Learning to Read Improves the Structure of the Arcuate Fasciculus

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The acquisition of literacy results from an effortful learning process that leads to functional changes in several cortical regions. We explored whether learning to read also leads to anatomical changes within the left intrahemispheric white matter pathways that interconnect these regions. Using diffusion tensor imaging tractography, we compared illiterates with ex-illiterates who learned to read during adulthood and literates who learned to read during their childhood. Literacy related to an increase in fractional anisotropy and a decrease in perpendicular diffusivity in the temporo-parietal portion of the left arcuate fasciculus. The microstructure within this pathway correlated with the reading performance and the degree of functional activation within 2 dominant brain regions involved in reading: The Visual Word Form Area in response to letter strings, and the posterior superior temporal cortex in response to spoken language. Thus, the acquisition of literacy is associated with a reinforcement of left temporo-parietal connections whose microstructure predicts overall reading performance and the functional specialization of the Visual Word Form Area. This anatomical magnetic resonance imaging marker may be useful to predict developmental reading disorders.

Keywords: diffusion, language, literacy, plasticity, tractography

Introduction

Reading a word consists in identifying a letter string and using it to access language-related representations of the word's phonological pattern and stored semantic and grammatical knowledge. Those skills are not innately present, but result from a long and effortful learning process. Brain activation studies show pervasive functional differences between the literate and illiterate brain. With literacy, the Visual Word Form Area, in the left occipito-temporal visual cortex, dramatically enhances its activation to known scripts (McCandliss et al. 2003; Shaywitz et al. 2004; Baker et al. 2007; Dehaene et al. 2010) and acquires a script-specific and case-invariant prelexical representation of letter strings (Dehaene et al. 2001; Vinckier et al. 2007; Braet et al. 2012). The left perisylvian language cortex, particularly the "planum temporale", also increases its activation to spoken words and sentences (Dehaene et al. 2010) and encodes phonology (Chang et al. 2010) and grapheme–phoneme correspondences (van Atteveldt et al. 2004; Blau et al. 2010). In literates, information trafficking between those 2 brain systems is enhanced in both the bottom-up and top-down directions (Dehaene et al. 2010; Yoncheva et al. 2010).

The acquisition of reading, like other expert skills (Draganski and May 2008), may also be expected to induce anatomical changes accessible to structural imaging. Indeed, comparisons of the anatomy of illiterates and literates revealed an increase of gray matter in the bilateral angular, dorsal occipital, middle temporal, and in left supramarginal and posterior superior temporal gyri (Carreiras et al. 2009). As concerns white matter tracts, the only documented correlate of literacy in normal readers consists in a thickening of the splenium or the isthmus of the corpus callosum (Carreiras et al. 2009; Castro-Caldas et al. 2009). Such a scarcity of white matter changes may seem surprising, as one would rather expect increased anatomical connectivity between left occipito-temporal regions devoted to the processing of alphabetic strings (the Visual Word Form Area) and regions subtending phonological and semantic processes. Several tracts may support such connectivity. The most relevant ones, inasmuch as they interconnect the ventral visual cortex and frontal and temporal language areas, include the 3 branches of the arcuate (long fronto-temporal, posterior temporo-parietal, and anterior fronto-parietal segments; Catani et al. 2005), the inferior longitudinal and the inferior fronto-occipital fasciculi (Catani et al. 2003; Fig. 1).

Here, we studied the impact of literacy on the microstructure of those tracts by acquiring diffusion-weighted images (Basser et al. 2000; Jones 2008) in 31 Brazilian adults of identical social origin, but variable schooling and literacy: 10 illiterates who never learned to read; 10 ex-illiterates who learned to read during adulthood; and 11 literates who learned to read during their childhood.

Materials and Methods

Participants

Thirty-one participants were recruited for this study and divided into 3 groups according to their literacy profile. They underwent neuroimaging scans at the Brasilia unit of the SARAH Network of Neurorehabilitation Hospitals and were pretested at local community schools or at home. All subjects were right-handed (as estimated using the Edinburgh handedness test; Oldfield 1971). All participants gave their written informed consent (the consent form was read aloud and explained to illiterates).

The illiterate participants ($n = 10$) were from rural areas (5 subjects) or urban centers in the Brasilia vicinity. Participants were illiterates for social reasons, with no history of special difficulty other than the lack of access to schools. The families of all these participants were originally from rural areas, and their parents had been illiterate rural workers. The average age of the illiterates was 53.3 (±7 years). The
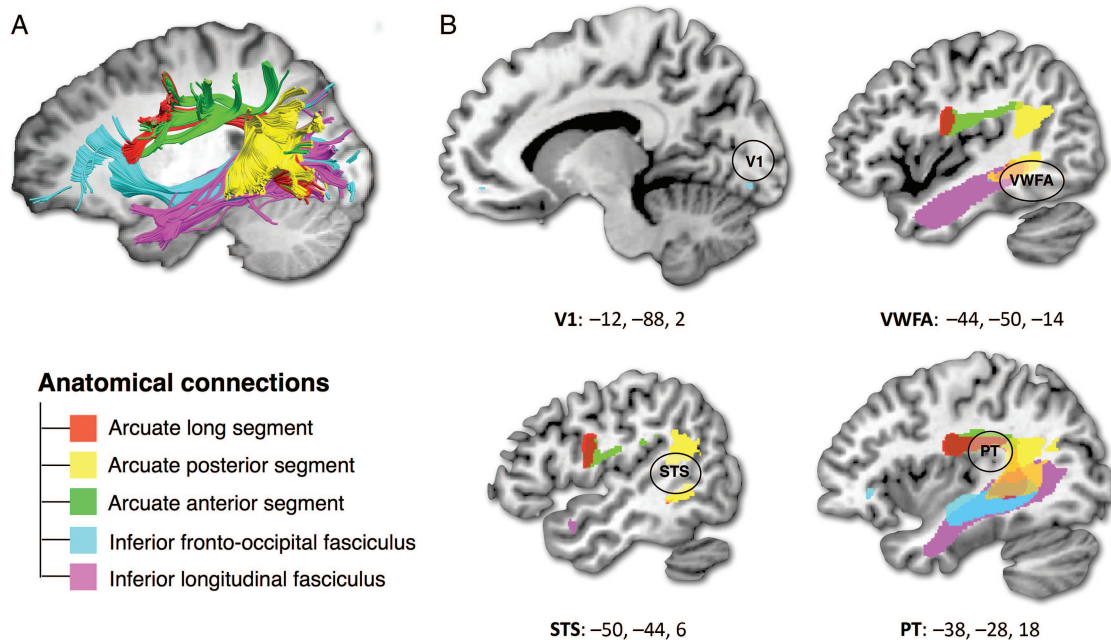
Figure 1. The extended reading network. fMRI has revealed a common network whose activation is modulated by the acquisition of literacy including the primary visual area (V1), the Visual Word Form Area (VWFA), the superior temporal sulcus (STS), and the planum temporale (PT; Dehaene et al. 2010). This network is highly interconnected via the arcuate fasciculus (long, posterior and anterior segment), the inferior fronto-occipital fasciculus, and the inferior longitudinal fasciculus, which therefore appear as prime candidates for a literacy-induced change in white matter organization. Tracts displayed in (A) come from a single representative participant, and in (B) from an atlas of human brain connections (http://www.natbrainlab.com, see Thiebaut de Schotten, ffytche, et al. 2011).

ex-illiterates group ($n = 10$) includes participants who had backgrounds similar to those of the illiterates (illiterate parents from rural areas). All had attended adult courses. The average age of the ex-illiterates was 49.5 (±10 years). The literate group ($n = 11$) comprised participants from the same social community as the illiterate group, but with 2–7 years of early education. The average age of the illiterates was 54.3 (±5 years). Full demographic information is reported in Table 1.

As a measure of reading performance, we assessed the number of words and readable pseudowords that could be read per minute (the same measure was used to identify functional magnetic resonance imaging (fMRI) correlates of reading expertize in the same participants; see Dehaene et al. 2010). For illiterates, who failed to identify even some single letters, the measure was set to 0.

Tractography Acquisition and Analysis

We used a 3-T whole-body system (Siemens Trio, Germany) to acquire 24 diffusion-weighted volume directions and 1 volume with no diffusion gradient applied covering the whole head of the participants with a resolution of $1.8 \times 1.8 \times 3.3$ mm. The diffusion weighting was equal to a b value of 1000 s/mm^{-2}. At each slice, raw diffusion-weighted data were simultaneously registered and corrected for subject motion and geometrical distortions using ExploreDTI (http://www.exploredti.com, see Leemans and Jones 2009). The tensor model was fitted to the data using the Levenberg–Marquardt nonlinear regression (Marquardt 1963). Fractional anisotropy (FA), a scalar value that describes the degree of diffusion anisotropy, was computed from the eigenvalues of the diffusion tensor (Basser and Pierpaoli 1996). Whole-brain tractography was performed using an interpolated streamline algorithm that propagates from voxel-to-voxel following a step length of 0.5 mm and a maximum angle threshold of 35°. Voxels showing a FA value inferior to 0.2 were excluded from the tractography (Jones et al. 2002; Jones 2003, 2004). The whole-brain tractography

Table 1

Demographical data and reading performance

Group	Age	Gender	Education	Profession	Reading score
Illiterate	49.7	F	1.5	Housewife	0
Illiterate	52.1	F	0.5	Housewife	0
Illiterate	47.5	F	0.3	Housemaid	0
Illiterate	55	M	3.5	Street vendor	0
Illiterate	62	M	0.9	Construction worker (master builder)	0
Illiterate	60.6	F	0.2	Housewife	0
Illiterate	64.4	F	0.9	Housewife	0
Illiterate	51.1	M	0.1	Rural worker	0
Illiterate	47	M	0.25	Rural worker	0
Illiterate	43.8	M	0.1	Public servant	0
Ex-illiterate	51.2	F	3	Housewife	8.25
Ex-illiterate	59.4	F	0.5	Housewife	7.75
Ex-illiterate	30.9	M	0.5	Construction worker (carpenter)	6.5
Ex-illiterate	41.6	M	2	Electrician	34.5
Ex-illiterate	60.7	M	1	Construction worker (master builder)	43.5
Ex-illiterate	50.9	M	1	Construction worker	18.75
Ex-illiterate	39.1	F	2.5	Housewife	17.75
Ex-illiterate	60	M	1	Taxi driver	42.25
Ex-illiterate	47.1	F	7	Housemaid	38.5
Ex-illiterate	54.5	F	2	Dressmaker	45.25
Literate	50.8	F	7.5	Housemaid	80.25
Literate	60.3	F	5	Housewife	39
Literate	53.4	F	6.5	Unemployed	57.75
Literate	49.8	F	8	Housemaid	119.25
Literate	58.5	M	5	Construction worker (master builder)	42.25
Literate	53.3	M	5	Construction worker (painter)	65.25
Literate	55.7	M	4	Construction worker (plumber)	26
Literate	58.1	F	7	Dressmaker	37.75
Literate	63.5	M	3	Rural worker	52.5
Literate	49.1	M	13	Yardman	79
Literate	55.6	M	10	Watchman	62

was imported to TrackVis (http://www.trackvis.org; Wedeen et al. 2008) using home-made software written in Matlab 2009b (http://www.mathworks.com). The fiber-tracking software allows for the identification of the tracts, visualization in 3-dimensional, and quantitative analyses on the delineated tracts. An expert anatomist, unaware of the group to which the participants belonged, performed the tractography dissections. Based on the previous tractography work, regions-of-interest (ROIs) were defined manually on the axial, coronal, and sagittal FA images of each participant and were used as seed regions for tracking. The trajectories of the 3 segments of the arcuate (i.e. long, anterior and posterior segments), the inferior longitudinal, and the inferior fronto-occipital fasciculi were obtained for both hemispheres, as previously described (Catani et al. 2007; Catani and Thiebaut de Schotten 2008). Average FA, perpendicular ($d_\perp$), and parallel diffusivities which are indirect measures of the white matter microstructural properties (Beaulieu 2002; Beaulieu 2009), were extracted along each tract.

As the number of streamlines and the tract volume may varies substantially between participants, we also used a recent diffusion tensor imaging (DTI) atlas (http://www.natbrainlab.com, see Thiebaut de Schotten, ffytche, et al. 2011; Catani et al. 2012; Catani and Thiebaut de Schotten 2012) to confirm our results using a ROI approach. We aligned individual whole-brain FA volumes to the FMRIB58 template using nonlinear registration as implemented in the FSL software package (http://www.fmrib.ox.ac.uk/fsl/, see Smith et al. 2004). We defined 5 specific brain regions in the FMRIB 58 space containing fibers of the posterior segment of the arcuate fasciculus, in order to identify between-group differences in FA.

fMRI Acquisition and Analysis

For each subject, as reported in a previous study (Dehaene et al. 2010), we collected the individual level of activation of the Visual Word Form Area to written strings relative to checkers, and the level of activation of the planum temporale in response to spoken sentences relative to the rest baseline. fMRI sequences were acquired using a gradient-echo planar imaging sequence sensitive to brain oxygen-level dependent contrast (40 contiguous axial slices, 3 mm thickness; TR = 2400 ms; flip angle = 81°, TE = 30 ms, in-plane resolution = 3 × 3 mm, matrix = 64 × 64). Auditory stimuli were presented via high-fidelity stereo headphones (MR Confon). An MR compatible LCD screen (12 × 17 cm) was used to present visual stimuli. The image on the screen was seen after reflecting on 2 mirrors, with a global visual angle of 17.3°.

Images of strings and checkers were presented in the MRI scan in short blocks of 12 stimuli (10.5 s), separated by a brief resting period with a fixation point only (3 s). Letter strings were pseudowords, 4 letters long, made of the lower-case letters 'bdmnpqiou' and were orthographically legal in Portuguese and 3.5 × 1.1° wide. The checker was an expanding circular grid of black-and-white designed to broadly cover the entire region where other stimuli could be presented. It was presented in a constantly expanding motion, starting at size of 4.9° and ending at 5.6° for the first checkerboard (duration 200 ms) as well as 7.1° for the second checkerboard (duration 500 ms).

The spoken language runs consisted in a lexical decision task on single spoken words (n = 40) and pseudowords (n = 40). The average duration of the stimuli was 660 ms. Within 1 fMRI run, all 80 stimuli were presented in random order, intermixed with an additional 20 rest trials in which no sound was presented. Each trial consisted in a short (100 ms) dimming of the fixation point, which served as a warning signal, followed 500 ms later by the presentation of a single word. There was an initial blank duration of 4 s, for a total duration of 5 min 24 s (324 s or exactly 135 TRs of 2.4 s). Each run was repeated 4 times in a different random order.

Participants were trained on all tasks inside a mock scanner before starting real data acquisition. A post-acquisition debriefing served to ensure that the subject correctly understood and performed the tasks. fMRI analysis relied on the Statistical Parametric Mapping software (SPM, http://www.fil.ion.ucl.ac.uk/spm/), as previously described (Dehaene et al. 2010).

Statistical Analysis

Statistical analysis was performed using SPSS software (SPSS, Chicago, IL). Bivariate Pearson correlations analyses were performed between the FA measurement of each single tract dissected and each participant's reading performance. Correlation significant at $P < 0.005$ survives Bonferroni correction for multiple comparisons (10 tracks). In our analysis, Gaussian distribution of the data was not confirmed for the reading score using the Shapiro–Wilk test (Shapiro and Wilk 1965). Therefore, results reported as significant with Pearson correlation were confirmed using the Spearman rank correlation coefficient (Spearman 1904). Independent sample 1-tailed t-tests and $d_{//}$ and $d_\perp$ 2-tailed correlations were performed for each tract revealed as significant by the correlations analyses between FA and the reading score.

Results

White Matter Microstructure and Literacy

Correlation analyses were used to quantify the relationship between anatomical and behavioral variables, revealing that better reading performance correlated with an increased FA in the posterior segment of the left arcuate fasciculus (Pearson $r = 0.531$; $P = 0.002$; Fig. 2A). This result was confirmed using bivariate Spearman rank correlation coefficient ($\rho = 0.482$; $P = 0.006$). Independent sample t-tests showed that, in the left posterior segment, illiterates had a lower FA than literates ($t_{19} = -2.683$; $P = 0.008$), and a lower FA than ex-illiterates ($t_{18} = -1.939$; $P = 0.034$). There was no significant difference between the ex-illiterate and literate groups ($t_{19} < 1$; Fig. 2B). Thus, FA in the posterior arcuate depended solely on literacy, not on early schooling, and was enhanced even when literacy was acquired in adulthood.

There was also a trend of correlation between reading score and FA in the right posterior segment ($r = 0.348$; $P < 0.055$). This trend was confirmed with nonparametric correlations ($\rho = 0.391$; $P < 0.030$). No significant correlation was observed in the left and right inferior longitudinal fascicles (left, $r = 0.277$; $P = 0.132$; right, $r = 0.255$; $P = 0.167$), inferior fronto-occipital fascicles (left, $r = 0.222$; $P = 0.230$; right, $r = 0.294$; $P = 0.108$), the anterior (left, $r = 0.054$; $P = 0.777$; right, $r = 0.297$; $P = 0.105$), and long segments (left, $r = 0.263$; $P = 0.153$; right, $r = 0.371$; $P = 0.089$) of the arcuate fascicles.

Measurements of FA along the posterior segment of the arcuate fasciculus using 5 axial ROIs confirmed that, for 4 of these 5 regions, illiterates had a lower FA than literates (ROI 1, $t_{19} = -2.647$; $P = 0.008$; ROI 2, $t_{19} = -1.970$; $P = 0.032$; ROI 3, $t_{19} = -2.265$; $P = 0.018$; ROI 4, $t_{19} = -1.799$; $P = 0.045$; ROI 5, $t_{19} < 1$; Fig. 2C).

FA is computed on the basis of parallel diffusivity along the fiber's direction ($d_{//}$), and of diffusivities along the 2 minor axes, which may be averaged to produce a measure of perpendicular diffusivity ($d_\perp$; Beaulieu 2010). To better interpret the observed differences in FA, we collected in each participant the average $d_{//}$ and $d_\perp$ along the left posterior segment of the arcuate fasciculus. The $d_\perp$ in the posterior segment correlated negatively with the reading score ($r = -0.375$; $P = 0.038$; Fig. 2D). This result was confirmed using bivariate Spearman rank correlation coefficient ($\rho = -0.389$; $P < 0.031$). No significant correlation was observed between $d_{//}$ and the reading score ($r = -0.021$; $P < 0.909$).
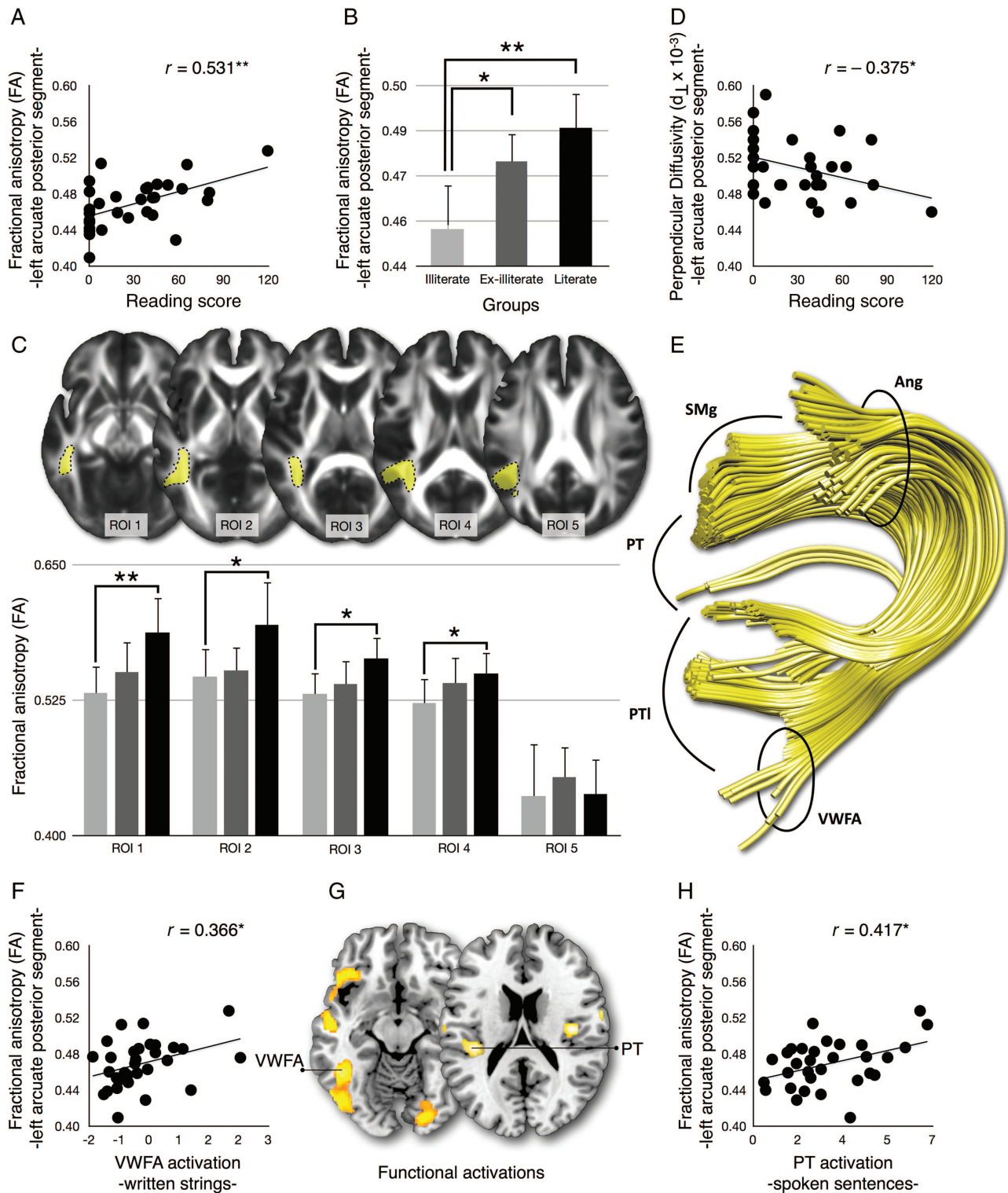
Figure 2. Links between the microstructure of the posterior segment of the arcuate fasciculus, behavioral reading scores, and functional neuroimaging correlates of literacy. (*A*) Correlation between the FA in the posterior segment of the left arcuate fasciculus and reading performance. (*B*) Average FA in the left posterior segment (with 95% confidence intervals) for the illiterate (light gray), ex-illiterate (dark gray), and literate groups (black). (*C*) Average measurements of FA along the left posterior segment of the arcuate fasciculus made using 5 regions of interest selected on axial slices. (*D*) Correlation between the $d_\perp$ in the left posterior segment of the arcuate fasciculus and reading performance. (*E*) The posterior segment of the arcuate fasciculus and its projections (posterior coronal view). (*F*) Correlation between the FA in the posterior segment of the left arcuate fasciculus and the level of activation of the VWFA to written strings relative to checkers. (*G*) Functional activations in response to letter strings (left) and to spoken language (right) ([Dehaene et al. 2010](#)). (*H*) Correlation between the FA in the posterior segment of the left arcuate fasciculus and the level of activation of the PT in response to spoken sentences. SMg: supramarginal gyrus; Ang: angular gyrus; PT: planum temporale; VWFA: Visual Word Form Area; PTl: posterior temporal lobe; **$P < 0.01$; *$P < 0.05$.

Temporo-Parietal Microstructure and Reading-Related Functional Activations

The posterior segment of the left arcuate fasciculus links the posterior temporal lobe, including the Visual Word Form Area, with the inferior parietal lobule and posterior superior temporal regions, including the supramarginal gyrus and posterior superior temporal gyrus/sulcus (Fig. 2E), involving in phonological coding and grapheme-to-phoneme translation (van Atteveldt et al. 2004; Binder et al. 2009; Blau et al. 2010; Graves et al. 2010). Its connections thus encompass 2 dominant sites of functional changes with literacy: The Visual Word Form Area in response to letter strings, and the superior temporal region in response to spoken language (Dehaene et al. 2010). Our findings suggest that reading acquisition may entail an enhanced communication between these 2 regions. If so, we would expect that its anisotropy would be directly correlated with the level of functional activation at these 2 sites.

To test this hypothesis, for each subject, we extracted 2 fMRI measures from our previous study (Dehaene et al. 2010): The level of activation of the Visual Word Form Area to written strings relative to checkers, a putative measure of orthographic learning; and the level of activation of the planum temporale in response to spoken sentences, a putative measure of the refined phoneme-level analysis (also called "phonological awareness") made possible by the acquisition of an alphabetical writing system. Both measures were found to correlate positively with FA across subjects (respectively, $r = 0.366$; $P = 0.043$, Fig. 2F–G and $r = 0.417$; $P = 0.02$, Fig. 2G–H). Furthermore, they made independent significant contributions to FA in a multiple-regression model with these 2 regressors (respectively, $t = 2.104$; $P = 0.044$ and $t = 2.446$; $P = 0.021$). Once reading score was entered in the model, however, this behavioral variable became the only significant predictor of FA, and fMRI activations no longer made an independent contribution. Overall, these findings are compatible with the hypothesis that learning to read is the causal variable that induces parallel changes both in the functional responses of the Visual Word Form Area and the planum temporale, and in the microstructure of the pathway connecting them.

Discussion

Our study is the first to report a change in the microstructure of the temporo-parietal portion of the left arcuate fasciculus in literate relative to illiterate subjects. Carreiras et al. (2009) previously explored the morphological brain changes induced by literacy acquisition in a group of unschooled adults with or without alphabetization courses, and uncovered a change in the callosal white matter. However, their study only relied on T_1-weighted anatomical images and voxel-based analyses of gray and white matter densities. Compared with this earlier and important work, here, we obtained detailed images of white matter organization in illiterates using the method of DTI. The sensitivity of this method allowed us to uncover subtle changes in the temporo-parietal portion of the left arcuate fasciculus.

In expert readers, the left posterior superior temporal region is involved in encoding the pronunciation of written letters (van Atteveldt et al. 2004) and words (Simos et al. 2002) and, thus, participates in the grapheme–phoneme conversion route for reading. The observed change in the microstructure of the posterior arcuate fasciculus may directly reflect the impact of literacy in training this grapho-phonological decoding route. Accordingly, and although findings are still not fully convergent, differences in reading performance in normal versus dyslexic populations have been correlated with structural features of the arcuate fasciculus (reviews in Rimrodt et al. 2010; Yeatman et al. 2011). We note, however, that the arcuate fasciculus may be involved in reading not only by supporting the phonemic route to the superior temporal lobe, but also by its projection to the angular gyrus, a route possibly subtending the translation of orthography to semantics (Vigneau et al. 2006). Thus, the posterior segment of the left arcuate fasciculus may well be involved in both lexical and non-lexical reading routes, explaining why it is the fascicle whose microstructure is modified the most through the acquisition of reading.

It is noteworthy that the difference in arcuate FA remained significant when restricting the analysis to the 2 groups of illiterate and ex-illiterate participants. These subjects came from the same communities and had been equally deprived of schooling during childhood, but only the ex-illiterates had eventually learned to read during adulthood, with variable degrees of performance. The fact that they showed an increased FA indicates that literacy acquisition can refine the organization of white matter well beyond childhood.

The change in microstructure reported in our study may be associated with a change in fiber density, myelination, or axonal diameter. As models of diffusion show, FA is most sensitive to the fiber packing density, and more specifically, the amount of extra-axonal space (Beaulieu 2002; Ball et al. 2009; Stikov et al. 2011). All else being equal, increases in myelination will tend to decrease the extra-axonal space and, thus, to increase FA. However, FA increases can also arise from an increase in axon density, holding myelination constant. Conversely, FA decreases can be caused by a reduction in packing density, as from Wallerian degeneration (Epelbaum et al. 2008).

Animal studies suggest that a decrease in $d_\perp$, as observed here, can be induced by an increased myelination (Ono et al. 1995; Gulani et al. 2001; Song et al. 2002; Nair et al. 2005; Tyszka et al. 2006; Harsan et al. 2007; Zhang et al. 2009; Beaulieu 2010). Thus, one possible interpretation of our results is an increased myelination of the arcuate with literacy. Such an effect would be compatible with animal studies demonstrating that increased axonal activity may lead to increased myelination (Demerens et al. 1996; Stevens et al. 1998; Stevens and Fields 2000; Zalc and Fields 2000; Stevens et al. 2002). However, this interpretation is not univocal, because of the possible complications induced for instance by the effects of crossing fibers or morphological considerations (e.g., thickness and shape of the fiber bundle) on the estimated diffusivity metrics (Alexander et al. 2001; Wheeler-Kingshott and Cercignani 2009; Vos et al. 2011, 2012). Most of the white matter contains a complex fiber architecture (Jeurissen et al. 2012), and new development in terms of reconstructing fiber trajectories (Dell'Acqua et al. 2010; Jeurissen et al. 2011; Thiebaut de Schotten, Dell'Acqua, et al. 2011) and estimating fiber-specific rather than voxel-specific microstructure (Dell'Acqua et al. 2012) will be needed in order to improve the neurobiological interpretation of our results and circumvent its pitfalls (Tournier et al. 2011; Dell'Acqua and Catani 2012; Jones et al. 2012).

In conclusion, the acquisition of literacy is associated with a reinforcement of left temporo-parietal connections whose microstructure predicts overall reading performance and the functional specialization of the Visual Word Form Area. Our study confirms that learning to read causes demonstrable changes in brain structure (Carreiras et al. 2009; Castro-Caldas et al. 2009). It also leads to a word of caution in interpreting the white matter and diffusion anomalies that are observed in developmental reading disorders. These anomalies may have a complex causal path: poor readers who may be endowed with suboptimal white matter pathways even prior to reading experience, but their white matter anomalies may also arise as a consequence of fewer hours of exposure to print (Ben-Shachar et al. 2007; Rollins et al. 2009). Further research should investigate whether the magnetic resonance imaging marker that we studied here can help to diagnose and predict developmental reading disorders (Rimrodt et al. 2010; Vandermosten et al. 2012).

Notes

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