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Peer reviewed
Cerebral asymmetry in children when reading Chinese characters

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Abstract
This study examined cerebral asymmetry, especially in the hierarchical visual system, when reading Chinese characters. Twelve right-handed Chinese children (mean age = 11.6 years) were scanned while performing semantic and phonological tasks. Strong leftward asymmetry was found in the left inferior frontal cortex (BA44/45/47), the parietal lobule (BA40), and the cingulate cortex (BA24/32). In the visual system, we found significant left-hemispheric dominance in the fusiform cortex (BA19/37), but no asymmetry was found in the primary visual cortex (BA17/18). The differential results for the primary visual cortex versus high-order visual cortex (i.e., the fusiform cortex) are discussed in terms of the contribution of the logographic nature of Chinese characters to the asymmetry pattern in the hierarchical visual system.

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1. Introduction
The question of whether there are specific neural networks for different language systems has long intrigued researchers (e.g., Refs. [53,54,69]). Because of the dramatic differences between logographic Chinese and alphabetical languages such as English, researchers have suspected that, if there are language-specific neural networks, they would appear in a comparison between Chinese and English. One specific hypothesis concerns whether the processing of Chinese shows left-hemispheric dominance as found for alphabetic languages (e.g., Refs. [73,80]). Research evidence is clear regarding left-hemispheric dominance in the processing of written English words (e.g., Refs. [2,17,24,57,86]). However, the processing of other holistic, visuospatial objects such as geometric shapes and faces showed right-hemispheric dominance [31,38,70] (also see Refs. [34,78] for a direct comparison between words and faces). Because Chinese characters originated from pictographs and remain logographic (i.e., a number of strokes packed into a square as a single unit), a question was raised as to whether the processing of Chinese characters is similar to that of pictures or symbols (thus right-lateralized) or to that of English words (thus left-lateralized).

Various methods have been used to examine the cerebral asymmetry of Chinese character processing. In the beginning, the visual hemifield procedure was used and results were mixed. Some researchers found evidence for right-hemispheric dominance [11,80], whereas others found left-hemispheric dominance [1], and still others found bilaterality [18,46].
One possible reason for these inconsistent results is the lack of spatial specification of the hemifield method: That is, this method can only show overall hemispheric dominance, but not asymmetry in specific brain regions for specific aspects of a task. ERP and fMRI provide a complementary approach to this problem. Most fMRI studies have suggested a general pattern of left-dominated frontal activation in reading Chinese characters [7–10,25,40–42,73–76,87,88]. Nevertheless, for certain brain regions such as the occipital–temporal region, bilateral or even right-dominated activation has been reported. For example, Tan et al. [73] found significant activation in the right occipital cortex. Bilateral occipital and occipitotemporal activation for the processing of Chinese characters has also been confirmed by several fMRI studies (e.g., Refs. [10,25,40–42,55,56,88]) and a study using high-density ERPs and Low-Resolution Electromagnetic Tomography (LORETA) [49].

The possibility of rightward lateralization in the occipitotemporal region (or even just bilateral occipitotemporal activation) for Chinese character processing is of potential significance because of its clear contrast with the leftward lateralization in the processing of alphabetical writings (e.g., Refs. [33,35,58,60,66,89]). Such a difference is consistent with the view that the processing of Chinese characters involves more visual–spatial information than the processing of alphabetical writings.

Within the occipitotemporal region, however, it is not known whether the whole region or only parts of the region showed laterality for Chinese processing. This region is hierarchically structured for visual processing [47,61–63,81,83]. The primary visual cortex (BA 17 and 18) is responsible for most visuospatial tasks, whereas BA19/37 is associated with higher-order object processing (see Refs. [5,62,63], for a review). In terms of word processing, the lower-level visual cortex is involved in the analysis of visual properties of words (see Ref. [16], for a review), whereas the higher-level visual cortex is mainly in charge of whole-word recognition [13,14,59,77,78]. One aim of the current study is to investigate lateralization at the sub-region level within the occipitotemporal region to help refine our understanding of neural networks specific for Chinese processing.

Another limitation in the existing literature in this area concerns methods used to draw conclusions about cerebral asymmetry. With few exceptions (e.g., Ref. [73]), conclusions about lateralization of Chinese character reading were drawn merely based upon observations of significant activation in one hemisphere and a lack of significant activation in the other, without a rigorous statistical test of the left/right activation differences. These observational and qualitative approaches may also have contributed to the mixed results in the asymmetry pattern in the occipital–temporal region when processing Chinese characters. For example, whereas Tan et al. [73] found strong rightward lateralization in occipital cortex, Fu and his colleagues [25] found that extrastriate visual cortex activation was bilateral or left-lateralized for Chinese characters.

The current fMRI study used a voxel-based comparison of left and right hemispheres to identify precisely the locations of cerebral asymmetries in the processing of Chinese characters. Voxel-wise whole-brain asymmetry analysis was originally developed to examine anatomical asymmetry of human brain [32,64,84] and introduced into fMRI language studies of functional asymmetry by Liegeois et al. [48]. It compares the left and right hemispheres (voxel-by-voxel) by a direct subtraction between the left–right flipped functional map and the original one (see the Methods section for details of the procedure). This method has several advantages (e.g., better reliability and higher spatial resolution) over the traditional regions-of-interest (ROI) analysis [48].

Although the voxel-based analysis would provide information for the whole brain, our focus is on the specific parts within the occipitotemporal region based on previously published research results discussed above. Given the hierarchical structure of the visual system, we hypothesized that the rightward laterality or bilaterality of Chinese processing found in the previous studies is limited to the primary visual cortex (BA 17 and 18) and does not extend to higher-level visual cortex such as BA 19 and 37.

2. Methods

2.1. Participants

Twelve primary-school students (6 male and 6 female), ranging in age from 10 to 12 years (mean age = 11.6 years), were recruited for this experiment. They and their parents gave informed consent in accordance with the guidelines set by the Beijing 306 Hospital. All subjects were native Chinese (Mandarin) speakers, had average academic performance, and had no previous history of mental diseases or head injuries. Snyder and Harris’s [71] handedness inventory was used to determine the handedness of our subjects. We adapted nine items of the inventory that involved tasks that can be done by only one hand, including writing, drawing, throwing, holding chopsticks, hammering, brushing teeth, cutting with scissors, striking a match, and opening a door. A 5-point Likert-type scale was used, with “1” representing exclusive left-hand use and “5” representing exclusive right-hand use. The scores on the nine items were summed for each subject, with the lowest score (9) indicating exclusive left-hand use for all tasks, and the highest score (45) indicating exclusive right-hand use. All subjects had scores higher than 42.

2.2. Materials

One hundred and sixty Chinese characters with precise meanings were selected from the reading textbook used by the subjects to ensure their familiarity with the stimuli. Half of the characters were used for semantic tasks and the other
half for phonological tasks. During the semantic task, paired Chinese characters were presented and subjects were asked to judge whether the two characters were semantically related or not. For the phonological task, subjects were asked to judge whether the two characters rhymed with each other (see Fig. 1). These two tasks were similar to those in Tan et al. [75]. We used these two tasks to see whether cerebral asymmetry was robust across different reading tasks. Block design was used in this fMRI study: 30 s for the experimental block and 21 s for the control block. Each pair of characters was presented for 2500 ms, followed by a blank screen for 500 ms. Subjects indicated a positive response by pressing the key corresponding to the thumb of their right hand and a negative response by pressing the key corresponding to the thumb of the left hand. For the control condition, a fixation cross was presented in place of the pairs of characters. Subjects were asked to fixate their eyes on the cross silently and no response was required.

2.3. Apparatus and parameters

Brain scans were performed with a 2.0-T GE/Elscint Prestige whole-body MRI scanner (Elscint, Haifa, Israel) at the MRI Center of the Beijing 306 Hospital. Stimuli, programmed with an IBM-compatible computer, were presented in black color on white background and projected onto a translucent screen. Subjects viewed the stimuli through a mirror attached to the head coil. A single-shot T2*-weighted gradient-echo, EPI sequence was used for functional imaging scan with the following parameters: TR/TE/θ = 3000 ms/60 ms/90°, FOV = 375 × 210 mm, matrix = 128 × 72, and slice thickness = 6 mm. Twenty contiguous axial slices were acquired to cover the whole brain. The anatomical MRI was acquired using a T1-weighted, three-dimensional, gradient-echo pulse-sequence. The parameters for this sequence were: TR/TE/θ = 25 ms/6 ms/28°, FOV = 220 × 220 mm, matrix = 220 × 220, and slice thickness = 2 mm. This provided high-resolution (1 × 1 × 2 mm) anatomic images of the entire brain.

2.4. Data analysis

We used SPM99 (Wellcome Department of Cognitive Neurology, London, UK) for image preprocessing and subsequent statistical analysis. This software is implemented in Matlab (Mathworks, Sherborn, Mass., USA). The image preprocessing steps included EPI functional image realignment, anatomic–functional image co-registration, and normalization [22]. During normalization, we used a symmetric anatomical template created by averaging the original and the left–right flipped MNI templates [48]. All functional images were smoothed with a cubic Gaussian filter of 8 mm full width at half maximum. General linear model was used to estimate the condition effect for each individual subject [23]. Boxcar convolved with HRF was selected as the reference function.

Individual activation maps were parametrically estimated by the following contrasts: the semantic or the phonological task minus the fixation task. These images were then flipped along x axis (i.e., left–right flip). Both the original and flipped images were entered into a paired t-test model for group analysis. In order to restrict our left/right comparison only to voxels that were ‘activated’ during the task condition, we added an external mask that only included the significantly activated voxels according to the group-averaged results (threshold: \( P < 0.001 \), uncorrected). In addition, to present a strict test of whether the asymmetry pattern for Chinese language processing was consistent across the two reading tasks, we did a direct contrast between the asymmetry maps of the semantic and the phonological tasks. The threshold for testing significant asymmetry between left and right hemisphere was \( P < 0.001 \), uncorrected. Small volume correction (SVC) was made to the activation data in the visual system, because of our a priori hypothesis in this region [85]. The SVC procedure was conducted using a program developed by Matthew Brett [4], with volumes of interests anatomically defined.

3. Results

3.1. Overall pattern of activation

The overall pattern of activation, acquired by normalizing the EPI data to a symmetric template, was projected onto a glass brain map (see Fig. 2). Results were shown separately for the semantic and phonological tasks. As is apparent from Fig. 2, similar activation patterns for the two tasks were observed. Activated regions included the inferior frontal cortex, the parietal cortex, the temporal–occipital conjunctive area, the occipital cortex, and the cingulate cortex. Significant results \(( P < 0.001 \), uncorrected\) from both comparisons were used as an inclusive mask for the voxel-wise asymmetrical comparisons.

3.2. Voxel-wise asymmetrical comparisons

As shown in Fig. 3, voxel-by-voxel comparisons between the left and right hemispheres revealed significant leftward (i.e., left > right) asymmetry in most of the activated regions,
including the inferior frontal gyrus (BA44/45/47), the inferior parietal lobule (BA40), the fusiform gyrus (BA37), the inferior temporal gyrus (BA19), and the cingulate cortex (BA32). For these regions, results were very similar for the two tasks. However, for the phonological task only, significant leftward asymmetry was also found in the precentral cortex (BA6), the postcentral cortex (BA43), and the anterior cingulate cortex (BA24). The foci with significant left–right differences are summarized in Table 1.

Within the visual system, as we hypothesized, there was evidence of bilaterality for the primary visual cortex (BA 17 and 18), but leftward laterality for the higher-level visual system (BA 19 and 37). For the fusiform asymmetry, the SVC corrected $P < 0.05$ corresponds to a $Z$ value of 3.82 for the phonological task and 3.86 for the semantic task. This result further confirmed our conclusions. Finally, a direct comparison between the asymmetry pattern for the semantic task and the phonological task showed that no voxels in the

Fig. 2. “Glass Brain” views of the overall pattern of activation for the semantic task (left) and the phonological task (right) relative to control task (fixation) ($P < 0.001$, uncorrected). These contrasts were used to mask voxel-wise analysis of language asymmetry.

Fig. 3. Group-averaged results showing significant difference between the left and right hemispheres. Results are overlaid onto different slices from a single-subject template from the Montreal Neurological Institution. The number on each slice indicates the relative position to the anterior–posterior intercommissural line.
visual system survived the threshold of $P < 0.05$ (small volume correction).

4. Discussion

This study used a voxel-based asymmetry analysis to evaluate the functional asymmetry of Chinese character processing. Our results revealed strong leftward (i.e., left > right) asymmetry when subjects performed either the semantic or the phonological tasks. Consistent with previous studies, leftward asymmetry occurred in the inferior frontal gyrus (IFG: BA44/45/47), which is commonly activated when reading English words (e.g., Refs. [58,65], also see Ref. [19], for a review) and Chinese characters and words [7–10,25,40–42,73,74,75]. The consistent activation in the left IFG by semantic tasks in different languages appears to support the view that such an activation may have top-down modulation, rather than being driven by the lower-level features of different languages [52]. In addition to left IFG, we also found significant leftward lateralization in the fusiform cortex (an area commonly activated by visual words), in the cingulate cortex (an important area for attention, e.g., Ref. [6]), and in the parietal lobule whose relevance to language processing is not clear (e.g., Ref. [68]).

Consistent with another study on Chinese children [69], our results indicated that Chinese children as young as 10 years old showed significant cerebral lateralization in language processing. This finding adds to the growing literature showing early development of lateralization in language processing. Although different patterns of brain asymmetry were once suggested for language processing by children and by adults (e.g., Ref. [45]), recent studies have consistently shown leftward asymmetry in language processing for children before 7 years old [26–30], perhaps even for infants of 30 months [15]. Direct comparisons between children and adults also showed no significant age difference in asymmetry [30]. Regardless, we should caution against generalizing our findings from children who are still learning the language to adults who are proficient readers. Further studies are needed to examine both cerebral asymmetry and within-hemispheric differences between Chinese children and adults (for results on alphabetical languages, see Refs. [3,65,79]). It will also be important to understand gender and other individual differences [24,67,81] as well as potential associations between anatomical asymmetry and language lateralization [20,21,36,37,50] for Chinese.

In the context of overall leftward lateralization for language processing, we were particularly interested in the visual system. We identified a hemispherically asymmetric pattern of activation within the hierarchical visual system. To our knowledge, this experiment is the first systematic examination of this kind in the study of Chinese language. Direct comparisons of activations between the two hemispheres revealed significant leftward asymmetry in the higher-order visual cortex (i.e., the fusiform cortex), but not in the primary visual cortex (i.e., BA17/18).

The significant leftward fusiform asymmetry in Chinese character processing is consistent with the results of studies of other language systems, including English (e.g., Ref. [78]), French (e.g., Refs. [13,14]), and Japanese Kanji and Kana [39]. The peak of the asymmetry location in Talairach coordinate [72] (−39 −68 −12) closely matches the visual word form area (VWFA) (−42 −57 −15) [13,14]. Neuroimaging and lesion research has shown that this area plays an important role in the recognition of abstract visual word forms (see Refs. [12,51] for a review). For example, it is reproducibly activated by reading tasks, and it is not sensitive to the location, fonts, color, or the letter case [59]. In addition, patients with lesion in this area show a disorder in whole-word recognition (e.g., Ref. [44]).
Consistent with these findings, our result suggests that the functional asymmetry of the fusiform cortex may be based on the linguistic, not visual, attributes of the stimuli. The visual complexity of the Chinese characters seems to have little to do with the pattern of asymmetry (i.e., left dominance) in the fusiform cortex. Further studies are needed to directly test this conjecture by requesting non-Chinese-speaking subjects to respond to Chinese characters (which would have visual complexity but no linguistic meanings to these subjects) or Chinese-speaking subjects to respond to visually complex non-Chinese scripts (e.g., Egyptian hieroglyphs). We expect that in these cases there would be little or no leftward asymmetry in the fusiform cortex.

In contrast to the leftward asymmetry of the fusiform cortex, the middle and inferior occipital regions showed bilateral activation for Chinese character processing. This finding is consistent with previous studies with Chinese adults that found significant right occipital activation [49,73]. This bilateral pattern for Chinese is different from the existing results for alphabetic languages, which showed consistent leftward asymmetry in the occipital region. These studies of alphabetic languages used various techniques for data collection such as ERPs [33], MEG [89], and PET [35,58,60,66]. The unique activation pattern in the primary visual cortex for Chinese character processing may be related to Chinese characters’ special visual and spatial properties (i.e., logography). Consistent with this explanation, a recent fMRI study [69] indicated that, compared to normal controls, Chinese dyslexic children who manifested abnormal frontal activation in reading showed more extensive right inferior occipital activation. This result suggests that the right occipital region may help to identify the visual–spatial structure of Chinese characters.

Our results contribute to current debate on cultural constraints on the neural substrates of language processing [53,54,69]. Together with emerging evidence from other studies of Chinese language [69,73,74,75] and of Chinese–English comparisons [49], the present study supports the view that neural strategies for language processing are dependent on culture [69]. Our results also showed, however, that such cultural constraints may be limited to sub-regions of the brain. In our case, the visual feature of a writing system may have more impact on the primary visual cortex than on the high-order visual cortex.

It should be noted that the asymmetric pattern found in the occipitotemporal region for Chinese character processing may or may not be limited to Chinese native speakers. For example, one study of Korean subjects found that the reading of Korean Hanja characters (i.e., Chinese characters used by Koreans) elicited rightward fusiform activation, whereas the processing of Hangul characters (logographic Korean writings) elicited more activation in bilateral inferior parietal lobules than the processing of Hanja [43]. Japanese subjects, on the other hand, showed leftward asymmetry in the middle occipital region when processing Japanese Kanji (i.e., Chinese characters used by Japanese) [82]. These inconsistencies may have been due to a number of factors such as language fluency (e.g., Koreans rarely use Hanja), degree of visual control (e.g., scrambled Kanji vs. crosshair), and analytical methods (e.g., qualitative comparison vs. voxel-wise asymmetry analysis).

Finally, we discuss two methodological issues related to the voxel-wise asymmetry examination approach. First, researchers need to deal with the slight differences in the spatial location and size of regions in the two hemispheres, as suggested by previous anatomical and volumetric MRI studies (e.g., Refs [20,21,36]). In the present study, special precautions were taken to minimize the likelihood of false functional asymmetry due to the structural differences. In the preprocessing steps, we adopted symmetry template and the images were smoothed with an 8-mm cubic Gaussian filter, which should decrease the structural differences between the two hemispheres. In addition, paired t tests were used to take advantage of the fact that the within-subject differences were much smaller than those between subjects in spatial locations of a given structure. As a result, the spatial resolution of fMRI images is acceptable for left–right comparisons [48]. The second methodological issue concerns the possibility that our results might have been influenced by negative activations. In the present study, an external mask was added to include only significantly activated voxels in subtractive analysis.

To summarize, the contrastive asymmetry pattern in lower- and higher-order visual system while processing visually presented Chinese characters suggest that the visual features of a writing system may affect the primary visual cortex, whereas its linguistic attributes may determine the functional asymmetry in the higher-order visual cortex. Further studies are certainly needed to replicate our findings and to examine how the brain circuits are shaped by the design principle of a writing system.

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