

**Pre-Reading Language Abilities and the Brain's Functional Reading Network in Young
Children**

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HIGHLIGHTS

- We acquired passive viewing fMRI and assessed pre-reading in 50 children aged 2-5
- Functional connectivity was measured from three key reading areas bilaterally
- Better pre-reading predicted stronger connectivity between reading and motor areas
- Better scores were related to decreased connectivity with visual and default mode areas

ABSTRACT

Early childhood is an important period for language development that lays the foundation for future reading abilities. Despite the importance of early language development, very little research has focused on the functional brain systems supporting pre-reading language abilities in typically developing children. Here, using passive viewing functional magnetic resonance imaging (fMRI), we investigated relationships between functional connectivity from key brain areas involved in reading (angular gyrus, superior temporal gyrus, inferior frontal gyrus bilaterally) in 50 healthy children aged 2.85-5.07 years (3.84 ± 0.60 years, 22 female/28 male). Children completed the NEPSY-II Phonological Processing and Speeded Naming subtests and underwent functional MRI scanning while watching a movie of their choice. Pre-reading language scores positively correlated with functional connectivity between seed regions and motor areas, and between the right angular gyrus and superior temporal gyrus. Better pre-reading scores were associated with stronger negative functional connectivity between seed regions and default mode network regions in the medial frontal lobe and posterior cingulate cortex, as well as posterior occipital regions. These results suggest that integration of reading and motor areas, and dissociation between reading areas and the default mode network, are apparent in young children with better pre-reading skills, even before formal reading instruction begins.

Keywords: preschool, early childhood, language, functional connectivity, fMRI, reading, default mode network, speeded naming, phonological processing.

1 INTRODUCTION

Language development in early childhood (~2-5 years) lays the foundation for future reading skills, and is associated with future mental health, academic achievement, and career success (Carroll and Snowling, 2004). Most children will learn to read without difficulty, but between 17-21% have persistent challenges despite adequate motivation, opportunity, and intelligence (Ferrer et al., 2015). Although dyslexia is typically not diagnosed until third grade, its correlates are evident in the preschool period; phonological skills in early childhood are a strong predictor of later reading ability (Gabrieli, 2009). Understanding the neural bases of language and pre-reading skills in early childhood is critical for designing and evaluating early reading interventions.

Functional magnetic resonance imaging (fMRI) studies have identified a reading network in the left hemisphere of the brain that includes specific inferior frontal, superior temporal, temporal-parietal, and temporal-occipital areas (Pugh et al., 2000; Schlaggar and McCandliss, 2007; Shaywitz and Shaywitz, 2003). These regions are consistently engaged during reading relative to non-reading control tasks. Activation in this network also distinguishes typical readers from school-aged children and adults with reading deficits (Norton et al., 2015; Richlan et al., 2009, 2011). A small number of task-based fMRI studies have shown that brain function is related to language abilities in children before children have learned to read. One study found that pre-reading children (~5.5 years) with a family history of dyslexia had reduced activation in left temporal-occipital and temporal-parietal regions during a sound-matching task compared to children without a family history of dyslexia (Raschle et al., 2012). During a passive listening task, 3-5 year old children with better vocabulary scores showed higher activation of the left angular gyrus, hippocampus, and thalamus (Sroka et al., 2015). These studies show that reduced

activation in left temporal-parietal and temporal-occipital regions is characteristic of reading difficulties in older children and youth, and thus suggest that the potential neurological bases for reading disability are present in young children even before reading begins.

Resting state fMRI (rs-fMRI) is a powerful, task-independent imaging tool for investigating coordination, or functional connectivity, between brain regions. While the rs-fMRI literature on reading deficits is relatively sparse, functional connectivity between reading regions is positively correlated with reading abilities in typical adults and school-aged children (Hampson et al., 2006; Koyama et al., 2011). In a longitudinal rs-fMRI study, increases in functional connectivity between the left posterior superior temporal area and bilateral inferior frontal areas from age 5 to 6 years were associated with gains in sentence comprehension (Xiao et al., 2016b). Rs-fMRI studies have also noted stronger functional connectivity from the left supramarginal gyrus to striatal regions in adults with poor decoding skills (Achal et al., 2016), and altered connectivity to visual and default mode areas (e.g., posterior cingulate) as well as increased right hemisphere connectivity in children with dyslexia (Finn et al., 2014), suggesting that individuals with reading difficulties may recruit limbic and default mode network areas that are not involved in reading processes in individuals without reading impairments.

While rs-fMRI is powerful, it is also highly sensitive to motion (Power et al., 2014). Staying still for the duration of a scan may be particularly difficult for children, making acquisition of rs-fMRI challenging. In traditional rs-fMRI studies, individuals are asked to close their eyes and think of nothing in particular or open their eyes and fixate on a cross. This can exacerbate head motion for individuals who get bored easily (e.g., young children). Thus, some recent studies have adopted passive viewing fMRI protocols where children watch excerpts from movies or TV shows. Watching movies reduces head motion and increases reliability during

fMRI (Greene et al., 2018; Vanderwal et al., 2017), and thus may improve and even enable data collection in populations and individuals that could otherwise not be studied with rs-fMRI. Indeed, several studies have successfully used passive viewing fMRI to acquire data in children younger than 5 years (Long et al., 2017; Moraczewski et al., 2018; Richardson et al., 2018; Rohr et al., 2016). Most passive viewing studies have all participants watch the same movie (Moraczewski et al., 2018; Richardson et al., 2018; Rohr et al., 2016; Vanderwal et al., 2015), while others allow participants to select their own video (Emerson et al., 2015; Long et al., 2017). In the current study, given that children were as young as 2 years, they selected their own movie to maximize their engagement and interest, and thus increase compliance and decrease head motion as much as possible.

Early childhood (~2-5 years) is an especially important period of rapid structural brain development (Brown and Jernigan, 2012; Lebel and Deoni, 2018), which also sees strengthening of long-range functional connectivity between classical reading areas such as inferior frontal, temporal-parietal, and temporal-occipital cortex (Long et al., 2017; Xiao et al., 2016a), as well as a shift toward more left-lateralized functional networks for language processing (Reynolds et al., 2019a; Xiao et al., 2016a; Yamada et al., 2011). A small number of studies show that brain structure is linked to pre-reading skills in children as young as 3 years (Saygin et al., 2013; Vandermosten et al., 2015; Walton et al., 2018); however, it is unclear whether functional connectivity in early childhood also shows relationships with pre-reading language skills.

Reading cannot be measured in young children, but pre-reading skills such as phonological processing and speeded naming can be assessed, and are strongly and independently associated with later reading abilities (Lonigan et al., 2009; Snowling and Hulme, 2011). Phonological processing measures the ability to separate and manipulate the sounds that

make up words, and relies on both phonological awareness and memory. Speeded naming assesses the ability to rapidly name familiar objects or pictures, relying on lexical access and motor articulatory skills. To examine the brain correlates of these skills, we selected three regions of interest (ROI) that are consistently activated during reading tasks in older children and adults: the posterior superior temporal gyrus (part of Wernicke's area), the pars triangularis in the inferior frontal gyrus (part of Broca's area), and the angular gyrus (Bolger et al., 2008; Houde et al., 2010; Koyama et al., 2011; Price et al., 2015). These three regions are involved in speech, language, and reading, with the inferior frontal gyrus supporting speech production, and the angular and superior temporal gyri supporting comprehension and phonological processing (Price, 2012; Schlaggar and McCandliss, 2007).

The aim of the current study was to determine the relationship between pre-reading language ability and functional connectivity within the reading network of young children (2-5 years) before they begin reading instruction. We measured Phonological Processing and Speeded Naming in 50 children aged 2-5 years. Children underwent fMRI while watching a movie of their choice, and functional connectivity was measured between key regions of the reading network (angular gyrus, superior temporal gyrus, inferior frontal gyrus). Previous work shows better integration of the reading network in school-aged children and adults with better reading abilities (Hampson et al., 2006; Koyama et al., 2011), as well as altered connectivity in default mode, striatal, and visual areas (Achal et al., 2016; Finn et al., 2014). Therefore, we hypothesized that Phonological Processing and Speeded Naming scores would positively correlate with functional connectivity between the seed regions (inferior frontal, superior temporal, angular gyrus) and negatively correlate with connectivity between seed regions and areas of the default mode network. Furthermore, given that leftward lateralization of language

processing increases with age (Reynolds et al., 2019a; Xiao et al., 2016a; Yamada et al., 2011), and that poor readers show more right hemisphere involvement (Finn et al., 2014), we expected to see more right hemisphere connectivity related to pre-reading scores than previous studies in adults.

2 METHODS

2.1 Participants

Fifty typically-developing children aged 2.85-5.07 years (3.84 ± 0.60 years) were included in this study (22 female/28 male, 5 left-handed/44 right-handed/1 undecided). Of an initial sample of 64, we excluded participants with excessive head motion ($n=8$) (see Data Preprocessing section below), an incidental finding ($n=1$), and children who fell asleep during the scan ($n=5$). The majority ($n=44$) of participants were Caucasian, with 5 participants of Asian descent and 1 participant of mixed race. Participants were from the ongoing Alberta Pregnancy Outcomes and Nutrition Study that recruited mothers during pregnancy and continues to follow their children (Kaplan et al., 2014) and from the local community. All children were born at full term (>37 weeks' gestation), were free from diagnosed neurocognitive or developmental disorders, spoke English as a primary language, had not yet received any formal reading instruction, and had no contraindications to MRI scanning. Information on informal reading instruction (e.g., at home) was not collected. Seven participants had an immediate family member (parent or sibling) with a reading disability and two had other family member(s) with reading disabilities (parent-reported). Years of maternal post-secondary education was obtained as a proxy for socioeconomic status (all mothers completed high school) and ranged from 1-10 years (mean = 5.3 ± 2.4 years). Informed consent was obtained from the participant's legal guardian(s), and

verbal assent was obtained from the children. This study was approved by the Conjoint Health Research Ethics Board at the University of Calgary (REB13-0020).

Participants who were excluded did not differ significantly from those included in age ($t = -1.63, p = 0.11$), sex (chi-square = 0.76, $p = 0.38$), handedness (chi-square = 0.05, $p = 0.82$), pre-reading language scores (Phonological Processing: $t = -1.33, p = 0.19$; Speeded Naming: $t = -1.39, p = 0.17$), or maternal postsecondary education ($t = 1.36, p = 0.18$).

2.2 Language Assessments

Participants' language skills were assessed using the Phonological Processing and Speeded Naming subtests from the standardized Developmental Neuropsychological Assessment-Second Edition (NEPSY-II) (Korkman et al., 2007). The Phonological Processing subtest measures a child's ability to separate and manipulate individual phonemes within words. In this age range, the examiner points to and names aloud three different pictures that contain similar and different sounds (e.g., a duck, a dog, and a door). Then the examiner says one sound (e.g., "uck") and asks the child to point to the corresponding picture. The Speeded Naming subtest involves rapid naming of colours and shapes. In the first part, the child is asked to name the colour of circles presented on a page as quickly as they can. In the second part, the child is asked to name shapes (circles and squares) as quickly as possible. Children are scored on number correct and time to complete.

Language assessments were conducted on the same day as the MRI scan, except for two children who had language assessments 10-11 days prior to their MRI. All 50 included participants successfully completed the Phonological Processing subtest; 46 completed the Speeded Naming subtest, either because of time constraints or because they opted out after

completing the Phonological Processing subtest. Language assessments were administered in a standardized manner according to the procedures outlined in the examiner's manual (Korkman et al., 2007). The subtests took 5-10 minutes each to complete, or 10-20 minutes total.

NEPSY-II provides age-standardized scores for participants aged 3-16 years. As some of the children who participated in this study were under three years of age (2.85, 2.89, 2.95, and 2.99 years), it would be inappropriate to convert the raw scores obtained on these measures to standard scores. Therefore, in order to take the age of the child into account, age-regressed residual values were computed for the children's scores on Phonological Processing and Speeded Naming. A similar data transformation approach has been used in previous research with children to take into account scores on various cognitive measures at different ages (Bergemann et al., 2012). The age-regressed unstandardized residual values of Phonological Processing were used in our analysis. The Speeded Naming test included two trials (colours and shapes), and each produced two variables (completion time and number of correct responses). To combine these, we first summed the scores across the two trials to create one score for each of completion time and total correct responses. We then took the inverse of the completion time score ($1/\text{time}$), so that higher scores indicated better performance. We then applied factor analysis to quantify and combine the two variables. Factor 1 extracted the majority of the shared variance (79.79%), and its age-regressed unstandardized residuals were used in the analysis.

A subset of participants ($n=41$) who were recruited through APrON (Kaplan et al., 2014) were assessed with the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV) (Wechsler, 2012).

2.3 Image Acquisition

MRI scanning was performed on a GE 3T MR750w scanner (General Electric, Waukesha, WI) system using a 32-channel head coil at the Alberta Children's Hospital. Children were scanned while awake watching a movie (Thieba et al., 2018). To increase the likelihood of compliance, children were allowed to choose their own movie from a set of preselected choices (the most common choices were Frozen or Despicable Me) or bring their own movie from home. Children watched the movie on a screen inside the bore of the magnet and listened to audio via headphones. Movie choice was not recorded.

Functional MRI data were acquired with a gradient-echo echo-planar imaging (EPI) sequence (240 volumes, TR = 2000 ms, TE = 30 ms, flip angle = 60°, 36 3.6 mm slices, voxel size = 3.6 x 3.6 mm isotropic; duration = 8.10 minutes). Anatomical scans were acquired using a high-resolution T1-weighted 3D FSPGR BRAVO gradient echo sequence (4:12 minutes; TR = 8.228 ms; TE = 3.76 ms; TI = 540 ms; flip angle = 12°; 210 slices; voxel size: 0.9 x 0.9 x 0.9 mm).

2.4 Data Preprocessing

Data preprocessing was performed using AFNI (Cox, 1996) and FSL (Jenkinson et al., 2012), and consisted of skull stripping, slice-time correction, spatial smoothing (6 mm FWHM Gaussian kernel), motion correction, band-pass filtering (0.009 -0.08 Hz), image registration, and normalization to a standard asymmetrical high-resolution 2mm isotropic pediatric template, optimized for children aged 33-44 months (Fonov et al., 2009). Head motion was regressed out based on six rigid body realignment motion parameters (x, y, z, pitch, raw, roll) from FSL's MCFLIRT linear motion estimation tool, as well as signal from white matter, cerebral spinal

fluid and the global signal (Jenkinson et al., 2012; Power et al., 2014). High motion corrupted volumes were identified by FSL MotionOutliers then censored if volumes exceeded both frame-wise displacement (FD) of 0.3 mm and 0.3% change in BOLD signal intensity (Power et al., 2014). Participants with less than 4.5 minutes (>105 censored volumes) of usable fMRI data were excluded from analysis. There are no clear recommendations for the minimum data that should remain after scrubbing (Power et al., 2015), and our 4.5 minute limit is similar to other resting-state fMRI studies, which exclude participants with less than 3-5 minutes of low-motion rs-fMRI data (Cechmanek et al., 2018; Khosla et al., 2019; Satterthwaite et al., 2013; Yan et al., 2013). Of an original 64, 8 participants were excluded for high motion data (6 were excluded for other reasons: 5 were sleeping, and 1 had an incidental finding). In the final sample of 50 children, the mean number of motion-corrupted volumes was 34.22 ± 26.96 (range: 0-94 volumes). The number of the corrupted volumes was significantly negatively correlated with age ($r = -0.35$, $p = 0.013$), but not with Phonological Processing ($r = -0.11$, $p = 0.45$), Speeded Naming ($r = -0.11$, $p = 0.49$), or different between boys and girls ($t = -0.91$, $p = 0.37$).

2.5 fMRI data analysis

Seed regions were the posterior superior temporal gyrus (part of Wernicke's area), the pars triangularis in the inferior frontal gyrus (part of Broca's area), and the angular gyrus; these have been consistently implicated in reading in both children and adults (Bolger et al., 2008; Houde et al., 2010; Koyama et al., 2011; Price et al., 2015). Based on coordinates provided in a meta-analysis including children (Houde et al., 2010), the seed ROIs for this study were selected in MNI space on an adult template. This template was co-registered to a pediatric template for children aged 33-44 months (also in MNI space) (Fonov et al., 2009), and then seed ROI

coordinates were transformed to the pediatric template using `img2imgcoord` in FSL and visually inspected to ensure they were correctly positioned. For reporting, coordinates of results were transformed back to adult MNI space using a reverse transform. To better understand the involvement of the right hemisphere in language development, we included the same regions from the right hemisphere by flipping the left ROI coordinates into the right hemisphere and manually adjusting them to the correct anatomical location. Each ROI was expanded from the centre to create a sphere of with a 6 mm radius.

Regions are shown in both hemispheres in Figure 1, and coordinates are provided in Table 1.

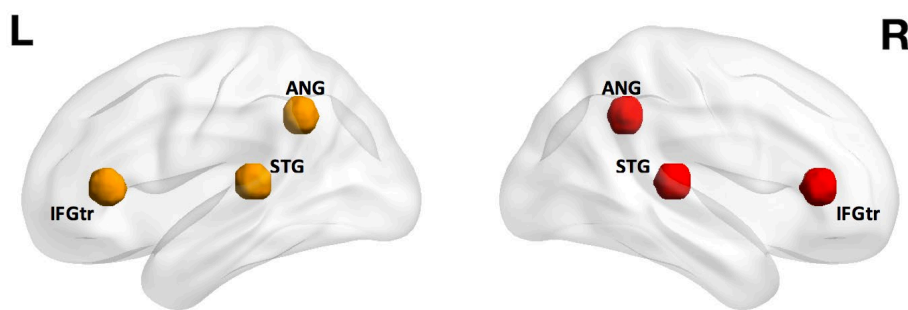


Figure 1. Brain Regions of Interest. Placement of the left (yellow) and corresponding right (red) seed regions are shown for the angular gyrus (ANG), superior temporal gyrus (STG), and inferior frontal gyrus, pars triangularis (IFGtr).

Table 1. Coordinates for regions of interest. Left hemisphere regions of interest were selected based on key regions identified in previous literature (Houde et al., 2010). Left hemisphere ROIs were flipped to the right hemisphere and manually adjusted to correspond to the analogous regions. All coordinates were expanded to create spheres with a 6 mm radius.

Region of Interest	MNI Coordinates			Pediatric Coordinates		
	x	y	Z	x	y	z
Left Hemisphere						
Angular gyrus	-48	-52	38	-39	-42	30
Inferior frontal gyrus, pars triangularis	-48	32	6	-39	26	5
Superior temporal gyrus	-53	-31	9	-43	-25	7
Right Hemisphere						
Angular gyrus	48	-52	38	39	-42	30
Inferior frontal gyrus, pars triangularis	52	32	6	43	26	5
Superior temporal gyrus	53	-31	9	43	-25	7

The average time course for each ROI was extracted and Pearson correlations with every other voxel in the brain of each participant were computed. The resultant whole-brain functional connectivity correlation maps were then normalized using Fisher's r-to-z transform. Group-level statistical analysis was performed using the mixed-effects modelling in FSL FEAT's FLAME 1, including age, sex, and the number of censored high motion volumes. The number of censored volumes was closely related to framewise displacement ($r=0.58$, $p=0.00001$), but we used it to account more specifically for the slightly less stable correlations that might be expected in participants with reduced datasets. Voxel-wise thresholding was set at $z > 2.3$, and cluster correction was set at $p < 0.05$ to correct for multiple comparisons. Relationships between connectivity between the seed regions and the rest of the brain, and language scores (Speeded

Naming and Phonological Processing) were tested using linear regression, controlling for age, sex, and the number of censored high motion volumes. Functional connectivity maps were generated in AFNI using 3dfim+ (Cox, 1996). Coordinates of the results were transformed back to adult MNI space in FSL img2imgcoord for reporting.

As a follow-up analysis to determine the specificity of the results, we conducted similar analyses examining relationships between functional connectivity from the seed regions and WPPSI-IV Full Scale IQ (FSIQ) scores.

2.6 Data availability

Neuroimaging data and raw and age-standardized language scores are available through the Open Science Framework as part of the Calgary Preschool MRI Dataset (<http://doi.org/10.17605/OSF.IO/AXZ5R>).

3 RESULTS

3.1 Language assessments

Phonological Processing Scaled Scores for the children ≥ 3 years ($n=46$) ranged from 6-16 ($M= 11.33 \pm 2.65$). Speeded Naming Combined Scaled Scores for children ≥ 3 years ($n=42$) ranged from 5-19 ($M= 12.40 \pm 2.96$). The standardized age-regressed residual values for Phonological Processing used in the analysis ranged from $-7.07 - 5.46$ (0 ± 3.19). The standardized age-regressed factor used for Speeded Naming in the analysis ranged from $-1.59 - 1.63$ (0 ± 0.71). These scores were not significantly correlated with each other ($r=0.08$, $p=0.60$),

and neither was significantly related to age or sex (Phonological Processing and sex: $r=-0.03$, $p=0.86$; Speeded Naming and sex: $r=0.20$, $p=0.19$; both scores with age: $r=0.00$, $p=0.99$).

WPPSI-IV FSIQ scores were available for 41 participants and ranged from 80-131 (110 ± 12). FSIQ was not significantly correlated with either pre-reading measure: FSIQ-Phonological Processing: $r=0.09$, $p=0.57$; FSIQ-Speeded Naming: $r=0.21$, $p=0.19$. The population mean score is 100 ± 15 . BASC-2 Internalizing T-scores ranged from 32-64 (47 ± 8). Higher BASC-2 scores indicate worse behavior, and T-scores ≥ 70 represent clinically-significant levels.

3.2 Functional connectivity patterns

Group average maps of functional connectivity to the left and right seed regions are shown in Figure 2. The angular gyrus seeds demonstrated positive connectivity with frontal lobes and the middle/inferior temporal gyrus, and negative connectivity to occipital lobes, superior temporal gyrus, inferior medial-frontal and sensorimotor cortex. The superior temporal gyrus had positive connectivity with neighboring regions, extending through middle temporal gyrus and superiorly into the medial parietal lobe and the precentral and postcentral gyrus. The superior temporal gyrus had negative connectivity with the bilateral frontal pole, precuneus and the occipital cortex. The inferior frontal gyrus (pars triangularis) had positive connectivity with the temporal-parietal and the middle/inferior frontal and temporal areas, but negative connectivity with areas of the inferior temporal, superior central parietal, and the lateral/middle occipital cortex. These patterns are broadly consistent with patterns observed in previous studies in adults (Ding et al., 2016; Tanaka and Kirino, 2019; Tomasi and Volkow, 2012) and sleeping children aged 3-5 years (Xiao et al., 2016a), though with slightly more extensive patterns of connectivity

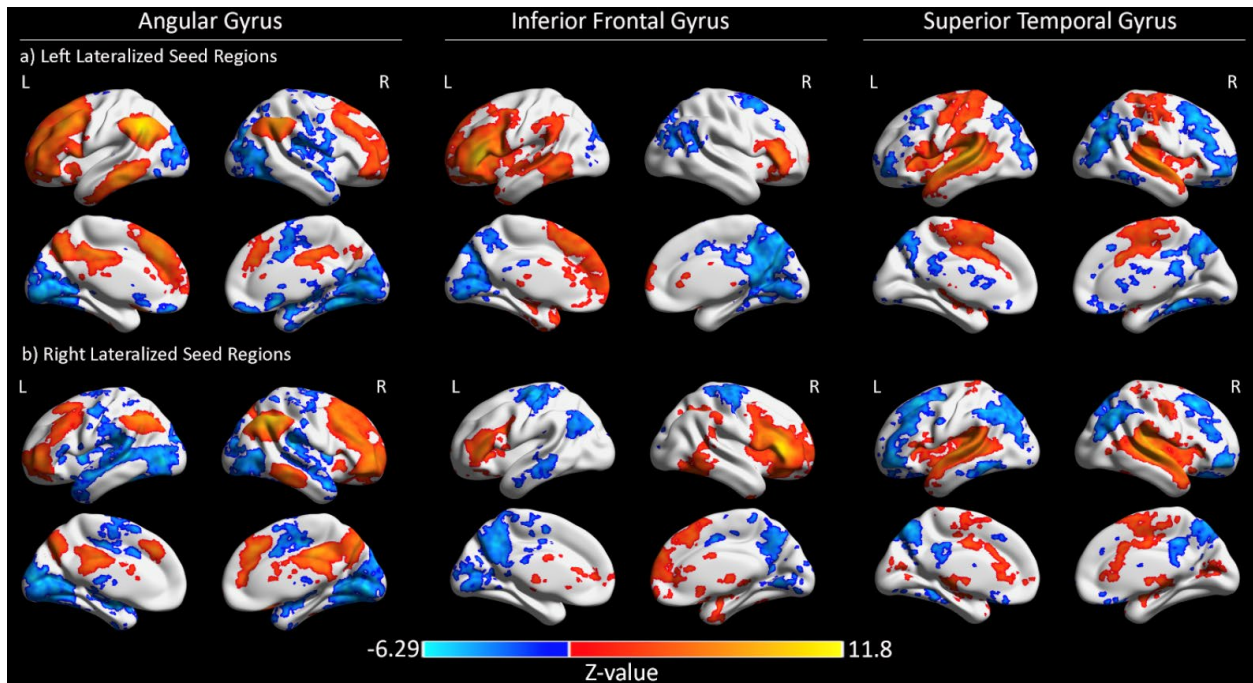


Figure 2. Group average connectivity maps from each of the seed regions of interest. Each seed region showed strong positive functional connectivity with adjacent areas and the contralateral region. The angular gyrus and inferior frontal gyrus show connectivity with each other in both hemispheres. The superior temporal gyrus shows strong connectivity with sensorimotor regions. For all three seed regions, negative connectivity to occipital regions was observed.

3.3 Connectivity and Phonological Processing

Phonological Processing scores were positively correlated with functional connectivity between the left angular gyrus and the right precentral and postcentral gyri. Phonological Processing scores were also positively correlated with functional connectivity between the right angular gyrus and the right superior temporal and precentral gyri (Figure 3; Table 2).

Phonological Processing scores were significantly positively associated with connectivity between the left superior temporal gyrus and the bilateral medial frontal gyrus.

Negative relationships were noted between Phonological Processing and connectivity between the (1) the left angular gyrus and right superior temporal gyrus, (2) the right pars triangularis and bilateral medial frontal gyrus, (3), the left superior temporal gyrus and left middle occipital gyrus, and (4) the right superior temporal gyrus and the right angular and middle temporal gyri (Table 2, Figure 3).

Table 2. Functional connectivity associated with Phonological Processing. Connectivity with the left and right angular gyri was associated with Phonological Processing; location of significant correlations is shown.

Seed	Connectivity Region	Number of Voxels	Cluster p-value	Z-Max	MNI coordinates [x, y, z]
Positive Relationships					
Left angular gyrus	Right pre/postcentral gyrus	2232	0.03	4.40	30, -41, 55
Right angular gyrus	Right superior temporal gyrus	766	0.03	4.44	51, -48, 22
	Right precentral gyrus	705	0.04	4.49	38, -11, 65
Left superior temporal gyrus	Bilateral medial frontal gyrus	661	0.02	3.97	14, 45, -11
Negative Relationships					

Left angular gyrus	Right superior temporal gyrus	1298	7.24E-04	-4.16	-62, -37, -2
Right pars triangularis	Bilateral medial frontal gyrus	780	0.02	-3.92	13, 35, 17
Left superior temporal gyrus	Left middle occipital gyrus	884	2.27E-03	-4.22	-39, -80, 10
Right superior temporal gyrus	Right angular gyrus	868	6.12E-03	-4.31	29, -45, 39
	Right middle/superior temporal gyrus	650	0.04	-4.20	45, -52, 23

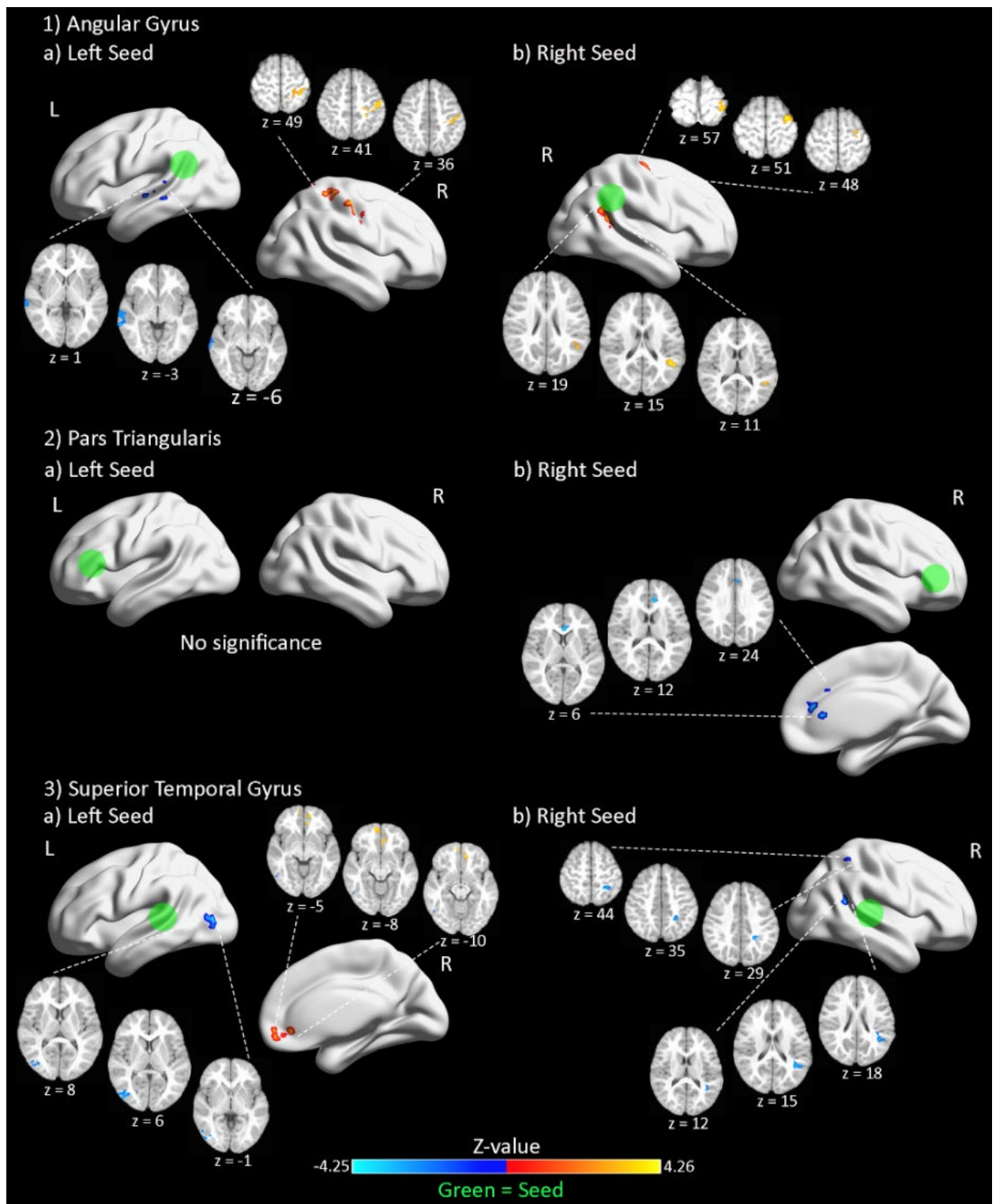


Figure 3. Correlations between Phonological Processing scores and functional connectivity.

Phonological Processing scores were correlated with connectivity between the angular gyrus (1a,

b), pars triangularis (2a, b), and superior temporal gyrus (3a, b) and other brain areas. Positive correlations are shown in red-yellow; negative correlations are shown in blue.

3.4 Connectivity and Speeded Naming

Speeded Naming scores were positively correlated with functional connectivity between the left pars triangularis and three clusters in the right superior temporal gyrus, left middle occipital gyrus, and the left insula. Connectivity between the right pars triangularis and the left precentral gyrus, as well as between the right pars triangularis and the bilateral thalamus were also positively correlated with Speeded Naming. Speeded Naming scores were also positively correlated with connectivity between the left superior temporal gyrus and the right cerebellum, and between the right superior temporal gyrus and the left angular gyrus. Speeded Naming scores were negatively correlated with connectivity between (1) the right angular gyrus and left inferior frontal and right superior occipital gyri, (2) the right pars triangularis and the left middle frontal gyrus, and (3) right superior temporal gyrus and the bilateral precuneus (Figure 4; Table 3).

Table 3. Functional connectivity associated with Speeded Naming. Location of significant correlations between Speeded Naming and functional connectivity are shown. There were no significant relationships found for functional connectivity with seeds in the left superior temporal gyrus or left angular gyrus. Note that the negative relationships below reflect stronger negative functional connectivity associated with better language scores.

Seed	Connectivity Region	Number of Voxels	Cluster p-value	Z-Max	MNI coordinates [x, y, z]
Positive Relationships					
Left pars triangularis	Right superior temporal gyrus	1669	6.29E-05	4.28	60, -29, 29
	Left middle occipital gyrus	1647	7.20E-05	3.73	-48, -53, 2
	Left insula	1167	1.66E-03	4.09	-24, 17, 9
Right pars triangularis	Left precentral gyrus	1067	5.98E-04	4.13	-38, -1, 47
	Bilateral thalamus	868	3.35E-03	4.04	-2, -11, 8
Left superior temporal gyrus	Right lobule VIII of cerebellum	545	0.05	3.85	35, -54, -52
Right superior temporal gyrus	Left angular gyrus	662	0.03	4.07	-64, -30, 39
Negative Relationships					
Right angular gyrus	Left inferior frontal gyrus	2128	7.97E-04	-3.90	-24, 46, -18
	Right superior occipital gyrus	762	7.39E-03	-4.42	18, -85, 26
Right pars triangularis	Left middle frontal gyrus	1199	0.04	-3.97	-20, 41, 23

Right superior temporal gyrus	Bilateral precuneus	1585	1.64E-05	-3.68	4, -52, 34
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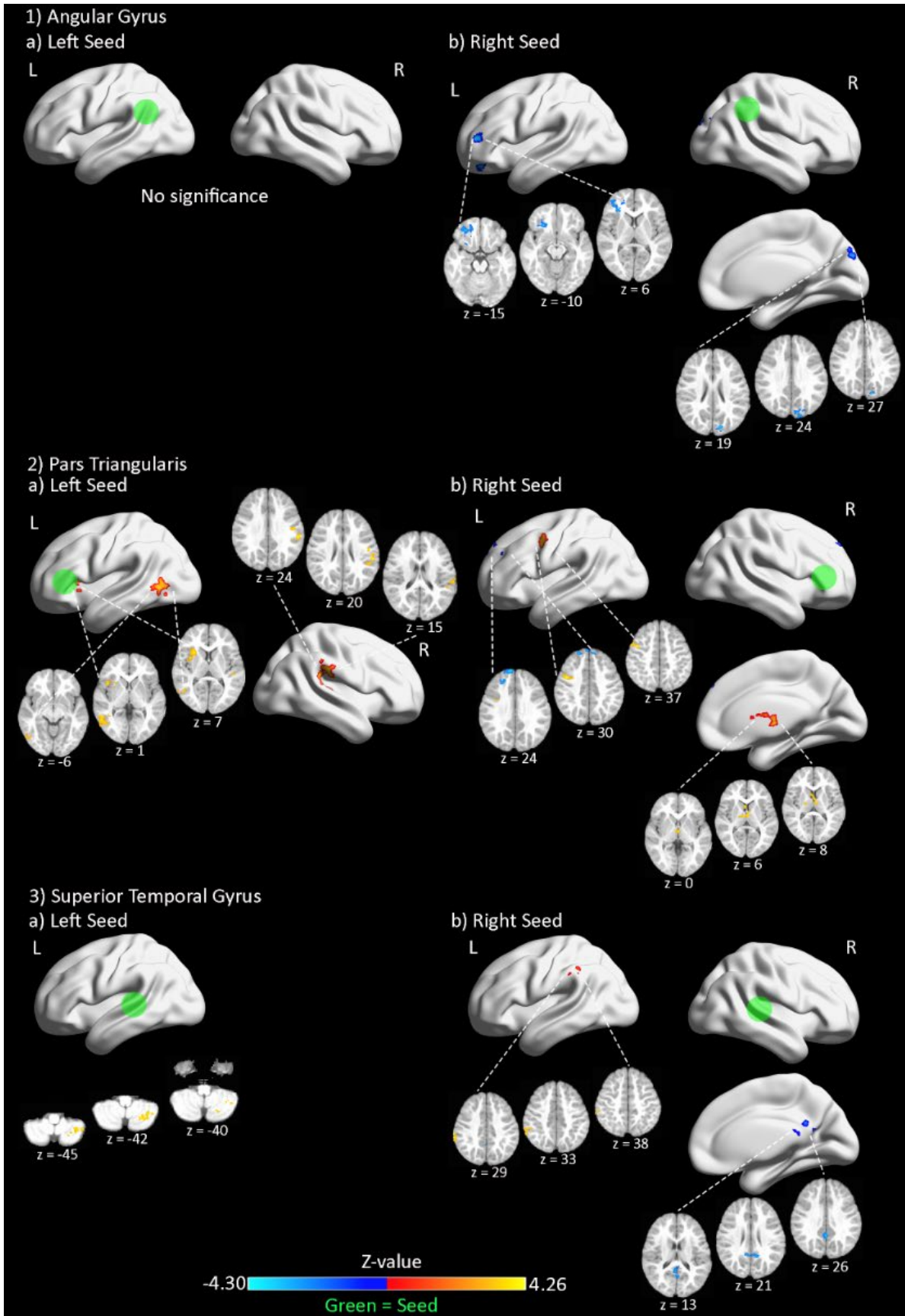


Figure 4. Correlations between Speeded Naming Scores and functional connectivity. (A)

Speeded Naming scores were correlated with connectivity between the angular gyrus (1a, b), pars triangularis (2a, b), and superior temporal gyrus (3a, b) and other brain areas. Positive correlations are shown in red-yellow; negative correlations are shown in blue.

3.5 Connectivity and FSIQ

Significant relationships between connectivity from seed regions and FSIQ are shown in Figure 5. Of particular relevance for this study are regions that also showed significant relationships with pre-reading scores.

None of the areas with relationships between connectivity with the left or right angular gyrus and Phonological Processing has significant relationships with FSIQ. Two small sections of clusters with negative relationships between their connectivity to the right angular gyrus and Speeded Naming also had negative relationships with FSIQ; these were located in the left frontal gyrus (pars orbitalis) and the right superior occipital gyrus. Connectivity between the right pars triangularis and the right medial frontal gyrus was negatively related to both Phonological Processing and FSIQ.

Subsections of most areas with relationships between Speeded Naming and connectivity with the bilateral pars triangularis showed relationships with FSIQ; the only exception was connectivity between the left pars triangularis and the left insula, which had positive relationships with Speeded Naming but not FSIQ.

Most areas that had relationships between connectivity with the superior temporal gyrus and Phonological Processing did not have significant relationships with FSIQ. Connectivity between the left superior temporal gyrus and cerebellum was positively related to Speeded Naming; it was also significantly positively related to FSIQ. Areas where connectivity with the right superior temporal gyrus was related to Speeded Naming were not significantly related to FSIQ.

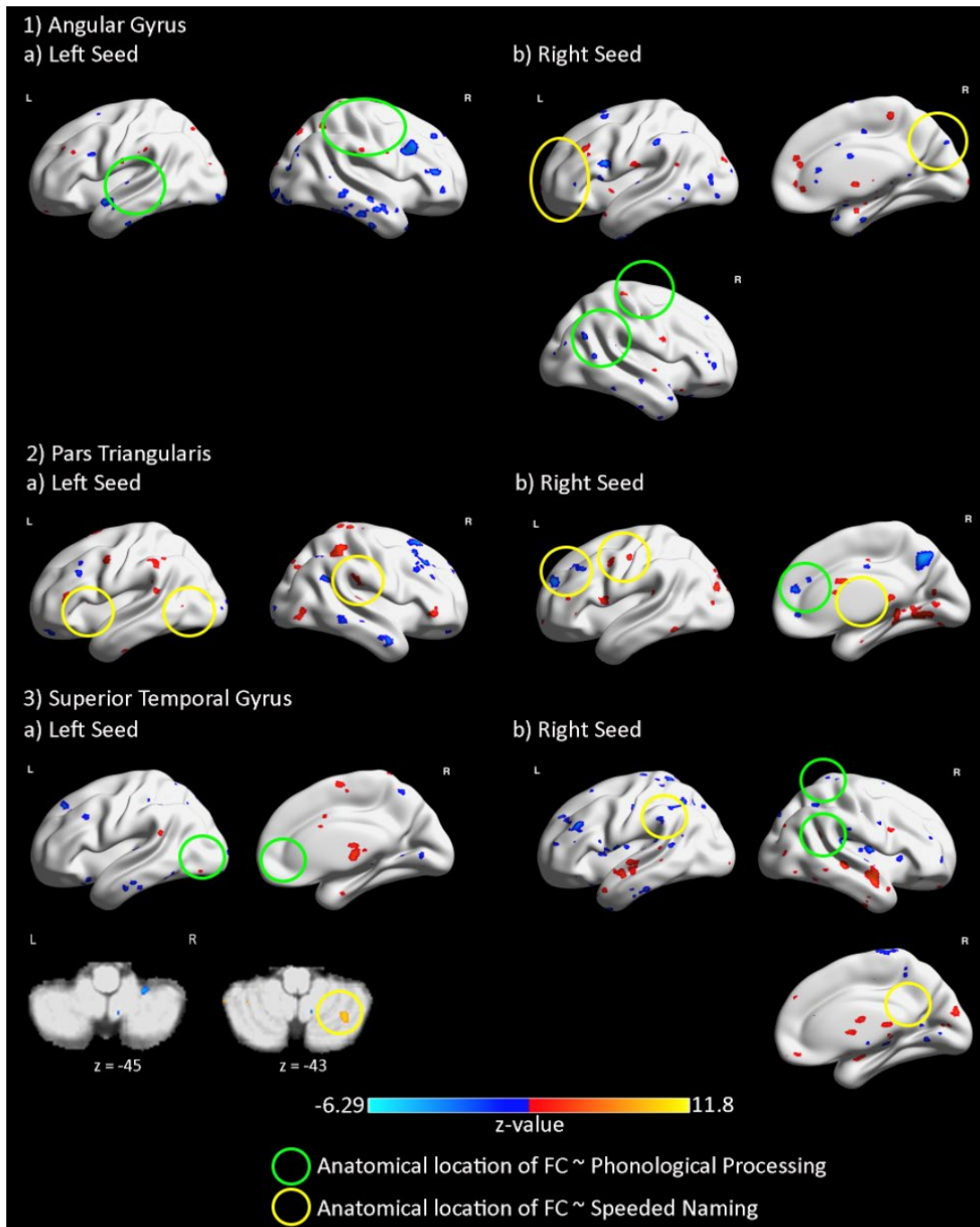


Figure 5: Relationships between connectivity and FSIQ. Significant relationships between FSIQ and connectivity between seed regions and other brain areas are shown. For comparison purposes, areas where connectivity with a seed region was significantly associated with Phonological Processing are circled in green; areas where connectivity with a seed region was

associated with Speeded Naming are circled in yellow.

(1) Areas where connectivity with the angular gyrus was associated with FSIQ. Areas where connectivity was associated with Phonological Processing (green circles) did not overlap with areas associated with FSIQ. Connectivity between the right angular gyrus and small areas in the left frontal gyrus (pars orbitalis) and right superior occipital gyrus were associated with Speeded Naming and FSIQ.

(2) Areas where connectivity with the pars triangularis was associated with FSIQ. Connectivity between the right pars triangularis the right medial frontal lobe showed relationships with both Phonological Processing and FSIQ scores. Most areas where connectivity with the pars triangularis was associated with Speeded Naming also showed relationships between connectivity and FSIQ, with a notable exception in the insula.

(3) Areas where connectivity with the superior temporal gyrus was associated with FSIQ. Note the lack of overlap between areas where connectivity was associated with Phonological Processing and FSIQ. Connectivity between the left superior temporal gyrus and the cerebellum was positively associated with Speeded Naming and FSIQ.

4 DISCUSSION

Here, we demonstrate stronger functional connectivity between seed regions involved in reading (inferior frontal gyrus, angular gyrus, and superior temporal gyrus) and motor areas in young children (2-5 years old) with better pre-reading language skills. Furthermore, we show that children with higher language scores have stronger negative connectivity between these seed areas and both visual areas and regions of the default mode network. These results suggest early

strengthening of connectivity between reading and motor areas in young children and dissociation from the default mode network occurs before formal reading instruction and may lay the foundation for future reading abilities.

The angular gyrus and superior temporal gyrus are associated with semantic processing in adults, while the inferior frontal gyrus tends to be more associated with speech production; all three regions are reliably activated by phonological tasks (Graves et al., 2010; Price, 2012; Schlaggar and McCandliss, 2007; Seghier et al., 2010). Here, we found stronger connectivity between the right pars triangularis and premotor areas was positively related to Speeded Naming. Better Phonological Processing scores were also related to connectivity with motor and premotor regions, specifically connectivity with the bilateral angular gyri. Motor and premotor areas are involved in articulatory control and auditory-motor integration (Friederici, 2011; Hickok and Poeppel, 2004), including processing of speech perception (Pulvermuller et al., 2006). A meta-analysis of task fMRI studies showed reliable activation of the precentral gyrus during reading in children (Houde et al., 2010). A previous rs-fMRI study found stronger connectivity among motor regions was associated with better reading competence in both children (8-14 years) and adults (Koyama et al., 2011). The stronger connectivity between the angular gyri and motor/premotor areas was not related to FSIQ, and thus appears to be specific to pre-reading language skills. On the other hand, connectivity between the right pars triangularis and the left precentral gyrus was related to FSIQ, and may be more generally related to cognitive abilities. Thus, our results support and extend previous findings to show that motor and premotor areas demonstrate stronger connectivity with temporal-parietal areas in children with better pre-reading skills.

Phonological Processing and/or Speeded Naming were correlated with functional connectivity between seed regions. Specifically, Phonological Processing was positively related to connectivity between the right angular gyrus and the right superior temporal gyrus, and Speeded Naming was positively related to connectivity between the right superior temporal gyrus and the left pars triangularis and between the right superior temporal gyrus and left angular gyrus. These results appear to be specific to pre-reading skills, as they did not overlap with regions showing connectivity associated with FSIQ. These areas are part of the classic reading network (Houde et al., 2010; Price, 2012), and task-based fMRI studies of reading have shown hypoactivation of similar areas in older children and adults with dyslexia (Cao et al., 2006; Hoeft et al., 2006; Hoeft et al., 2007; Richlan et al., 2009). Reduced activation has also been noted in right temporal-parietal and occipital areas of children with dyslexia during reading tasks (Hoeft et al., 2006; Shaywitz et al., 2002). Even before reading begins, reduced activation during a sound-matching task was observed in bilateral occipital-temporal areas in children (age 5.5 years) with a family history of dyslexia versus those without (Raschle et al., 2012). Using rs-fMRI in young children, gains in sentence comprehension ability from age 5-6 years were associated with strengthening functional connectivity from the left superior temporal gyrus to bilateral inferior frontal areas (Xiao et al., 2016b). Thus, the stronger connectivity among these classical reading areas seen here may reflect faster learning processes occurring in the children with better language abilities.

Connectivity between the left pars triangularis and the left insula, part of the salience network, was positively related to Speeded Naming scores. The insula is known to be associated with language, with the left insula being activated during both expressive and receptive language tasks in adults (Oh et al., 2014); the left insula is also involved in articulatory control in children

(Chang et al., 2018), a skill critical to accurate and rapid naming. Notably, insula-pars triangularis connectivity was not associated with FSIQ or Phonological Processing, suggesting that our results are related specifically to Speeded Naming in young children, rather than more general cognitive or language abilities. Children with better Speeded Naming scores also had stronger connectivity between the right pars triangularis and the thalamus bilaterally. The thalamus is a sensory relay station, has been previously implicated in syntactic and semantic language in adults (Wahl et al., 2008), though its role in language remains somewhat controversial (Klostermann et al., 2013). Previous studies have suggested that the thalamus is more heavily involved in language processing in children than in adults (Houde et al., 2010; Koyama et al., 2011). Furthermore, a longitudinal fMRI study of children aged 5-11 years found reduced involvement of the left thalamus during word generation as children got older (Szaflarski et al., 2006). Thus, our findings of thalamus relationships in even younger, pre-reading children, support the idea of thalamus involvement in language skills at early ages.

Pre-reading abilities were negatively associated with connectivity to visual and auditory regions. Specifically, Phonological Processing was negatively associated with connectivity between the left angular gyrus and left auditory cortex, and connectivity between the superior temporal gyrus and left occipital areas involved in vision. Connectivity between the right angular gyrus and right posterior occipital areas was negatively correlated with Speeded Naming. Areas that showed relationships with Phonological Processing were not associated with FSIQ, suggesting they are specific to phonological skills. On the other hand, connectivity between the right angular gyrus and the right posterior occipital gyrus was associated with FSIQ, suggesting it may represent a more general relationship. Both auditory and visual areas have been consistently highlighted as important for skilled reading, and are active during fMRI studies of

reading (Price, 2012). However, as the children in this study had not received reading instruction, and were not yet skilled readers, it may be that the functional connections between our reading-related seed regions and visual and auditory areas are not yet established. Indeed, visual deficits are commonly seen in older children and adults with dyslexia, but are not apparent in young children and appear to be a consequence of poor reading that appears later (Olulade et al., 2013). Longitudinal studies including children prior to and after they learn to read may be able to better elucidate the nature of connectivity between reading and visual areas, as it pertains to reading-related skills.

Connectivity between the right pars triangularis and the medial frontal region was negatively correlated with Phonological Processing, while connectivity between the right superior temporal gyrus and the posterior cingulate/precuneus was negatively related to Speeded Naming. Both areas are involved part of the default mode network, a network that tends to be most active during rest (Raichle, 2015). Our findings show a negative correlation, suggesting that activation of the reading areas used here as seed regions is related to deactivation of default mode areas. Previous work in adults has shown that the default mode and language networks are distinct from one another and are activated by separate tasks (Mineroff et al., 2018). The results seen here suggest not that the default mode network is unrelated to pre-reading skills, but in fact that more negative connectivity to default mode areas is beneficial for language skills. This negative relationship suggests that the more a child can disengage the default mode network, the better their pre-reading abilities. Previous studies in adults have shown that connectivity between reading areas (superior temporal gyrus, fusiform gyrus) and the default mode network is negatively correlated with reading ability (Zhang et al., 2014). Interestingly, one previous study showed negative associations between the fusiform gyrus and default mode areas in adults but

did not find similar relationships in children aged 8-14 years (Koyama et al., 2011). Our results somewhat contrast these previous findings and suggest this negative relationship between reading and default mode areas may in fact be present in young children before formal reading instruction begins. Given that substantial brain development occurs between early childhood and adulthood in these brain networks for both structure and function (Fair et al., 2007; Lebel et al., 2017; Long et al., 2017; Reynolds et al., 2019b), there may be complex relationships that vary with age. Future studies with wider age ranges will be able to better explore the developmental processes that may influence relationships between these networks.

Multiple areas of the right hemisphere had connectivity that was associated with pre-reading abilities, and results were broadly consistent in both hemispheres (stronger connectivity to motor areas, negative connectivity to default mode areas and sensory areas). Reading is predominantly left-lateralized in adults (Schlaggar and McCandliss, 2007), but less so in children. Lateralization of language function in the brain tends to increase during early childhood (Reynolds et al., 2019a; Xiao et al., 2016a; Yamada et al., 2011), and remain relatively stable after age 6 (Weiss-Croft and Baldeweg, 2015), with only slight increases in lateralization of frontal areas during later childhood (Szaflarski et al., 2006). Children with dyslexia show more right hemisphere connectivity than controls (Finn et al., 2014), and increases in leftward lateralization of reading during adolescence is strongly linked to performance (Weiss-Croft and Baldeweg, 2015). Thus, our results support the idea that leftward lateralization develops in parallel with reading skills, and that young pre-reading children have a much more symmetric arrangement of brain function.

Development of the brain network supporting reading occurs throughout childhood. Rs-fMRI studies have shown increases in long-range connectivity in the language network both

during early childhood (2-6 years) and between later childhood and adulthood (Fair et al., 2007; Long et al., 2017). Furthermore, task-based fMRI studies in children show that activation in inferior frontal and sensorimotor regions increases with age and with gains in language abilities (Weiss-Croft and Baldeweg, 2015), while activation in the default mode network decreases as language abilities improve (Weiss-Croft and Baldeweg, 2015; Yu et al., 2018). Thus, our results showing that children with better pre-reading language abilities tend to have stronger connectivity between seed regions and motor areas, and negative correlations between seeds and areas of the default mode network suggest that these children show a more mature pattern of brain connectivity than those with weaker pre-reading skills.

Phonological processing and speeded naming in early childhood are strong and independent predictors of later reading abilities (Lonigan et al., 2009; Snowling and Hulme, 2011). Scores on both assessments were positively related to connectivity among language areas and between language areas and the precentral gyrus, and both were negatively related to connectivity to default mode areas. Notable differences include thalamus and cerebellum connectivity, which were related to Speeded Naming, but not Phonological Processing scores. To further assess specificity, we conducted similar analyses on the subset of 41 participants who had FSIQ scores from the WPPSI-IV and BASC-2 Internalizing T-Scores. Most results related to connectivity with the angular gyrus or superior temporal gyrus were unique to pre-reading scores and not also significantly related to FSIQ or BASC-2 scores. On the other hand, most areas whose connectivity with the pars triangularis was related to Phonological Processing or Speeded Naming were also related to FSIQ. Many studies have established the importance of the inferior frontal gyrus in reading and language (Pugh et al., 2000; Schlaggar and McCandliss, 2007; Shaywitz and Shaywitz, 2003), and its connectivity is related to pre-reading language abilities in

the sample of young children here. However, the overlapping connectivity that is related to FSIQ suggests these relationships are not specific to pre-reading language skills at this young age and are instead more broadly related to cognitive abilities.

The fMRI data used here were collected while children were watching videos. This more naturalistic condition can reduce head motion and increase compliance compared to the traditional rest conditions (Vanderwal et al., 2015), which enabled us to collect data even in children as young as 2 years. Network patterns are generally similar between rest and passive viewing (Bray et al., 2015; Vanderwal et al., 2015); however, in this study children were permitted to choose their movie, and movie choice was not recorded. Therefore, differences in linguistic content, visual stimuli, or social information of the movies could not be controlled and may confound our results. This may be a particularly important limitation given that some areas in which connectivity was associated with language abilities, in particular the superior temporal gyrus, are also associated with social cognition (Blakemore, 2012). However, while different social stimuli in the movies may confound the results seen here, the differences are unlikely to be systematic and all movies included both dialogue and music. Regardless, future studies using consistent viewing or rest conditions, or a systematic analysis of how varying language and social content influences functional connectivity, are necessary to further understand pre-reading and brain function. Furthermore, the scan time used here was relatively short, which may limit the stability of the functional connectivity estimates.

In conclusion, we found that stronger functional connectivity between reading areas and motor regions was associated with better pre-reading language skills in young children who had not yet begun formal reading instruction. Furthermore, stronger negative connectivity between reading areas and the default mode network as well as visual areas was associated with better

pre-reading language skills, suggesting increased negative connections of these brain networks. Our results extend previous findings in school-age children who had already begun reading and suggest that altered functional connectivity associated with later reading skills may be apparent even in young children who have not yet had formal reading instruction. Our findings highlight the enormous potential language researchers and professionals may have to predict future reading impairments and develop more targeted early interventions that result in improved reading outcomes for children at risk for dyslexia.

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