seen, the seed region in the inferior parietal lobe/temporal-parietal junction, clustered roughly in the area of the angular gyrus, shows the greatest degree of coupling with other seeds.

DISCUSSION

Adding to the literature on the distributed nature of word knowledge and linguistic skill in the brain, we find that individual differences in vocabulary ability are closely tied to the degree of CT covariation across distributed regions of cortex in typically developing youth. Specifically, higher scores on a standardized vocabulary test were associated with greater CT coupling in the left inferior parietal and temporal gyri, left middle and superior frontal gyri, and the right inferior and precentral gyri. Thus, consistent with prior sMRI and fMRI studies [Grossman et al., 2002; Lee et al., 2007; Sowell et al., 2004], the neural correlates of semantics appear to be bilateral in this young sample, albeit much more diffuse on the left.

Unlike the majority of structural imaging studies of cognitive abilities in youth, this study did not focus on the absolute size of brain structures but rather on the degree to which the thickness of different regions of cortex covaried. Thus, it complements the existing literature by providing information about the possible importance of structural covariation in the neural systems that underlie linguistic skills in youth. Another unique feature of this study is its focus on individual differences and how CT coupling may provide important information about the underpinnings of exceptional vocabulary performance,

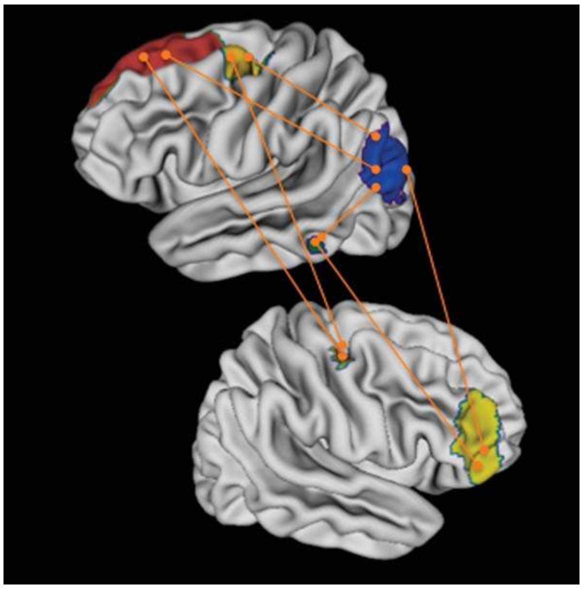

Figure 4.

Coupling among seed regions in both the left and right hemispheres that varies as a function of vocabulary ability. To examine coupling among the six seed regions identified in prior analyses as being associated with stronger vocabulary performance, a series of linear regression analyses were completed using the following equation: Seed_i peak vertex thickness $=$ Intercept $+\ \beta_1(\text{Seed}_j$ peak vertex thickness$)\ +\ \beta_2(\text{Vocabulary})\ +\ \beta_3(\text{Seed}_j$ peak vertex thickness $\times$ Vocabulary$)$. (Note that seed vertex thickness is a residualized score with variance associated with age, age squared, and sex removed, and vocabulary is a residualized score with variance associated with the two WASI nonverbal subtests [Block Design and Matrix Reasoning] removed). The six seed regions are projected onto the cortical sheet, and orange lines are used to indicate when the relationship between two seeds varied significantly as a function of vocabulary performance (i.e., the seed peak vertex × vocabulary interaction *t*-statistic was statistically significant; $P < 0.05$). As can be seen, the seed in the left inferior parietal lobe/temporal-parietal junction appears to be coupled with the largest swath of cortex, suggesting that it is a key node that relates to individual differences vocabulary knowledge.

both for low and high performers. Even within this sample of typical children with a mean vocabulary score that is approximately two-thirds of a standard deviation above the national average, differences in cross-cortical correlations for high and low performers were striking and suggest that far greater differences may have been apparent if more children with poor vocabulary skills were included.

The results of this investigation converge with the larger literature on the neural underpinning of semantic knowledge or language comprehension more generally. In fact, many of the regions identified as being more strongly coupled with the rest of cortex in those more adept at vocabulary in this paper overlap with those reported to be part of the "semantic system" in a meta-analysis of fMRI studies completed by Binder et al. [2009]. Of the seeds or nodes identified here, the seed in the inferior parietal lobe/temporal-parietal junction, corresponding roughly to the angular gyrus, was coupled with the largest swath of cortex. In fact, when the peak vertex within the angular gyrus was used as a seed, statistically significant interactions were found in approximately 33% of vertices across the cortex, such that stronger coupling with this seed was associated with better vocabulary skills. Furthermore, it is worth noting that several of the regions identified here as being more coupled with the angular gyrus/inferior parietal seed were similar to those reported to be "functionally connected" to the angular gyrus/superior temporal sulcus in an investigation of resting state connectivity in brain regions relevant to language comprehension conducted by Turken and Dronkers [2011]. These authors note that this region (among others in the left middle temporal gyrus) appears to be ..."part of a richly interconnected network that extends to additional frontal, parietal, and temporal regions in the two hemispheres" (p. 1). While the current study does not directly address "connectivity" (either functional connectivity or white matter tracts), the results suggest that in healthy children with strong vocabulary skills, there is a high degree of coupling between the inferior parietal lobe/temporal-parietal junction and the rest of the cortex on the left and the right.

What role might the angular gyrus/temporal-parietal junction play in vocabulary ability? In a recent review of the anatomy and functionality of the angular gyrus, Seghier [2013] reports that it has been implicated in subserving several cognitive functions in the neuroimaging literature, including (but not limited to) semantic processing, reading comprehension, number processing, attention/spatial cognition, conflict resolution, and social cognitive abilities, such as theory of mind. The review highlights the integrative role the angular gyrus may play in processing concepts and suggests that the angular gyrus "...resembles a ' core facility' used by different subsystems to access concepts when interfacing perception-to-recognition-to-action" (p. 52). When viewed within this context, it seems sensible to think of this region as being an important node in a neural network subserving semantic knowledge and language comprehension more generally.

Prior to discussing mechanisms that may be responsible for the higher degree anatomical coupling observed in those with stronger vocabulary skills, we will briefly mention the two seed regions in the right hemisphere that were more coupled with the rest of cortex in children with poorer vocabulary scores, namely, the inferior occipital and superior temporal gyri. These regions are parts of the visual and auditory association cortices, respectively. Speculatively, it may be the case that the cortex of children who perform less well on vocabulary tasks is characterized by greater coupling among sensory regions without the concurrent coupling of higher-level integration regions, such as the angular gyrus. Clearly, further research is needed to investigate this possibility. For example, it may be informative to examine anatomical coupling in children with developmental disorders of language, as these children offer an opportunity to examine the nature of cortical covariance when word knowledge is clinically impaired.

What mechanisms may be involved in the development of individual differences in cross-cortical correlations reported here? Parallel distributed processing approaches [Davis and Gaskell, 2009; McClelland, 1998] suggest that two learning mechanisms may be involved: (1) a slower, distributed system that relies on statistical or Hebbian learning [Hebb, 1949] to incorporate new information into representational systems and permit within-category semantic generalization, and (2) a much more rapid, error-driven system thought to be important for making arbitrary, nonoverlapping associations. The former system is thought to be characteristic of the neocortex while the latter is thought to be characteristic of the hippocampus.

Accordingly, individual differences in vocabulary knowledge may be accounted for by differences in the functioning of these learning mechanisms. Given that this study focused on the neocortex exclusively and research on new word learning suggests that statistical learning principles are important to this process [Saffran et al., 1996], there is a suggestion that differences in Hebbian learning efficiency (which is thought to be instantiated through the processes of presynaptic and postsynaptic long-term potentiation and depression; O'Reilly and Munakata, 2000] may contribute to individual differences in vocabulary ability. Unfortunately, this research is not equipped to answer questions about the biological mechanisms that underlie differences in anatomical coupling; a shortcoming of this descriptive, cross-sectional study. Clearly, longitudinal and/or experimental studies are needed to elucidate the mechanisms responsible for the development of individual differences in cross-cortical correlations over time.

Another limitation of this study is the use of a standardized vocabulary test as a measure of word knowledge, given that multiple linguistic (and nonlinguistic) processes are involved in completing such a task. To lessen the impact of this limitation, we regressed the variance associated with our estimate of nonverbal IQ from the WASI (the Block Design and Matrix Reasoning subtests) out of Vocabulary scores. This may have reduced some of the variance in Vocabulary scores related to general cognitive ability rather than to word knowledge, per se. However, regressing nonverbal IQ scores out of Vocabulary scores did not permit us to disambiguate which linguistic processes (e.g., semantic vs. phonological) relate to different aspects of our findings. Finally, by focusing on the cortical sheet alone, we were not able to examine how individual differences in vocabulary skills relate to white matter covariance or cortical–subcortical covariance. Thus, this is an obvious next step for future investigations.

Despite these limitations, this is the first study to examine how anatomical coupling relates to individual differences in word knowledge, thus, opening the door to future investigations of the cross-cortical correlates of different aspects of cognitive functioning. Furthermore, this study's findings have implications for clinical research seeking to identify the neural correlates of developmental learning disorders. Future studies in our laboratory will examine how cross-cortical correlations differ between typically developing children and children with genetic disorders characterized by language impairments (e.g., Klinefelter syndrome). Relations between vocabulary skill and cross-cortical correlations will also be investigated longitudinally to begin to describe the developmental unfolding of cortical covariance and its relation to word knowledge. Finally, twin studies of the heritability of cross-cortical covariance may begin to elucidate the genetic and environmental mechanisms contributing to individual differences in vocabulary skill and the neural systems that subserve it.

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