Language-general and -specific white matter microstructural bases for reading

Mingxia Zhang, Chuansheng Chen, Gui Xue, Zhong-lin Lu, Leilei Mei, Hongli Xue, Miao Wei, Qinghua He, Jin Li, Qi Dong

Abstract

In the past decade, several studies have investigated language-general and -specific brain regions for reading. However, very limited research has examined the white matter that connects these cortical regions. By using diffusion tensor imaging (DTI), the current study investigated the common and divergent relationship between white matter integrity indexed by fractional anisotropy (FA) and native language reading abilities in 89 Chinese and 93 English speakers. Conjunction analysis revealed that for both groups, reading ability was associated with the FA of seven white matter fiber bundles in two main anatomical locations in the left hemisphere: the dorsal corona radiate/corpus callosum/superior longitudinal fasciculus which might be for phonological access, and the ventral uncinate fasciculus/external capsule/inferior fronto-occipital fasciculus which might be for semantic processing. Contrast analysis showed that the FA of the left temporal part of superior longitudinal fasciculus contributed more to reading in English than in Chinese, which is consistent with the notion that this tract is involved in grapheme-to-phoneme conversion for alphabetic language reading. These results are the first evidence of language-general and -specific white matter microstructural bases for reading.

Introduction

There are over 6000 languages in the world. It is believed that an unimpaired person can theoretically learn any language because humans are equipped with universal mechanisms for language acquisition. Similarly, reading any language should involve similar cognitive processes in the brain (Yang et al., 2009, 2013), namely, to integrate signals from visual, phonological, semantic and other linguistic processing (Price, 2000; Schlaggar and McCandliss, 2007; Turkeltaub et al., 2002; Vigneau et al., 2006; Wandell, 2011). Given the vast differences in writing systems (e.g., alphabetic and logographic languages), however, reading different languages may require unique neural circuits to map visual materials to sounds (Perfetti et al., 2005; Siok et al., 2004, 2008).

In the past decade, several studies have identified common cortical regions for reading across different languages as well as cortical regions that are only activated by alphabetic or logographic language reading. For example, the left occipitotemporal region, anterior part of superior temporal gyrus and superior posterior part of inferior frontal gyrus were found to be involved in reading different languages (Bolger et al., 2005; Thuy et al., 2004; Zhang et al., 2013a). These regions might be responsible for grapheme-to-phoneme conversion which is more important for reading alphabetic languages. The left middle frontal cortex and the right occipitotemporal cortex are involved specifically in logographic Chinese reading whereas the left posterior part of superior temporal gyrus and temporoparietal area are relevant to alphabetic language reading (Bolger et al., 2005; Sakurai et al., 2000; Siok et al., 2008; Tan et al., 2005). The former regions might be recruited because of the greater visual analysis of spatial information when reading logographic Chinese and the latter regions might be responsible for grapheme-to-phoneme conversion which is more important for reading alphabetic languages.

Previous cross-linguistic imaging research on reading has relied almost exclusively on functional MRI studies. Little attention has been paid to white matter that connects the cortical regions. Intriguingly, several recent studies have discovered that white matter properties could be the efficient neural markers for reading abilities (for reviews see Ben-Shachar et al., 2007; Vandermosten et al., 2012). Using DTI, studies
revealed significant associations between reading skills and white matter integrity, mostly indexed by fractional anisotropy (FA) of superior or longitudinal fasciculus, corona radiate and inferior fronto-occipital fasciculus (temporo-parietal region and fronto-temporal regions) (Beaulieu et al., 2005; Deutsch et al., 2005; Klingberg et al., 2000; Niogi and McCandliss, 2006; Steinbrink et al., 2008; Yeatman et al., 2011) as well as other white matter tracts (e.g., corpus callosum) (Cumming and Boliek, 2013; Dougherty et al., 2007; Frye et al., 2008; Lebel et al., 2013) in the left hemisphere.

These findings of FA-reading ability relationships have important implications for understanding the white matter pathway for reading. However, all these studies focused on native readers of alphabetic languages. Only one study tested the relationship between white matter maturation and Chinese reading and revealed an association between reading and FA of the internal capsule (Qiu et al., 2008), which was recently confirmed by a study of English readers (Lebel et al., 2013). Thus far, no study has directly evaluated the relationship between white matter connectivity and reading abilities across different writing systems.

Using tract-based spatial statistics (TBSS) of DTI, we investigated how white matter connectivity (indexed by FA) was associated with individual differences in native language reading abilities in alphabetic English and logographic Chinese speakers. To directly compare the FA-reading ability relationship between the two groups, we recruited two samples of college students, administered reading tests with the same format and conducted DTI scans. Conjunction and contrast analyses were conducted to identify the white matter connections that were associated with reading performance for both English and Chinese readers or for either of them.

Method

Subjects

Data for this study came from two samples. The American sample included 93 college students (age range: 18–30 years, mean age = 20.8, SD = 2.2; 54 females and 39 males) from the University of California, Irvine and the University of Southern California. The Chinese sample included 89 college students (age range: 19–25 years, mean age = 21.7, SD = 1.7; 45 females and 44 males) from Beijing Normal University. Because second-language is a requirement in secondary schools and colleges in both China and the United States of America, all students had learned a second language to some level of proficiency. For the American sample, because their second language varied greatly (e.g., Spanish, Chinese, Armenian, Russian, and French), we did not test their second language reading level. Based on participants’ self-report, some participants (n = 12) viewed their fluency in their second-language so low that they considered themselves as monolingual, whereas the remaining participants (n = 81) had a moderate reading level. The average second language reading level was 3.3 on a 7 point scale: (1: only a little; 7: native-level proficiency). For the Chinese sample, all participants learned English as their second language starting in elementary school and passed the college entrance examination of English. We used a standardized English reading ability test (TOWRE-SWE, Form A) of the Test of Word Reading Efficiency (TOWRE), a nationally normed measure of word reading accuracy and fluency in America for individuals from 6 to 24 years of age (Torgesen et al., 1999). (The other subtest of TOWRE, Pseudoword Decoding Efficiency [PDE], was not used because there are no pseudowords [pronounceable but illegal words] in logographic Chinese). Reading ability was indexed by the number of printed real words (out of 104 words) that were accurately read within 45 seconds. Test items were arranged in order of difficulty from easy to difficult items. For subjects who accurately read all 104 items in less than 45 s, the reading scores were calculated as (104/time in s) * 45 (i.e., estimated number of words that would have been read if they used all 45 s).

Native reading ability of Chinese subjects was measured by the Chinese Character Reading Efficiency Test (CCRET). This test was developed in the format of TOWRE-SWE. There are also 104 items in the CCRET selected from the Chinese character psycholinguistic norms (Liu et al., 2007) with word frequency ranging from 4 to 5636 (mean = 196), number of strokes ranging from 2 to 14 (mean = 7.3), and number of units ranging from 1 to 5 (mean = 2.4). Reading ability was indexed by the number of printed Chinese characters that were accurately read in 45 seconds. Test items were also arranged in order of difficulty from easy to difficult items. Again, for subjects who accurately read all 104 items in less than 45 s, the reading scores were calculated as (104/time in s) * 45 (i.e., estimated number of words that would have been read if they used all 45 s). Both tests (TOWRE-SWE and CCRET) have been used in our previous studies that examined the structure and resting state functional connectivity correlates of reading skills (Zhang et al., 2013a, 2013b). Because American and Chinese subjects took reading tests in their native languages, their scores could not be directly compared. Instead, we used the standardized reading scores within each sample for correlational analyses with the DTI data.

To identify reading-specific correlates, a non-verbal reasoning (or intelligence) test, Raven’s Advanced Progressive Matrices, was also used in the current study and regressed out in the group-level of DTI data analysis. This test has been widely used in previous studies (e.g., Zhu et al., 2010). Table 1 shows subjects’ basic demographic information and test scores.

DTI data acquisition

DTI data of the Chinese and American subjects were acquired in the Brain Imaging Center at Beijing Normal University and the Dana and Dornsife Cognitive Brain Imaging Center at University of Southern California, respectively. Both samples were scanned with the same type of scanner (3.0 T Siemens Magnetom Trio with TIM) equipped with a standard head coil. Data collection from both samples was performed for about 11 min using echo-planar spin echo, with the same imaging parameters: 70 axial slices, slice thickness = 2 mm with no interslice gap, TE = 100 ms, TR = 10000 ms, 64 diffusion directions

<table>
<thead>
<tr>
<th>Table 1: Characteristics of the subjects.</th>
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<tbody>
<tr>
<td>U.S. subjects</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Gender (F/M)</td>
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<tr>
<td>Handedness</td>
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<tr>
<td>Raven’s Progressive Matrices</td>
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<tr>
<td>Scores</td>
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<td>Time (minutes)</td>
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<tr>
<td>Reading ability</td>
</tr>
<tr>
<td>Raw scores</td>
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<tr>
<td>Standardized Scores</td>
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</tbody>
</table>

Note: Standard deviations are shown in parentheses and ranges in brackets.
with $b = 1000 \text{s/mm}^2$, and an additional image without diffusion weighting (i.e., $b = 0 \text{s/mm}^2$), acquisition matrix = $128 \times 128$, FOV = $256 \text{mm} \times 256 \text{mm}$, average = 1, parallel imaging = GRAPPA (acceleration factor 2).

**Data analysis**

**Data preprocessing**

Image preprocessing was carried out using FSL (version 4.1.8) [FMRIB Software Library, http://www.fmrib.ox.ac.uk/fsl]. First, diffusion images were corrected for eddy-current distortion and head motion [Jenkinson and Smith, 2001]. B-vectors were also rotated according to the log file generated from the eddy-current correction procedure. Then, a binary mask (Smith, 2002) was extracted from the no-diffusion image for subsequent diffusion tensor fitting. Finally, using dtifit, original diffusion images: V1 (first eigenvector), V2 (second eigenvector), V3 (third eigenvector), L1 (first eigenvalue), L2 (second eigenvalue), L3 (third eigenvalue), FA, MD (mean diffusivity), and S0 (raw T2 signal with no diffusion weighting) were created in the brain mask by fitting a tensor model to the corrected data (Behrens et al., 2003). The preprocessing steps were repeated for each subject.

**Tract-based spatial statistics (TBSS)**

FA images from the preprocessing step were then analyzed by the standard protocol of TBSS (v1.2) [Smith et al., 2006], which is part of FSL. Using the TBSS script, we first eroded the FA images slightly and zeroed the end slices (to remove likely outliers from the diffusion tensor fitting). Then, the FA data were aligned into a $1 \times 1 \times 1 \text{mm}$ standard space using the nonlinear registration tool FNIRT [Andersson et al., 2007a, 2007b], which resulted in a standard-space version of each subject's FA image. Because the current study involved subjects from two countries who might have different overall brain morphology, we contrasted the degree of warping (indexed by mean squared displacement of the brain) between subjects in America and China to detect potential differences in fiber tracts' locations. No group difference in warping was found. Next, the standard-space FA images of all subjects were merged and averaged to create a single mean FA image. This mean image was fed into the FA skeletonisation program to create a skeleton that only included voxels that were identified as white matter. Finally, a threshold of FA $> 0.2$ was applied to the skeleton and the resulting binary skeleton mask defined the set of voxels used in all subsequent cross-subject statistical analyses.

Three sets of statistical analyses were conducted in the whole skeleton from TBSS (with age and Raven's score as the covariates). First, we correlated skeletonized FA with reading abilities in American and Chinese subjects separately by using the nonparametric permutation test with a correction for multiple comparisons (5000 times, $p < 0.05$) (using the command Randomize in FSL) [Nichols and Holmes, 2002]. This resulted in maps of white matter fiber tracts whose FA was associated with reading abilities in the two samples. Second, to establish the language-general white matter fiber tracts, we conducted a conjunction analysis, in which the significant maps of white matter fiber tracts were binarized (significant white matter fiber tracts in the last step became $z = 1$ maps) and summed. The common white matter fiber tracts were then created at the threshold of $z = 2$. Finally, to determine language-specific white matter fiber tracts, we conducted direct statistical comparisons on the tracts showing either FA-reading ability relationship in Americans (Americans minus Chinese) or Chinese (Chinese minus Americans), again, by using the nonparametric permutation test with a correction for multiple comparisons (5000 times, $p < 0.05$) (Nichols and Holmes, 2002).

**Interscanner reliability analysis**

Because of the use of two separate scanners, we wanted to ascertain interscanner reliability for white matter integrity. Six additional subjects (Chinese adults, age range: 29–35 yrs., mean age = 31; 2 females, 4 males) were scanned in both machines using the same acquisition protocol as used for the study (see above for details). The same preprocessing and TBSS analysis were conducted (also see above for details). Each subject’s mean FA values of white matter clusters in the whole brain were extracted. Using Cronbach's $\alpha$ test on these FA values (Beyer et al., 2013; Morey et al., 2010), we found excellent interscanner reliability: $\alpha = 0.93$ for mean FA in clusters of the whole brain.

**Reading and other diffusion properties**

Besides FA, several previous studies investigated reading and other diffusion properties such as tangential (the first eigenvalue), radial (the second and third eigenvalues) and mean diffusivity (Cummings and Boliek, 2013; Dougherty et al., 2007; Frye et al., 2008; Lebel et al., 2013; Qiu et al., 2008; Steinbrink et al., 2008; Yeatman et al., 2011). We also explored the utility of these properties in predicting reading proficiency in our study. Results and discussion are presented in the supplementary materials.

**Results**

As shown in Table 2, FA in five white matter fiber bundles was positively associated with reading abilities of American subjects. They are located in the corpus callosum, bilateral external (internal) capsule, inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, superior longitudinal fasciculus, corona radiate and left uncinate fasciculus (see Fig. 1, the blue tracts). For Chinese subjects, FA in 11 white matter fiber bundles was positively associated with reading ability. They are located in the corpus callosum, bilateral corona radiate, left thalamic radiation, external (internal) capsule, cerebral peduncle, uncinate fasciculus, superior longitudinal fasciculus, inferior fronto-occipital fasciculus and right corticospinal tract (see Fig. 1, red). There was no negative FA-reading ability relationship in any white matter cluster in either American or Chinese subjects.

Further conjunction analysis revealed that the FA of seven white matter fiber bundles in two main anatomical locations in the left hemisphere was commonly associated with reading abilities in both American and Chinese subjects (see Table 3, also see Fig. 1, green, emphasized via TBSS command tbs_fill). One is the left superior corona radiate/body of the corpus callosum/superior longitudinal fasciculus (CR/CC/SLF) located in the parietal-frontal region (278 voxels, MNI coordinates) and the other is the left uncinate fasciculus/external capsule/inferior fronto-occipital fasciculus (UF/EC/IFO) located in the insular area (149 voxels). Direct comparisons (Americans minus Chinese) on the tracts that showed FA-reading ability relationship in Americans revealed that the FA of one white matter fiber bundle located in the left SLF (temporal part) was more strongly associated with reading in English than in Chinese (77 voxels, $x = -46$, $y = -28$, $z = -10$) (see Fig. 2, red, emphasized via TBSS command tbs_fill). Direct comparisons (Chinese minus Americans) on the tracts showing FA-reading ability relationship in Chinese did not find any significant results.

**Discussion**

The primary purpose of the current study was to test language-general and -specific white matter microstructural bases for reading. The conjunction analysis identified white matter fiber bundles in two locations in the left hemisphere whose FA was associated with reading abilities in both English and Chinese speakers and the contrast analysis revealed one white matter fiber bundle in the left hemisphere whose FA specifically contributed to English reading.

One white matter fiber bundle for language-general FA-reading ability relationship was located in the left CR/CC/SLF. The CR/CC/SLF has been the focus of many previous studies of FA-reading relationship. Klingberg et al. (2000) firstly reported a positive correlation between the FA in left temporo-parietal area and reading ability ($x = -28$, $y = -20$, $z = 28$ in Talairach coordinates). Subsequent studies have
Table 2
Fiber clusters whose FA showed significant associations with reading abilities of American and Chinese subjects.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Voxels in cluster</th>
<th>Peak (MNI)</th>
<th>Anatomical location of cluster (≥ 5% probability on these tracts)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>American</td>
<td>3970</td>
<td>−3, −24, −22</td>
<td>L external (internal) capsule/inferior longitudinal fasciculus/inferior fronto-occipital fasciculus</td>
<td>.02</td>
</tr>
<tr>
<td></td>
<td>2853</td>
<td>36, −5, −22</td>
<td>R external (internal) capsule/inferior longitudinal fasciculus/inferior fronto-occipital fasciculus</td>
<td>.02</td>
</tr>
<tr>
<td></td>
<td>1158</td>
<td>13, 22, 20</td>
<td>R superior corona radiate/body (genu) of corpus callosum</td>
<td>.04</td>
</tr>
<tr>
<td></td>
<td>340</td>
<td>−11, 24, 18</td>
<td>L superior corona radiate/body (genu) of corpus callosum</td>
<td>.04</td>
</tr>
<tr>
<td></td>
<td>122</td>
<td>9, 30, 6</td>
<td>R genu of corpus callosum/anterior corona radiate/</td>
<td>.05</td>
</tr>
<tr>
<td>Chinese</td>
<td>1479</td>
<td>−23, −53, 9</td>
<td>L posterior (superior/anterior) corona radiate/body (splenium) of corpus callosum/posterior thalamic radiation/inferior fronto-occipital fasciculus</td>
<td>.02</td>
</tr>
<tr>
<td></td>
<td>885</td>
<td>−40, −8, −23</td>
<td>L anterior (superior) corona radiate/external capsule/uncinate fasciculus/superior longitudinal fasciculus</td>
<td>.03</td>
</tr>
<tr>
<td></td>
<td>312</td>
<td>−9, −3, −7</td>
<td>L internal capsule</td>
<td>.04</td>
</tr>
<tr>
<td></td>
<td>77</td>
<td>−17, −23, −6</td>
<td>L cerebral peduncle</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>−10, 24, 15</td>
<td>L genu of corpus callosum</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>−14, −23, −3</td>
<td>L anterior thalamic radiation</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>20, −25, 49</td>
<td>R corticospinal tract</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>−12, −26, −5</td>
<td>Unclassified</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>27, −42, 25</td>
<td>R posterior corona radiate</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>21, −29, 48</td>
<td>R corticospinal tract</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>−8, −21, 1</td>
<td>L anterior thalamic radiation</td>
<td>.05</td>
</tr>
</tbody>
</table>

L, left hemisphere; R, right hemisphere.

Fig. 1. Tracts whose FA was related to reading abilities of Americans (blue) or Chinese (red) or both (green, emphasized via TBSS command ths_fill) (corrected p < .05) and the scatter plot of associations between reading and FA of two main anatomical locations in left hemisphere (dorsal CR/CC/SLF and ventral UF/EC/IFO). L, left hemisphere; R, right hemisphere; CR, superior corona radiate; CC, body of corpus callosum; SLF, superior longitudinal fasciculus; UF, uncinate fasciculus; EC, external capsule; IFO, inferior fronto-occipital fasciculus.
generally confirmed their findings of FA differences between good and poor readers in the temporoparietal areas (Beaulieu et al., 2005; Carter et al., 2009; Deutsch et al., 2005; Lebel et al., 2013; Niogi and McCandliss, 2006; Odegard et al., 2009; Rimrodt et al., 2010; Steinbrink et al., 2008), although studies disagreed in terms of the specific tracts for this effect. Kingberg et al. found most voxels of this effect exhibited anterior–posterior orientation and suggested that they were within the arcuate fasciculus (a component of the SLF), the main pipeline between language regions of Wernicke’s and Broca’s areas. Other studies, however, placed this effect mainly in the CR oriented in the superior–inferior direction (Beaulieu et al., 2005; Deutsch et al., 2005; Niogi and McCandliss, 2006) or within the callosal pathways (CC) between left and right hemispheres (Ben-Shachar et al., 2007; Dougherty et al., 2007). The CR connects the cerebellum, thalamus, brainstem, and spinal cord with dorsal cortical motor and somatosensory regions. However, given the complexity of white matter tracts (e.g., different tracts may interdigitate), Beaulieu et al. (2005) also suggested that “other relevant white matter fibers crossing at this level, such as the adjacent SLF, could be responsible for the correlation with reading ability” (Beaulieu et al., 2005).

The other fiber bundle that exhibited common FA-reading ability relationship in both English and Chinese speakers was located in the left UF/EC/IFO (the insular area). This tract has been described in several previous tractography reports of reading (or language) pathways

<table>
<thead>
<tr>
<th>Voxels in cluster</th>
<th>Centre of gravity (MNI)</th>
<th>Anatomical location of cluster (&gt;5% probability on these tracts)</th>
<th>Pathways</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
</tr>
<tr>
<td>142</td>
<td>18</td>
<td>4</td>
<td>34</td>
</tr>
<tr>
<td>104</td>
<td>5</td>
<td>18</td>
<td>12</td>
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<tr>
<td>65</td>
<td>17</td>
<td>9</td>
<td>37</td>
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<tr>
<td>61</td>
<td>15</td>
<td>10</td>
<td>32</td>
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<tr>
<td>27</td>
<td>9</td>
<td>3</td>
<td>-19</td>
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<tr>
<td>18</td>
<td>13</td>
<td>10</td>
<td>32</td>
</tr>
<tr>
<td>16</td>
<td>3</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

L, left hemisphere; R, right hemisphere; CR, corona radiate; CC, corpus callosum; SLF, superior longitudinal fasciculus; UF, uncinate fasciculus; EC, external capsule; IFO, inferior fronto-occipital fasciculus.

Fig. 2. Tract whose FA was specifically related to reading abilities of Americans (red, emphasized via TBSS command tbs_fill) (corrected p < .05) and the scatter plot of associations between reading and FA of this tract (the left temporal SLF). L, left hemisphere; R, right hemisphere; SLF, superior longitudinal fasciculus.
The role in GPC. Future research is needed to replicate this finding and to test specifically the role of this tract in GPC with designs that can rule out the confounds of other linguistic and nonlinguistic differences between English and Chinese (i.e., visual analysis, lexical processing and language production).

In sum, by comparing the FA-reading ability relationships across languages and identifying two language-general white matter fiber bundles and one alphabetic language-specific white matter fiber tract, the current study extended previous cross-language research on functional neuroanatomical correlates of reading to white matter microstructural bases. Our results have important implications for understanding white matter pathway of reading different languages.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2014.04.080.

References


