

An anatomical signature for literacy

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Language is a uniquely human ability that evolved at some point in the roughly 6,000,000 years since human and chimpanzee lines diverged^{1,2}. Even in the most linguistically impoverished environments, children naturally develop sophisticated language systems³. In contrast, reading is a learnt skill that does not develop without intensive tuition and practice. Learning to read is likely to involve ontogenic structural brain changes⁴⁻⁶, but these are nearly impossible to isolate in children owing to concurrent biological, environmental and social maturational changes. In Colombia, guerrillas are re-integrating into mainstream society and learning to read for the first time as adults. This presents a unique opportunity to investigate how literacy changes the brain, without the maturational complications present in children. Here we compare structural brain scans from those who learnt to read as adults (late-literates) with those from a carefully matched set of illiterates. Late-literates had more white matter in the splenium of the corpus callosum and more grey matter in bilateral angular, dorsal occipital, middle temporal, left supramarginal and superior temporal gyri. The importance of these brain regions for skilled reading was investigated in early literates, who learnt to read as children. We found anatomical connections linking the left and right angular and dorsal occipital gyri through the area of the corpus callosum where white matter was higher in late-literates than in illiterates; that reading, relative to object naming, increased the interhemispheric functional connectivity between the left and right angular gyri; and that activation in the left angular gyrus exerts top-down modulation on information flow from the left dorsal occipital gyrus to the left supramarginal gyrus. These findings demonstrate how the regions identified in late-literates interact during reading, relative to object naming, in early literates.

After decades spent fighting, members of the guerrilla forces have begun re-integrating into mainstream Colombian society, introducing a sizeable population of illiterate adults who have no formal education. Upon putting down their weapons and returning to society, some had the opportunity to learn to read for the first time in their early twenties, providing the perfect natural situation for experiments investigating structural brain differences associated with the acquisition of literacy in the absence of other types of schooling or maturational development. To this end, we obtained high-resolution T₁-weighted magnetic resonance imaging (MRI) scans from 42 right-handed healthy adults: 20 late-literates who had completed a literacy program in adulthood in their native tongue (Spanish) and 22 age- and culturally matched illiterates who had not yet started that literacy program. Thus, unlike in studies of developmental dyslexia, there were no known between-group differences in reading potential. Moreover, our analyses factored out variability in more general cognitive skills.

The results of a voxel-based morphometry (VBM) comparison (experiment one; Fig. 1) showed that late-literates had more grey

matter than illiterates in five posterior brain regions that form a subset of those activated in functional imaging studies of reading^{7,8}. Specifically, grey-matter density increases were identified in bilateral dorsal occipital areas associated with higher-level visual processing, in left supramarginal and superior temporal areas associated with phonological processing and in the angular gyri and posterior middle temporal regions associated with semantic processing. In addition, and as observed previously^{5,6}, the ability to read was associated with a greater amount of white matter in the splenium of the corpus callosum (SCC), which is frequently damaged in pure alexic patients who are unable to read despite good language function⁹. These structural differences in known reading areas were observed even in subgroups of participants who were closely matched on a range of different cognitive abilities (Fig. 1). They are therefore likely to be consequences of learning to read, consistent with longitudinal studies that have shown regional changes in brain structure with the acquisition of new skills in adults⁴ as well as in children¹⁰.

Although the identified areas are all within the known reading network^{7,8}, neither the voxel-based structural analysis nor previous results indicate how the areas are anatomically or functionally connected to one another. The aim of our second experiment was to integrate the grey- and white-matter results from experiment one using tractography analyses with diffusion tensor imaging (DTI). Specifically, we looked for an interhemispheric white-matter track that linked left- and right-hemisphere homologues (that is, angular gyri and/or dorsal occipital areas) through the region of the SCC area where white-matter amount differed according to literacy. In ten adults who learnt to read English in childhood, we found strong interhemispheric paths linking the left angular and dorsal occipital gyri with the right angular and dorsal occipital gyri through the precise region of the SCC identified in the first experiment (Fig. 2). Long range connections through the SCC are laid down *in utero* and will therefore be present irrespective of literacy experience. On the basis of experiment two, we suggest that learning to read in adulthood alters the properties of the interhemispheric links between the left and right angular and dorsal occipital gyri. This perspective integrates the grey- and white-matter findings from experiment one into the same anatomical system; however, we can not rule out the possibility that the white-matter differences in late-literates relative to illiterates pertain to other tracts through the same area of the corpus callosum (for example, those connecting the temporal lobes).

To investigate the functional connectivity within the identified anatomical system, our third experiment used functional magnetic resonance imaging (fMRI) and dynamic causal modelling (DCM) in 20 adults who learnt to read English in childhood. Reading activity was compared with object-naming activity in the regions showing structural differences between late-literates and illiterates in experiment one. We chose object naming as the baseline to control for

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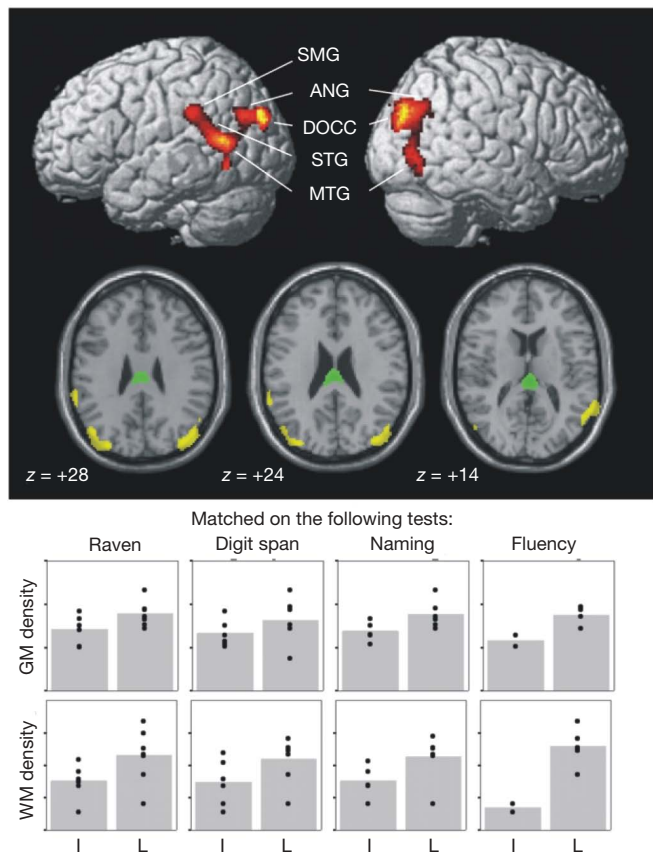


Figure 1 | The effect of literacy on brain structure. Upper images show the locations of grey-matter increases in 20 literates relative to 22 illiterates, with a height threshold of $P < 0.001$ and an extent threshold of $P < 0.05$, corrected for multiple comparisons across the whole brain. Data were processed using VBM procedures in the brain-imaging software SPM5 with covariates of no interest that factored out the effects of age, gender, global intensity and neuropsychological performance. The images below these are axial slices (left side of image corresponds to left hemisphere) showing grey-matter (yellow) and white-matter (green) differences with literacy. Peak x , y and z coordinates in MNI (Montreal Neurological Institute) space were $(-47, -74, +28)$ and $(+50, -72, +32)$ in the left and right angular gyri (ANG), respectively; $(-34, -86, +26)$ and $(+34, -86, +26)$ in the left and right dorsal occipital gyri (DOCC), respectively; $(-54, -62, +10)$ and $(+60, -72, -4)$ in the left and right middle temporal gyri (MTG), respectively; $(-64, -38, +30)$ and $(-62, -46, +22)$ in the left supramarginal gyrus (SMG) and the posterior superior temporal gyri (STG), respectively; and $(0, -26, +16)$ and $(-6, -36, +6)$ in the left- and right-hemispherical corpus callosum, respectively. No differences in left ventral occipito-temporal grey matter were identified even when the statistical threshold was reduced to $P < 0.05$ uncorrected. Bottom rows: Grey-matter (GM) and white-matter (WM) (density in arbitrary units) extracted from and summed over all the identified voxels in the VBM analysis for subgroups of illiterates (I) and literates (L) who were matched for scores on four tests of intellectual ability. Each dot represents the value for an individual subject, and the height of the bar indicates the average of these values. See Supplementary Table 1 for full details.

processes involved in the recognition of complex visual stimuli, name retrieval and speech production¹¹. Although our DCM analyses only included the areas that in experiment one were associated with learning to read in adulthood, the influence of all other reading areas is implicitly assumed (Supplementary Information).

Our first functional connectivity analysis showed that reading, relative to object naming, increased interhemispheric functional connectivity between the left and right angular gyri but not between the left and right dorsal occipital regions (Fig. 3a). Therefore, the results of all three experiments associate interhemispheric connections with the left and right angular gyri. Moreover, the results of experiments one and three highlight the importance of these connections for

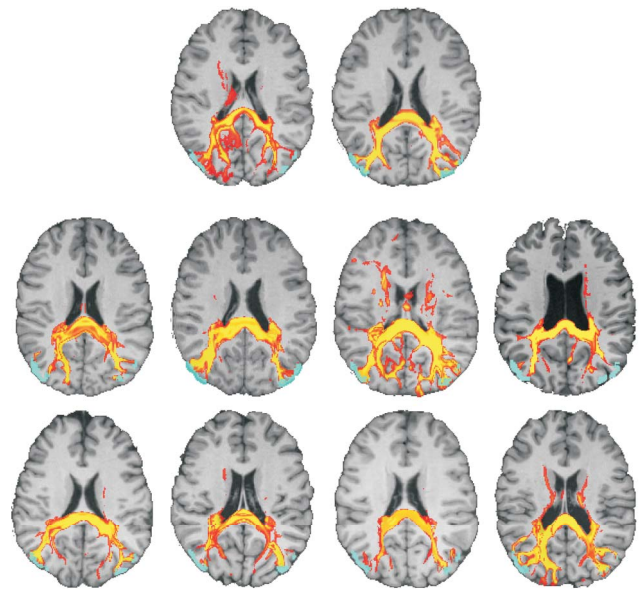


Figure 2 | Anatomical connectivity results. Diffusion-weighted magnetic resonance images from ten early-literates were acquired with a b value of $1,000 \text{ s mm}^{-2}$ uniformly distributed across 60 gradient directions. Paths through the corpus callosum region of interest were identified using a Markov-chain Monte Carlo technique with 25,000 samples in each voxel in the left and right angular and dorsal occipital gyri that was structurally different (at $P < 0.001$) in the late-literates and illiterates (shown in blue). The resulting images (yellow/red) represent empirically determined probability distributions linking the left and right hemisphere regions of interest in each subject.

reading. This correspondence across experiments was observed despite the use of different methods (VBM, DTI and DCM) in different populations varying in age of reading acquisition, language spoken and reading ability.

Experiment three also allowed us to investigate how activity for reading, relative to object naming, is propagated through the left-hemisphere anatomical system identified in experiment one. The results (Fig. 3b) suggest that reading increased the functional coupling from visual (DOCC) to phonological (SMG) processing areas either directly or by means of semantics (in MTG). This is consistent with reading increasing the demands on the retrieval and assembly of speech sounds^{11–16}. In addition, the angular gyrus had a top-down modulatory effect on dorsal occipital activity. This may reflect top-down constraints on the discrimination of visually similar words with different meanings (for example, chain and chair).

Our findings can now be used to revisit structural and functional imaging studies of acquired and developmental dyslexia. In particular, an understanding of the anatomical mechanisms that support the process of learning to read can be used to determine whether neuronal abnormalities are a cause or a consequence of the inability to read. For example, many studies have shown that developmental dyslexics have reduced left temporoparietal grey matter^{17–20} and reduced SCC white matter^{21–23}. The effect of literacy in the present study suggests that this might be the consequence of reading experience rather than the cause of reading difficulties.

Finally, we consider why experiment one did not reveal structural brain differences for literates relative to illiterates in the left ventral occipito-temporal region, where damage can result in pure alexia¹⁰. Previous functional imaging studies of children have shown that in the early stages of learning to read English, dorsal parietal activation predominates, after which skilled reading utilizes more ventral occipito-temporal areas^{24,25} that also support object naming¹¹. We therefore predict that the dorsal system may be more important than the ventral system in early stages of reading—when reading is less proficient and not yet automatic—and in transparent orthographies (like Spanish)

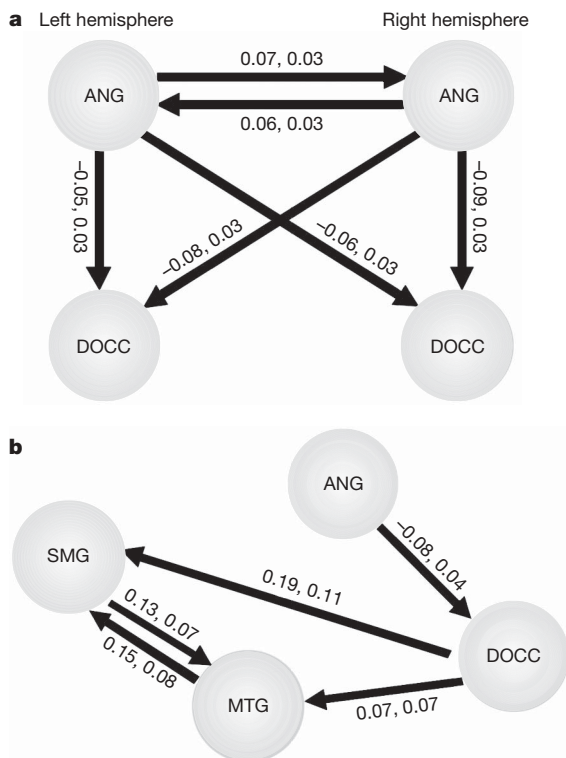


Figure 3 | Functional connectivity results. Two dynamic causal models were defined and estimated in each of 20 literate subjects using standard procedures in SPM5. All forward and backward connections were specified (fully connected dynamic causal models) but only illustrated where the modulatory effect of reading was significantly stronger ($P < 0.05$) than that for object naming. The values on each connection refer to the strengths of intrinsic connections and modulatory effects, respectively (in hertz).

a, Assessment of the interhemispheric effective connectivity between left and right dorsal occipital gyri and left and right angular gyri. Driving inputs (words and objects) were connected to left and right occipital gyri. Only the interhemispheric connections that involved the angular gyrus were significant. **b**, Assessment of the interactions of the four left-hemisphere regions that belong to the anatomical system identified in experiment one. Driving inputs (word and objects) were connected to the left occipital gyrus. Note that the only significant top-down (backward) modulation to this input region is exerted by the angular gyrus.

in which there is a consistent relationship between spelling and sound. In contrast, the ventral system may be more important in later stages—when skilled reading is fast and automatic—and in deeper orthographies (like English²⁶) that necessitate parallel letter processing because of the inconsistent spelling–sound relationships. Future longitudinal studies are required to test these predictions.

In conclusion, we have identified structural brain differences in late-literates relative to illiterates and used these results to guide anatomical and functional connectivity analyses in early-literates. Our findings shed light on neurological models of reading. First, they suggest that learning to read strengthens the coupling between left and right angular gyri and that this coupling is mediated by anatomical white-matter pathways through the SCC. Second, they show that when words are read aloud, the angular gyrus provides top-down constraints on the functional interactions between visual processing in the dorsal occipital gyrus and speech processing in the supramarginal gyrus. This contradicts the classic version of the neurological model, which posits that information flows from visual areas through the angular gyrus to the superior temporal gyrus^{27–30}. We suggest that reading increases the functional connectivity between the left and right angular gyri and on information flow from the left dorsal occipital gyrus to the left supramarginal gyrus, with the left angular gyrus playing a top-down modulatory role.

Future studies are required to investigate anatomical and functional connectivity in late-literates and to tease apart which components of their literacy training were effective in generating the structural brain differences. Nevertheless, this study demonstrates that learning to read in adulthood can have a significant effect on the structure of brain regions that are important for skilled reading in early-literates.

METHODS SUMMARY

Experiment one compared structural MRI scans from 22 late-literates and 20 culturally matched illiterates. Grey- and white-matter density was estimated on the basis of T_1 -weighted anatomical whole-brain images acquired using a GE 1.5T MRI system. VBM statistical analyses were conducted using SPM5 separately for grey- and white-matter images. Linear contrasts produced two t -statistic maps, one for activation that was greater in literates than in illiterates and one for activation that was greater in illiterates than in literates.

Experiment two used DTI and tractography analyses in 10 adults who learnt to read in childhood (early-literates). Diffusion-weighted magnetic resonance images were collected using a 1.5T Siemens Sonata MRI system. The aim of the tractography analyses was to investigate the link between the grey- and white-matter regions identified in experiment one.

Experiment three used fMRI to compare reading and object naming in 20 early-literates. There were three conditions: naming pictures of objects, reading the written names of the objects and articulating “1, 2, 3” in response to unfamiliar symbols and pictures. The fMRI analysis using SPM5 investigated regional activation differences for reading relative to picture naming in the significant regions of interest identified in the VBM analysis. Peak activations were identified using the peak coordinates from experiment one with a 6-mm-radius search volume. In addition, a DCM analysis was performed to investigate how the brain regions interacted during reading relative to object naming. For each region, eigenvectors were extracted in each participant at the closest maxima within a distance of 4 mm from the group peaks. The first dynamic causal model tested the effective connectivity between left and right hemispheres in DOCC and ANG regions. The second dynamic causal model tested the effective connectivity between the left-hemisphere regions of interest from the anatomical reading system identified in experiment one.

Full Methods and any associated references are available in the online version of the paper at www.nature.com/nature.

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Supplementary Information is linked to the online version of the paper at www.nature.com/nature.

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Author Contributions M.C., M.L.S., J.T.D. and C.J.P. designed the experiments, performed the data analyses and wrote the paper. S.B., A.E. and A.L. performed experiment one.

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METHODS

We conducted three different experiments (see Supplementary Information for full discussion).

Experiment one: structural imaging of late-literates and illiterates. This study was approved by the ethics committee of the University of La Laguna.

Forty-two right-handed³¹ native Spanish-speakers from Colombia provided written consent to participate. Most were members of the Colombian guerrilla forces that had put down their weapons. The rest were housewives from a similar socio-economic background. The 22 illiterates (11 males and 11 females, with a mean age of 32.8 years) were about to start a literacy program. The 20 literates (10 males and 10 females, with a mean age of 31.5 years) had already completed the literacy program in adulthood. This was primarily based on learning to recognize words on the basis of spelling–sound relationships in Spanish. All 20 literates had been actively reading and writing in Spanish for at least five years. They had a normal neuropsychological profile^{32–37} (see Supplementary Table 1 for details) and performed at ceiling on standardized tests of Spanish reading designed for 7–12-year-old children³⁸. When tested for comprehension of sentences and small texts, they responded 98% correctly to the comprehension questions asked afterwards, showing a good reading level. Finally, on the most difficult task (text comprehension³⁸) they scored an average of 85% (range, 64–100%). Overall, these results confirm a good level of reading proficiency, consistent with the increased grey matter that they expressed in known reading areas.

The criteria for inclusion in the illiterate sample were as follows: (1) lack of formal schooling, owing to there being no opportunity to gain any; (2) inability to read more than five simple words following tests including the reading and writing of words, the reading of sentences and the comprehension of a text³⁸, as administered to the literate participants; (3) normal performance in daily-life activities according to their socio-cultural environment; (4) right-handedness according to the Edinburgh inventory³¹; and (5) a normal neuropsychological profile^{32–37} (see Supplementary Table 1 for details) on the Raven test (Raven), digit span (Digit), picture naming (Naming) and verbal fluency (Fluency).

Focal grey- and white-matter densities were estimated on the basis of T₁-weighted anatomical whole-brain images acquired in a GE 1.5T MRI system. We used a whole-brain three-dimensional (3D) sequence to acquire two structural images in the axial and coronal planes that were subsequently averaged to ensure the best signal contrast. The 3D spoiled-gradient-recalled acquisition sequence was obtained with the following acquisition parameters: TR = 15.8 ms; TE = 4.2 ms; TI = 450 ms; flip angle, 20°; slice thickness, 1.5 mm; field of view, 24 cm; matrix size, 256 × 192 pixels.

Data were processed using the SPM5 software package (Wellcome Trust Centre for Neuroimaging; <http://www.fil.ion.ucl.ac.uk/spm/>) after checking all images for artefacts. The unified segmentation algorithm in SPM5 involves alternating between tissue classification, bias correction and spatial normalization in the inversion of a single generative model³⁹ and outputs grey- and white-matter probability images that were smoothed using an isotropic Gaussian kernel with a full-width at half-maximum (FWHM) of 12 mm. Statistical analyses were conducted separately for grey- and white-matter images with proportional scaling to remove global signal-intensity differences. Each analysis used the general linear model with two groups (literate and illiterate) and seven covariates of no interest that factored out the effect of age, gender and performance on the five neuropsychological tests^{32–37} (digit span, Raven, picture naming, phonological fluency and mini-mental state examination). Neither gender nor age differed between groups (for example, the mean age was 31.5 years for the literates and 32.8 years for the illiterates, and the age range was 21–52 years for the literates and 20–52 years for the illiterates; see Supplementary Table 1). By modelling age and gender as covariates of no interest in the multiple regression, we aimed to reduce within-group error variance. As expected, performance in the five neuropsychological tests was higher on average in the literate and illiterate groups. This is likely to be a consequence of learning to read^{40,41}. Nevertheless, we wanted to factor out this variance to ensure that our findings focused on structural changes related to reading ability rather than other cognitive skills.

Linear contrasts produced two *t*-statistic maps, one for activation that was greater in literates than in illiterates and one for activation that was greater in illiterates than in literates (after factoring out the effect of the seven additional regressors). Regional differences were reported as significant at $P < 0.05$ after family-wise error correction for multiple comparisons either at the height or the volume level. In addition, we checked specifically for differences between literates and illiterates in the left occipito-temporal region that is sometimes referred to as the visual word form area⁴² by defining a 10-mm-radius spherical region of interest around the coordinates (−42, −56, −14). No significant effects were observed in this region even when the statistical threshold was reduced to $P < 0.05$ uncorrected (*Z*score, >1.64).

Experiment two: diffusion tensor imaging. Data for experiment two were collected at the Oxford Centre for Magnetic Resonance imaging in the UK because the protocols and facilities were not available in Bogotá. However, as indicated above and in the main text, the basic pattern of long-range connections that this study identified are laid down *in utero* and are therefore expected to be present irrespective of literacy experience. In other words, learning to read will not generate *de novo* anatomical connections; instead, it modifies existing pathways. Moreover, there were advantages to collecting corresponding data in a different sample of individuals. In particular, experiment two allows us to confirm predictions from experiment one.

Diffusion-weighted magnetic resonance images were collected from ten healthy, literate volunteers (six male, four female) aged 18–37 years (mean, 24 years), all of whom provided informed consent after explanation of the protocol. Scanning was performed at the Oxford Centre for Magnetic Resonance Imaging on a 1.5T Siemens Sonata with a maximum gradient strength of 40 mT m^{−1}. Two sets of echo-planar images of the whole head were acquired (60 2.5-mm thick axial slices; in-plane resolution, 2.5 mm × 2.5 mm). Each set comprised three non-diffusion-weighted and 60 diffusion-weighted images acquired with a *b* value of 1,000 s mm^{−2} uniformly distributed across 60 gradient directions⁴³. These were pre-processed to correct for eddy currents and remove minor head motions⁴⁴, averaged to improve the signal-to-noise ratio and converted into voxel-wise 3D probability density functions assuming a single fibre direction except where the evidence merited increasing the model complexity by including crossing fibres⁴⁵. Finally, we also acquired a high-resolution T₁-weighted image (3D FLASH sequence; TR = 12 ms; TE = 5.60 ms; flip angle, 19°; voxel size, 1 mm × 1 mm × 1 mm) for anatomical localization.

The aim of the tractography analyses was to investigate the link between the grey- and white-matter VBM results. Specifically, we tested the hypothesis that the white-matter differences in the SCC reflected an interhemispheric anatomical connection between left- and right-hemisphere homologue regions where there were significant grey-matter differences in the structural comparison of grey matter in literates and illiterates in both hemispheres. The only two areas with significant effects (corrected for multiple comparisons) in both left and right hemispheres in experiment one were the angular gyrus and the dorsal occipital cortex. We did not include the temporal regions, because the location of the effects in the left and right middle temporal areas were more than 14 mm apart ((−54, −62, 10), (+60, −72, −4)), and the effects in the supramarginal/superior temporal areas only reached significance in the left hemisphere.

Corticocortical connections linking the left and right angular gyri were traced using a probabilistic tractography algorithm⁴⁶ in each of the ten subjects. Because the VBM findings were group results localized in MNI space but the tractography was carried out in individuals (in native space), the first step was to map the VBM results from experiment one onto each participant's anatomy. This involved the following procedure. First, structural images for each of the ten subjects were converted to MNI space using a linear transformation. The voxels showing significant effects in experiment one ($P < 0.001$ uncorrected) were then transposed onto the structural image in MNI space. To ensure that registration was accurate, we only excluded voxels if they had a 20% or less chance of being grey matter. In other words, the only voxels used to seed each DTI analysis were those from the VBM results that were present in that individual's angular gyrus and dorsal occipital gyrus grey matter. These were manually checked to verify the accuracy of this process. For all tractography analyses, each of the seed voxels was converted back into native space by reversing the linear transformation.

Paths were determined three times using a Markov-chain Monte Carlo technique with 1,000, 5,000 or 250,000 samples per seed voxel. All paths that did not intersect the SCC identified by the VBM white-matter analyses (and mapped on the individual's own corpus callosum) were excluded. The resulting images represent empirically determined probability distributions linking left- and right-hemisphere voxels through the region of the SCC identified in the VBM white-matter analysis. The results revealed a clear pathway linking the left- and right-hemisphere seed regions through the SCC irrespective of whether 1,000, 5,000 or 250,000 samples were used. This suggests that the pathway is robust and easily traced. It was also present across a range of different seed voxels (Fig. 3).

Experiment three: functional imaging of reading versus picture naming. Data for experiment three were collected at the Wellcome Trust Centre for Neuroimaging. The study was approved by the joint ethics committee of the Institute of Neurology and University College London Hospital.

Twenty healthy, right-handed skilled readers (8 males and 12 females; age range, 13–71 years; mean, 35 years) gave written informed consent to participate in this study. All were literate, native English-speakers, had normal or corrected-to-normal vision, with no history of neurological or psychiatric disorders. They were all highly educated and are therefore likely to have been much more proficient readers than the adult literates included in experiment one. Critically, however, we looked for consistencies between studies rather than differences.

There were three tests: naming pictures of objects that have familiar names of three to six letters, reading the written names of the objects used for picture naming and articulating “1, 2, 3” in response to unfamiliar symbols and pictures of three unfamiliar 3D shapes. Responses were spoken aloud and recorded with an in-house MRI-compatible auditory recording system. To facilitate task switching, the conditions were blocked with 12 stimuli per block that alternated with 14.4 s of fixation. Within a block, the 12 stimuli were presented in four sequential trials (one each 4.3 s) with three stimuli per trial, one above fixation and two below fixation. The participants were asked to name the objects or read the word in the same order (top, bottom left, bottom right) and to say “1, 2, 3” in response to the unfamiliar stimuli while looking sequentially at the top, bottom-left and bottom-right pictures. Over the experiment, each participant responded to 32 trials (96 stimuli) of each condition. Within subject, a different set of objects was used for picture naming and reading, but across subjects, articulation was matched for picture naming and reading. Thus, we had a total of 192 objects, divided into sets A and B. Half the subjects saw set A as pictures and set B as written names; the other half saw set B as pictures and set A as written names. Name agreement across subjects was ensured by a pilot study. The total scanning time for all conditions was 12 minutes in two separate six-minute runs.

To ensure that the task was understood correctly, all subjects were provided with detailed instructions and underwent a short training session before entering the scanner. To minimize artefacts from head motion, participants were instructed to whisper their response with minimal mouth movement. Their movement within the scanner was assessed. The 20 participants included in the analyses reported below were selected from a larger sample after excluding those who moved more than 1.5 mm in any direction in the scanner.

Data were acquired on a 1.5T Siemens Sonata MRI system. Functional imaging comprised an echo-planar-imaging gradient-echo sequence (TR = 3,600 ms; TE = 50 ms; flip angle, 90°; FOV = 192 mm; 40 axial slices with 3 mm × 3 mm × 3 mm voxel size). The echo-planar-imaging gradient-echo sequence used here was optimized to minimise signal dropout by adjusting the slice tilt, the direction of the phase encoding and the z-shim moment⁴⁷. Functional, scanning was always preceded by 14.4 s of dummy scans to ensure tissue steady-state magnetization.

Data processing and statistical analyses were performed using SPM5. All functional volumes were spatially realigned, unwarped, normalized to the MNI space using the unified normalization-segmentation procedure of SPM5 (ref. 40) and smoothed with an isotropic Gaussian kernel with 6-mm FWHM, with resulting voxels size of 2 mm × 2 mm × 2 mm. Time series from each voxel were high-pass filtered (1/128-Hz cut-off) to remove low-frequency noise and signal drift. The pre-processed functional volumes for each subject were then submitted to a fixed-effects analysis, using the general linear model at each voxel. The onset of each stimulus was modelled as an event encoded in condition-specific ‘stick-functions’. Correct and incorrect responses were modelled separately. The resulting stimulus functions were convolved with a canonical haemodynamic response function to form regressors for the general linear model. Parameter estimates (that is, beta images) were assessed using least-squares regression analysis. The appropriate contrast image (that is, a contrast of maximum-likelihood-parameter estimates) was then entered into a second-level random-effects analysis to allow inferences at the group level in the regions showing structural differences between literates and illiterates (Supplementary Table 1 and Supplementary Fig. 1). This analysis was used to identify regional activation differences for reading and picture naming and to extract the time series for each region from the F map for all conditions.

First we created a mask of the significant voxels in the structural comparison (experiment one). Then we applied this mask to the second-level analysis of the functional data. Peak activations were identified using the peak coordinates from experiment one using a 6-mm-radius search volume. The coordinates of the six local F-map peaks closest to our regions of interest from experiment one were as follows: left DOCC at (−30, −88, +20), right DOCC at (+30, −88, +20), left ANG at (−48, −74, +28), right ANG at (+50, −70, +32), left MTG at (−54, −54, +10) and left SMG at (−52, −42, +26). See Supplementary Table 2 for comparison of structural imaging results (experiment one) and functional imaging results (experiment three).

For the rationale behind DCM and our choice of analysis, please see Supplementary Information. The procedures were as follows. For each region, eigenvectors (that is, time series) were extracted in each participant at the closest maxima within a distance of 4 mm from the group peaks (individual map threshold, $P < 0.05$) from experiment one. Critically, this 4-mm limit ensured that DCM models were comparable across participants⁴⁸. Regions of interest were extracted for each session separately within a 4-mm-radius sphere and the principal eigenvariables were adjusted to the F contrast of each participant. For each subject, we extracted region-of-interest time series that were concatenated over the two runs and incorporated in two DCM models. The first DCM model

(Supplementary Fig. 2a) tested the effective connectivity between left and right hemispheres in left DOCC and ANG regions. It was a fully connected model between left and right DOCC and left and right ANG regions; the driving inputs (that is, objects, words, symbols and non-objects) were connected to both the left and the right DOCC regions; and object naming and word reading were used as modulatory inputs on all connections.

The second DCM model (Supplementary Fig. 2b) tested the effective connectivity between the different regions of the anatomical reading system identified in experiment one (that is, four left-hemisphere regions). It was a fully connected model (all forward and backward connections specified) between the left DOCC and ANG regions, the MTG and the SMG; the driving inputs (that is, objects, words, symbols and non-objects) were connected to the left DOCC region; and word reading and object naming were used as modulatory inputs on all connections to estimate the change in connection strengths as a function of the context (for example reading versus naming). Both DCM analyses identified the interactions that increased selectively during reading aloud when visual processing and articulation were controlled.

All parameters of both DCM models (intrinsic and modulatory values) and their posterior probabilities were assessed using Bayesian inversion by means of expectation and maximization^{49,50}. The intrinsic and modulatory effects of each subject were submitted to *t*-tests at the group level to infer consistent findings across our 20 subjects⁵⁰. Critically, only connections that showed stronger modulatory effects for word reading than for object naming ($P < 0.05$) are considered relevant in our context. For the first DCM model, we also carried out a factorial analysis (that is, analysis of variance) on the strength of the modulatory effects, to test the effects of task (reading or naming), region (left DOCC or ANG) and interhemispheric coupling (left to right versus right to left). Significant effects for these factors and their interactions were reported at $P < 0.05$.

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