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Developmental dyslexia in Chinese and English populations: dissociating the effect of dyslexia from language differences

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Previous neuroimaging studies have suggested that developmental dyslexia has a different neural basis in Chinese and English populations because of known differences in the processing demands of the Chinese and English writing systems. Here, using functional magnetic resonance imaging, we provide the first direct statistically based investigation into how the effect of dyslexia on brain activation is influenced by the Chinese and English writing systems. Brain activation for semantic decisions on written words was compared in English dyslexics, Chinese dyslexics, English normal readers and Chinese normal readers, while controlling for all other experimental parameters. By investigating the effects of dyslexia and language in one study, we show common activation in Chinese and English dyslexics despite different activation in Chinese versus English normal readers. The effect of dyslexia in both languages was observed as less than normal activation in the left angular gyrus and in left middle frontal, posterior temporal and occipitotemporal regions. Differences in Chinese and English normal reading were observed as increased activation for Chinese relative to English in the left inferior frontal sulcus; and increased activation for English relative to Chinese in the left posterior superior temporal sulcus. These cultural differences were not observed in dyslexics who activated both left inferior frontal sulcus and left posterior superior temporal sulcus, consistent with the use of culturally independent strategies when reading is less efficient. By dissociating the effect of dyslexia from differences in Chinese and English normal reading, our results reconcile brain activation results with a substantial body of behavioural studies showing commonalities in the cognitive manifestation of dyslexia in Chinese and English populations. They also demonstrate the influence of cognitive ability and learning environment on a common neural system for reading.

Keywords: dyslexia; fMRI; language processing; cognitive impairment; developmental neuroimaging

Abbreviations: LIFS = left inferior frontal sulcus; LpSTS = left posterior superior temporal sulcus; WISC-III = Wechsler Intelligence Scale for Children

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Introduction

Reading is an increasingly important communication skill in modern society. It is therefore important to understand why dyslexics have difficulties learning to read despite normal intelligence and educational opportunities. Functional imaging studies have shown differences in the pattern of reading activation in dyslexic and skilled readers but it is not yet clear how these differences depend on the language spoken and its orthography (writing system). Evidence to date suggests common effects of dyslexia in languages that use alphabetic writing systems (Paulesu *et al.*, 2001) but differences in dyslexics that read Chinese versus alphabetic writing systems (Siok *et al.*, 2004, 2008). In alphabetic writing systems, dyslexia has consistently been associated with atypically low activation in posterior occipito-temporal and/or temporoparietal regions such as the angular gyrus (Rumsey *et al.*, 1997; Brunswick *et al.*, 1999; Paulesu *et al.*, 2001; Shaywitz *et al.*, 2002, 2003; Kronbichler *et al.,* 2006; Hoeft *et al.*, 2007; Meyler *et al.*, 2007). In contrast, the first neuroimaging studies of Chinese dyslexics reported atypically low activation in the left middle frontal cortex (Siok *et al.*, 2004, 2008). This suggests a different neural basis for Chinese and English dyslexia. Critically, however, behavioural studies emphasize a similar cognitive profile in Chinese and English dyslexics (see below) and no previous neuroimaging study has directly and statistically compared brain activation for reading in Chinese and English dyslexics. Therefore we investigated whether the effect of dyslexia on brain activation differs in Chinese and English monolingual readers when the experimental paradigm and procedures are matched.

The expectation that the effect of dyslexia will differ in Chinese and English arises from the well known differences in the orthographies used. The English and Chinese writing systems differ in the visual features of their orthographies and in how these visual features are linked to the sounds of words. English is an alphabetical language that uses letters and letter combinations to represent the sounds of words at the level of phonemes. In contrast, the Chinese writing system uses square-shaped characters that link directly to monosyllabic sounds but not to phonemes. A critical distinction here is that the sounds of English words can be assembled from the phonemic components, but Chinese characters map directly to syllables in an arbitrary way and all Chinese words are composed of such syllables (morphemes).

In normal readers (i.e. those with no history of dyslexia), recent evidence suggests differences in brain activation for reading in Chinese and English. Specifically, the left posterior superior temporal cortex is activated in English but not Chinese reading, while the left middle/inferior frontal cortex is more activated in Chinese than English readers (Tan *et al.*, 2003, 2005). A plausible explanation for these brain activation differences in Chinese and English is that higher left superior temporal activation for English versus Chinese reading reflects phonological decoding, i.e. the process of assembling the sounds of letter combinations into the sounds of whole words (Tan *et al.*, 2005). In contrast, left middle frontal activation in Chinese readers may be involved in the direct mapping of visual characters to their monosyllabic sounds which, in the absence of phonemic cues, increases the demands on visual and verbal short-term memory (Siok *et al.*, 2004, 2008). By directly comparing brain activation in Chinese and English readers, with and without developmental dyslexia, we independently manipulated the effects of dyslexia from differences in Chinese and English reading. This allowed us to determine whether the left frontal region, reported to be more activated in Chinese normal readers than Chinese dyslexics (Siok *et al.*, 2004, 2008), is the same as the left frontal region that is expected to be more activated in Chinese relative to English normal readers (Tan *et al.*, 2003, 2005).

In contrast to the prediction that the effect of dyslexia on brain activation will be different in Chinese and English, there are also reasons to predict commonalities in brain activation for Chinese and English dyslexia (Ziegler, 2006). Numerous behavioural studies have demonstrated that both Chinese and English dyslexics have difficulty computing and remembering how phonology is linked to written symbols (Bradley and Bryant, 1983; Ho *et al.*, 2000; Ziegler and Goswami, 2005). Moreover, although English orthography carries phonological cues at the phonemic level, this is not consistently helpful in English. Consequently, English readers tend to use multi-letter clusters, rhyme analogy strategies (e.g. using ‘sink’ as the basis of reading ‘link’) and whole word knowledge (Goswami, 1986, 1988; Goswami *et al.*, 1997; Ziegler *et al.*, 2001; Ziegler and Goswami, 2005), which in turn depends on vocabulary knowledge (Hanley *et al.*, 2004). Thus, despite differences in the Chinese and English writing systems, learning to read in both languages requires good visual perceptual skills (Li *et al.*, 2009), phonological awareness at the syllable level (Ho and Bryant, 1997; Ho *et al.*, 2000; Chung *et al.*, 2008; Cheung *et al.*, 2009) and verbal short-term memory (Mayringer and Wimmer, 2000; Siok and Fletcher, 2001; Ho *et al.*, 2006). Impairments at any of these levels can lead to difficulties in learning to read that will be most pronounced when the individual suffers from multiple deficits (Ho and Bryant, 1997; Ho *et al.*, 2002; Snowling, 2008). Cross-linguistic behavioural studies of dyslexia therefore predict commonalities in the neural markers for Chinese and English dyslexics.

In summary, previous neuroimaging studies suggested that the effect of dyslexia on brain activation will be different in Chinese and English populations, while the behavioural data presented a similar cognitive profile for Chinese and English dyslexia. This discrepancy in the neuroimaging and behavioural literature requires further investigation. We therefore directly compared the neural mechanisms that support reading in English dyslexics, Chinese dyslexics, English normal readers and Chinese normal readers, while controlling for all other experimental parameters (see ‘Materials and methods’ section). This allowed us to provide the first direct statistically based investigation into how the effect of dyslexia on brain activation is influenced by the Chinese and English writing systems. It also allowed us to determine whether the effect of Chinese or English dyslexia is manifest in the same regions where activation differs for Chinese and English normal readers.

All our participants were monolingual and tested in their own countries using closely matched experimental stimuli, tasks and protocols. Our dyslexic readers had concurrent difficulties with reading, spelling and phonological tasks (Supplementary Fig. 1), despite good educational opportunities and the absence of sensory or neurological damage (see 'Materials and methods' section for details). The activation task of interest involved semantic word matching. This required a right hand index or middle finger press response to indicate which of two written object names had a closer semantic relationship with a target word (Fig. 1). Prior investigation has shown that this task involves orthographic, semantic and phonological processing in both English (Van Orden, 1987) and Chinese (Tan and Perfetti, 1999; Perfetti *et al.*, 2005).

In addition to semantic decisions on written words, our paradigm also involved semantic decisions on photographs of objects, perceptual decisions on unfamiliar letters and non-objects, reading aloud and object naming (Fig. 1). These conditions allowed us to investigate condition specific differences and control for sensory and motor processing. However, for the group specific differences in Chinese versus English readers and normal versus dyslexic readers, we focused on the semantic word matching task because we were able to record accurate measurements of in-scanner performance, which was not possible for the speech output tasks. We could therefore carefully equate accuracy across participant groups (Table 1 and Supplementary Fig. 1) so that any group differences in activation could not be attributed to in-scanner accuracy differences. We were also able to ensure that there were no response time differences in the Chinese and English groups, although dyslexics were slower than normal readers in both languages. Finally, to ensure that any group differences were in the context of successful rather than unsuccessful performance, our analysis identified activation for correct trials only and excluded activation related to errors. This allowed us to interpret group activation differences in terms of the impact of different writing systems and/or reading abilities on the functional mechanisms that support successful reading.

Figure 1 Functional imaging stimuli. Each trial presented three stimuli simultaneously. Their forms were either familiar or unfamiliar. Participants matched one of the lower stimuli to the target (above) according to the closer semantic relationship (for familiar words and pictures) or perceptual identity (for unfamiliar letters and non-objects). The right middle finger was used to indicate the right lower stimulus and the right index finger was used to indicate the left lower stimulus. The words and unfamiliar letter strings depended on the language spoken. The majority of Chinese words were the direct translation of the English object names but some stimuli were different in Chinese and English (Supplementary Table 1) because (i) the participants used different vocabularies; (ii) pictorial representations of the items were different in Chinese and English; and (iii) changes to one stimulus in a triad sometimes necessitated changing all the stimuli in a triad. The pictures of objects for English subjects corresponded to the written English object names and the pictures of objects for Chinese subjects corresponded to the written Chinese object names.

Aims and predictions for group differences during the semantic word matching task

Our aim was to determine: (i) whether reading activation differs in Chinese and English dyslexics; and (ii) whether the effect of dyslexia in Chinese and/or English corresponds to the effect of Chinese versus English in normal readers. For the effect of dyslexia, we expected reduced activation in the left middle/inferior frontal cortex for Chinese dyslexics relative to Chinese normal readers (Siok *et al.*, 2004), and in the left posterior middle temporal and left occipitotemporal areas for English dyslexics relative to English normal readers (Paulesu *et al.*, 2001; Kronbichler *et al.*, 2006). We also predicted that activation in the left angular gyrus would be lower for English dyslexics than English normal readers, as previously reported during semantic or sentence verification tasks (Shaywitz *et al.*, 1998, 2002; Meyler *et al.*, 2007). For the effect of Chinese versus English normal readers we predicted increased activation in the left middle/inferior frontal cortex for Chinese than English, and in the left posterior superior temporal cortex for English than Chinese (Tan *et al.*, 2003).

Materials and methods

The English part of the study was approved by the National Hospital and Institute of Neurology's joint ethics committee. All Chinese subjects signed a formal consent as required by the Institute of Linguistics, Xuzhou Normal University. All participants were adolescents (13–16 years of age), right handed, monolingual with good educational opportunities and no history of sensory, neurological or psychiatric impairment or attention deficit disorder.

English participants

Our initial sample included 45 English participants: 28 had a diagnosis of developmental dyslexia from a prior educational assessment and 17 were normal readers with no history of learning difficulties. All 45 participants were re-assessed at the time of the experiment using standardized assessments. Reading and spelling were assessed with the Wechsler Objective Reading Dimensions (Rust *et al.*, 1993).

Table 1 **In-scanner behaviour**

	Chinese		English	
	Normal	Dyslexic	Normal	Dyslexic
Raw data				
Accuracy (%)				
Word match	92.4 (6.7)	89.1 (3.3)	88.6 (5.7)	86.5 (3.8)
Picture match	83.6 (9.5)	84.8 (8.9)	88.3 (4.7)	90.5 (5.3)
Same letters	99.2 (2.1)	99.2 (2.2)	97.5 (4.4)	98.4 (3.9)
Same picture	98.5 (2.8)	100.0 (0.0)	98.8 (4.0)	99.1 (3.0)
Response times (ms)				
Word match	1874 (273)	2137 (209)	1912 (263)	2369 (236)
Picture match	2195 (201)	2266 (213)	1797 (252)	2034 (242)
Same letters	1354 (225)	1518 (234)	1158 (145)	1383 (179)
Same picture	1164 (270)	1329 (243)	1197 (228)	1412 (271)

	The effect of dyslexia		Chinese versus English		Interaction	
	F (1,33)	*P*-value	*F*(1,33)	*P*-value	*F*(1,33)	*P*-value
Statistics						
Word match	19.4	0.000	2.7	1.4	0.108	0.245
Picture match	4.0	0.053	16.9	0.000	1.2	0.289
Same letters	9.1	0.005	6.6	0.015	0.22	0.639
Same picture	5.0	0.032	0.47	0.50	0.09	0.769

Mean accuracy in percentages, response times in milliseconds and statistics for group differences for each semantic and perceptual matching task. Standard deviation is given in brackets.

Phonological skills were assessed using the Phonological Assessment Battery (Frederickson *et al.*, 1997). Verbal and non-verbal IQ scores were assessed using the Wechsler Intelligence Scale for Children (WISC-III) (Wechsler, 1955). We then excluded four dyslexics whose full scale IQ on the WISC-III was below 80 (i.e. they were not consistent with our definition of dyslexics); and seven dyslexics whose scores on the reading, spelling or Phonological Assessment Battery assessments were within the range of our own control subjects (i.e. they were not dyslexic according to our assessment). Following functional MRI data collection and analysis we also excluded six dyslexics and seven controls because: (i) performance was <80% in the semantic word matching task in the scanner; and/or (ii) they moved more than 3 mm during image acquisition. Our final selection of English participants included 10 normal readers and 11 dyslexics with accurate performance. The motivation for these strict selection criteria (in English and Chinese) was to minimize error variance from confounding group differences. Confirmation that our analyses had sufficient statistical power is provided by the remarkably consistent replication of previous findings (see main text for details). Moreover, none of our conclusions are based on null effects. The mean age of the selected English dyslexics was 13.8 (range 12.1–16.0) and five were female. The mean age of the English normal readers was 13.6 (range 13.0–14.3) and four were female.

Chinese participants

As described in Siok *et al*. (2004), the classification of children's reading ability in Chinese is primarily based on their school performance and their teacher's recommendation because standardized tests of dyslexia are not available in Chinese. Therefore, we tested a large population of 548 adolescents (13–16 years of age) to calculate the norms and standard deviation. The first round of paper and pencil testing involved: (i) orthographic decisions (35 trials); and (ii) lexical decisions (20 trials) on single Chinese characters or single Chinese words; (iii) phonological decisions (rhyme judgement on 40 pairs of Chinese characters); (iv) semantic decisions (chose one or four words to complete a written sentence, 15 trials); and (v) spelling (writing 20 characters to dictation). Each correct answer was given a score of 1. The mean and standard deviation of all scores was calculated over all 548 participants. From this population, 52 participants had scores more than 1.5 SD below the mean and were therefore judged to be potentially dyslexic.

From the 52 participants with low scores, we excluded participants who were not in the lowest 20% for reading as judged by their Chinese class teacher, or who were not below 1.5 SD on the mean score from the two most recent examinations for Chinese language and literature, which mainly test students' knowledge of Chinese vocabulary, and their reading and writing skills. After excluding participants who were within the normal range on this task, our sample of potential dyslexics was reduced to 38. Forty five normal readers were chosen, at random, from those who scored within 1.5 SD of the mean.

The selected samples of 38 potential dyslexics and 45 normal readers were then tested on a second set of tasks: (i) naming Arabic digits (20 trials); and (ii) Chinese characters (20 trials) presented on a computer so that response times could be measured; (iii) digit span from the WISC-III; (iv) spoonerisms (15 trials); and (v) Raven's standard progressive matrices. Correlation analysis demonstrated the results of the spoonerism task were the best predictor of performance on the formal Chinese examinations. This is consistent with dyslexia resulting from a phonological impairment, as observed in the English dyslexics. Finally, four dyslexics were excluded because their performance was below 10% of the mean on the Raven's standard progressive matrices tasks or within the normal range on the spoonerisms task. Thus, the Chinese dyslexic sample, like the English dyslexic sample, was selected on the basis of phonological impairments.

The remaining 34 dyslexics and 45 normal readers were invited to participate in the functional MRI experiment but only 11 dyslexics and

14 normal readers agreed. After applying the inclusion criteria used with the English participants, our samples were further reduced to eight dyslexics and eight normal readers. As indicated above, this was sufficient to replicate the findings of previous functional MRI comparisons of dyslexic and good reader Chinese reading (Siok *et al.*, 2004, 2008) and to generate novel interpretations and conclusions that were not based on null effects. The mean age of the selected Chinese dyslexics was 14.1 years (range 13.1–14.7) and all were male. The mean age of the Chinese normal readers was 14.5 (range 13.2–15.2) and two were female.

As the English and Chinese participants were administered different tests outside the scanner, their scores are not directly comparable. However, what we show is that both the English and Chinese dyslexics showed similar difference relative to their culturally matched normal readers for reading, spelling and spoonerisms.

Experimental design and stimuli for the functional MRI experiment

There were four experimental sessions/runs. In two sessions, participants made a finger press response to indicate the semantic relationship between (i) words; or (ii) pictures of objects; or judged the perceptual relationship between (iii) unfamiliar letters; or (iv) non-objects (Fig. 1). In the other two sessions, participants (i) read aloud the words; (ii) named the pictures; and (iii) said *'1, 2, 3'* to the unfamiliar letters; or (iv) non-objects.

Over the experiment, the participants were presented with 192 written object names and their corresponding pictures. In English, the majority ($n = 140$) of these object names were monosyllabic (e.g. bell, bus, horse, dog), 47 were bisyllabic (carrot, flower, spider, window) and five were trisyllabic (camera, onion, piano, potato, tomato). In Chinese, the translations (or their culturally-appropriate changes) were primarily bisyllabic ($n = 153$), with 24 monosyllabic, and 15 trisyllabic words. Thus, the names of the English stimuli had fewer syllables than the names of the Chinese stimuli, which may impact upon the level of phonological processing in Chinese and English during naming, reading and word matching but was not expected to impact upon group differences in semantic picture matching or perceptual matching that do not involve overt phonological processing. The 192 stimuli were organized in triads, with one target stimulus above and two choices below (see Fig. 1 and Supplementary Table 1 for details). For the semantic conditions, there were 64 triads where the target had a close semantic relationship with one of the two choices (e.g. anchor and ship in Fig. 1). Note that where a stimulus word was changed in an English triad for cultural reasons this necessitated further changes on occasions to ensure meaningful response (Supplementary Table 1). In the naming and reading conditions, the semantic relationship between the three items was minimized (e.g. anchor, carrot, broom).

During the perceptual matching conditions, unfamiliar Greek letters were presented to the English participants and Korean characters were presented to the Chinese participants. This controlled for early visual processing in the English words and Chinese characters respectively. The pictures of unfamiliar non-objects were photographs of wooden or plastic constructions. The same non-objects were presented to the English and Chinese participants.

Conditions were blocked, with four triads per block. However, our analysis was event related so that we could exclude incorrect trials. Each triad remained on the screen for 4.32 s followed by 180 ms of fixation. The resulting block length was therefore 18 s for each condition. Each block was preceded by 3.6 s of instructions. Over the experiment, there were eight blocks (32 triad stimuli) of each condition and 10 blocks of fixation (lasting 14.4 s). The order of conditions was counterbalanced within session and the order of sessions was counterbalanced across subjects.

Stimulus presentation was via a video projector, a front-projection screen and a system of mirrors fastened to a head coil. Each picture was scaled to take $7.3 \times 8.5^{\circ}$ of the visual field. English words were presented in lower case Arial and occupied 4.9° (width) and 1.2° (height) of the visual field. Chinese characters were presented in Kai font and occupied around 4° (width) and 1° (height), which corresponded to the size that was most comfortable for reading. For semantic and perceptual matching, accuracy and response times were measured via right hand finger presses on a key pad. For the naming and reading conditions, it was only possible to record in-scanner accuracy for the English participants, using a noise cancellation procedure, and training to whisper their responses and minimize jaw and head movements in the scanner. In-scanner accuracy was not measured for the naming and reading tasks in the Chinese participants. Instead, accuracy was estimated by asking the Chinese participants to name and read the items again after scanning. For this reason, we focus our comparison of English and Chinese activation on the semantic and perceptual tasks where performance was precisely recorded and matched across groups.

MRI acquisition

All data were acquired using whole brain Siemens 1.5T MRI scanners. The English data were acquired on the Sonata and the Chinese data were acquired on the Symphony. Functional imaging consisted of an echo planar imaging, gradient recalled echo sequence (repetition time = 3600 ms, echo time = 50 ms, flip = 90°; matrix = 64×64). English participants were scanned at the Wellcome Trust Centre for Neuroimaging, London, UK, with 40 axial slices, acquired with $3 \times 3 \times 3\,mm^3$ voxels. Chinese participants were scanned at the P.L.A. No. 97 Hospital, Xuzhou, China, with 30 axial slices acquired with 3 mm thickness and a gap of 1 mm. Each of the four functional scanning sessions was always preceded by 14.4 s of dummy scans to ensure tissue steady-state magnetization. Whole brain, high resolution, anatomical images were acquired for all participants using a T_1-weighted sequence with a voxel size of $1 \times 1 \times 1\,mm^3$.

Functional MRI data analysis

All data were analysed using Statistical Parametric Mapping (SPM5) software package (Wellcome Trust Centre for Neuroimaging, London, UK, http://www.fil.ion.ucl.ac.uk/spm), running under MATLAB 7.0 Mathworks, Sherbon, MA, USA). Functional volumes from each subject were spatially realigned and unwarped to remove movement-related signal intensity changes. They were then spatially normalized to the Montreal Neurological Institute space using the unified normalization-segmentation procedure in SPM5 with a resulting voxel size of $2 \times 2 \times 2\,mm^3$. Spatial smoothing was performed using 6 mm full-width half maximum isotropic Gaussian kernel to compensate for residual variability after spatial normalization and to permit application of Gaussian random-field theory for corrected statistical inference.

The pre-processed functional volumes for each subject were then submitted to a first level (fixed-effects) statistical analysis. Although the stimuli were blocked by condition, we used an event related analysis to increase sensitivity (Mechelli *et al.*, 2003) and dissociate correct from incorrect responses. This involved event-related delta functions, convolved with a canonical haemodynamic response function, which modelled correct responses for each of the eight conditions separately, the instructions and the errors (over all conditions). Condition effects were estimated using the general linear model at each voxel. To exclude low frequency confounds, the data were high-pass filtered using a set of discrete cosine basis functions with a cut-off period of 128 s. Statistical contrasts were computed for each condition relative to fixation. All effects were based on correct trials only.

At the second level, we computed two different ANOVAs. The first included the contrast images for the four semantic and perceptual conditions relative to fixation (within subject) for each of the four groups (between subject). This resulted in 16 conditions with a correction for non-sphericity on the within subject factor. From this analysis, we computed the following statistical contrasts:

(i) Normal readers > Dyslexics for semantic word matching, over Chinese and English; for Chinese only and for English only.
(ii) Dyslexics > Normal readers for semantic word matching, over Chinese and English; for Chinese only and for English only.
(iii) Chinese > English for semantic word matching, over dyslexic and normal readers; for normal readers only and for dyslexics only.
(iv) English > Chinese for semantic word matching, over dyslexic and normal readers; for normal readers only and for dyslexics only.

The second ANOVA included the contrast images for reading aloud, naming, semantic word matching and semantic picture matching relative to fixation for each of the four groups, i.e. 16 conditions with a correction for non-sphericity on the within subject factor. The focus of this analysis was on within group differences in activation for speech output tasks (naming and reading) and semantic matching tasks (on pictures and words). Between-group differences were only significant for the comparison of English normal readers to Chinese normal readers. We did not interpret the presence or absence of group differences in this analysis because there was a wide range of accuracy between and within groups that would make group activation differences difficult to interpret. We therefore focused on the following statistical contrasts, for each group separately:

(i) Reading aloud and picture naming > Semantic word and picture matching.
(ii) Semantic word and picture matching > Reading aloud and picture naming.
(iii) The interaction of Task (speech versus button press) and Stimuli (words versus pictures).

Statistical threshold

The threshold for significance was set at $P < 0.05$ after a family wise error correction for multiple comparisons in height or extent and either across the whole brain or in spherical regions of interest (6 mm radius) centred on the co-ordinates from previous studies (Table 2).

Results

In-scanner response times

The response times for each task were analysed using a 2×2 between subjects ANOVA with the factors Normal readers versus Dyslexics and Chinese versus English. The main effect of Dyslexia (slower responses in dyslexics than normal readers) was significant for semantic word matching and both perceptual tasks, but did not reach significance for the semantic picture matching task. There was no evidence that the effect of Dyslexia differed in Chinese or English ($P > 0.24$ for the interaction term in each of the four tasks, see Table 1 for details). The main effect of Chinese versus English (dyslexics and normal readers) was not significant for semantic word matching or the non-object perceptual task but response times were slower for Chinese than English normal readers during semantic picture matching and perceptual matching of unfamiliar letter strings. This is because the pictures were initially selected for the English participants and may have been less familiar to the Chinese participants. Likewise, the Korean letters used in the perceptual task with the Chinese participants may have been visually less familiar or more complex than the Greek letters used in the perceptual task with the English participants. Details of the response times and all statistics are provided in Table 1 and Supplementary Fig. 1.

Functional MRI activation

Below we report group differences in activation during the semantic word matching task for Normal readers versus Dyslexics, and Chinese versus English. We then investigate how differences in Chinese and English reading are influenced by task and stimuli.

The effect of dyslexia

Both the Chinese and English dyslexics showed reduced activation relative to culturally matched normal readers in the left middle frontal gyrus, left posterior middle temporal gyrus, left occipito-temporal cortex and left angular gyrus. These effects were identified at $P < 0.001$ uncorrected in the whole brain analysis but were also significant at $P < 0.05$ following a correction for multiple comparisons in regions of interest from previous studies (Table 2). Figure 2 illustrates that there is a remarkable correspondence in the effect of dyslexia in Chinese and English, despite different orthographies, ethnicities and laboratories.

At a statistical threshold of $P < 0.001$ in the whole brain analysis, we also observed reduced activation for dyslexics in the right middle frontal cortex and cerebellum (Table 2). We report these effects for completeness but do not discuss them further because they were not predicted *a priori*, and were not significant following a correction for multiple comparisons across the whole brain.

There were no other areas where there was a main effect of dyslexia (lower or higher than normal readers) at a statistical threshold of $P < 0.001$ in the whole brain analysis. However, when we focused on regions showing differences in Chinese versus English normal reading (see below), we found that English dyslexics had more activation than English normal readers in the left inferior frontal sulcus (LIFS) while Chinese dyslexics had more activation than Chinese normal readers in the left posterior superior temporal sulcus (LpSTS).

Table 2 Reduced semantic word matching activation for dyslexics relative to normal readers, in regions of interest from previous studies

Region	Region of interest				Normal > Dyslexic readers												Each group separately			
					Main effect				Chinese only				English only				English		Chinese	
	x	y	z		x	y	z	Zsc.	x	y	z	Zsc.	x	y	z	Zsc.	Nor. Zsc.	Dys. Zsc.	Nor. Zsc.	Dys. Zsc.
Left middle frontal	−51	+10	+38	S	−52	+16	+32	3.8	−52	+16	+32	3.7	−50	+16	+28	2.2	5.5	4.4	7.5	4.6
Left middle temporal	−60	−56	0	P	−52	−56	−2	3.6	−54	−56	−4	2.6	−50	−58	0	3.4	3.3	ns	3.2	ns
Left occipitotemporal	−52	−60	−14	P	−46	−58	−14	3.1	−46	−58	−14	2.8	−44	−58	−12	2.6	5.8	4.4	6.3	4.4
Left angular gyrus	−36	−66	+32	M	−36	−60	+40	3.5	−30	−62	+36	3.1	−36	−60	+40	3.4	3.6	ns	4.9	2.2
Right middle frontal					+48	+10	+40	3.5	+46	+12	+40	2.8	+46	+8	+38	2.4	3.8	ns	4.3	1.7
Cerebellum					−4	−56	− 2	3.5	− 6	−60	0	2.3	−2	−56	−2	3.4	5.5	ns	ns	ns

Regions of interest from previous studies of dyslexia referred to as S (Siok *et al.*, 2004), P (Paulesu *et al.*, 2001) and M (Meyler *et al.*, 2007).
Dys. = dyslexics; Nor. = normal; *x y z* = co-ordinates in Montreal Neurological Institute space; Zsc. = *Z*-scores; ns = not significant ($Z < 1.64$; $P > 0.05$ uncorrected).

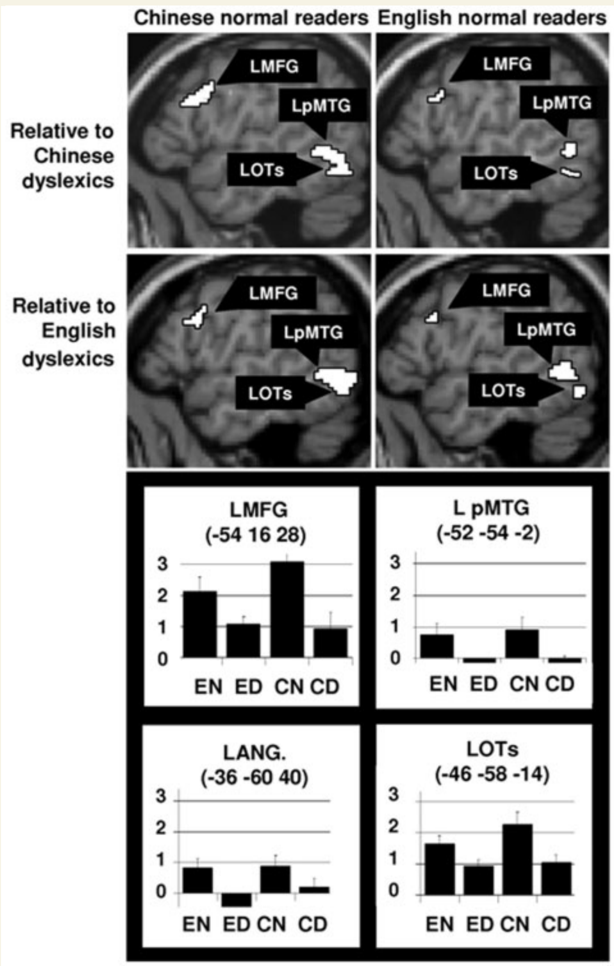

Figure 2 Reduced activation for Chinese and English dyslexics. *Top:* activation (in white) is shown in the left middle frontal gyrus (LMFG), left posterior middle temporal gyrus (LpMTG) and left occipito-temporal sulcus (LOTs) for the comparison of each of the good reader groups to each of the dyslexic groups. Statistical threshold = $P < 0.05$ uncorrected to compare all effects. *Bottom*: parameter estimates for semantic word matching relative to fixation are plotted for each of the regions showing reduced activation for dyslexics compared to normal readers (common to English and Chinese). LANG. = left angular gyrus. See Fig. 3 for details of plots.

Chinese versus English normal readers

The activation patterns for semantic word matching were remarkably similar for Chinese and English monolingual normal readers (Supplementary Fig. 2), as observed in studies of Chinese–English bilinguals (Chee *et al.*, 1999). Nevertheless, a direct comparison of activation for semantic word matching in Chinese and English monolingual readers also demonstrated differences that were consistent with studies of Chinese–English bilinguals (Tan *et al.*, 2001, 2003). Specifically, we found that semantic word matching activation was greater in Chinese than English readers in the LIFS on the boundary between the left middle and inferior frontal gyri with peak co-ordinates in Montreal Neurological Institute space at $x = -46$, $y = +6$, $z = +30$, a *Z*-score of 3.4 and 20 voxels at $P < 0.001$. The peak co-ordinates are in close proximity to those that Tan *et al*. (2001) first identified with Chinese reading ($x = -45$, $y = +13$, $z = +30$) and our effect was highly significant following small volume correction for multiple comparisons ($P < 0.02$ corrected) based on Tan *et al.*'s previous result. In contrast, English readers had greater activation than Chinese readers in the LpSTS. The peak co-ordinates ($x = -56$, $y = -38$, $z = +6$) for this effect were also within the area (from $x = -57$, $y = -42$, $z = +21$ down to $z = +6$) that Tan *et al*. (2003) reported when English monolinguals read English but not when Chinese–English bilinguals read English.

Chinese versus English dyslexic readers

Surprisingly, activation was not significantly different in Chinese versus English dyslexics in a whole brain analysis thresholded at $P < 0.001$ uncorrected, and when we lowered the statistical threshold to $P < 0.05$ uncorrected in the LIFS and LpSTS areas where we found activation differences in Chinese versus English normal readers. Further investigation revealed that both LIFS and LpSTS were activated in both groups of dyslexics, even though normal readers activated either LIFS (Chinese but not English) or LpSTS (English but not Chinese) (Tables 2 and 3, and Fig. 3). Thus, Chinese dyslexics activated the LpSTS like both groups of English readers, while English dyslexics activated the LIFS like both groups of Chinese readers.

Table 3 **Increased semantic word matching activation for dyslexics relative to normal readers, in regions differentially activated by Chinese versus English in normal readers**

Region	Chinese versus English						Dyslexic > Normal readers								Each group separately			
	Normal readers				Dyslexics	Interaction	Chinese only				English only				English		Chinese	
	x	*y*	*z*	Zsc.	Zsc.	Zsc.	*x*	*y*	*z*	Zsc.	*x*	*y*	*z*	Zsc.	Nor. Zsc.	Dys. Zsc.	Nor. Zsc.	Dys. Zsc.
Left LIFS	–46	+6	+30	3.4	ns	3.3				ns	–48	+6	+32	3.1	2.1	5.5	6.0	5.0
Left PSTS	–56	–38	+6	3.8	ns	2.9	–54	–38	+4	2.6				ns	3.2	3.0	ns	2.5

Dys. = dyslexics; Nor. = normal; *x y z* = co-ordinates in Montreal Neurological Institute space; Zsc. = *Z*-scores; ns = not significant ($Z < 1.64$; $P > 0.05$ uncorrected).

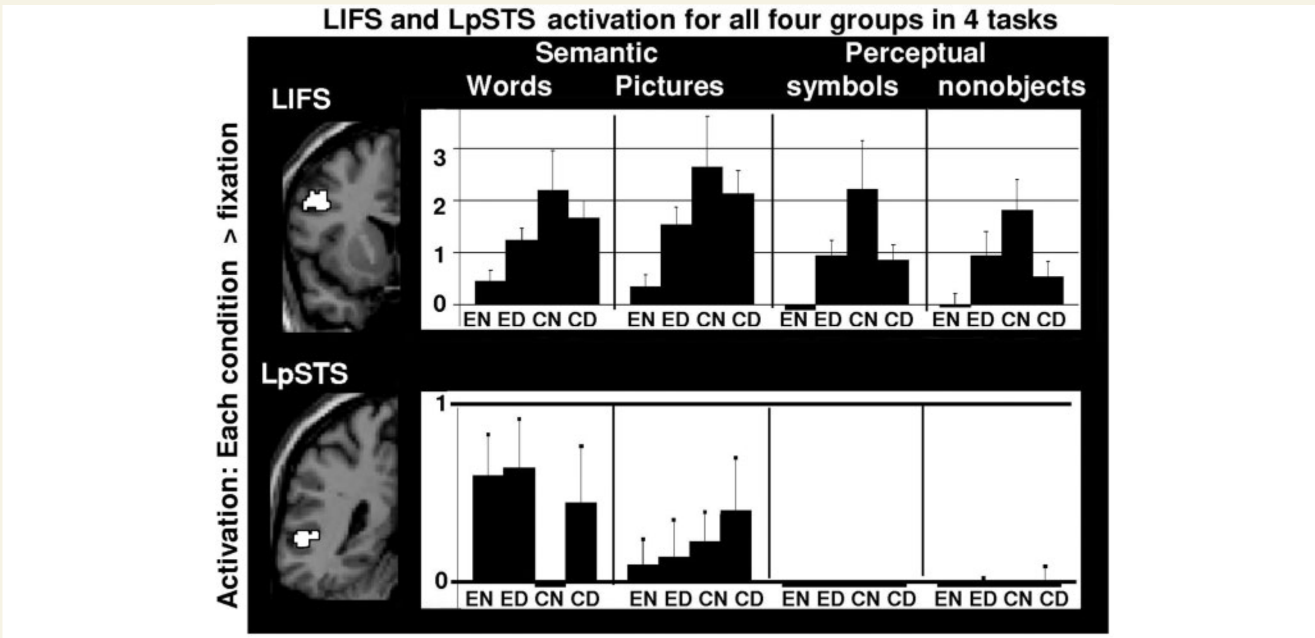

Figure 3 Activation for all four groups across all four tasks in LIFS and LpSTS. The location and parameter estimates of group differences in activation for semantic word matching relative to fixation are shown in LIFS (Chinese > English normal readers) and LpSTS (English > Chinese normal readers) on left hemisphere coronal slices at $y = +6$ mm and $y = -40$ mm, respectively for each of the four button press conditions separately in each of the four participant groups. EN = English normal readers; ED = English dyslexics; CN = Chinese normal readers; CD = Chinese dyslexics.

Dissociating the effect of dyslexia from differences in Chinese versus English reading

Critically, the area in the left middle frontal gyrus where activation was less for dyslexics than normal readers in both languages was 10 mm more anterior than the LIFS area where activation was higher for Chinese than English normal readers (Fig. 4). Likewise, the area in the left middle temporal gyrus ($x = -60$, $y = -56$, $z = 0$) where activation was less for dyslexics than normal readers was 10 mm more posterior than the LpSTS area ($x = -56$, $y = -38$, $z = +6$) where activation was higher for English than Chinese normal readers. The effect of dyslexia therefore dissociates from the effect of Chinese versus English reading.

The effects of other tasks and stimuli

The differences in Chinese and English normal reading reported above were derived from the semantic word matching task because this allowed us to ensure that group differences were not confounded by performance. Nevertheless, having identified the LpSTS and LIFS areas where activation differed in Chinese and English normal readers, we examined the effects of task and stimuli to illustrate the functions of each of these areas.

In LIFS, activation was observed for Chinese normal readers and both groups of dyslexics during perceptual matching as well as semantic matching (Fig. 3), but it was not observed for English normal readers in any task and it was not observed for naming and reading in any group. Statistical comparisons identified stronger activation ($P < 0.001$ uncorrected) for (i) Chinese normal readers than for English normal readers during perceptual as well as

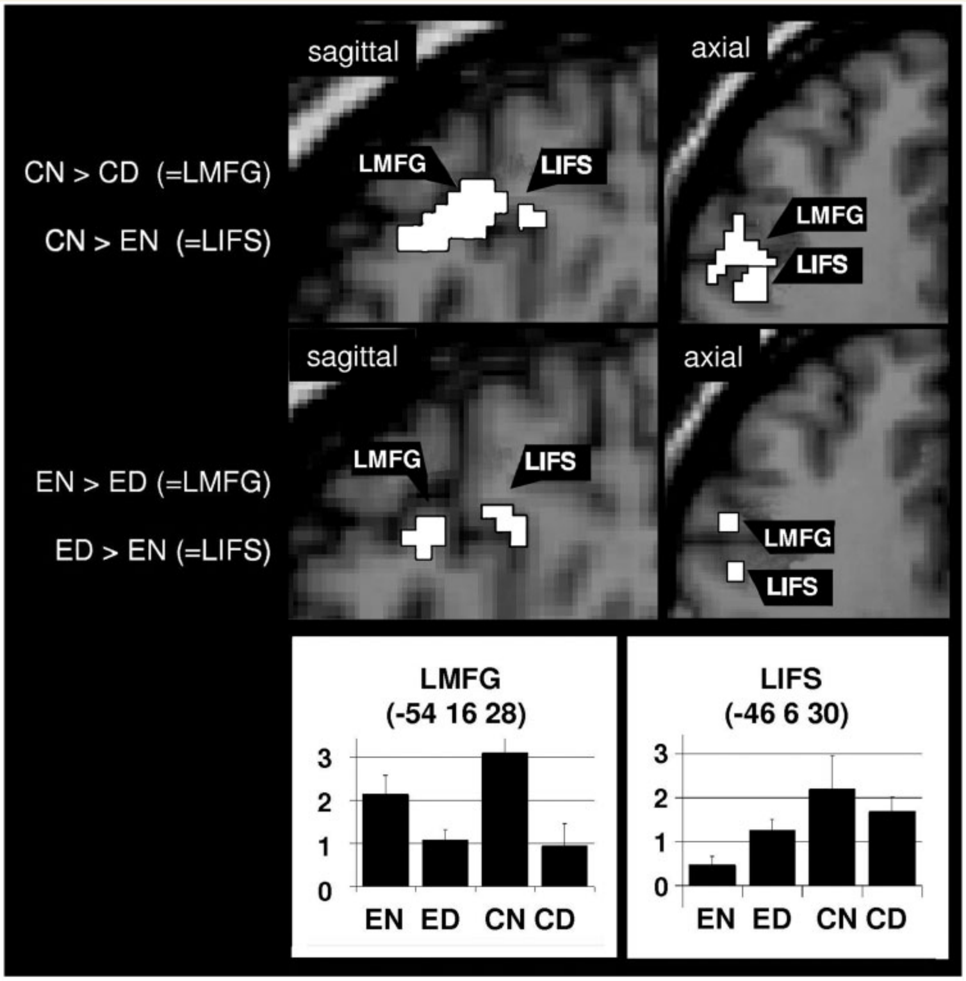

Figure 4 Dissociating left inferior frontal sulcus and left middle frontal gyrus activation. Even when the statistical threshold was lowered to $P < 0.05$ uncorrected, there was no overlap in left inferior frontal sulcus (LIFS) activation and left middle frontal gyrus (LMFG) activation on sagittal ($x = -50$ mm) and axial ($z = +30$ mm) slices for top: CN > CD (= LMFG) and CN > EN (= LIFS) and middle: EN > ED (= LMFG) and ED > EN. *Bottom*: parameter estimates (with standard error) for semantic word matching relative to fixation. EN = English normal readers; ED = English dyslexics; CN = Chinese normal readers; CD = Chinese dyslexics; see Fig. 3 for details of plots.

semantic matching (Fig. 3); and (ii) semantic decisions than for naming and reading in each group, except for the English normal readers who did not show LIFS activation in any condition. There was no significant difference ($P > 0.05$ uncorrected) in LIFS activation for semantic versus perceptual matching or word versus picture matching. Nor was there any corresponding relationship between LIFS activation and response times on any of the tasks. In short, LIFS was activated when Chinese normal readers and both groups of dyslexics were matching stimuli, irrespective of whether the task was perceptual or semantic and irrespective of whether the stimuli were words or pictures.

A very different pattern of effects was observed in LpSTS. Here, activation was related to the demands on phonological processing because it was observed for naming and reading in all four participants groups, but it was not activated during perceptual matching in any of the groups. In Chinese normal readers who did not activate LpSTS during semantic word matching, there was significantly greater activation ($P < 0.001$ uncorrected) for naming and reading versus during semantic word and picture matching. Thus LpSTS was activated by Chinese normal readers when the demands on phonological processing were increased.

Finally, we examined how task and stimuli affected activation in those regions with reduced activation in dyslexics compared to normal readers. All were more activated for semantic than perceptual matching in both normal readers and dyslexics and the difference between normal readers and dyslexics was more significant for written words than pictures (Table 4). Although both groups of dyslexics were slower than normal readers on the perceptual decisions (see above and Table 1), the effect of dyslexia on the perceptual tasks was not significant at the whole brain level or in our regions of interest.

Discussion

Our study reports the first direct and statistically based investigation into how the effect of dyslexia on brain activation is influenced by the Chinese and English writing systems. Critically, our

Table 4 Semantic more than perceptual matching in regions of interest from previous studies of dyslexia

Region	Region of interest				Pictures and words						Pictures only			Written words only		
	x	y	z		x	y	z	Nor. Zsc.	Dys. Zsc.	Nor. >Dys. Zsc	Nor. Zsc.	Dys. Zsc.	Nor. >Dys Zsc.	Nor. Zsc.	Dys. Zsc.	Nor. >Dys. Zsc.
Left LIFS	−51	+10	+38	S	−48	+16	+28	7.7	5.9	2.7	5.3	4.1	2.0	5.3	3.2	2.7
Left middle temporal	−60	−56	0	P	−54	−56	−4	4.1	3.1	2.6	3.7	3.3	ns	3.0	1.8	2.8
Left occipitotemporal	−52	−60	−14	P	−52	−54	−14	4.6	4.6	ns	5.2	4.9	ns	4.2	3.3	2.8
Left angular gyrus	−36	−66	+32	M	−36	−64	+36	3.3	2.7	3.8	3.1	3.9	ns	3.2	2.3	3.3

Regions of interest from previous studies of dyslexia referred to as S (Siok *et al.*, 2004), P (Paulesu *et al.*, 2001) and M (Meyler *et al.*, 2007).
Dys. = dyslexics; Nor. = normal; *x y z* = co-ordinates in Montreal Neurological Institute space; Zsc. = *Z*-scores; ns = not significant ($Z < 1.64$; $P > 0.05$ uncorrected).

participants were all monolingual and tested in their own countries using closely matched experimental stimuli, tasks and protocols. We focused on two questions: (i) does reading activation differ in Chinese and English dyslexics? and (ii) how does the effect of dyslexia in Chinese and English compare to differences in activation for Chinese versus English normal reading? Below we provide a discussion of the answers to each of our questions. We then consider the functional role of the areas that differ in Chinese and English normal reading.

Does reading activation differ in Chinese and English dyslexics?

Our findings show that Chinese and English dyslexics have remarkably similar brain activation, during semantic word matching, with reduced activation relative to normal readers in the left middle frontal cortex, left occipitotemporal cortex, left middle temporal cortex and the left angular gyrus. The consistent effect of dyslexia across Chinese and English cultures is a novel functional imaging conclusion. Nevertheless, the details of each result are in accordance with previous studies because reduced activation for dyslexics compared to normal readers has previously been reported (i) in left middle frontal cortex for phonological and lexical decisions in Chinese (Siok *et al.*, 2004, 2008) and for lexical decisions in French, which is an alphabetical language (Quaglino *et al.*, 2008); (ii) in left occipitotemporal cortex for lexical decisions in Chinese (Siok *et al.*, 2004, 2008) and for a range of silent reading tasks in alphabetic languages (Paulesu *et al.*, 2001; Shaywitz *et al.*, 2002; Meyler *et al.*, 2007); and (iii) in left temporoparietal regions (in middle temporal cortex and the angular gyrus) during semantic or sentence verification tasks in English (Shaywitz *et al.*, 1998, 2002; Meyler *et al.*, 2007). Our study is the first to show an effect of Chinese dyslexia in the left middle temporal cortex and left angular gyrus. We suggest that this is because we used a semantic matching task, whereas previous functional imaging studies of Chinese dyslexia reported the results of phonological and lexical decision tasks but not semantic decisions.

By investigating the effects of dyslexia (normal versus dyslexic) and Chinese versus English reading within the same study, we can also further our understanding of why the effect of dyslexia in the left middle frontal cortex is more noticeable in Chinese than English (Siok *et al.*, 2004, 2008). As shown in Table 2, we found that the *Z*-score for the effect of dyslexia in the left middle frontal cortex was higher in Chinese (3.7) than English (2.2) (Table 2). These differences arose at the level of the control groups, not at the level of the dyslexics because left middle frontal activation was higher for Chinese normal readers than English normal readers (Fig. 2). Critically, however, the direct comparison of Chinese and English normal readers located the peak activation difference in LIFS, not left middle frontal cortex. We are therefore suggesting that left middle frontal activation is higher for Chinese normal readers because (i) this area is in close proximity with LIFS; (ii) the Chinese normal readers are the only group to activate strongly both LIFS and left middle frontal cortex; and (iii) strong activation in both frontal regions, and the inherent spatial smoothing, might enhance activation in each of these frontal areas in the Chinese normal readers. Nevertheless, we acknowledge the possibility that left middle frontal activation may be significantly greater for Chinese than English normal readers in other paradigms, for example, when the task involves phonological rather than semantic decisions. Our point is that understanding differences in Chinese and English dyslexia necessitates the statistical comparison of Chinese and English dyslexics and normal readers in the same study.

Despite the novelty of our brain imaging conclusions, numerous behavioural studies have highlighted similarities in Chinese and English dyslexia by showing that dyslexia is characterized by impaired phonological processing in all the languages tested to date (Bradley and Bryant, 1983; Snowling, 2000; Ziegler and Goswami, 2005). In addition to difficulties with remembering and using phonological knowledge, both Chinese and English dyslexics have been reported to have difficulties with visual processing and working memory (Bradley and Bryant, 1983; Riddell *et al.*, 1990; Huang and Hanley, 1995; Siok and Fletcher, 2001; Eden *et al.*, 2003; Wilmer *et al.*, 2004; Ho *et al.*, 2006; Ram-Tsur *et al.*, 2008). We can therefore infer that a common pattern of reduced activation for Chinese and English dyslexics is likely to reflect the impact of weak phonological, verbal and/or visuospatial working memory processes on the neural mechanisms used to retrieve the semantics of written words. However, we are not able to distinguish whether low activation was the cause or consequence of reading difficulties in our Chinese or English dyslexics. Nor are we able to comment on whether or how the behavioural manifestation of dyslexia might differ in Chinese and English dyslexics, particularly since our samples were selected according to similar criteria (poor phonological and reading skills) and the in-scanner behaviour indicated that both groups of dyslexics were slower than the normal readers when making perceptual as well as semantic decisions. Future studies are therefore required to investigate how the interaction of writing system and dyslexia depends on task and individual differences in cognitive abilities and reading experience (Ramus *et al.*, 2003; Pernet *et al.*, 2009; Siok *et al.*, 2009).

How does the effect of dyslexia in Chinese and English compare to differences in Chinese versus English normal reading?

Consistent with previous studies, we found that LIFS activation was higher for Chinese than English normal readers and LpSTS activation was higher for English than Chinese normal readers. These differences in Chinese and English reading were not observed in the dyslexic groups. By investigating Chinese and English dyslexics and normal readers in the same study, we were able to show that LIFS activation was higher in English dyslexics than English normal readers and LpSTS activation was higher in Chinese dyslexics than Chinese normal readers (Table 3). Thus, both Chinese and English dyslexics activate both LIFS and LpSTS even though normal readers activate either LIFS (in Chinese) or LpSTS (in English).

The finding that both Chinese and English dyslexics activate LIFS and LpSTS demonstrates that activation in these regions reflects the cognitive ability of the participants as well as the processing demands of the orthography. Specifically, LIFS activation in English dyslexics suggests that activation in this area is not specific to Chinese reading. It may therefore be recruited to support word recognition in the context of weak links between orthography and phonology, regardless of whether these weak links are the result of the type of orthography (Chinese versus English) or reading ability (dyslexic versus normal). Likewise, LpSTS activation was not specific to English reading because it is also activated in Chinese dyslexics during semantic decisions and all Chinese participants during reading and naming. It may therefore be activated to support word recognition in the context of weak links between orthography and semantics, irrespective of whether these weak links are the result of the type of orthography (English versus Chinese) or reading ability (dyslexic versus normal).

The functional role of the areas that differ in Chinese and English normal reading

With respect to the functional role of LpSTS, the expectation from cognitive models of reading is that activation that is higher for English than Chinese will reflect phonemic decoding strategies (Tan *et al.*, 2005). However, our findings were not entirely consistent with this conclusion because we observed LpSTS activation for Chinese dyslexics performing semantic matching on Chinese words that have no phonemic cues. We also observed LpSTS activation when Chinese normal readers were naming pictures that have no phonemic cues. It is therefore more likely that LpSTS activation is involved in phonological processing in general rather than being specific to phonemic decoding (Price *et al.*, 2006). Higher LpSTS activation for English than Chinese normal readers may reflect the use of a phonological strategy to facilitate semantic access. Alternatively, there might be greater phonological processing in English because implicit phonology (that is incidental to the task) is available at the phonemic as well as syllabic and whole word levels. Likewise, higher LpSTS activation for Chinese dyslexics than Chinese normal readers during semantic word matching may reflect a phonological processing strategy that facilitates semantic access, or may reflect increased phonological processing (relative to Chinese normal readers) because of the additional time spent attending to the stimulus when semantic access is delayed.

With respect to the functional role of LIFS, the expectation from cognitive models is that reading Chinese will increase the reliance on visuospatial working memory in order to maintain the visual representation while perceptual, semantic or phonological information is retrieved (Li *et al.*, 2009). LIFS activation in our paradigm may therefore reflect visuospatial working memory. Indeed, the inclusion of a range of tasks and stimuli in our paradigm provided three novel observations that are consistent with an explanation of LIFS activation in terms of the demands on visuospatial working memory. First, we found that Chinese normal readers and both groups of dyslexics activate LIFS during perceptual as well as semantic tasks, irrespective of the stimuli tested (Fig. 3). Second, we found that LIFS activation was greater during semantic and perceptual tasks than naming and reading tasks. This is consistent with the involvement of visuospatial working memory function that holds semantic or perceptual representations in memory while a common theme is determined. Third, we found that English normal readers had low LIFS activation relative to all other groups during perceptual as well as semantic tasks, even when the task and stimuli were held constant (i.e. perceptual decisions on non-objects) (Fig. 3). The absence of LIFS activation in the English normal readers during either semantic or perceptual tasks (Fig. 3) suggests that activation in this region is strategy dependent. In this case, the strategy appears to have been used for semantic and perceptual decisions in both Chinese groups and English dyslexics, but not English normal readers.

Our observation that LIFS activation was higher in Chinese normal readers than English normal readers during perceptual tasks further suggests that learning to read impacts upon the neural processing of perceptual information. Although this observation may be specific to our experimental context that interleaved perceptual with semantic matching, it is consistent with reports by Tan and colleagues (2003, 2008), who found that perceptual processing was influenced by language learning.

Conclusions

Previous studies have suggested that the effect of developmental dyslexia on brain activation is different in Chinese and English. In contrast, behavioural experiments have identified common patterns of deficits in Chinese and English dyslexics indicative of culturally independent effects. Here, in a direct comparison of

Chinese and English monolingual reading, we show for the first time that reduced brain activation for Chinese and English dyslexics is remarkably similar during semantic word matching. Furthermore, these similarities contrast with the activation differences for Chinese and English normal readers that we localized to the LIFS and LpSTS, respectively. This pattern of similarities and differences strongly suggests a common neural basis for dyslexia regardless of the language spoken and its orthography.

By including dyslexics and normal readers in the same study, with exactly the same experimental tasks and protocols, we are also able to show for the first time that LIFS activation is not specific to normal Chinese reading and LpSTS activation is not specific to normal English reading. Instead, dyslexics from both cultures activated both LIFS and LpSTS, consistent with the use of culturally independent strategies when reading is less efficient. This illustrates that reading activation is determined by the interaction of cognitive abilities and learning environment.

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Supplementary material

Supplementary material is available at *Brain* online.

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