Individual Differences in Crossmodal Brain Activity Predict Arcuate Fasciculus Connectivity in Developing Readers

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Abstract

■ Crossmodal integration of auditory and visual information, such as phonemes and graphemes, is a critical skill for fluent reading. Previous work has demonstrated that white matter connectivity along the arcuate fasciculus (AF) is predicted by reading skill and that crossmodal processing particularly activates the posterior STS (pSTS). However, the relationship between this crossmodal activation and white matter integrity has not been previously reported. We investigated the interrelationship of crossmodal integration, both in terms of behavioral performance and pSTS activity, with AF tract coherence using a rhyme judgment task in a group of 47 children with a range of reading abilities. We demonstrate that both response accuracy and pSTS activity for crossmodal (auditory–visual) rhyme judgments was predictive of fractional anisotropy along the left AF. Unimodal (auditory-only or visual-only) pSTS activity was not significantly related to AF connectivity. Furthermore, activity in other reading-related ROIs did not show the same AV-only AF coherence relationship, and AV pSTS activity was not related to connectivity along other language-related tracts. This study is the first to directly show that crossmodal brain activity is specifically related to connectivity in the AF, supporting its role in phoneme–grapheme integration ability. More generally, this study helps to define an interdependent neural network for reading-related integration. ■

INTRODUCTION

In its most basic form, reading requires the ability to fluently integrate phonological and orthographic information, or letter sounds and shapes, to form heteromodal word representations. A complex network of brain regions supports this integration, including areas responsive to input in each modality and regions involved in crossmodal processing. Although some of the white- and gray-matter brain systems supporting this integration have previously been separately described, little work has so far examined the relationships between behavioral integration ability, functional activity, and structural connectivity. We here aim to determine the relationships between crossmodal task performance and activity in the posterior STS (pSTS) during this task with arcuate fasciculus (AF) connectivity in a sample of typically developing children with a range of reading abilities.

Letter–sound integration ability has been repeatedly demonstrated to be one of the most important skills for reading success, potentially because it reflects an individual's ability to match crossmodal phonemic and graphemic information and form a stable whole. Early integration ability is a significant predictor of later reading ability: Kindergarten letter–name (Blomert & Willems, 2010; Evans, Bell, Shaw, Moretti, & Page, 2006; Treiman,

2006; Foulin, 2005) and first grade letter–sound (Ellefson, Treiman, & Kessler, 2009) knowledge are important precursors for and the strongest predictors of future reading. Indeed, Blomert and Willems (2010) demonstrated that kindergarten phonological awareness was not predictive of first-grade reading but that response to letter–sound integration training was. This phoneme–grapheme binding becomes automatic for most readers by second grade, after sufficient practice and experience (Blomert, 2011; Froyen, Willems, & Blomert, 2011), resulting in a stable integrated "graphoneme" object representation (Whitney & Cornelissen, 2005). However, for some individuals, this process remains difficult, reflected in lower reading ability. Poorer readers have been demonstrated to be able to learn phoneme–grapheme pairings similarly to typical readers but do not automatically draw on this information even after years of instruction and practice (Froyen et al., 2011, p. 644; Mittag, Thesleff, Laasonen, & Kujala, 2013). Thus, this integration of auditory phonological and visual orthographic linguistic information is critical for reading acquisition, and individual differences in this skill may directly impact reading ability.

The neural systems supporting this integration have been investigated using fMRI. Unimodal processing of letters and words may draw most heavily on sensory-specific cortices. Auditory phonological processing evokes activity in the left Heschl's gyrus and the anterior to middle superior temporal gyrus (Hickok & Poeppel, 2007; Liebenthal,

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Binder, Spitzer, Possing, & Medler, 2005; van Atteveldt, Formisano, Goebel, & Blomert, 2004; Caplan, Gow, & Makris, 1995). Visual orthographic processing of letters and words has been localized to the left posterior to mid-fusiform gyrus (Glezer, Jiang, & Riesenhuber, 2009; Dehaene, Cohen, Sigman, & Vinckier, 2005; James, James, Jobard, Wong, & Gauthier, 2005; McCandliss, Cohen, & Dehaene, 2003; Cohen et al., 2002; Dehaene, Le Clec'H, Poline, Le Bihan, & Cohen, 2002). The integration of phonemes and graphemes has been shown to involve both activity in unimodal regions as well as specific activity in heteromodal parts of the left pSTS. The left pSTS has been noted to be particularly sensitive to crossmodal processing across multiple types of stimuli. Calvert (2001) has shown that activity in the left pSTS is increased for auditory–visual speech processing (i.e., lip movements) relative to either unimodal condition, especially when the two modalities demonstrate congruent (matching) information (see Calvert, Campbell, & Brammer, 2000; Calvert et al., 1999). Others have demonstrated increased activity for pictures of complex objects and auditory samples of their sounds (e.g., a drill-*buzz*, Beauchamp, Lee, Argall, & Martin, 2004; or musical instruments, Werner & Noppeney, 2010a, 2010b), indicating that this region may also host an integrated representation of the object. Most relevant to the current study, Blau and van Atteveldt have demonstrated that activity in the left pSTS is increased for passive simultaneous bimodal letter–sound presentations in both typically developing adults and children, especially for congruent trials (Blau et al., 2010; Blau, van Atteveldt, Ekkebus, Goebel, & Blomert, 2009; van Atteveldt, Roebroeck, & Goebel, 2009; van Atteveldt et al., 2004). Active integration tasks have also found a similar left pSTS activity increase for linguistic auditory–visual integration, as in the case of learning new phonograms (Callan, Callan, & Masaki, 2005), character–speech matching judgments (Hashimoto & Sakai, 2004), and letter identification (Raij, Uutela, & Hari, 2000; but see Kast, Bezzola, Jancke, & Meyer, 2011, for right pSTS group differences). In summary, left pSTS activity plays a crucial role in crossmodal integration processing, including for aural and visual language.

Other regions are also involved in multimodal integration. Most notably, the inferior frontal gyrus has been demonstrated to show increased activity for stimuli with incongruent auditory–visual information (van Atteveldt, Formisano, Goebel, & Blomert, 2007; Booth et al., 2002) and decreased activity for congruent stimuli (Werner & Noppeney, 2010b; Calvert et al., 2000), the reverse of the pattern seen in the pSTS. Importantly, the inferior frontal gyrus seems to be involved only for tasks requiring active auditory–visual integration and not for passive perceptual tasks (such as van Atteveldt et al., 2004) and perhaps not even for active tasks using single-letter stimuli instead of words (Hein et al., 2007). Hagoort, Baggio, and Willem (2009) have proposed that, whereas the pSTS is involved in the retrieval of integrated object representations from memory, the inferior frontal gyrus may be particularly

important in the construction or formation of new multi-modal representations (i.e., "unification"). As such, the increased activity noted for conflicting trials may reflect an attempt to determine whether a new representation for this pairing should be created (see also Blomert, 2011). The inferior frontal gyrus may thus be important for crossmodal processing, but at a later stage than the pSTS. Unimodal cortices may also show some multimodal sensitivity. Calvert et al. (2000) demonstrated some potentially superadditive auditory and visual cortex responses to congruent crossmodal audiovisual speech stimuli, although no subadditive suppression was found for incongruent trials. However, these responses were weaker than those from the pSTS, indicating that the pSTS is the primary site for heteromodal integration.

More recently, investigations of the white matter connecting these reading-related brain regions have been undertaken using diffusion tensor imaging (DTI). DTI measures the degree and directionality of the diffusion of water within brain voxels. White matter voxels show a high degree of diffusivity parallel to the direction of the tract, as water can more easily diffuse along than perpendicular to myelinated axons. Fractional anisotropy (FA) values reflect the degree of this directional diffusivity. Higher FA values are taken to reflect increased integrity of and structural coherence in a tract, which may indicate greater connectivity between the endpoint brain regions and thus more efficient processing of information passing along the tract.

Although less work has examined the brain structure as compared with function supporting reading, the literature has consistently noted connectivity along the left AF to be related to reading skill. The AF arcs from the temporal lobe to the inferior frontal gyrus. This tract tends to be left lateralized, with most adults demonstrating greater FA and increased tractography streamlines in the left hemisphere (Lebel & Beaulieu, 2009; Vernooij et al., 2007; Catani, Jones, & Ffytche, 2005; but see Wahl et al., 2010). The AF may be synonymous with (Friederici, 2009) or in part parallel to (Makris et al., 2005) the superior longitudinal fasciculus (but see Duffau, 2008). Among other functions, connectivity along the left AF may particularly support the integrative processing necessary for reading (Vandermosten, Boets, Poelmans, et al., 2012; Catani et al., 2005). From a functional–anatomical perspective, the AF thus connects the temporal regions, especially important for auditory processing and usage of crossmodal information, with the inferior frontal region particularly involved in the formation of integrated representations for new or unfamiliar items (see Blomert, 2011; Hagoort et al., 2009).

Individual differences in reading ability have been demonstrated to be related to AF connectivity. Scores on tests of single-word reading consistently correlate with FA in the AF, including word (Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012; Beaulieu et al., 2005) and pseudoword reading (Yeatman et al., 2012), reading fluency (Nagy, Westerberg, & Klingberg, 2004), and lexical decision speed

(Gold, Powell, Xuan, Jiang, & Hardy, 2007). In addition, phonological skills such as elision have been shown to uniquely explain FA in the AF even beyond word identification or spelling verification abilities (Vandermosten, Boets, Poelmans, et al., 2012; Yeatman et al., 2011). If reading requires connections between phonology and orthography (Blomert, 2011; Snowling, 1980) and the AF supports this integration, its integrity and coherence may directly impact reading ability.

Other work has also demonstrated significant relationships between reading ability and connectivity along other tracts, such as the left superior corona radiata (Rimrodt, Peterson, Denckla, Kaufmann, & Cutting, 2010; Odegard, Farris, Ring, McColl, & Black, 2009; Niogi & McCandliss, 2006), the left inferior fronto-occipital fasciculus (Vandermosten, Boets, Poelmans, et al., 2012; Odegard et al., 2009; Rollins et al., 2009; Richards et al., 2008; Steinbrink et al., 2008), and the splenium of the corpus callosum (Hasan et al., 2012; Odegard et al., 2009; Frye et al., 2008; Rumsey et al., 1996). However, the specific reading function supported by each of these tracts has not been detailed, making links between connectivity and specific behavioral abilities or task-specific brain activities more speculative.

Phonological–orthographic integration ability may be related to pSTS activity and AF tract coherence even beyond general population variation, as in the case of developmental dyslexia. Dyslexia is defined by specific difficulty in reading despite typical intelligence, motivation, and instruction (Shaywitz & Shaywitz, 2005; Lyon, Shaywitz, & Shaywitz, 2003) and is estimated to affect 5–10% of the population (Shaywitz, Shaywitz, Fletcher, & Escobar, 1990). Although a causal mechanism has not yet been determined, the most prominent theory posits that phonological deficits are the most likely candidate (see Shaywitz & Shaywitz, 2005; Vellutino, Fletcher, Snowling, & Scanlon, 2004; Ramus et al., 2003). Poorly specified phonological representations (Swan & Goswami, 1997) may lead to exaggerated difficulties learning and using phoneme–grapheme relationships (Brady & Shankweiler, 1991), which then in turn directly impact reading performance. For example, normal readers showed decreasing response times on a letter–speech sound identification task through elementary school, whereas readers with dyslexia did not improve after early grades, although task accuracies eventually did not differ between groups (Blomert, 2011). Dyslexic children may thus be able to learn the associations between letters and sounds, but these links may not become automatic or easily accessible. Between-group neural differences in reading-related integration have also been demonstrated. Participants with dyslexia show less activity relative to controls in the left pSTS across a wide variety of linguistic and reading-related tasks (Richlan, Kronbichler, & Wimmer, 2009; Shaywitz & Shaywitz, 2005; McCandliss & Noble, 2003; Shaywitz et al., 2002); furthermore, neither dyslexic adults nor children demonstrate crossmodal activity enhancement in the pSTS for audiovisual letter presenta-

tions (Blau et al., 2009, 2010). Participants with dyslexia also demonstrate decreased FA in the left AF, both for adults (Vandermosten, Boets, Poelmans, et al., 2012; Richards et al., 2008; Steinbrink et al., 2008; Klingberg et al., 2000) and children (Rimrodt et al., 2010; Carter et al., 2009; Keller & Just, 2009; Deutsch et al., 2005; see Vandermosten, Boets, Wouters, & Ghesquiere, 2012, for a recent review). As such, reading ability may thus be directly tied to crossmodal activity in the pSTS and connectivity along the AF.

The pSTS and the AF appear to be of particular importance for the automatic crossmodal integration of letters and sounds underlying successful fluent reading. Furthermore, individual differences in activity or tract connectivity may be directly related to reading ability, whether resulting in variability within typical populations or clinical deficits. However, the relationships between AF coherence and behavioral integration skill and between coherence and crossmodal activity in the pSTS have not been directly described. We here sought to investigate these relationships in a group of typically developing children with a range of reading abilities. We aimed to replicate the finding that word reading skill is related to left AF connectivity but also to examine the specificity of this relationship by investigating whether word reading ability is more strongly related to left AF FA than is phonological awareness ability. We further investigated whether behavioral performance on an experimental crossmodal integration task (i.e., audiovisual word rhyme judgment) is more strongly predictive of left AF FA than unimodal task performance (auditory-only or visual-only rhyme judgment). We also aimed to replicate the finding that crossmodal integration processing results in increased activity in the left pSTS as compared with unimodal processing. Importantly, we extend this work by directly examining the relationship of activity in this region to white matter coherence: We expected activation in the left pSTS for crossmodal task processing to be more strongly associated with FA along the left AF than activation for unimodal processing. Given our specific a priori hypotheses as to the involvement of the pSTS and AF, we used an ROI approach with several comparative ROIs to demonstrate the specificity of these relationships.

METHODS

Participants

Participants were 47 children (20 girls), aged 8–14 years (mean = 11.2 years) recruited from the Chicago metropolitan area. Parents of children were interviewed to ensure that children met the inclusion criteria of the study. Children were all native English speakers with normal hearing and normal or corrected-to-normal vision. All were right-handed, with no history of attention deficit hyperactivity disorder, psychiatric illness, or neurological disorder or damage, and were not taking medication affecting

CNS function. Informed consent was obtained from participants and their parents, and all procedures were approved by the institutional review board at Northwestern University.

Standardized Testing

Children first participated in a comprehensive standardized testing session to ensure that all participants were of at least average intelligence quotient (IQ) and reading ability. Tests included the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999), using two verbal (vocabulary, similarities) and two performance (block design, matrix reasoning) subtests; the Woodcock–Johnson III Tests of Achievement (Woodcock, McGrew, & Mather, 2001), including the word identification subtest; the Tests of Word Reading Efficiency (Torgesen, Wagner, & Raschotte, 1999), including the sight word efficiency subtest; and the Comprehensive Test of Phonological Processing (Wagner, Torgesen, & Rashotte, 1999), including the phonological awareness subtests. A real-word reading score was calculated from the average of the Woodcock–Johnson and Tests of Word Reading Efficiency subtest standardized scores. All children demonstrated full-scale IQ standardized scores between 89 and 145 and real-word reading standardized scores between 85 and 125 (see Table 1 for demographic and standardized test score information).

Experimental Task

During functional scanning, children participated in a rhyming task. Children were presented with two words sequentially and were asked to decide whether the pair of words rhymed or did not rhyme and to give a button-press response as quickly and accurately as possible. Each word was presented for 800 msec, followed by a 200-msec blank interval. Participants could respond at any point after the second stimulus presentation. A red fixation cross appeared on the screen for 2200, 2600, or 2800 msec after the second word, signaling the participant to respond if they had not already done so. This jittered interval allowed for better condition signal deconvolution. For each scanning session, stimuli were presented in one of three modality conditions. In the

Table 1. Demographic Information

	Mean (SD)	Range
Age, years; months	11;2 (1;7)	8;2–14;6
Single-word reading	102.8 (12)	85–127.5
Phonological awareness	105 (11)	76–124
Full-scale IQ	117 (16)	89–145

unimodal conditions, both words were presented in the auditory (AA) or visual (VV) modality. In the crossmodal condition, the first word was presented auditorily and the second was presented visually (AV). Previous investigations of crossmodal linguistic processing research (e.g., Froyen, Van Atteveldt, Bonte, & Blomert, 2008) similarly employed auditory then visual presentations, motivating the task design for that modality condition. In all cases, stimulus presentation, trial timing, and response recording were achieved using E-Prime presentation software (Psychological Software Tools, Pittsburgh, PA).

Twenty-four word pairs were presented in each of four lexical conditions that independently manipulated the orthographic and phonological similarity between words. The same word pairs were used in each presentation modality. In the two nonconflicting conditions, paired words were either similar in both orthography and phonology (O+P+, e.g., *dime–lime*) or different in both orthography and phonology (O−P−, e.g., *staff–gain*). In the two conflicting conditions, paired words had either similar orthography but different phonology (O+P−, e.g., *mint–pint*) or different orthography but similar phonology (O−P+, e.g., *jazz–has*). This manipulation of orthographic and phonological similarity ensured that rhyme decisions could not be based only on orthographic information. Current analyses collapsed across lexical conditions. All included participants demonstrated response accuracies of at least 50% across all experimental trials in each modality condition, removing any participants with a possible response bias or inability to perform the task at least at chance.

Two nonlexical control conditions were also included. Fixation trials (24 per run) were included as a baseline and required the participant to press the "yes" button when a fixation cross at the center of the screen turned from red to blue. Perceptual trials (12 per run) required participants to determine whether sequentially presented abstract symbol strings (tones [AA], nonalphabetic glyphs [VV], or tones followed by glyphs [AV]) matched in pattern (increasing/becoming larger, decreasing/becoming smaller, or steady in pitch or height). The timing for the fixation and perceptual trials was the same as for the lexical trials.

Experimental Procedure

After obtaining informed consent and assent and completion of the standardized test battery, participants were invited for a practice session during which they learned the experimental task and became acclimated to the MRI environment in a mock scanner in the laboratory. Participants were thus familiar with the task and the scanning environment before scanning sessions. Experimental MRI sessions took place within a 6-month period (mean interval between first and last scans = 2.7 months). During each scanning session, participants completed the rhyming task in one modality condition. Participants first performed

the VV task, then AV, and last, AA. In instances where data processing had indicated data quality issues for a previously acquired run (e.g., because of excessive head movement), up to one attempt was made to reacquire that data in a subsequent session. In total, 10 sessions were reacquired for this experiment (four for the VV condition, four for AV, and two for AA); with the exclusion of one participant who did not respond to more than half of the trials on his initial visit, participant accuracy did not significantly differ between initial and reacquired sessions ($t(1, 8) = 0.094$, $p > .9$), indicating that reacquisition performance was not artificially improved by task training and should still reflect general rhyme-judgment skill.

MRI Data Acquisition

MRI images were acquired at the Northwestern University Center for Translational Neuroimaging. Participants were positioned in the MRI scanner with their head position secured using foam pads. An optical response box was placed in the participant's right hand to log responses. Visual stimuli were projected onto a screen, which participants viewed via a mirror attached to the inside of the head coil. Participants wore sound-attenuating headphones to minimize the effects of the ambient scanner noise. Images were acquired using a 3.0-T Siemens Trio MRI scanner, using a standard 16-channel head coil.

Two functional runs, with 202 repetitions each, were administered for each of the modality conditions. In each, the BOLD signal was measured using a susceptibility-weighted single-shot EPI method. Functional images were interleaved from bottom to top for whole-brain acquisition. The following parameters were used: echo time (TE) = 20 msec, flip angle = 80°, matrix size = 128 × 120, field of view = 220 × 206.25 mm, slice thickness = 3 mm (0.48-mm gap), number of slices = 32, and repetition time (TR) = 2000 msec.

In the first scanning session, a high-resolution T1-weighted 3-D structural image (MP-RAGE) was acquired for each participant (TR = 1570 msec, TE = 3.36 msec, matrix size = 256 × 256 mm^2, field of view = 240 mm, slice thickness = 1 mm, number of slices = 160).

In the second scanning session, a diffusion-weighted image (echo-planar spin echo imaging) was acquired for each participant (TR = 9512 msec, TE = 89 msec, matrix size = 128 × 128 mm^2, field of view = 256 × 256 mm^2, slice thickness = 2 mm, b = 1000 s/mm^2, 64 non-collinear diffusion-encoding directions). Additionally, one set of images with no diffusion weighting (b = 0 s/mm^2) was acquired.

## MRI Image Analysis

fMRI Analysis

fMRI data were processed using SPM8 (Wellcome Department of Cognitive Neurology, London, United

Kingdom, www.fil.ion.ac.uk/spm). Preprocessing for all runs for each participant included the following steps. Slice timing was applied to minimize timing errors between slices, and realignment was performed. Images were smoothed using a 2 × 2 × 4 nonisotropic Gaussian kernel. ArtRepair software (Mazaika, Hoeft, Glover, & Reiss, 2009) was used to correct for participant movement. Images were realigned in Art Repair, which identified and replaced outlier volumes associated with excessive movement (>4 mm in any direction) or spikes in the global signal, using interpolated values from the two adjacent nonoutlier volumes. No more than 10% of the volumes from each run and no more than four consecutive volumes were interpolated in this way. Functional images were coregistered with the anatomical image and normalized to the Montreal Neurological Institute ICBM152 T1 template, which is an average of 152 normal adult MRI scans. This template is well defined with respect to a number of brain atlas tools and the Montreal Neurological Institute coordinate system. Moreover, stereotaxic space for children within the age range included in our study has been shown to be comparable with that of adults (Kang, Burgund, Lugar, Petersen, & Schlaggar, 2003; Burgund et al., 2002). Thus, it was deemed preferable to use the standard adult SPM template rather than create an average-based template.

First-level statistics. All functional runs from each individual were analyzed together using a mass-univariate approach based on the general linear model with a canonical hemodynamic response function. Modeled factors included modality (three: AA, VV, AV), word-pair consistency condition (four: O+P+, O+P−, O−P+, O−P−), perceptual controls, and fixation controls. A high-pass filter with a cutoff period of 128 sec was applied.

ROI analysis. Previous literature suggested the pSTS as a region particularly important in the integration of auditory and visual information, including for reading (Blau et al., 2009, 2010; van Atteveldt et al., 2004, 2009; Beauchamp et al., 2004; Hashimoto & Sakai, 2004; Calvert, 2001; Calvert et al., 1999, 2000; Raij et al., 2000). Individually based ROIs were created for this region through two steps. First, an anatomical pSTS ROI was created using the automated anatomical labeling atlas (Tzourio-Mazoyer et al., 2002). A mask of the overlap of the superior and middle temporal gyri was created by selecting the intersection of these two structures, each dilated by two units in the WFU PickAtlas tool in SPM8, yielding the complete extent of the STS. This mask was truncated anterior to $y = −25$ to yield the pSTS ($k = 390$; see Figure 1 for diagram). Second, the average beta value of the top 50 voxels within this region was then extracted for each participant in each modality condition, greater than fixation (e.g., AV > fixation). As the AV perceptual controls also involve

Figure 1. Left pSTS activity in word rhyming tasks. The left pSTS was created by taking the overlap of the left superior and middle temporal gyri posterior to $y = -25$ ($k = 390$, purple; $x = -57$, $y = -41$, $z = 10$). The average beta value of the top 50 voxels within this region was then extracted for each participant in each task. Beta values were significantly greater for audiovisual (AV) task than for unimodal visual (VV) or unimodal auditory (AA) task (*$p < .001$; error bars show *SEM*). All figures show left-hemisphere structures on the right side of the figure.
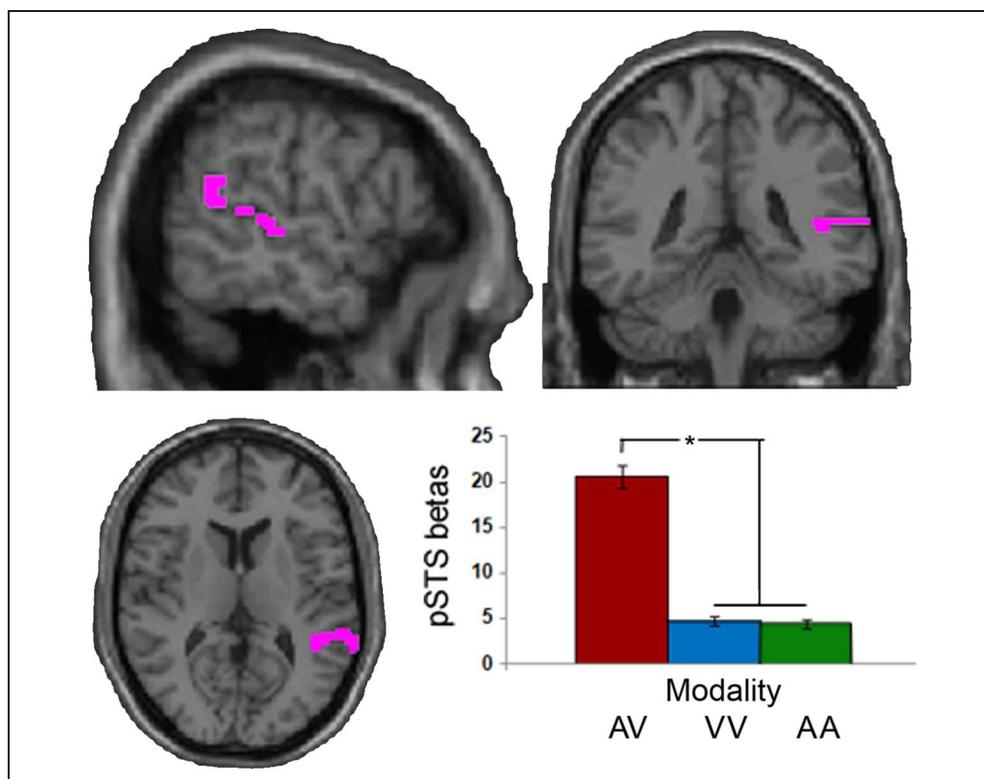
crossmodal matching, versus the unimodal VV and AA perceptual controls, a contrast against fixation was chosen so as to best examine any crossmodal processing activity. Secondary comparative analyses also used ROIs, similarly created using the WFU PickAtlas definitions of the mid-fusiform gyrus and the superior temporal gyrus. The superior temporal gyrus region was truncated posterior to $y = -25$ to yield the anterior to mid-superior temporal gyrus, excluding any potential pSTS voxels. Individualized ROIs for each participant for each modality condition were created using the same process as for the pSTS.

DTI Analysis

DTI data analysis was performed using FMRIB Software Library (FSL) software (www.fmrib.ox.ac.uk/fsl). All images were first examined for artifact by creating mean, standard deviation (*SD*), and signal-to-noise maps using the fslmaths command. Between-volume motion was also inspected; all participants demonstrated run motion of <0.5 mm across the scan. Preprocessing steps for all participants included eddy current correction, brain extraction (fractional intensity threshold = 0.25), and diffusion tensor fitting. FA maps were then calculated for each participant. FA maps were normalized to the adult FMRIB58 1-mm template image and used the template skeleton.

Tract-based spatial statistics were implemented to determine voxels where FA values were predictive of behavioral or fMRI measures. Only voxels with FA greater than 0.25 were included in the analysis (Smith et al., 2006). Three

regressions (standardized test scores, response accuracy, and pSTS activity) were run using the Randomise tool, each including all variables to test for the unique effects of each measure. Randomise implements Monte Carlo permutation testing to determine significance; all results are reported at $n = 5,000$ iterations, with $p < .05$, corrected for multiple comparisons, and $k > 5$, using the threshold-free cluster enhancement option (Smith et al., 2006). p values were corrected using the false discovery rate (FDR) tool available in the FSL package (fsl.fmri-b.ox.ac.uk/fsl/fslwiki/FDR). Post hoc correlations between regressor values and participants' mean FA in significant voxels are included to help describe significant relationships.

All analyses in this study were conducted first within restricted anatomical masks from the John Hopkins University white-matter tractography atlas (Wakana et al., 2007; Mori et al., 2002). As such, only skeleton mask voxels corresponding to the left AF in at least 25% of atlas participants were examined in the initial analyses (see Figure 2 for the diagram of AF). We describe clusters as occurring within the parietal, frontal, or temporal sections of the AF, with the parietal section expected to be of particular importance for reading-related integrative processing. Secondary comparative analyses used similarly created ROIs of the left superior corona radiata, left inferior fronto-occipital fasciculus, and bilateral splenium of the corpus callosum. Finally, exploratory whole-brain voxel-based analyses were performed. No significant relationships with FA were seen in any analysis condition (standardized test

Figure 2. Left AF mask with tract skeleton. Tract-based spatial statistics were performed within an anatomical mask of the left AF (purple).

$x = -37$ $z = 24$ $y = -44$
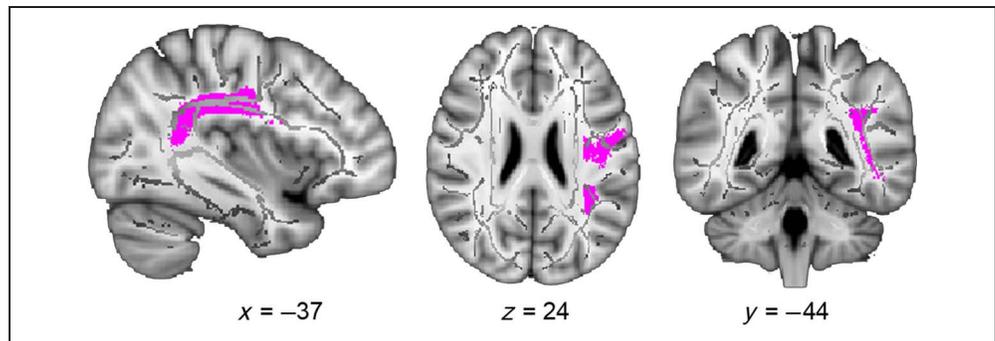
scores, accuracy in any modality, pSTS activity in any modality), with $p < .05$, FDR corrected.

RESULTS

Behavioral Performance

Task accuracy in each modality was first assessed using a 1×3 (Modality) repeated-measures ANOVA. There was no significant difference on response accuracy between modality conditions ($F < 1$), $\eta^2 = .106$. Response accuracy was correlated between modalities (AV–VV: $r = .627$, $p < .001$; AV–AA: $r = .488$, $p = .001$; VV–AA: $r = .458$, $p = .001$), wherein participants who performed well in one modality tended to perform well in the others.

Response time was then assessed. A 1×3 (Modality) repeated-measures ANOVA demonstrated a significant effect of Modality on Response Time, $F(2, 92) = 34.343$, $MSE = 800892$, $p < .001$, $\eta^2 = .427$, wherein response time was faster for AV trials (mean = 1169.69 msec, $SD = 289.95$ msec) than VV trials (mean = 1319.8 msec, $SD = 310.54$ msec), which were in turn faster than AA (mean = 1429. 74 msec, $SD = 301.92$ msec); the slowed responses for AA are likely an artifact of the auditory presentations, where information is delivered over time. Response times were correlated between modalities (AV–

VV: $r = .762$, $p < .001$; AV–AA: $r = .739$, $p < .001$; VV–AA: $r = .730$, $p < .001$), wherein participants who were faster in one modality tended to be faster in the others.

Relationships between participant age and behavioral performance were also investigated. Age was significantly correlated with VV accuracy ($r = .439$, $p = .002$), but not with either AV ($r = .133$, $p > .3$) or AA ($r = -.022$, $p > .8$) accuracy. Age was not significantly correlated with response time in any modality (all $rs > -.25$, $ps > .05$). Age was included as a regressor in structural analyses to partial out any variance attributable to maturational effects, allowing examination of independent modality-specific relationships.

A Priori ROI Results

fMRI ROI Results

Differences in activity in the pSTS ROI between modalities were then examined. A 1×3 (Modality) repeated-measures ANOVA demonstrated a significant effect of Modality on the experimental > fixation beta values extracted, $F(2, 92) = 123.764$, $MSE = 4043$, $p < .001$, $\eta^2 = .729$, where activity was greater for AV trials (mean = 20.61, $SD = 8.48$) than VV (mean = 4.69, $SD = 3.33$) or AA (mean = 4.39, $SD = 3.26$) trials (see Figure 1).

Table 2. Standardized Test Scores: AF Relationship

Test	Tract	x	y	z	k
Real Word	L AF parietal	−36	−50	26	52
	L AF parietal	−43	−30	32	9
	L AF frontal	−44	−13	27	9
Phonological Awareness	L AF parietal	−32	−36	37	17
	L AF parietal	−36	−36	31	12
	L AF frontal	−48	−20	28	12
Real Word > Phonological Awareness	L AF parietal	−35	−35	25	31
	L AF parietal	−38	−42	20	14
Phonological Awareness > Real Word	None				

L = left.

Figure 3. Relation of real-word reading and phonological awareness scores to AF FA. Both real-word reading (red) and phonological awareness standard scores (green) were predictive of FA in the anterior and parietal sections of the left AF ($x = -38, y = -44, z = 28$). Scatterplot shows higher word reading scores (red, dashed line), and higher phonological awareness scores (green, dotted line) were associated with greater FA extracted from group-level predictive voxels.
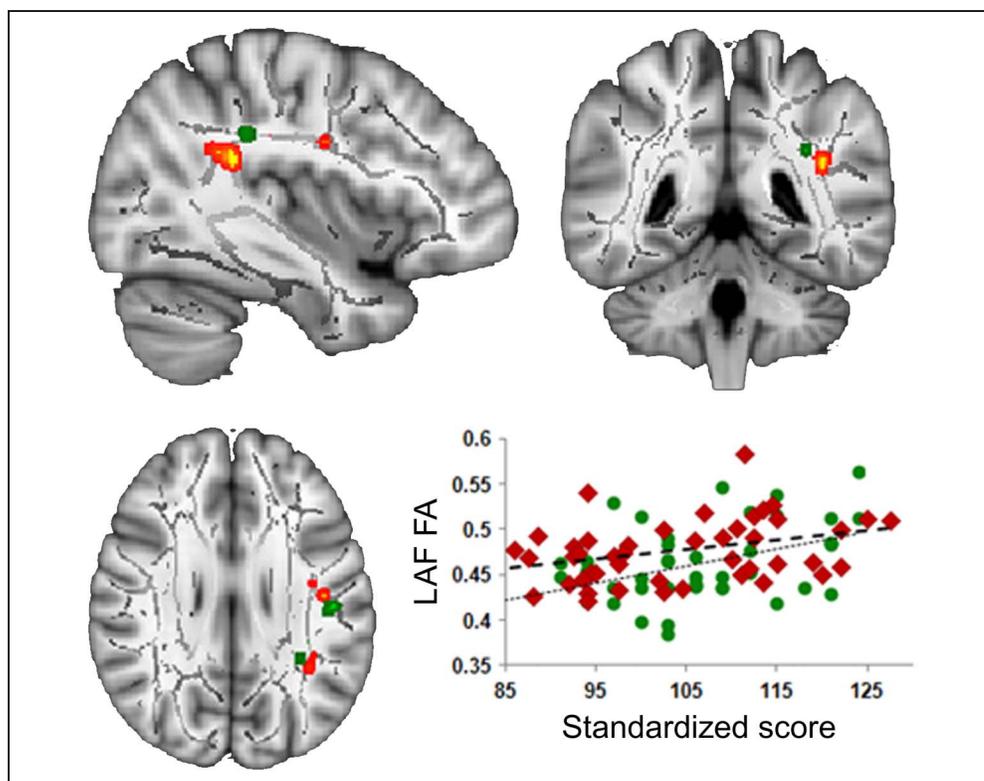
Betas were not correlated across modalities ($ps > .35$, $rs < .15$). Furthermore, age was not correlated with pSTS activity in any modality ($ps > .15$, $rs < .2$).

DTI Results

Standardized test score—AF FA relationship. The relationships between real-word reading ability, phonological awareness, and FA in the left AF were first examined. Participants' average real-word reading standard score and phonological awareness standard score were entered into a regression to determine if it either was predictive of FA in the AF; age (in months) was also included in this model (see Table 2, Figure 3). Both real-word reading ability and phonological awareness skills were significantly predictive of FA in the parietal and frontal sections of the tract. Real-word reading was significantly more strongly related to FA than was phonological awareness in the parietal subsections; phonological awareness was not more related to FA than word reading at any points.

Response accuracy—AF FA relationship. The relationship between response accuracy in each modality and FA in the left AF was then examined. Experimental trial response accuracy in each modality and participant age in months were entered into a regression to determine if any factors were uniquely predictive of FA in the AF (see Table 3, Figure 4). Response accuracies in all three modalities were predictive of FA in the AF, although in

different regions. AV was most predictive of response accuracy in the parietal and anterior frontal sections, whereas VV and AA were predictive in the middle frontal section. AV was significantly more related to FA than was VV in an anterior cluster and more than AA in a temporal cluster.

pSTS activity—AF FA relationship. The relationship between activity in the pSTS for each modality and FA in the left AF was then examined. Beta values for activity in each modality and participant age in months were entered into a regression (see Table 4, Figure 5). Only AV activity was significantly predictive of FA in the AF in parietal and

Table 3. Accuracy by Modality: AF Relationship

Modality	Tract	x	y	z	k
AV	L AF frontal	−49	−5	20	13
	L AF parietal	−37	−52	19	12
	L AF temporal	−39	−52	2	5
VV	L AF frontal	−36	−10	35	25
	L AF frontal	−33	−26	38	5
AA	L AF frontal	−59	−5	15	8
AV > VV	L AF frontal	−49	−5	19	8
AV > AA	L AF temporal	−39	−52	2	5

Figure 4. Relation of word rhyming accuracy to AF FA. Audiovisual (AV, red) accuracy was significantly predictive of FA in the temporal, parietal, and anterior sections of the left AF ($x = -37$, $y = -52$, $z = 19$). Unimodal visual (VV, blue) and unimodal auditory (AA, green) accuracies were predictive of FA in the anterior sections of the left AF. Scatterplot shows higher accuracy scores were associated with greater FA extracted from group-level predictive voxels (AV: red, dashed line; VV: blue, solid line; AA: green, dotted line).
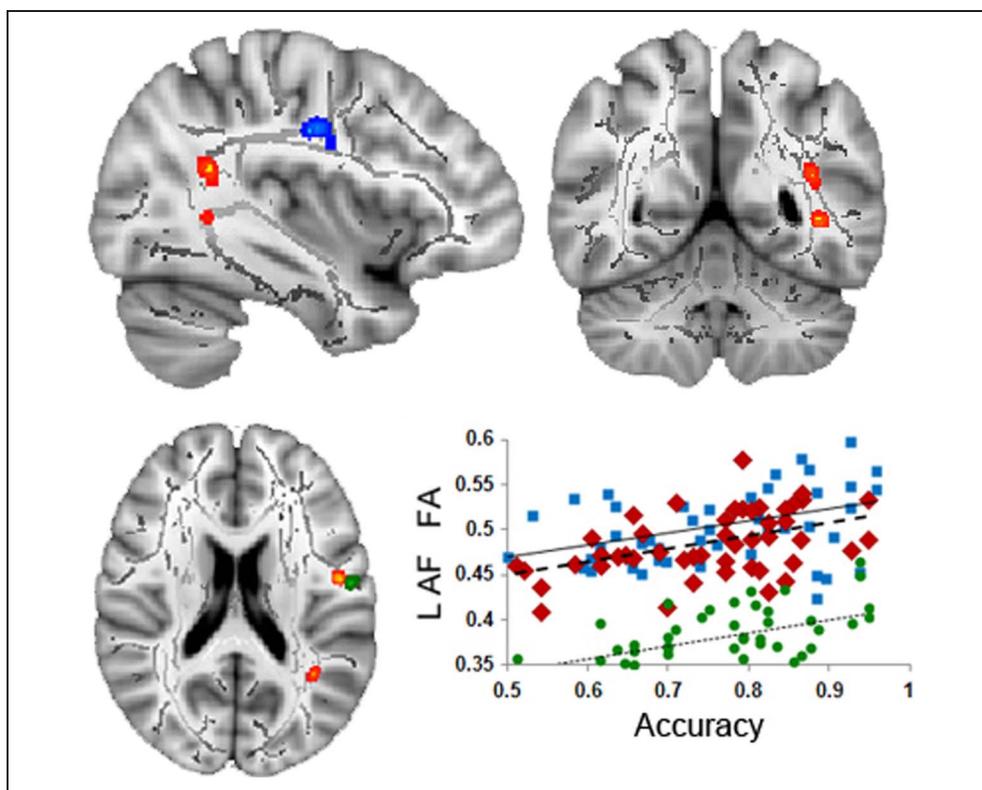
frontal sections of the tract. Furthermore, AV activity was significantly more predictive of FA than VV in both parietal and frontal sections.

Effect Specificity Results

To demonstrate that the unique relationship between AV pSTS activity and AF coherence is significant and specific, we conducted several further analyses examining whether only AV activity in other reading-related regions was correlated with AF FA and whether only AV pSTS activity was correlated with white-matter coherence in other reading-related tracts.

Table 4. pSTS Betas by Modality: AF Relationship

| Modality	Tract	x	y	z	k
AV	L AF parietal	−42	−46	29	53
	L AF frontal	−51	−7	20	22
VV	None				
AA	None				
AV > VV	L AF parietal	−36	−53	20	280
		−44	−40	33	14
	L AF frontal	−35	−16	30	14
AV > AA	None				

Activity—AF FA Relationship

The relationships between activity in the mid-fusiform gyrus and the anterior superior temporal gyrus in each modality and FA in the AF were examined. First, beta values for mid-fusiform gyrus activity in each modality and participant age in months were entered into a regression (see Table 5). Both AV and VV activities were significantly predictive of FA in the AF in the parietal (AV) and frontal (VV) sections of the tract. Then, beta values for anterior superior temporal gyrus activity in each modality and participant age in months were entered into a new regression. Both AV and AA activities were significantly predictive of FA in the AF in the parietal (AV) and frontal (AA) sections of the tract. No AV-only relationships were found in either analysis.

Standardized Test Score—FA Relationship

The relationships between real-word reading ability, phonological awareness, and FA in the left superior corona radiata, bilateral splenium of the corpus callosum, and left inferior fronto-occipital fasciculus were first examined. Participants' average real-word reading standard score and phonological awareness standard score were entered into a regression to determine if it either was predictive of FA in the AF; this analysis was performed separately in each tract. No significant relationships were found between score on either test and FA in any tract, $p > .05$, FDR corrected.

Figure 5. Relation of audiovisual word rhyming pSTS activation to AF FA. Audiovisual (AV) activation in pSTS was significantly predictive of FA in the parietal and anterior sections of the left AF ($x = -37$, $y = -43$, $z = 24$). Scatterplot shows greater AV activation in pSTS was associated with greater FA extracted from group-level predictive voxels.
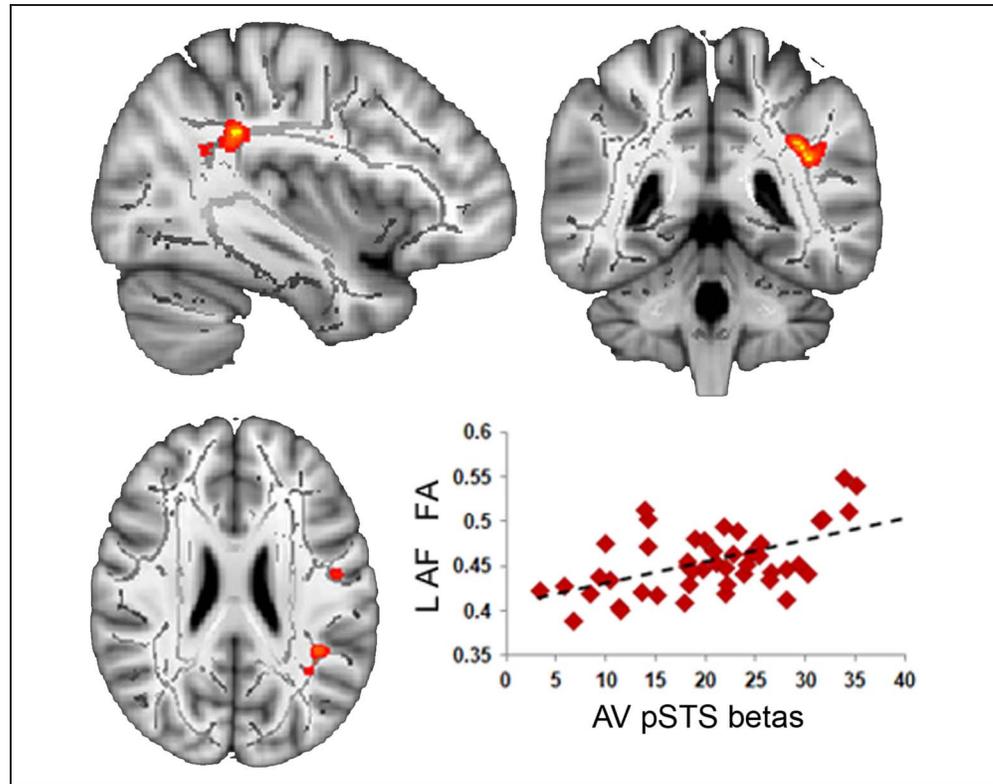
pSTS Activity—FA Relationship

The relationships between activity in the pSTS and FA in the left superior corona radiata, bilateral splenium of the corpus callosum, and left inferior fronto-occipital fasciculus were then examined. pSTS betas (for each modality) and participant age in months were entered into a regression to determine whether activity was predictive of FA; this analysis was performed separately in each tract. No significant relationships were found between pSTS activity and FA in any tract, $p > .05$, FDR corrected. As such, the crossmodal-specific relationship between pSTS activity and AF FA was not found when using either activity

from other regions or connectivity measures with other tracts.

Age Comparisons

Given the large age range of the sample, we performed split-group analyses to ensure that these AF results were

Table 5. Comparison ROI Betas by Modality: AF Relationship

	Tract	x	y	z	k
Mid-fusiform Gyrus					
AV	L AF parietal	−40	−33	28	11
VV	L AF frontal	−40	−6	28	27
	L AF frontal	−32	−18	34	7
AA	None				
Mid-superior Temporal Gyrus					
AV	L AF parietal/temporal	−38	−52	14	15
VV	None				
AA	L AF frontal	−59	−5	15	10

Table 6. pSTS Betas by Modality: AF Relationship, Split by Age Group

	Tract	x	y	z	k
Younger Participants					
AV	L AF frontal	−47	−10	24	44
	L AF frontal	−34	−22	36	7
	L AF parietal	−40	−39	32	5
	L AF temporal	−42	−43	9	5
VV	None				
AA	None				
Older Participants					
AV	L AF parietal	−38	−42	28	18
	L AF frontal	−54	−9	20	10
VV	None				
AA	None				

Figure 6. Relation of audiovisual word rhyming pSTS activation to AF FA in each age group. Audiovisual (AV) activation in pSTS was significantly predictive of FA in the parietal, anterior, and temporal sections of the left AF in younger participants (A: $x = -41$, $z = 32$) and in the parietal and anterior sections in older participants (B: $x = -38$, $z = 28$).
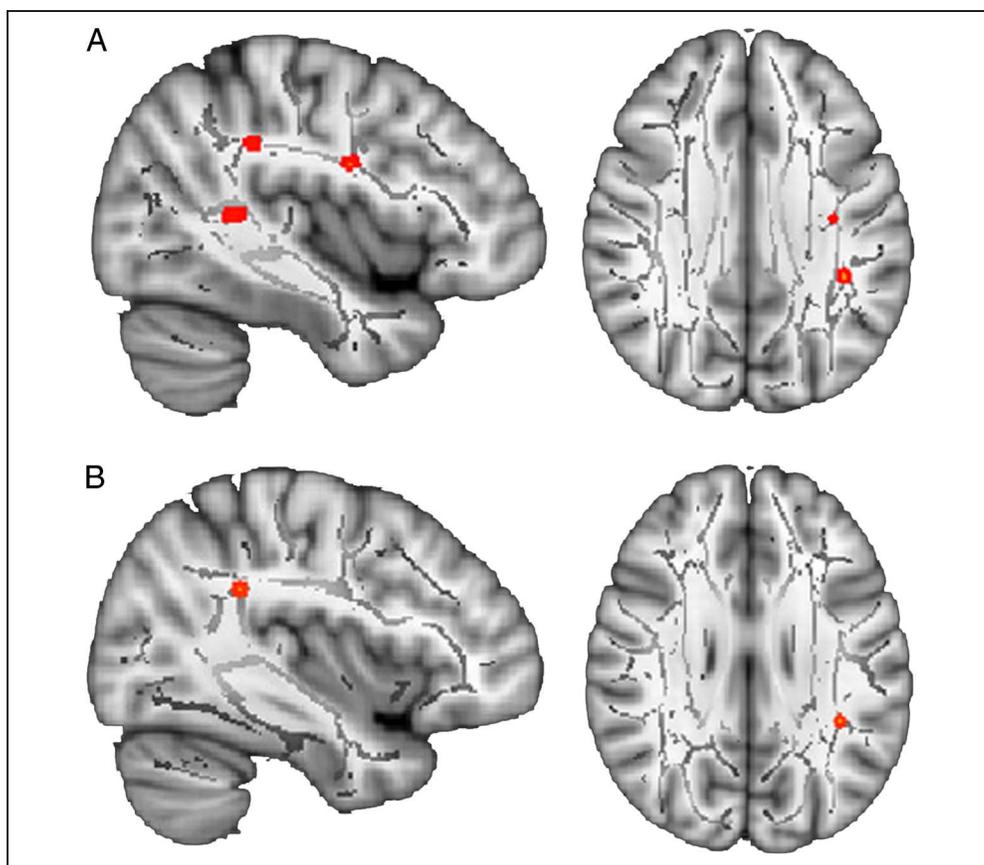
not driven only by older or younger participants (see Table 6, Figure 6). Younger participants (age = 8.2–11.0, $N = 23$) demonstrated a significant relationship only for AV pSTS betas and FA in the parietal, frontal, and temporal AF; no significant correlations were found with VV or AA pSTS activity. Older participants (age = 11.1–14.5, $N = 24$) demonstrated a significant relationship only for AV pSTS betas and FA in the parietal and frontal AF; no significant correlations were found with VV or AA pSTS activity. As such, the significant and specific relationship found between pSTS activity and AF connectivity for AV was conserved in both older and younger participants, indicating that this effect was not driven by one age group.

DISCUSSION

The goal of the current study was to directly investigate the relationship of behavioral performance and brain function related to phoneme–grapheme integration to white-matter tract structure. Although previous work has noted relationships between behavioral phoneme–grapheme knowledge and either pSTS activity or AF connectivity, to our knowledge, no research has directly linked this crossmodal activity to tract connectivity. This brain–brain correlation may allow for more specificity in our understanding of the processing supported by each of these areas. Our use of activity from a region

sensitive to crossmodal information in tasks that vary only in modality allows us to determine whether the unique relationship found with arcuate coherence for crossmodal processing may be because of the crossmodal integration required and not other variables. Consistent with previous literature, we demonstrate that behavioral performance in crossmodal word processing was correlated with FA in the AF, but we additionally and critically demonstrated that crossmodal pSTS activity was specifically related to the coherence of this white-matter tract. As the ability to fluently process crossmodal linguistic information is critical for reading, our demonstration of a specific relationship between crossmodal pSTS activity and AF connectivity suggests that reading-related audiovisual integration may rely on the AF and describes an interdependent neural network supporting letter–sound integration ability.

First, we demonstrated that a composite real-word reading measure and phonological awareness skill were each significantly predictive of FA in the AF in frontal and parietal sections, although word reading ability was more predictive of FA than phonological awareness in the parietal lobe. Although the sample of children in our study did not include any participants with word reading scores lower than 1 *SD* below the mean, this demonstrated relationship is consistent with correlations previously found across typically developing and reading-disabled participants using a variety of measures similar to the ones used here (word

identification: Yeatman et al., 2012; Beaulieu et al., 2005; Deutsch et al., 2005; pseudoword decoding: Frye et al., 2008; Steinbrink et al., 2008; Klingberg et al., 2000). The finding of a stronger relationship for word reading supports the idea that the parietal AF is involved in reading-related integrative processing, as these reading and decoding tests require conversion from visually presented graphemic information to a phonological representation for oral naming. Other work including both typical and dyslexic or high-risk readers has found phonological awareness to be correlated with tract coherence along the AF (Vandermosten, Boets, Poelmans, et al., 2012; Yeatman et al., 2011). Furthermore, because both the word reading and phonological measures used involve oral responses, our finding of significant correlations between skill and frontal AF FA may support previous conceptualizations of an anterior subtract of the AF specific to articulation (Vandermosten, Boets, Poelmans, et al., 2012; Catani et al., 2005).

These measures are relatively broad and rely on multiple subskills, including exception word recognition, fluent letter–sound association, naming speed, elision, and blending. Although audiovisual integration is certainly involved in word reading, it is only an indirect measure of integration ability. Additionally, some phonological awareness tasks may engage orthographic representations (Castles, Wilson, & Coltheart, 2011; Ehri & Wilce, 1980) and therefore engage integration mechanisms to some degree, making the distinction between these skills less clear. Our experimental rhyme-judgment task, however, can allow for more direct investigation of the role that the AF plays in crossmodal integration.

Our rhyming judgment task allowed for a comparison between stimuli that were crossmodally presented (auditory and visual, AV) to those that were unimodally presented (auditory-only [AA] or visual-only [VV]). We found that performance on all three tasks were predictive of AF connectivity, although in different subregions. AV performance was most related to posterior connectivity in anterior, parietal, and temporal areas, whereas AA and VV performances were predictive of only frontal FA. These differences may be reflective of the relative integration demands in the modalities. Only the AV condition explicitly required integration, given the crossmodal stimuli, thus drawing on connectivity across the tract. VV trials may be considered implicitly integrative in the sense that words were presented visually but required conversion to phonological representations to perform the rhyming task. Interestingly, the significant anterior connectivity relationship for the VV task is similar in location to previous findings of a correlation between word reading skill and connectivity (see Vandermosten, Boets, Wouters, et al., 2012), which also involves processing only orthographic information. The AA task requires skills similar to those for phonological awareness, which also demonstrated a significant relationship with anterior FA. No previous studies have included a specifically crossmodal

behavioral task, making our finding of a more posterior parietal–temporal connectivity relationship with AV performance novel and interesting.

Our study also demonstrated both the importance of the pSTS for crossmodal processing and served to link AF structural integrity with integrative brain activity. The increased activity for the AV task, relative to VV and AA activities, in the pSTS is consistent with the conceptualization of this region as a critical site for active integration of audiovisual information (Blau et al., 2009, 2010; van Atteveldt et al., 2004, 2009; Calvert, 2001) or for access to these integrated representations (Noppeney, Josephs, Hocking, Price, & Friston, 2008). Most importantly, we demonstrated a significant and specific relationship between pSTS activity during the AV task and AF connectivity. Individuals with increased pSTS activity for crossmodal word stimuli also show increased tract coherence and integrity along the AF, although no relationships were found with activity in either unimodal condition, supporting the hypothesis that connectivity along this tract is particularly related to integration. These demonstrated relationships between crossmodal rhyme judgment activity and AF FA are thus consistent with the previously reviewed works noting AF connectivity to particularly support reading ability (see Vandermosten, Boets, Wouters, et al., 2012) and extend this literature by directly linking crossmodal brain activity to this connectivity.

Phoneme–grapheme integration is a critical skill for reading and one that may be deficient or less fluent in individuals with dyslexia. We were specifically interested in the relationship between integrative processing and brain structure and so first investigated activity in the pSTS and connectivity along the AF. However, because other brain regions have been demonstrated to be particularly important for both reading generally and crossmodal integration specifically, we included several functional and structural comparison ROIs to determine if the AV-only relationship found was unique to the pSTS and AF. Importantly, no crossmodal-specific relationships were found between fusiform gyrus or anterior superior temporal gyrus activity and AF coherence, and no relationships were found between pSTS activity and FA in any of the three comparison tracts, indicating that the AV-only relationship we demonstrate is limited to the pSTS and AF. Thus, although the AF may also support other functions and processing, the functional–anatomical connection between these particular regions seems to be particularly important in supporting reading-related crossmodal integration.

The children included in the current study range in age from 8 to 14 years. Maturational effects on AF FA have been established previously, with connectivity showing age-related increases in groups of typical readers (Yeatman et al., 2012; Rollins et al., 2009). Age was included as a variable in both our behavior-DTI and function-DTI analyses, allowing us to properly account for FA changes associated with development separate from our modality-based effects of interest. Furthermore, a supporting analysis

upheld our pSTS activity—AF coherence relationship in both older and younger participant subgroups. As such, although there is a significant relationship between age and FA in the AF, our associations of AV behavioral performance and pSTS activation with FA in the AF should not be attributable only to maturational effects.

This experiment involved performing rhyme judgments on pairs of words in three distinct modality conditions; however, the word pairs used were the same across modalities. Furthermore, all participants completed the experiment in the same modality order (VV–AV–AA) because we did not want to provide the auditory pronunciation of the word before participants were required to read it. It is possible that implicit training occurred over the course of participation in the experiment, potentially leading to better performance in later conditions than would otherwise be found if order had been counterbalanced. The AV-specific relationships seen may not be because only of such learning; if training were to induce such effects, we would expect to also find significant relationships for AA, as it was the last condition performed. As such, the potential for implicit learning is an important point to be considered, especially in simple comparisons of modality response performance, but is unlikely to fully account for the FA relationships results found.

Rather than being a unitary structure, new DTI tractography work has demonstrated that the left AF may be separable into subtracts with distinct subfunctions. The current work uses tract-based spatial statistics to find AF voxels wherein FA was significantly related to individual differences on task performance or brain activity. This technique does not rely on tractography and so cannot be used to classify voxels as belonging to specific subtracts, as in the most prominent three-subdivision model proposed by Catani et al. (2005) or the alternate two or four subdivisions advanced by other groups (Glasser & Rilling, 2008; Makris et al., 2005, respectively). As such, we describe clusters as occurring within parietal, frontal, or temporal portions of the AF but note that this methodology is not able to directly determine whether connectivity along the direct, anterior, or posterior subtracts is related to these measures. Future work including tractography may be able to determine the relationships between subtract connectivity and integration ability.

This study demonstrates the relationship of crossmodal processing, both in terms of behavioral performance and activity within the pSTS, with AF connectivity. This work increases specificity in the definition of the brain systems supporting reading-related integration and thus can potentially help in understanding reading disabilities such as dyslexia. Given the importance of crossmodal integration in fluent reading and previous demonstrations that deficient letter–sound knowledge may lead to future reading difficulties (Blomert & Willems, 2010; Ellefson et al., 2009; Evans et al., 2006; Treiman, 2006; Foulin, 2005), identification of the neural systems supporting individual differences in integration skill is an important step in eventually describing networks particularly affected in disordered reading.

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