Shared anomalies in cortical reading networks in Chinese and French dyslexic children

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Abstract

To determine whether the neural anomalies underlying developmental dyslexia are universal across languages or influenced by the writing system, we tested 10-year-old Chinese and French children, with or without dyslexia, in a cross-cultural fMRI paradigm. We compared their brain responses to words written in their known script, faces and houses while they were asked to detect a rarely presented star. We observed that impaired reading scores were correlated with a decreased activation to words in several key regions of the reading circuit, including left fusiform gyrus, superior temporal gyrus/sulcus, precentral and middle frontal gyrus. In ROIs previously reported as sensitive to dyslexia, we observed main effects of dyslexia common to Chinese and French readers, without interaction with the children's native language, suggesting a cross-cultural invariance in the neural anomalies underlying dyslexia. Multivariate pattern analyses further confirmed that dyslexics exhibit a reduced activation to written words in the left fusiform gyrus and left posterior superior temporal gyrus, and not merely a greater inter-individual variability. The impairments in these regions may reflect the causes as well as the consequences of orthographic and phonological deficits in dyslexia in different languages. The current study highlights the existence of common brain mechanisms for dyslexia even in highly different writing systems.

Keywords: developmental dyslexia, writing system, cross-cultural invariance, fMRI,

Introduction

A large proportion of published studies on reading concern English, even though this language may be considered as an outlier within alphabetic writing systems, compared to Finnish or Italian for example, due to its highly opaque grapheme-phoneme correspondences. Thus, international efforts are needed to extend the results obtained in English subjects, or more generally in Western languages, to other writing systems and languages notably during childhood. Daniels and Share listed 10 dimensions that might affect reading acquisition and dyslexia phenotypes, and fall into three main classes: the structure of the oral language, the complexity of the visual shapes, and the translation rules between those two domains [1]. With regard to language, the number of phonemes, the syllabic structure and the complexity and regularity of morphological markers can modulate the ease with which children construct explicit representations of speech, which need to be converted in, or deduced from, writing [2]. The visual shapes of letters and characters also vary in number, uniformity, and complexity [1]. Finally, the sound-character mappings vary on several dimensions across writings, including granularity, complexity, transparency, and consistency. All these factors may influence the speed and effectiveness with which children learn to read, and at least one of these dimensions, orthographic transparency, has been robustly reported to affect reading acquisition in Western languages [3], with a reported impact on brain activation in the reading circuit [4].

Beyond these surface differences, the fundamental logic of reading remains the same from one writing system to another: all of them operate as visual means of accessing the spoken language network. Although access to linguistic information from the visual system is a natural possibility for the brain, as demonstrated by the capacities for image naming, lip reading or sign language, writing introduces an additional step that involves converting an arbitrary visual form into speech. Grapheme-phoneme correspondences are arbitrary and have been shown to depend on a precise region of the visual system, the visual word form area (VWFA) and on the posterior superior temporal cortex, as shown by numerous brain imaging studies in adult readers [5-7]. However, most of those brain imaging studies suffer from the bias noted above, as they concern mainly adults in Western alphabetic languages. Despite the existence of a few previous investigations [8-11], controversy still surrounds the question of whether different cognitive and neural processes are involved in reading non-alphabetic material or whether reading is

based on a similar network regardless of the language, with only minor variations in the degree of involvement of the different nodes of the network according to the linguistic grain size that predominates in a given writing system [12]. For instance, Chinese characters map onto phonology at the syllable level, with no parts in a character corresponding to phonological segments such as phonemes.

An additional source of bias in the literature is that most publications on brain imaging have focused on adults, i.e., reading experts, but the acquisition of reading in children may yield different results. Children may rely on different and possibly broader regions of the brain before converging onto the adult expert network for reading [13]. Functional neuroimaging studies of young children, although difficult, are therefore highly desirable [14]. In all alphabetic languages as well as in Chinese, early linguistic skills are a good predictor of reading ability [15-17]. In particular, phonological awareness and morphological awareness (lexical compounding) in 4-year-old Chinese children predict their character recognition at 11 years of age, while naming speed (RAN) and vocabulary predict reading fluency [18]. These results, consistent with those obtained in alphabetic languages linking phonological awareness to reading accuracy and RAN to reading fluency [19, 20], suggest similar learning mechanisms. This pattern can be reinforced by current pedagogy, which uses pinyin, a phonetic alphabet, during the first few months of learning.

Another approach to studying the universality of the neurocognitive bases of reading is to study whether dyslexic children from alphabetic and non-alphabetic languages exhibit similar brain anomalies. Functional imaging studies of dyslexia have revealed common neural deficits in different alphabetic languages, with consistently decreased activation in several left-hemispheric posterior regions, including the left temporoparietal and left ventral occipitotemporal regions [21-23]. According to two recent meta-analyses, the left ventral posterior occipitotemporal cortex (including the Visual Word Form Area, VWFA) appears to be the most reproducible and consistent site exhibiting hypoactivation in dyslexic individuals across alphabetic writing systems regardless of orthographic depth [24]. Given its sensitivity to visual features (e.g. line junctions) and its efficient reciprocal projections to language areas [25-27], this area is one of the candidates for a universal effect of reading impairment [24, 28].

However, several neuroimaging studies of Chinese dyslexics did not report hypoactivation

in this region in dyslexics compared to controls but rather pointed to another region, the left middle frontal gyrus (MFG) [29-31]. The latter region showed reduced activation and decreased volume of grey matter that was not observed in any alphabetic language. These results were interpreted as showing a clear dissociation of the biological basis of reading disability between alphabetic and logographic writing systems. However they contradict behavioral data that show similar profiles in Chinese and alphabetic-language dyslexics [12, 32] and a more recent fMRI study showing remarkably few differences in brain activity between English and Chinese dyslexic adolescents when all confounding variables (e.g. stimuli and task in fMRI) were controlled for [33]. Furthermore, fMRI research in normal adult readers, comparing French and Chinese reading, found that the left MTG is not specific to Chinese writing, but comprises a representation of handwriting gestures which is engaged in both alphabetical and non-alphabetical languages [10].

To clarify the question of the universal bases of reading, we report here on a cross-cultural fMRI study, using a similar experimental protocol in four well-matched groups of Chinese and French, normal and dyslexic, 10-year-old readers. All children performed the same passive viewing task with words, faces and houses, with the mere goal to detect an occasional target star. We studied the effect of reading proficiency in whole-brain analyses and in specific ROIs identified from the literature, in both Chinese and French children.

In addition to activations to words, we were also interested in how the acquisition of writing, in French and Chinese, may reorganize cortical maps of other visual categories. Several studies suggest that, during reading acquisition, words and faces compete for cortical territory within the fusiform gyri [5, 13, 34]. Given the complexity of Chinese characters and their frequently reported bilateral activation, we investigated whether face activation would be affected differently in Chinese and French children. It was also suggested that because of the complexity of ideograms, Chinese children may exhibit better visual skills than children learning alphabetic writing [35]. We examined these issues using classical analyses of response intensity and location in the different groups, but also a multi-voxel pattern analysis (MVPA) in order to evaluate whether the differences between dyslexics and normal-readers are merely related to a greater spatial dispersion of activation in dyslexics or to a genuine decrease in brain activity.

Materials and Methods

Participants

Ninety-six children participated in the current study, including 24 Chinese dyslexics (mean age = 123 months, standard deviation [SD] = 10), 24 Chinese controls (mean age = 123 months, SD = 11), 24 French dyslexics (mean age = 123 months, SD = 10) and 24 French controls (mean age = 123 months, SD = 11). All children reported normal hearing and corrected-to-normal vision and no history of neurological or psychiatric disorder. Nonverbal IQ, assessed by Raven's Standard Progressive Matrices in Chinese children and Wechsler Intelligence Scale in French children, was in the normal range for all participants. The study was approved by local institutional review boards in Beijing (China) and Kremlin-Bicêtre (France), respectively. Written consent was obtained from all children and their parents.

Chinese participants: Because standardized tests of dyslexia are not available in Chinese, we tested a large population of 2554 primary school children in Beijing (3rd grade- 6th grade, 10-13 years of age) to calculate the standard norms in the following tests. The first round of tests involved: (1) Chinese Character Recognition Test (CCRT) [36], (2) Reading Comprehension Test (RCT) [37], (3) Raven Progressive Matrices Test [38], and (4) Digit Cancellation Test [39]. Children with a CCRT Z-score below -1.25 SD were identified as potential dyslexics. We then invited these children and their parents to take part in a second-round of tests, which involved MRI scanning and several individually-administered tests: (5) Chinese Phonological Awareness Test (CPAT), (6) Character Reading Test (CRT) [40], and (7) Rapid Automatized Naming Test. A total of 103 children with different reading abilities were scanned and more information about these children can be found in a previous paper [41]. Once those potential dyslexic children (CCRT Z-score < -1.25 SD) as screened in the first-round test also had CRT Z-score or CPAT Z-score below -1.5 SD as measured in the second-round test, they were considered dyslexics and their brain data were included in the current study. An equal number of control children (above -0.5 SD in all reading-related tests) matched in age, sex, and non-verbal IQ with the dyslexic group, was also selected (Table 1 and Table S1).

French participants: To match the Chinese children, we selected 24 dyslexics and 24 controls from two previously published French studies: 21 dyslexics and 18 controls from the Monzalvo et al's study (2012) [42], and 3 dyslexics and 6 controls from the population of

Altarelli et al's study [43]. French and Chinese children were matched in age and sex in each group. Detailed information of behavioral tests and the criterion for identifying French dyslexia can be found in Monzalvo et al (2012) and Altarelli et al., 2013 (see also Table 1 and Table S2).

Stimuli and task

The experimental procedure was similar to Monzalvo et al (2012) but adapted to Chinese children (Chinese words and Asian faces replacing French words and Caucasian faces). While being scanned, Chinese and French children viewed short blocks of words, faces and houses and of a revolving checkerboard (30 frequent regular words known by young readers and 30 black and white pictures in each category) followed by a fixation cross during 10.5 s (total bloc duration 28.5 s). In each block, 10 pairs of different images belonging to the same category (200 ms presentation for the first picture/word, 200 ms inter-stimulus, 500 ms presentation for the second picture/word) were presented, separated by a 600 ms fixation period. Besides, two stars were randomly inserted in each block, 1500 ms for each star. Children were instructed to press a button with their right index finger whenever a target star appeared. This task was designed to keep their attention focused on the visual stimuli, but without any explicit reading requirement. For Chinese children and the older French children, a supplementary category (tools) was added but not included in the present analyses as this category was not presented in the original study [42] and thus missing in most of the French children reanalyzed here.

In each run, there were two blocks of each visual category and only one block of checkerboard. All the blocks were presented in a random order. Chinese children performed two runs and French children performed four runs in Monzalvo et al (2012), and only one run in Altarelli et al (2013).

fMRI Acquisition Parameters

fMRI data were acquired on Siemens 3T scanners using a 12-radiofrequency-channel head coil and the same gradient-echo planar imaging sequence in France and China with the following parameters: 40 contiguous 3mm isotropic axial slices, TE/TR = 30/2400 ms, flip angle = 81°, voxel size = 3 × 3 × 3 mm, matrix = 64 × 64. A high-resolution T1 weighted volume was also acquired with the following parameters: 176 1mm isotropic axial slices, TE/TR =

4.18/2300 ms, flip angle = 9°, matrix = 256 × 256.

Prior to the scanning session, all children underwent a training session in a mock scanner. This training session aimed to help children become familiar with the MRI environment and task instructions, and to teach them to keep their head motionless during the scan.

Data pre-processing and statistical analyses

Preprocessing and analyses of the data were done using SPM12. The French and Chinese data were processed together. The functional images were first corrected for differences in slice-acquisition time and realigned to the first volume in the scanning session. ArtRepair toolbox was used to detect and repair bad volumes [44]. Two criteria were used to detect bad volumes: (1) 1.5 % variation in the global average BOLD signal from scan to scan and (2) 0.5 frame-wise displacement, reflecting the sum of all head movements from scan to scan (calculated from realignment parameters). The damaged volumes that exceeded these criteria were replaced by linear interpolation of previous and subsequent images or by nearest-neighbor interpolation when several consecutive images were affected.

For the anatomical image, we first checked for scanner artefacts and gross anatomical abnormalities, then we manually set the origin of T1 image to the anterior commissure for each subject. We normalized each child's anatomy to the Montreal Neurological Institute (MNI) template using the DARTEL approach to improve segmentation accuracy and local registration among participants. Functional images were co-registered to their corresponding anatomy. Then the parameters obtained during the DARTEL wrapping process were applied to the functional images which were finally smoothed using a 6 mm Gaussian kernel.

The pre-processed functional images were then submitted to a first level statistical analysis: in each subject, a general linear model was built in which a hemodynamic response function and its time derivative were convolved with block onsets for each category and the 6 motion parameters entered as regressors of non-interest.

Data-driven Analyses

We implemented a mixed-model analysis of variance (ANOVA) with Language (French vs. Chinese) and Dyslexia (control vs. dyslexic) as between-subject factors, and Category

(Words vs. Faces vs. Houses) as a within-subject factor. The ANOVA analysis was intended to test the main effect of Category (One category > mean of the other two categories) across the whole group (N = 96). We report effects at a threshold of $p < 0.001$ at the voxel level and $p < 0.05$ family wise error (FWE) corrected for multiple comparisons at the cluster level (denoted p_{FWE_corr}). We also separately report these category effects in each group (N = 24) at a threshold of $p < 0.001$ at the voxel-level, non-corrected at the cluster-level to provide the reader with the full information on activation patterns in each group.

To deepen our analyses of the differences between groups in their response to words (vs. fixation), we focused our analyses on a mask of voxels corresponding to the word-specific activation across all children determined as by the Words > [Faces, Houses] contrast ($p < 0.001$ voxel level and $p_{FWE} < 0.05$ cluster level). We performed an ANOVA with Language (French vs. Chinese) and Dyslexia (control vs. dyslexic) as between-subject factors. To provide readers with full information, we report these results at the threshold of voxel-level $p < 0.001$, non-corrected at the cluster-level.

Brain-behavioral correlation analysis

The above analyses were based on a binary distinction between dyslexics and controls. To better understand the effect of reading on brain activations, we replaced the categorical distinction (controls vs dyslexics) by a continuous variable of reading performance (standard scores in dyslexia screening measures) across both Chinese and French children (N = 96) and studied the correlation between this variable and word activation across the entire brain. We report effects at a threshold of $p < 0.001$ at the voxel level and $p < 0.05$ FWE corrected for multiple comparisons at the cluster level.

Literature driven Analyses

To increase the statistical power of comparisons between controls and dyslexics, we focused on Regions of Interest (ROI). We first searched published meta-analyses of imaging studies reporting brain regions showing functional dysfunction in dyslexics in alphabetic languages. To create representative ROIs for these dyslexia-related regions, we collected all of the foci reported in each meta-analysis corresponding to the anatomical location under

consideration (see Table S4), and averaged the reported coordinates (x, y, z respectively) to create a 6-mm-radius sphere of the averaged locus as a ROI (Fig 3).

Due to the limited number of published neuroimaging studies of Chinese dyslexia, no meta-analysis was available to summarize the available evidence into a pooled estimate. However, atypical activation in a lateral prefrontal region within BA 9 has been reported in Chinese dyslexics [30, 31] and this region was repeatedly found to be more involved in reading Chinese than alphabetic languages [10, 45, 46]. Besides, previous studies also often reported that Chinese reading networks are more symmetrical in the ventral visual system. We thus included the foci in both left middle frontal gyrus and right occipital cortex that were reported in several meta-analyses on Chinese typical reading [45-48] and created representative ROIs as above (see Table S5). In total, we obtained 10 ROIs related to dyslexia in alphabetic languages and 3 additional ROIs potentially related to Chinese typical reading and dyslexia (Fig 3).

We extracted the mean contrast-weighted beta values for the words vs. fixation contrast in each ROI in each child and entered these values in an ANOVA with Language (Chinese vs. French) and Dyslexia (controls vs. dyslexics) as between-subject factors. The false discovery rate (FDR) multiple-comparison method was implemented to take into account the multiple ROIs. We did the same analyses in the same ROIs for the contrasts of faces vs fixation and houses vs fixation. The FDR corrected p value is denoted as $p_{\mathrm{FDR_corr}}$.

Anterior-to-Posterior ROI Analysis in the visual cortex

To visualize whether the anterior-to-posterior and lateral-to-medial organization of activation to words (or to other categories) in the ventral visual cortex was similar between dyslexics and controls among both Chinese and French participants, a sliding-window ROI analysis was also conducted. We moved the ROI along the y-axis in the left hemisphere with constant x and y coordinates (respectively x = -48 and z = -16). Along the y-axis, six 6-mm-radius spheres were regularly spaced along the anterior-posterior axis, with the center positioned at y = -73, -64, -55, -46, -37, -28 respectively. The x-axis and z-axis were set based on the peak of the word-specific activation (Words > [Faces, Houses]) in all participants. To better characterize bilateral activation of ventral visual system in reading, counterparts of these ROIs in the right hemisphere were also included in the analysis.

First, we examined the responses to words vs fixation along this anterior posterior axis in an ANOVA with Language and Dyslexia as between-subject factors, ROI (6 y-axis position = -73, -64, -55, -46, -37, -28) and Hemisphere (left and right) as within-subject factors. Second, we investigated the responses to the other two visual categories following the same logic. We determined two x-axis sites (x = ± 39, x = ± 30) based on the location of the peak of Faces > other categories and Houses > other categories in our participants (see Table 2) and performed two separate ANOVAS with the same factors than above (Language, Dyslexia, 6 y-axis positions and Hemisphere). In each ANOVA, we corrected for multiple comparisons using the FDR method.

Individual peak analyses

To investigate whether the dyslexic children had a greater inter-individual variability in brain localization, we conducted individually defined ROI analyses. We focused on those regions showing significant main effects of dyslexia or language in the group activation analysis (i.e. left FFG, MFG, precentral, STS, pSTG, and SPL). We searched for active voxels (Words > fixation) in a sphere (radius = 12 mm) centered on the peak coordinates identified by the whole group activations (Words > [Faces, Houses]). We eliminated voxels with z-value inferior to 1 and selected the 10 strongest activated voxels within the search area. We first derived the individual center of mass of these voxels by averaging their x, y, z coordinates. We calculated the distance between this center of mass and the group peak coordinates in each child. Second, we averaged the beta values measured in these voxels to obtain the maximal activation in each child. We then entered those measures into Language × Dyslexia ANOVAs to investigate whether dyslexic children differed in peak location and activation intensity compared to control children. We performed a similar analysis on the face responses in the bilateral fusiform face areas (FFA) to investigate whether dyslexic children had greater inter-individual variability in the location and intensity of face activations.

Multivariate Pattern Analysis (MVPA)

In the MVPA analysis, we also focused on the regions showing significant main effects of dyslexia or language in the univariate activation analysis. We drew a sphere with 9-mm radius

centered on the averaged coordinates of foci reported in meta-analyses, and then intersected each sphere with the whole group activations (Words > [Faces, Houses]) to obtain a group mask (~3052 mm^3). All the voxels within the mask were included for MVPA analysis.

Secondly, within each ROI, we used the correlation-based multi-voxel pattern analysis to quantify the within-subject reproducibility of activation patterns. Thus, we calculated the correlation coefficients between the pattern of response evoked by words relative to fixation during the first run and the pattern of response evoked by each category (words, faces and houses) relative to fixation during the second run in each subject. The correlation coefficients were further converted into Z-scores. For each ROI, we then entered these correlation coefficients into an ANOVA with Language (Chinese vs French), Dyslexia (control vs dyslexia), and Condition (within-category correlation, e.g. words with words, vs between category correlation, e.g. words with faces, words with houses, and faces with houses) as factors.

We performed a similar MVPA analysis in the bilateral face fusiform areas to investigate whether dyslexic children showed reproducible activation patterns to faces. Bilateral face ROIs were spheres with a 9-mm radius centered on the reported peak coordinates in the face-selective activation in previous studies (left [-39, -45, -18], right [39, -45, -18]) [49]. We intersected each sphere with the whole group activations (Face > [Words, Houses]) to obtain a mask (~3052 mm3). All the voxels within the mask were included for MVPA analysis. We then calculated the correlation coefficients between the pattern of response evoked by faces relative to fixation during the first run and the pattern of response evoked by each category (faces, houses and words) relative to fixation during the second run in each subject.

Note that six French controls and three French dyslexics finished only one run of the visual task, so that they were not included in this MVPA analysis. For those children who had 4 runs, we used their first two runs to calculate the correlation coefficients between runs. The FDR multiple-comparison method was again used as a correction for the multiple ROIs tested.

Results

Behavioral Results

As shown in **Table 1**, the four groups were matched in age and sex. Because the reading tests are not directly comparable due to the writing differences, we did not compare French and

Chinese scores directly. However, both Chinese and French dyslexia performed worse than their respective controls in the dyslexia screening measures (CCRT for Chinese children, t = 18.03, $p < 0.001$ and "L'alouette" for French children, t = 14.66, $p < 0.001$). More information on the behavioral profile of Chinese and French children is presented in the supplementary material (see Table S1 and S2).

Within the scanner, although Chinese children responded faster to the target star than French children (main effect of Language: $F(1,92) = 60.94$, $p = 0.001$), there was no significant effect of dyslexia (F (1,92) < 1) nor Language × Dyslexia interaction (F (1,92) < 1) (Chinese controls: 534.95 ± 71.47 ms, Chinese dyslexics: 536.13 ± 72.84 ms; French controls: 661.15 ± 102.29 ms, French dyslexics: 689.32 ± 99.35 ms).

Category-specific activations

We first examined the brain activations to each category (i.e. Words, Faces, and Houses) relative to the other two categories among all participants (see Fig 1A and Table 2). The Words > [Faces, Houses] analysis yielded the usual reading-related regions: fusiform gyrus, posterior superior temporal region, *planum temporale*, intra-parietal sulcus and inferior frontal regions in the left hemisphere and the posterior superior temporal gyrus in the right hemisphere. We also observed the classic mosaic of category-specific ventral visual areas, with category-specific activation to Houses occupying a medial parahippocampal location, Faces an intermediate fusiform location, and Words a lateral location in the left occipito-temporal sulcus (VWFA). Amygdala responses to Faces were also clearly seen. Those results were seen in each of the four groups of subjects, with the interesting exception that the left VWFA seemed to be missing in both Chinese and French dyslexics (Fig 1B and Table S3).

Reading-related differences

Across all children, reading scores were significantly correlated with fMRI activation in the words vs fixation contrast in several regions: bilateral fusiform gyrus (left: [−42 −45 −18], Z = 4.36, 37 voxels, $p_{FWE_corr} = 0.055$ and right: [42 −66 -24], Z = 4.27, 66 voxels, $p_{FWE_corr} = 0.004$), bilateral precentral regions ([−36 −3 57], Z = 4.54, 56 voxels, $p_{FWE_corr} = 0.010$ and [54 18 33], Z = 4.21, 48 voxels, $p_{FWE_corr} = 0.02$), bilateral middle frontal gyrus ([-36 12 27], Z =

4.12, 88 voxels, p_{FWE_corr} = 0.001 and [45 6 54], Z = 4.32, 38 voxels, p_{FWE_corr} = 0.050), left superior temporal sulcus ([-57 -24 0], Z = 4.26, 56 voxels, p_{FWE_corr} = 0.010), and right middle occipital gyrus ([27 −69 42], Z = 4.37, 65 voxels, p_{FWE_corr} = 0.005) (see Fig 2 and Table 3).

When a categorical distinction was made between normal readers and dyslexics, no significant cluster differed between these two groups in either direction (dyslexics > normal readers and normal readers > dyslexics), when analyzing either the words > fixation or the words > others contrast. However, a few voxels reached the voxel threshold (p = 0.001) in regions corresponding to the above, more sensitive correlation analysis, including the left fusiform gyrus, left precentral and left superior temporal sulcus (see figure S7A).

When restricting the analysis to the word-specific mask (i.e. a mask comprising all voxels showing preference for words relative to the two other categories across all participants), a main effect of dyslexia in the left precentral (79 voxels, p_{FWE_corr} = 0.027, Z = 3.69 at [-51 15 33]) survived the mask-level multiple correction with voxel-wise $p < 0.005$. Besides, a main effect of language was observed in the left intra-parietal sulcus (55 voxels, p_{FWE_corr} = 0.004, Z = 4.29 at [-30 -60 39]) due to larger activation in Chinese than French children. No region showed a significant Language × Dyslexia interaction even in the word-mask restricted analysis and with a very lenient voxel-wise threshold of $p < 0.05$ (see figure S7B).

ROI-Level analysis

We next conducted ROI-based analyses specifically focused on regions reported in previous studies of dyslexia. Figure 3A presents all foci reported in four recently published meta-analyses of dyslexia in alphabetic languages [22, 50-52] and in four meta-analysis of Chinese typical reading [45-48]. As seen in figure 3A, dyslexia in alphabetic languages is consistently characterized by dysfunctions in the left occipito-temporal, temporoparietal and frontal regions. We added the left middle frontal gyrus (BA 9) and two regions in the right ventral visual system because previous studies suggested a specific role of these regions in Chinese reading (see method and Fig 3B). All ROIs (except two ROIs in the right-hemisphere) fell within the reading circuit identified in our participants (Words > other categories; see Fig 4 and Fig S8).

We submitted the activation to words relative to fixation in each ROI to an ANOVA with

Language and Dyslexia factors. Below, we report only the *p*-values that survived an FDR correction over the 13 ROIs. There was a significant main effect of Dyslexia in the left fusiform gyrus ($F(1,92) = 21.08$, $p < 0.001$, $p_{FDR_corr} < 0.001$), middle frontal gyrus ($F(1,92) = 10.17$, $p = 0.002$, $p_{FDR_corr} = 0.009$), superior temporal sulcus ($F(1,92) = 11.88$, $p = 0.001$, $p_{FDR_corr} = 0.006$), and precentral gyrus ($F(1,92) = 7.78$, $p = 0.006$, $p_{FDR_corr} = 0.020$), always due to a reduced activation in dyslexics relative to controls. Importantly, all of these effects were significant within each language group (see Fig 4).

A significant main effect of Language was observed in the left middle frontal gyrus ($F(1,92) = 15.23$, $p < 0.001$, $p_{FDR_corr} < 0.001$), superior parietal lobule (SPL, $F(1,92) = 8.13$, $p = 0.005$, $p_{FDR_corr} = 0.022$) and posterior superior temporal gyrus (pSTG, $F(1,92) = 9.04$, $p < 0.003$, $p_{FDR_corr} = 0.020$), always due to larger activation in Chinese readers than in French readers. Importantly, no ROI showed a significant Language × Dyslexia interaction (see Fig 4 and Fig S8). Only the pSTG showed a significant effect of Dyslexia within French, but not within Chinese participants, but the interaction was far from significance ($F(1,92) = 2.815$, $p = 0.097$ without FDR correction).

Finally, when these analyses were replicated for the activation to houses and to faces, no main effect nor interactions were found in these ROIs.

Anterior-to-Posterior gradient in the visual cortex

We then examined the anterior-posterior gradient of responses for the different categories vs fixation. Keeping constant x = ± 48 and z = -16, we studied the activation to Words vs fixation along the y-axis (ranging from -79 to -22). Those results are reported in detail in Supplementary Results and Fig S9B. Firstly, we observed greater response to words in Chinese children compared to French children in the right hemisphere at several y coordinates, leading to a significant triple interaction of Language × Hemisphere × ROI. Secondly, we observed larger activation in the posterior relative to anterior sites as revealed by the main effect of ROIs. Crucially, the Dyslexia × ROI interaction was significant. In more detail, compared to controls, dyslexic children had decreased activation to words at several consecutive sites (y axis at -64, -55, -46 and -37). However, when we examined the differences between dyslexics and controls separately in Chinese and French children, only one site (y = -46) survived correction for

multiple comparison in both Chinese and French children. This site is only slightly anterior to the classic VWFA site [53].

Keeping constant x = ± 39 and z = -16, we also studied the activation to Faces vs fixation along the y-axis (ranging from -79 to -22). We observed a significant Hemisphere × ROI interaction. This effect was due to greater right than left face activation at several y coordinates. Besides, the main effect of dyslexia reached significance, due to a lower activation to faces in dyslexics compared with controls bilaterally and in both languages (see Fig S9C).

Along the medial house specific activation at x = ± 30 and z = -16, we similarly studied the activation to Houses vs fixation. We found a significant triple interaction of Language × Hemisphere × ROI. French children had greater right than left activation at each of the six anterior-posterior y coordinates (all $p_{FDR_corr} < 0.005$) while Chinese children had the same pattern only at four sites (y = -73, -46, 37, 28). We also observed a significant Dyslexia × ROI interaction, with decreased activation to Houses in dyslexics in several sites (see Fig S9D).

Individual peak and multivariate pattern analyses

The above analyses were carried out in a standardized way at the group level. It is therefore possible that the observed group differences were due to a greater inter-individual variability in brain localization in the dyslexic group than in the control group. This possibility would lead to a completely different interpretation of the results: each dyslexic child might have a well-organized brain activity for reading, with the only anomaly of a greater anatomical dispersion in the dyslexic group compared to the control group. To test this possibility, we performed two individual-based analyses, one based on the comparison of the location and activation values of the most responding voxels and the other examining the stability of the pattern of responses across runs through a multi-voxel pattern analysis (MVPA).

As for the locations of the individual centers of mass for words (left FFG, MFG, STS, PCG, pSTG, SPL) and faces (bilateral fusiform face areas, FFA), their Euclidean distance to the group peaks did not differ between dyslexic and control children (Table S6), suggesting a similar dispersion among dyslexic participants and controls. By contrast, even after having selected the best responding voxels in each child, the word activation remained weaker in dyslexics than controls in the left FFG, MFG, STS, PCG, and pSTG (all $p_{FDR_corr} < 0.05$). French had also

weaker activations than Chinese children in the left MFG, pSTG and SPL (all $p_{FDR_corr} < 0.05$). There was no significant interaction Language × Dyslexia in any of these analyses. These results thus confirmed the standard analyses.

As a further test of the possibility of more dispersed brain localization in the dyslexic group, we used multi-voxel pattern analysis (MVPA) to analyze the within-subject reliability of the activation patterns between runs, and thus the stability of the representations across the two successive fMRI runs within each subject. Dyslexics might have more dispersed activations without focal peaks that would also create weaker responses at the group-level, but a reproducible pattern of activations. In that case, the within-subject reproducibility of multivariate activation patterns should not differ between normal-readers and dyslexics.

For this MVPA analysis, we focused on the regions showing significant effects of dyslexia (i.e. left FFG, MFG, PCG and STS) and language (i.e. SPL and pSTG) in the univariate analysis. We computed the similarity separately for within-category patterns (words in run 1 and words in run 2) versus between-category patterns (average of words-faces, words-houses and faces-houses, each in run 1 versus run 2). If the representation of words is more stable than that of other categories in these regions, then we should observe a significant main effect of condition (a greater correlation within than between-category). If the activation pattern is less reproducible in dyslexics than in controls, a significant interaction of condition × dyslexia should be found. In all these regions, when pooling over all subjects, there was an overall replicable pattern of activation evoked by words, as indicated by a significant main effect of condition, with a greater correlation coefficient within than between categories (all $p_{FDR_corr} < 0.001$) (see Fig 5 and Fig S10A). Crucially, we also observed a significant interaction of Condition × Dyslexia (control vs dyslexia) in the left FFG ($F(1, 83) = 10.14$, $p = 0.002$, $p_{FDR_corr} = 0.006$) and in the left pSTG ($F(1, 83) = 15.75$, $p < 0.001$, $p_{FDR_corr} < 0.001$). Post-hoc analysis found that normal readers, but not dyslexics, exhibited a significantly similar pattern of activation from one run to the next. Those results show that the above differences between normal readers and dyslexics were not due to an artifact of group averaging, and that individual dyslexics exhibited a genuinely less reproducible activation patterns in these regions (Fig 5).

For the MVPA analysis in the bilateral fusiform face areas (FFA), only the main effect of condition reached significance ($p_{FDR_corr} < 0.001$), with a greater correlation coefficient for

within-category patterns (faces-faces) than for between-category patterns (faces-words, faces-houses, words-houses). Neither the main effect of dyslexia nor the condition × dyslexia interaction reached significance. These results suggest an equally replicable pattern of activation to faces in normal and dyslexic children bilaterally in the fusiform face area (see fig S10B).

Discussion

In the present study, we examined whether similar impairments in reading circuits were observed in Chinese and French dyslexics. Our goal was to study whether the same neurobiological mechanisms were involved in reading disorders, independently of the size of the speech units mapped to characters, and of the complexity of the characters. We investigated this question in 10-year-old children using a similar paradigm in both countries with a minimally demanding task which was equally easy for everyone (i.e. detecting a star), in four matched groups (French and Chinese × dyslexics and normal readers).

First, in a whole-brain analysis, we recovered the classical category-specific activations for words, faces and houses in extra-striate visual areas across all participants but also in each group (Figure 1). Second, reading scores were correlated with the word activations in common key-regions of the reading circuit (left VWFA, posterior superior temporal gyrus/sulcus, middle frontal gyrus and precentral gyrus) but also in the right hemisphere (middle occipital and fusiform gyri and precentral). Third, analyses based on ROIs from the literature confirmed these results, and surprisingly, further identified a main effect of dyslexia in the left middle frontal gyrus whose dysfunction was previously claimed to be specific to Chinese dyslexia [29, 30]. In all these analyses, no Language × Dyslexia interaction was significant, emphasizing common neural anomalies in both languages. These results were replicated even when the best voxels in these areas were chosen. However, we did observe some differences in activations depending on the children's native language. Chinese reading tended to engage more symmetrical activations in the visual system, with stronger activations in the right hemisphere than French readers when we specifically tested the anterior-posterior organization of the fusiform region. Chinese children also had stronger activations than French children in the left parietal region, middle frontal region and posterior STG.

We concluded our analyses by examining the reproducibility of the activation patterns between runs. The within-subject pattern of activity evoked by words was reproducible across runs in normal readers in all key reading regions, underscoring that even in children, the reading circuit is stable after 3 years of learning to read and can be reliably measured in a single fMRI run. However, such was not the case for dyslexics, whose activity was significantly less reliable in left fusiform and posterior superior temporal gyrus in both Chinese and French dyslexics. We now discuss each of these results in turn.

Common reading network in different languages

A long-standing debate in reading research is whether the neurobiological circuitry for reading is universal across languages. Previous cross-cultural fMRI studies have compared brain activations in adult readers in different languages and suggested that the expert reading network may be universal across languages [4, 9, 10]. The current study extends this finding to young children by showing common activation patterns to words in children in both alphabetic and non-alphabetic writing systems. These cultural-invariance findings are in agreement with the neuronal recycling hypothesis, according to which recent cultural acquisitions (e.g. reading) rely on the preemption of universal pre-existing circuits of the human brain, with only small culture-dependent modulations [54]. In any language, reading recruits circuits for the visual recognition of orthographic symbols and for spoken language processing [9]. Successful literacy acquisition is thus the result of the convergence of visual and speech processing systems, both of which are likely to be largely universal and laid down under genetic control. Indeed, the spoken language network is already present at its usual left-hemispheric location in 2-month-old babies [55-57]. The specific subpart of the ventral visual pathway which is used to recognized written characters seems to be, at least in part, determined by its pre-existing connections with this language network [25-27]. Thus, according to the neuronal recycling hypothesis, in spite of variations in language and writing systems, a considerable amount of inter-cultural convergence should be expected.

In our study, although the main areas for reading were common to both groups, we also observed modulations of the amplitude of brain activity within culturally universal brain circuits. Chinese children had larger activations than French children in the (1) left middle

frontal gyrus (BA 9); (2) right hemisphere occipitotemporal regions (3) left intraparietal sulcus. These findings are in agreement with previous meta-analyses of Chinese reading [45-47]. The greater activation in the left middle frontal gyrus has been explained by greater demands on addressed phonology [46], visuospatial working memory [47], or a top-down model of handwriting gestures [10]. The more bilateral activations in the visual system and the greater involvement of the intraparietal sulcus in Chinese reading may be tentatively related to the complex visual-spatial configurations of Chinese characters, which possess a number of intricate strokes packed into a square shape [45, 46].

Besides, in our study with young children, who were still in the process of automatizing reading, we found that Chinese children showed slightly larger activation than French children in the posterior superior temporal gyrus/sulcus. This region is associated with phonological processing and grapheme-phoneme conversion [58]. Previous findings in adults suggested that it is more engaged in alphabetic than in logographic languages [45, 46] while our study showed an opposite pattern. In Chinese writing, a large number of written characters correspond to the same syllable, thus phonological information is insufficient to access semantics of a printed character. As a result, Chinese readers must rely more heavily on the direct route from orthography to the lexicon [59, 60]. However, phoneme-level representation still plays an essential role in learning to read Chinese, especially in beginners who relies on Pinyin which allows children manipulate different phonological units such as decomposing a syllable into onset, rime, tone and phonemes. More importantly, both phonological and morphological awareness (lexical compounding) are predictors of reading in all writing systems, including in Chinese children [18, 61, 62]. With proficiency, children reduce their reliance on phonology and develop more direct connections between orthography and meaning [63]. The involvement of the posterior superior temporal gyrus in Chinese reading may reflect the phonological role of this region for young readers of Chinese. Besides, when carefully comparing the activation of the posterior temporal gyrus with other regions, we found that the greater activation in Chinese may be mainly due to relatively weak activation in French dyslexics, even though the language × dyslexia interaction was not significant.

Overall, our findings indicate that the large-scale neural network for reading is largely invariant across cultures and only modulated by culture-dependent characteristics in the

intensity and spatial extent of its activation.

A universal neural phenotype for dyslexia

Some authors have also proposed that the cortical regions mediating dyslexia are different in Chinese and alphabetic languages (left middle frontal gyrus in Chinese versus left temporo-parietal regions in alphabetic languages) [29, 30]. On the contrary, our results are strikingly similar in Chinese and French dyslexic children tested with the same paradigm, thus suggesting a universal neural phenotype for dyslexia. Dyslexic children were impaired in all classical reading-related regions, most notably the VWFA in the left FFG and the left posterior STG, regions that have been consistently reported to show lower activations in dyslexics relative to controls in alphabetic languages [24, 64, 65]. The present study confirms that these hypoactivations can be observed since childhood in all writing systems, whether alphabetic systems with deep or shallow orthographies, or in Chinese characters. Hu et al [33] reached a similar conclusion by comparing Chinese and English dyslexics.

Thanks to the individual peak location and intensity analyses, as well as the multivariate pattern analyses, we could reject an alternative interpretation which, to the best of our knowledge, was not explicitly tested in previous studies: the possibility that the hypoactivations are an artifact of group averaging, solely due to greater inter-individual variability in the localization of reading-related circuits in the dyslexic brain. Using individual peak, we observed that the brain localization to words were not more dispersed among dyslexic participants than among controls. Using MVPA, we showed that, within individual subjects, the activation patterns in the VWFA in response to written words were less reproducible across runs in dyslexics than in normal readers. This was solely the case for words, not for the other visual categories. We did observe a slightly reduced activation to faces and houses in dyslexics relative to controls, as previously reported in illiterate subjects [34], as well as seen in response to non-word stimuli (numbers, abstract strings) [66] and faces in dyslexics [42, 67]. However, the pattern of activity for faces was stable from one run to the next, contrary to what was found for words in the MVPA analyses. This observation suggests that the reduced activation to written words does not reflect a general disorganization of the extra-striate visual areas, but rather a specific difficulty with written words.

Given that the VWFA is also under-activated by written words in illiterates [34, 68] and in normal children before they learn to read [13], its under-activation in dyslexia may simply reflect the lack of reading practice – in other words, it might be a consequence rather than a cause of the reading deficit. Dyslexia is likely to be a heterogeneous deficit with a variety of different causes, including a phonological deficit in many children, but also visual attentional deficits, plausibly anywhere along the complex processing chain that leads from print to sound and meaning [69-71]. The present study cannot distinguish cause from consequence, but merely observe that a reduced VWFA activation is one of dylexia dominant fMRI signatures.

The other major site of impairment reported in the dyslexia literature is the left posterior STG, a region involved in grapheme-phoneme conversion [58, 72] although this location is less consistently found in children than in adults [52]. In our data, only French dyslexic children had a significantly lower activation relative to controls at this location, but there was no significant Language × dyslexia interaction. In both languages, dyslexics exhibited an unstable activation pattern across fMRI runs, suggesting fragile phonetic representations evoked by written stimuli. In agreement with this interpretation, Vandermosten et al [73] also observed disrupted phonological representation in a multivariate pattern analysis but not in the univariate activation analysis in beginning readers with a family risk for dyslexia. Again, because this site is also hypoactivated in illiterates and in preliterate children [34] we cannot ascertain whether its anomalous activation is a cause or a consequence of dyslexia. Indeed, it could be both, as phonological awareness is known to be both a predictor of future reading impairments [74, 75], and a consequence of learning to read in an alphabetical language [76].

Finally, we also observed an impairment in the left middle frontal gyrus as reported in Chinese dyslexics by Siok et al. [29, 30]. Activation at this location was modulated by both reading score and language: overall, Chinese children had larger activation than French children at this site, but in both languages, dyslexics also exhibited weaker activation than their controls: effects of dyslexia and language on that region seemed to be additive. This result indicates that, once again, an impairment in this region is not specific to Chinese but part of a universal phenotype of dyslexia.

Unlike readers of alphabetic languages who can use grapheme–phoneme correspondences, readers of Chinese must learn the phonology of characters as a whole and they may rely on

writing as a means for memorizing the large number of characters. This hypothesis is consistent with the finding that writing skills could predict reading ability in Chinese children [77]. The greater activation of the left MFG may reflect the greater reliance of Chinese children on writing and the dysfunction of this region in Chinese dyslexia may reflect their impairment in linking spelling with phonology through motor memories for writing [78]. Interestingly, novice readers in alphabetic languages are also known to rely on a motor memory for hand gestures when recognizing written words [79]. A recent study found that the motor representation can be accessed automatically for subliminal words, in both Chinese and French adult readers [10]. Our findings on children further suggest that the left MFG is likely to play a pivotal role in successful reading acquisition that is independent of the writing system.

Conclusions

Thanks to several convergent analyses, we revealed that the neural anomalies underlying developmental dyslexia are largely similar in French and Chinese readers. Across these very different writing systems, the cultural invention of reading relies on similar brain resources. As previously noted in an adult fMRI study [10], cultural variability is merely reflected in the variable emphasis that different writing systems put on phonemes, syllables and whole words, which in turn may modulate the severity of dyslexia and the degree of anomaly that can be detected at different locations along the brain's reading circuitry.

Conflict of interest The authors declare no conflict of interest

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Table 1. Characteristics of the four groups

	Chinese		French	
	Control	**Dyslexia**	**Control**	**Dyslexia**
Sample size	24	24	24	24
Age in months (SD)	123 (11)	123 (10)	123 (11)	123 (10)
Sex	13M/11F	16M/8F	13M/11F	16M/8F
Reading ability (z-score)	0.67 (0.44)	-1.74 (0.45)	0.73 (0.81)	-2.16 (0.52)

Table 2. Regions of significant activations for each visual category vs the two others across all participants

Region	MNI coordinates	Peak *p*-value	Peak z-value
Words > others			
Left inferior frontal gyrus	-48 12 30	2.06e-19	8.93
Left precentral	-39 0 36	1.45e-18	8.72
	-51 6 39	2.91e-14	7.51
Left superior temporal gyrus/sulcus	-57 -30 3	2.39e-19	8.92
Left middle temporal gyrus	-51 -42 6	7.89e-18	8.52
Left fusiform gyrus	-48 -57 -15	1.69e-17	8.43
Left Inferior parietal sulcus	-45 -39 42	4.29e-14	7.46
Right superior temporal sulcus	57 -27 3	8.94e-10	6.02
Faces > others			
Left fusiform gyrus	-39 -48 -21	3.28e-17	8.35
Right fusiform gyrus	42 -54 -18	6.14e-26	10.47
Right amygdala/ hippocampus	18 -9 -18	6.11e-22	9.56
Left amygdala/ hippocampus	-18 -9 -18	3.91e-15	7.77
Houses > others			
Left fusiform gyrus	-30 -48 -6	9.01e-53	15.24
Right fusiform gyrus	30 -45 -9	2.90e-50	14.86
	27 -63 -9	2.40e-22	9.65
Left calcarine	-18 -54 9	8.66e-10	6.02

Table 3. Regions significantly correlated with reading scores across all participants at the whole-brain level

Region	MNI coordinates	Peak *p*-value	Peak z-value	R-value
Left fusiform gyrus	-42 -45 -18	6.65e-6	4.36	0.490
Right fusiform gyrus	42 -66 -24	9.96e-6	4.27	0.512
Left precentral	-36 -3 57	2.75e-6	4.54	0.467
Right precentral	54 18 33	1.29e-5	4.21	0.432
Left middle frontal gyrus	-36 12 27	1.92e-5	4.12	0.468
Right middle frontal gyrus	45 6 54	7.72e-6	4.32	0.460
Left superior temporal sulcus	-57 -24 0	1.00e-5	4.26	0.510
Right middle occipital gyrus	27 -69 42	6.34e-6	4.37	0.448

Figures

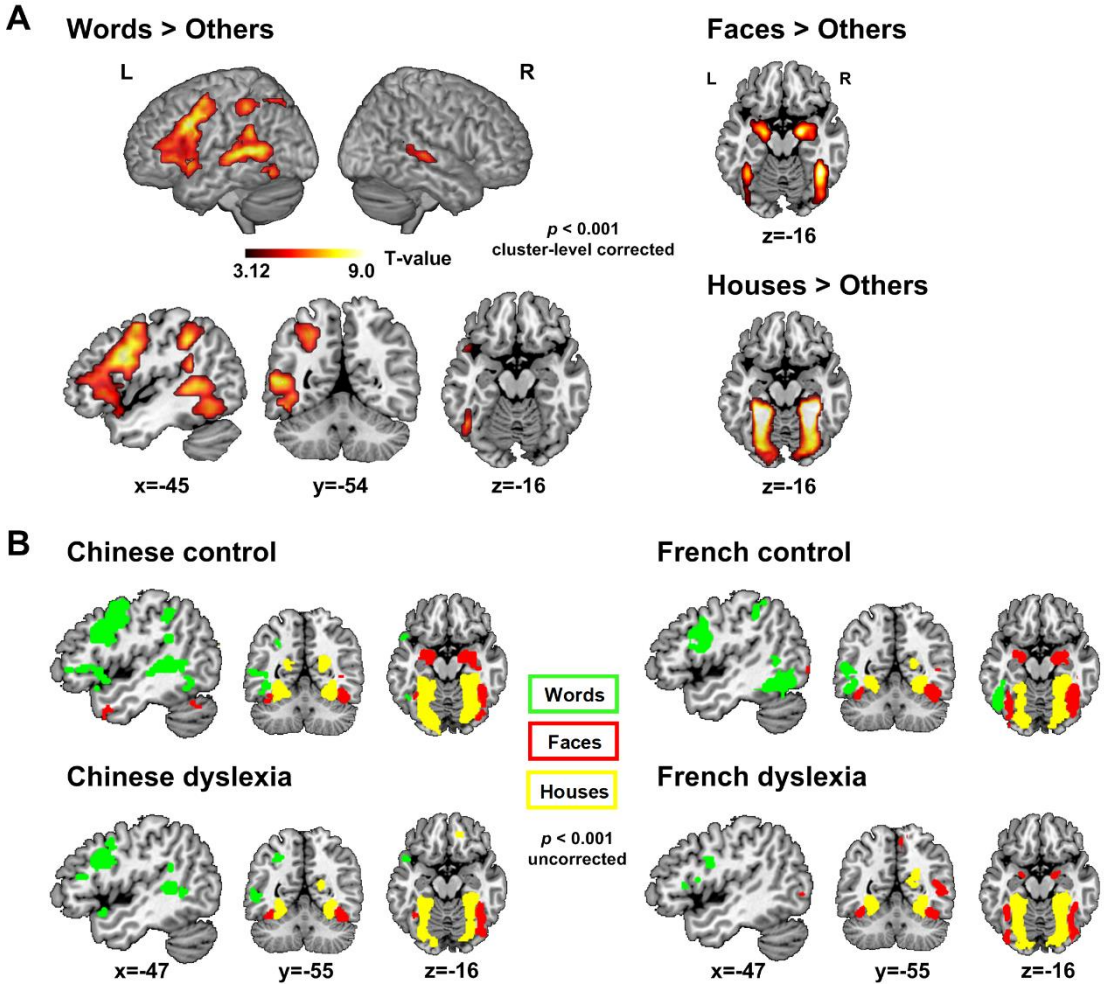

Figure 1. (A) **Category-specific circuits across all participants** (voxel-level $p < 0.001$, cluster-level FWE corrected $p < 0.05$)**.** On the left, the reading circuit identified by the contrast Words > [Faces, Houses] and on the right: Face-selective (Faces > [Words, Houses]) and House selective regions (Houses > [Words, Faces]). (B) **Separate category-specific activation in four groups** (voxel-level $p < 0.001$, cluster-level uncorrected)**.** On the left, category-specific activation in Chinese controls (above) and Chinese dyslexics (below). On the right, category-specific activation in French controls (above) and French dyslexics (below). Green: regions selectively activated by words (Words > [Face, House]); Red: regions selectively by faces (Face > [Word, House]); Yellow: regions selectively activated by Houses (House > [Word, Face];

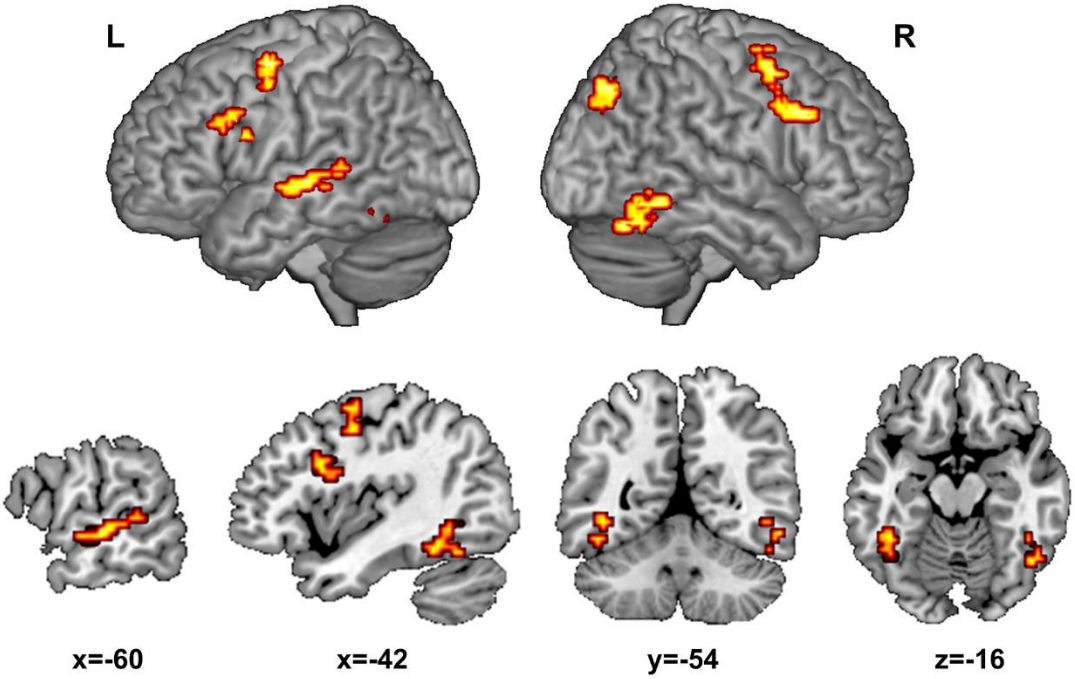

Figure 2. Neural correlates of inter-individual variability in reading scores. The figure shows the regions whose activation in the words versus fixation contrast was significantly correlated with reading scores across all participants at the whole-brain level (voxel-wise $p < 0.001$ and cluster-wise $p < 0.05$ FWE corrected).

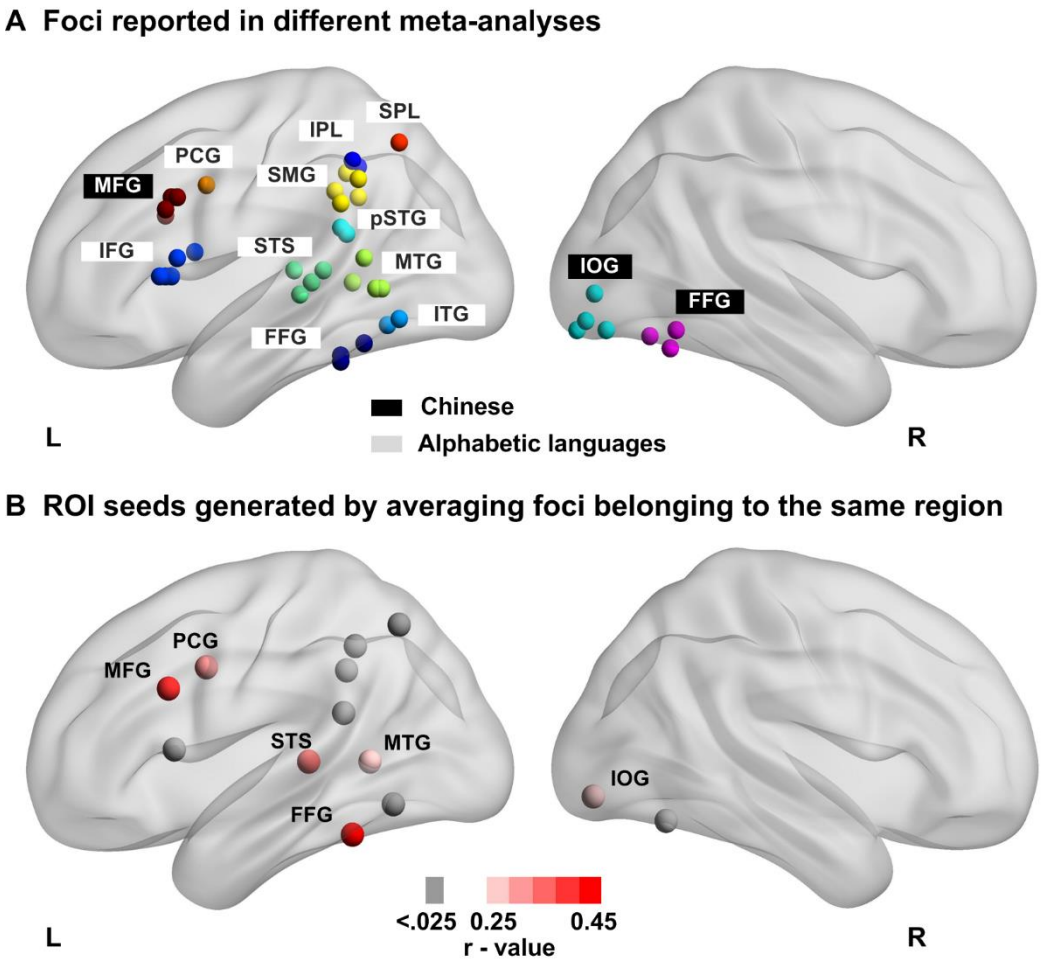

Figure 3: Regions of interest (ROIs) used to analyze the data. (A) Each sphere represents a peak reported in the literature; Labels in white background indicate foci reported in meta-analyses of dyslexia in alphabetic languages; Labels in black background indicate foci reported in meta-analyses of Chinese reading. (B) ROIs used in the current study. Coordinates of foci (see the upper graph) belonging to the same functional region were averaged to create 6-mm-radius spheres at the averaged coordinates. Dots are colored according to their correlation with reading scores across all participants. Red dots represent ROIs whose activation to words versus fixation were significantly correlated (pFDR < 0.05). MFG: Middle Frontal Gyrus, PCG: Pre-Central Gyrus, STS: Superior Temporal Sulcus, MTG, Middle Temporal Gyrus, FFG: Fusiform gyrus, IOG: Inferior Occipital Gyrus.

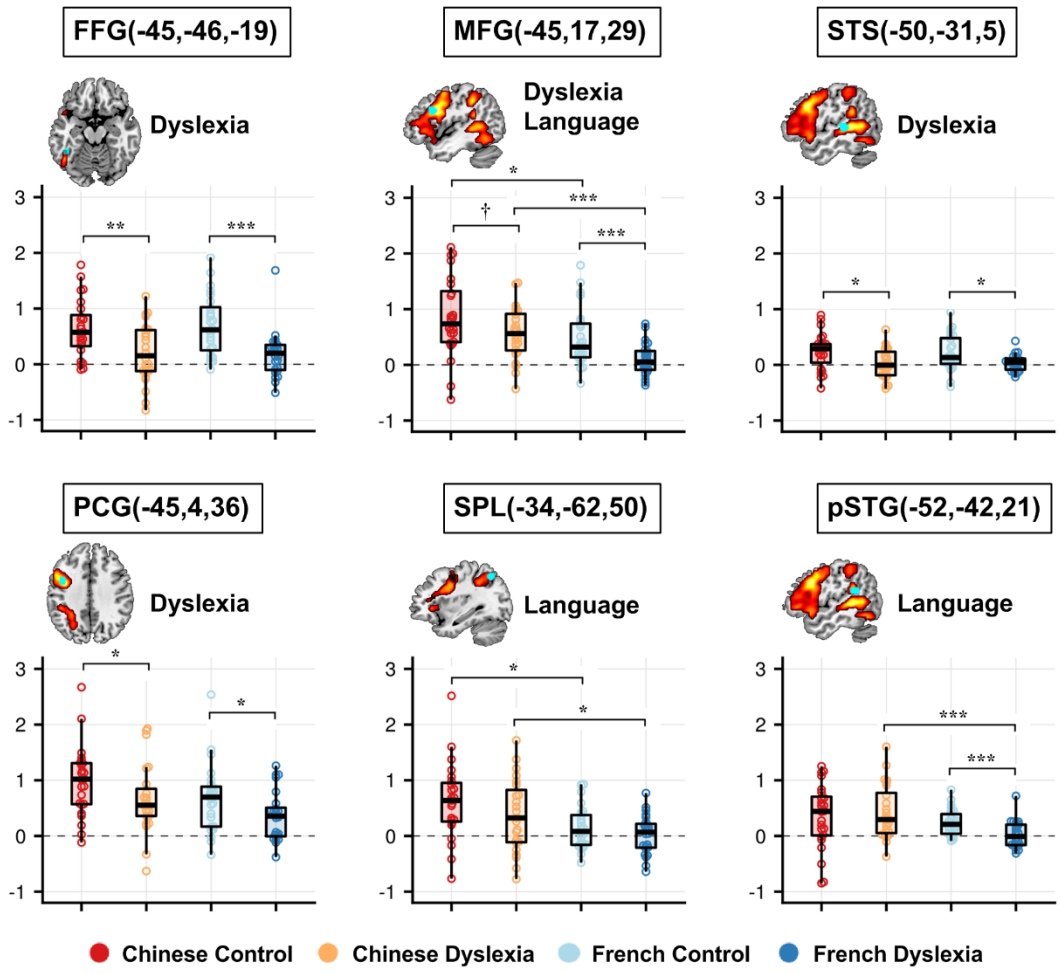

Figure 4. Effects of dyslexia and language on the words versus fixation contrast in the selected ROIs. Brain slices showed the literature-based ROIs (cyan) overlaid on the reading circuit (red-yellow) in our participants (Words > [Faces, Houses]). Plots show the mean activation for words > fixation, in each of the four groups and ROIs. The words "Dyslexia" and "Language" indicate a significant main effect of Dyslexia and a main effect of Language in the ANOVA (after FDR correction for a total of 13 ROIs). Note that no ROI showed a significant interaction of Language × Dyslexia. Brackets indicate significant post hoc analyses: ** $p <$ 0.005, ** < 0.01, * < 0.05, † = 0.07.

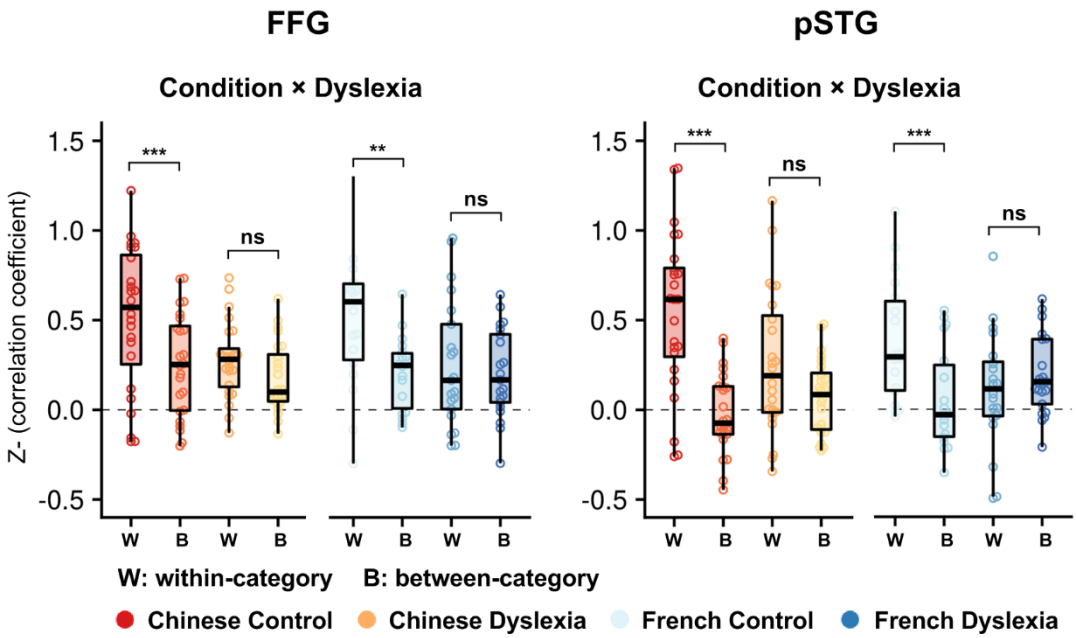

Figure 5: Multivariate pattern analysis indicates that the word-induced activation is not simply more anatomically variable, but is less reproducible in dyslexic children. Within the designated ROISs, we computed the correlation coefficient of the multivoxel patterns for the word versus fixation contrast in run 1 and in run 2 (within-category correlation, W). For the between-category coefficient (B), the plots show the average correlation coefficient between words and faces, words and houses and faces and houses between run 1 and run 2. In each plot, the correlation is presented for the Chinese children on the left of the plot and for French children on the right. The words "Condition × Dyslexia" indicate a significant interaction between condition (within vs between) and the status of children (normal vs dyslexic) (after FDR correction for a total of 13 ROIs). Normal readers, but not dyslexics, exhibited a significant similar pattern of activation to words from one run to the next in the left FFG and pSTG, suggesting that the activation pattern for words was not simply anatomically variable, but was genuinely less reproducible in dyslexics than in normal readers.