Published in final edited form as:

Neuroimage. 2011 April 1; 55(3): 1346–1356. doi:10.1016/j.neuroimage.2010.12.062.

Left fusiform BOLD responses are inversely related to word-likeness in a one-back task

Xiaojuan Wang¹, Jianfeng Yang^{2,*}, Hua Shu¹, and Jason D. Zevin^{3,*}

¹State Key laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, China

²Institute of Psychology, Chinese Academy of Science, China

³Sackler Institute for Developmental Psychobiology, Weill Cornell Medical College, USA

Abstract

Although its precise functional contribution to reading remains unclear, there is broad consensus that activity in the left mid-fusiform gyrus is highly sensitive to written words and word-like stimuli. In the current study, we take advantage of a particularity of the Chinese writing system in order to manipulate word-likeness parametrically, from real characters, to pseudo-characters that vary in whether they contain phonological and semantic cues, to artificial stimuli with varying surface similarity to real characters. In a one-back task, BOLD activity in the left mid-fusiform was inversely related to word-likeness, such that the least activity was observed in response to real characters, and the greatest to artificial stimuli that violate the orthotactic constraints of the writing system. One possible explanation for this surprising result is that the short-term memory demands of the one-back task put more pressure on the visual system when other sources of information cannot be used to aid in detecting repeated stimuli. For real characters and, to a lesser extent for pseudo-characters, information about meaning and pronunciation can contribute to performance, whereas artificial stimuli are entirely dependent on visual information. Consistent with this view, functional connectivity analyses revealed a strong positive relationship between left mid-fusiform and other visual areas, whereas areas typically involved in phonological and semantic processing for text were negatively correlated with this region.

Left fusiform gyrus has been understood to play a role in reading since an association between damage to this region and "pure alexia" was described by Déjerine (1892). A preponderance of neuropsychological (e.g., Behrmann, Nelson, & Sekuler, 1998; Leff et al., 2001; Cohen et al., 2003) and neuroimaging (e.g., Polk & Farah, 1998; Polk et al., 2002; Hasson, Levy, Behrmann, Hendler, & Malach, 2002; Cohen et al., 2000, 2002) studies confirm that this region is somehow involved in reading. Nonetheless, the nature of its functional role remains controversial.

One popular proposal is that the left fusiform functions as a "visual word form area (VWFA)", whose role in reading is to extract the information needed to identify linguistically significant information from text independent of variability in script, font, size and retinal position (Polk et al., 2002; Dehaene et al., 2004). This view is related both to

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*Address for Correspondence: Jason D Zevin, Box 140, Sackler Institute for Developmental Psychobiology, Weill Cornell Medical College, New York, NY, USA 10021, jdz2001@med.cornell.edu, yangjf@psych.ac.cn.

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neuropsychologically-inspired models of reading (Fiebach, Friederici, Müller, & Cramon, 2002; Kronbichler et al., 2006), and homology with the function of the right "fusiform face area" (Hasson et al., 2002). The VWFA has also been described as having an emergent specialization for words as a result of perceptual expertise and configural processing (McCandliss, Cohen, & Dehaene, 2003; Schlaggar & McCandliss, 2007), or as "recycling" of visual functions that evolved to support other functions of high-level vision (Dehaene & Cohen, 2007).

Studies that contrast responses to words with a wide range of control stimuli including checkerboards (Cohen et al., 2000, 2002; Cohen & Dehaene, 2004), line drawings (Hasson et al., 2002; Nobre, Allison, & McCarthy, 1994), geometric symbols (Tarkiainen, Helenius, Hansen, Cornelissen, & Salmelin, 1999), and black-and-white pictures of faces and houses (Gaillard et al., 2006; Fiebach, Rissman, & D'Esposito, 2006) can be thought of as demonstrating that words and well-formed pseudo-words reliably elicit strong responses in the left fusiform – in the tradition of characterizing receptive fields in visual cortex. In this sense the notion of the left fusiform as VWFA is relatively uncontroversial.

An alternative approach to understanding the function of the left fusiform has been to consider the wide range of non-reading tasks in which activity is observed for this region (Price & Devlin, 2003), and attempt to characterize its role in terms of mappings among perceptual and conceptual processes related to reading (Mechelli, Sartori, Orlandi, & Price, 2006; Devlin, Jamison, Gonnerman, & Matthews, 2006). The critical distinction between this view and the description of left fusiform as VWFA is its focus on the affordances of stimuli with respect to different tasks, rather than the structural properties of relatively abstract visual codes. Whereas a highly structured pattern of specialization emerges during tasks in which the critical stimuli are essentially incidental to performance (Binder, Medler, Westbury, Liebenthal, & Buchanan, 2006; Glezer, Jiang, & Riesenhuber, 2009; Vinckier et al., 2007), differences between stimulus classes in left fusiform are less consistent in tasks that involve processing more akin to natural reading or at least require explicit processing of the critical stimuli (Bruno, Zumberge, Manis, Lu, & Goldman, 2008; Kronbichler et al., 2004, 2007; Vigneau, Jobard, Mazoyer, & Tzourio-Mazoyer, 2005).

One difficulty in deciding between these two accounts has been that it is extremely difficult, in alphabetic scripts, to manipulate orthographic structure without simultaneously changing the semantic and phonological affordances of the stimuli. Sublexical cues to meaning are weak and difficult to quantify, so that the presence of print-to-meaning mappings is naturally confounded with lexicality. Further, because alphabets are structured as transcriptions of spoken language, pronounceable pseudo-characters are necessarily more consistent with the statistical regularities of writing system than typical control stimuli such as unpronounceable consonant strings. The Chinese writing system provides an opportunity to unconfound these properties by permitting manipulations of word-likeness that are, to a much greater degree than is possible in alphabetic scripts, independent of semantic and phonological mappings. Here we explore the function of the left fusiform region by manipulating word-likeness for Chinese characters, pseudo-characters and artificial stimuli, and presenting them in a one-back task.

Method

Participants

Participants were 18 university students (14 female) from Beijing Normal University. All participants were native speakers of Mandarin Chinese with normal or corrected-to-normal vision, aged between 19 and 25, with no history of neurological disease or learning disability. They provided written informed consent and were paid an hourly stipend.

Materials

Chinese orthography permits parametric manipulations of word-likeness that are to a large extent orthogonal to mappings among print, sound and meaning. The closest equivalent to single letters in an alphabet is the radical. There are 560 of these (Chinese National Language Affairs Commission, 1997) and, unlike letters, they can be arranged into complex spatial configurations, rather than necessarily being linearly combined into sequences. Further, although they often convey probabilistic information about either the sound or meaning of the character in which they appear, many radicals lack a canonical pronunciation, or a clear meaning (see Kang, 1993; Li & Kang, 1993 and Yang, McCandliss, Shu, & Zevin, 2008, 2009, for more detailed discussion, with particular attention to how this might shape the reading system). Some combinations of radicals form "components" that appear either as characters on their own, or as sublexical units in larger characters. Like radicals, components vary with respect to whether they contain probabilistic information about meaning or sound, or are simply cohesive orthographic units. Thus, it is possible to construct well-formed "pseudo-characters" that vary with respect to whether they contain sublexical information about meaning or sound or either. With respect to investigating the selectivity of the left fusiform, this is a distinct advantage over alphabetic stimuli, for which orthographic well-formedness and pronunciation are naturally confounded.

The stimulus list in the current study is built around characters with a left/right organization, i.e., there are two radicals or components, organized horizontally. This is the most common arrangement of Chinese characters (Li & Kang, 1993), many of which are called "phonograms" because they combine probabilistic semantic information with probabilistic phonological information (Kang, 1993). Three types of real characters were used: phonograms (abbreviated PS, because they are Words with Phonological and Semantic information), characters with only semantics (OS) and characters with only orthographic structure (OO). Pseudo-characters were constructed by recombining semantic and phonological components into configurations that do not correspond to real words, these comprise pseudo-characters with phonological and semantic cues (PS), pseudo-characters with only semantic cues (OS) and pseudo-characters with only orthographic cues (OO). Finally, Artificial stimuli were designed to violate orthographic constraints: the reversed radicals (RR) condition was composed by reversing the position of components in the OO Pseudo-characters. The NN condition was composed by randomizing the individual strokes that made up the RR stimuli (see Figure 1 for examples of all stimulus classes).

The goal of these manipulations was to create a continuum of word-likeness from least word-like (RR) to most (Pseudo PS) for non-word stimuli. Each class of stimuli had 20 items and the stimuli were matched for the number of radicals, strokes and frequency of occurrence for each component across all characters, and in its modal position (left or right) according two Chinese corpora: *Tsinghua Balanced Corpus* (Sun, 2006) and *Modern Chinese Frequency Dictionary* (Language and Teaching Institute of Beijing Linguistics College, 1986).

Procedure

fMRI experiment—Participants lay comfortably in the scanner and viewed stimuli via rear projection during the one-back task. A stimulus was presented on each trial, and participants were instructed to press a button with their right index finger whenever the stimulus was repeated from the previous trial. Each stimulus was presented for 500 ms at the center of the screen followed by a two second response interval. Two fonts (Songti and Bold) were pseudorandomly intermixed; participants were instructed to ignore font in making "repeat" responses.

A blocked design was used in which six stimuli of the same type were presented in 15 second blocks, followed by 12.5 seconds of fixation (""). The number of repeated stimuli per block was varied from zero to two, so that nearly every stimulus would be potentially task-relevant. In each scanning run, nine fixation blocks and one stimulus block per condition (i.e., eight stimulus blocks) were presented. Eight scanning runs were conducted, requiring 320 stimuli. Because only 160 stimuli were employed, the experiment was designed in halves, with the same stimuli re-cycled in the second half. The task was completed in approximately one half hour.

Behavioral experiment—The sixteen participants were brought back one week after the fMRI experiment to participate in a lexical decision task outside the scanner. Participants sat a comfortable distance from the screen (about 60 cm) and were instructed to decide whether the stimulus presented was a real character or not, and press one of two buttons to indicate their response. On each trial, a fixation cross appeared for 450 ms, after which the screen was cleared for 200 ms and a single character was presented for up to 2000 ms (or until a response was made). Stimuli were the same used in the fMRI experiment, and were presented centrally, in white against a black background using 36pt Songti font. Stimulus presentation and response latency collection was controlled using the E-Prime 1.1 (Psychology Software Tools, Pittsburgh, PA).

Data analysis

MRI acquisition—Functional and Anatomical images were collected using 3T Siemens Magnetom TrioTim syngo MR system in the State Key Laboratory of Cognitive Neuroscience and Learning of Beijing Normal University in China. Functional images were collected using a gradient-recalled-echo echo-planar imaging sequence sensitive to the BOLD signal. Forty-one axial slices were collected with the following parameters: TR = 2500 ms, TE = 30 ms, flip angle = 90°, FOV = 20 cm, matrix = 64 × 64, 3mm thickness, yielding a voxel size of 3.125 × 3.125 × 3mm, interleaved slices with no gap. A total of 8 functional runs were collected (93 TRs in each run). Following the acquisition of functional data, high resolution T1-weighted anatomical reference images were obtained using a 3D magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence, TR = 2530 ms, TE = 3.45 ms, flip angle = 7°, FoV = 25.6 cm, matrix = 256 × 256 with 1 mm thick sagittal slices.

MRI Data Analysis—Functional data were analyzed using AFNI (Cox, 1996, program names appearing in parenthesis below are part of the AFNI suite). Cortical surface models were created with FreeSurfer (available at <http://surfer.nmr.mgh.harvard.edu/>), and functional data projected into anatomical space using SUMA (Saad, Reynolds, Argall, Japee, & Cox, 2004; Argall, Saad, & Beauchamp, 2006, AFNI and SUMA are available at <http://afni.nimh.nih.gov/afni>).

Preprocessing of functional data—After reconstructing 3D AFNI datasets from 2D images (to3d), the anatomical and functional datasets for each participant were co-registered using positioning information from the scanner. The first 3 volumes were discarded, and functional datasets preprocessed to correct slice timing (3dTshift) and head movements (3dvolreg), reduce extreme values (3dDespike) and detrend linear and quadratic drifts (3dDetrend) from the time series of each run. Percent signal change was also calculated for each run.

General linear models and contrasts—Preprocessed data for all 8 runs were analyzed in general linear model (3dDeconvolve) including seven regressors of no interest (six estimates of head movement from motion correction from 3dVolreg, and one regressor for

"repeat" trials, to remove response-related activity). The eight experimental regressors were hypothetical hemodynamic response functions (HRFs) constructed by convolving the block onsets and durations of each condition (Real PS, OS, OO; Pseudo PS, OS, OO; RR and NN) with a model HRF (waver).

The results of this initial GLM analysis were then used to create a series of contrasts. First, a task > rest contrast was created by combining all of the active conditions and testing these against zero. Next, three "super-conditions" were created: 1) Real characters, which combined the responses to PS, OS and OO, 2) Pseudo-characters, which combined the responses to PS, OS and OO, and 3) Artificial stimuli, which combined the responses to RR and NN. These super-conditions were then compared to one another in a set of direct contrasts: Real > Pseudo, Pseudo > Artificial and Real > Artificial.

Surface reconstruction and projection of functional data into surface space—

Surfaces were made from structural T1-weighted MRI images with Freesurfer: cortical meshes were extracted from the structural volumes, then inflated to a sphere and registered anatomically (Fischl et al., 1999). SUMA (Argall et al., 2005) was used to resample each mesh into a standard space, and to generate an average mesh that was then converted to a volume and talairach (Talairach & Tournoux, 1988) transformed (@auto_tlrc, to the N27 template) for visualization and reference purposes. Functional data were then mapped into surface space (3dVol2Surf). In this way, the volume datasets of time series and the results of contrasts from GLM analysis were placed on the cortical surface for each participant.

Group analysis—Group analyses were conducted for each contrast by comparing the mean coefficients from all participants to zero for each node in the standard surface (3dtttest). The resulting surface was mapped to an AFNI volume based on a mesh of averaged brain (3dSurf2Vol), resulting in maps with t statistics for each voxel for each condition and contrast. The volume datasets were then converted to Talairach space (@auto_tlrc, using the N27 template) at $2 \times 2 \times 2$ mm resolution. Activation maps and regions reported as active in tables were obtained by first thresholding individual voxels at $p < 0.005$ (uncorrected), and then applying a subsequent cluster-size threshold based on Monte Carlo simulations (AlphaSim), resulting in a corrected threshold of $p < 0.05$.

Overlap maps—In order to visualize the specificity (or lack of specificity) or activation across conditions, we generated overlap maps by combining the thresholded task > rest contrast for the three super-conditions: Real, Pseudo and Artificial characters. These are then visualized with additive color mixing, so that primary colors indicate regions active for only one condition, secondary colors indicate combinations of two conditions, and white for regions common to all three. The proportion of voxels of each type for each region is also reported.

Gradient maps—A gradient analysis was conducted according to methods reported in Vinckier et al. (2007). We divided the contrast image (against fixation) of each stimulus class by the contrast image of the NN condition (note that, in the Vinckier et al. study, the real word condition yielded the greatest activation, and thus gradients were expressed as a proportion of that condition). The resulting images are masked so that only voxels that pass threshold for the omnibus task > rest contrast are displayed.

A priori regions of interest (ROI)—To test for internal functional organization of the fusiform gyrus and adjacent sites, six nonoverlapping spherical ROIs (4 mm radius, 33 voxels) were defined from posterior to anterior sampling the left occipitotemporal cortex, taken directly from Vinckier et al. (2007). The mean β value of those ROIs were compared across all eight conditions.

Functional connectivity analysis—To test for functional connectivity, a simple correlation was computed based on the mean time series from a seed volume selected by joint consideration of anatomical and functional criteria: the seed volume comprised all voxels in left fusiform cortex (based on anatomical information from the FreeSurfer parcellation) that were active in a task > rest contrast (voxel-wise $p < 0.005$, cluster-wise corrected $p < 0.05$). Drift effects, head motion and repeat trials were removed from the original time series (3dSynthesize), and the resulting clean data used in all subsequent steps. The mean time series was extracted from the seed volume, and correlated with activity in every voxel in the data set. For the purpose of group analysis, the R^2 from the regression was converted to Fisher's Z with normal distribution. A group t-test was then conducted (3dttest), following general procedures for group analysis.

Results

Behavioral results

Lexical decision—We first consider "yes" responses for real characters, then turn to the "no" responses for non-word stimuli. Performance on real words was very accurate (90%) and quite rapid (673 ms). As shown in Figure 2, a significant effect of sublexical information was observed both for response latency ($F(2,30) = 3.03$, $p = 0.054$) and accuracy ($F(2,30) = 13.48$, $p < 0.01$). Paired t-tests (Bonferroni corrected) revealed stimuli containing both semantic and phonological cues (PS) were faster than stimuli with only semantic information (OS) ($t(15) = 2.62$, $p < 0.05$), and more accurate than OS ($t(15) = 5.44$, $p < 0.01$) and OO ($t(15) = 4.21$, $p < 0.01$). There was no difference between OS and OO for either latency ($t(15) = 1.47$, $p = 0.16$) or accuracy ($t(15) = 1.26$, $p = 0.23$). Thus, although there was some effect of sublexical information for the real word stimuli, the effect was not monotonically related to the amount of information: only an advantage of both phonological and semantic information over the other two conditions was reliably observed.

For "no" responses, a graded effect of word-likeness was observed both for response latency ($F(4,60) = 69.04$, $p < 0.01$) and accuracy ($F(4,60) = 42.17$, $p < 0.01$), such that responses to the artificial stimuli were faster ($t(15) = 10.60$, $p < 0.01$) and more accurate ($t(15) = 8.42$, $p < 0.01$) than responses to pseudo-characters constructed to be similar to real Chinese characters.

Among pseudo-characters, there was a monotonic effect of sublexical information for response latency ($F(2,30) = 31.60$, $p < 0.01$) and accuracy ($F(2,30) = 16.60$, $p < 0.01$), such that items containing both semantic and phonological cues were the most difficult to reject, and stimuli containing neither were the easiest. Response on PS condition was slower ($t(15) = 5.80$, $p < 0.01$) and less accurate ($t(15) = 3.88$, $p < 0.01$) than OS condition, while response on OO condition was faster ($t(15) = 2.24$, $p < 0.05$) and more accurate ($t(15) = 1.44$, $p = 0.09$, one-tail test), than OS condition.

Responses to the artificial stimuli were more accurate (99%) and faster (556 ms) than responses to words – a pattern that is rarely observed for "no" responses in a lexical decision task – likely reflecting the unusually high distinctiveness of these stimuli as unwordlike.

One-back task—The behavioral data from the one-back task revealed a graded effect of familiarity across all eight conditions, which was only marginally significant for response latency, $F_1(7, 119) = 1.84$, $MSE = 6916.02$, $p = 0.09$ by subjects, $F_2(7, 56) = 1.11$, $MSE = 2502.96$, $p = 0.37$ by items, and significant for accuracy, $F_1(7, 119) = 3.73$, $MSE = 0.03$, $p = 0.001$, $F_2(7, 56) = 2.08$, $MSE = 0.011$, $p = 0.061$. Real characters produced faster and more accurate responses than Pseudocharacters, which in turn were easier to detect as repetitions than the Artificial stimuli. When treated as three super-conditions in this way, the

effect of word-likeness was highly reliable for both response latency $F(2, 34) = 4.26$, $MSE = 9379.08$, $p < 0.05$, $F(2, 61) = 3.373$, $MSE = 7160.55$, $p < 0.05$ and accuracy $F(2, 34) = 11.13$, $MSE = 0.03$, $p < 0.01$, $F(2, 61) = 5.24$, $MSE = 0.03$, $p < 0.01$. Post Hoc t-test (Bonferroni corrected) revealed Artificial stimuli produced less accurate responses than Real ($p < 0.01$) and Pseudo ($p < 0.05$) characters, and slower response latencies than Pseudo ($p < 0.05$) but not Real characters. There was a marginal difference between the Real and Pseudocharacters for accuracy ($p = 0.06$), but not for latency. Thus, familiarity had a strong influence on the participants' ability to detect stimulus repetitions.

Task- and stimulus-driven activity throughout the reading network

An omnibus contrast of task > fixation (Table 1) reveals activity throughout much of the typical reading network observed cross-linguistically – including bilateral fusiform and inferior frontal gyri, and much of the superior parietal lobule, as well as the middle frontal gyrus, which appears to be specifically engaged by written forms with complex spatial arrangements (Tan et al., 2003; Siok, Perfetti, Jin, & Tan, 2004; Yoon, Chung, Kim, Song, & Park, 2006; Bolger, Perfetti, & Schneider, 2005). One further difference from the pattern typically observed in alphabetic writing systems is the lack of significant activation in left superior or middle temporal regions or perisylvian temporoparietal regions (Price, 2000; Schlaggar & McCandliss, 2007); this is a common feature of fMRI studies of Chinese reading (Tan, Laird, Li, & Fox, 2005; Y. Liu, Dunlap, Fiez, & Perfetti, 2007), and is often interpreted as evidence that spelling-to-meaning mappings are less critical in this writing system (McBride-Chang et al., 2005; Perfetti, Tan, & Siok, 2006).

When viewed side-by-side, patterns of activity associated with different stimulus classes are clearly quite similar (Figure 3A). The extent of this similarity is visualized in Figure 3B and quantified in Table 1. Thus, activity throughout reading related areas is robust to all three classes of stimulus, and there is relatively little stimulus selectivity as measured by conjunction analyses of this type.

When direct comparisons between stimulus classes are considered, a number of striking contrasts are observed (Figure 4). When the Real and Pseudo-character conditions are compared directly to the Artificial stimuli, greater activity is observed in superior temporal, angular, supramarginal and post-central gyri (all bilateral). These regions are often associated with mappings among spelling, sound and meaning (Booth et al., 2006; Lee et al., 2004). These contrasts must be interpreted cautiously in light of the fact that none of these regions were identified in any of the task > rest analyses (see Figure 3) – indeed, further analyses indicated that activity in these regions was negatively correlated with task regressors for all stimulus classes, but less so for more word-like stimuli (see Figure 5). The same contrasts are negative in a large portion of visual cortex including the fusiform, middle frontal gyrus, posterior portions of the superior parietal lobe (all bilateral), indicating greater activity in these regions to the Artificial stimuli than the other stimulus classes.

Control analyses for task difficulty effects—In order to rule out the possibility that differences between stimulus conditions were the result of differences in time-on-task between conditions, we conducted a control analysis on the residuals of the task > rest contrast. The effect of task difficulty was then modeled by convolving a hemodynamic response function with a predictor scaled to the response latency of each stimulus class. In this way, we attempted to isolate effects of difficulty or time-on-task in the oneback task itself, which is moderately correlated with word-likeness. No significant activations were observed in this analysis.

"Reversed" pattern of stimulus selectivity in left fusiform

Figure 6B shows the β value across all eight stimulus types for the task > rest ROI identified in left ventral occipito-temporal cortex. The pattern is just the opposite of what we would predict based on the evidence for "word-likeness" from the LD task data, if the fusiform were behaving as it does during experiments designed to identify its "best stimulus:" greater activity was consistently observed for less word-like stimuli.

When three "super-conditions" were considered (Figure 6A, left), there was a main effect of stimulus class on activity ($F(2,34) = 33.07, p < 0.01$), with greater activity for less word-like than more word-like stimuli in each pairing – Pseudo > Real ($t(17) = 5.00, p < 0.01$) and Artificial > Psuedo ($t(17) = 4.86, p < 0.01$). Impulse response functions expressed as percent signal change reveal that this difference between conditions is sustained throughout the duration of stimulus blocks (Figure 6A, Right).

A similar pattern emerged when smaller gradations in word-likeness were considered in an ANOVA within the Pseudo-characters, with a large main effect of sublexical information, $F(2,34) = 8.39, p < 0.01$. The stimulus class with the least information (orthographic only) elicited stronger responses than the stimuli that contained either semantic only ($t(17) = 3.59, p < 0.01$) or phonological and semantic ($t(17) = 3.22, p < 0.01$) information. The β value was weakest for stimuli with both phonological and semantic information, but this condition did not differ significantly from the semantic only stimuli, $t(17) = 1.17, p = 0.26$.

We also undertook analyses that conceptually replicate the procedures used by Vinckier et al. (2007) to relate different levels of linguistic structure to subregions of the left fusiform. Figure 7A shows gradient maps that express activity as a proportion of the activity in the Artificial condition (NN). In addition to the obvious difference that the maximal activity in the Vinckier et al. data was to real word stimuli, another striking difference is a lack of clear structure in the gradients as related to level of linguistic structure, despite graded differences in word-likeness across conditions.

Figure 7B shows the pattern of activity across all stimulus classes in the same discrete ROIs selected by Vinckier et al. (2007). In the ROIs closest to the typical location of VWFA in previous studies (2,3 and 4), and in one more anterior and superior site (5), a pattern was observed similar to what was found for the fusiform ROI identified in this study: responses were strongest to the least word-like stimuli. In contrast, the more peripheral regions (1 and 6) were not significantly activated by any of the stimulus categories in this study.

Functional connectivity of fusiform reveals a trade-off of visual processing against using sound and meaning in the one-back task

In order to explore the relationship between activity in the left fusiform and other regions in the reading network, we characterized functional connectivity by correlating the mean time series of the activation in a functionally defined portion of left fusiform gyrus with the time series of every other voxel in the data set. The results, shown in Figure 8, suggest a trade-off between visual and more abstract (semantic, phonological) processing related to holding stimuli in working memory from moment to moment. The strongest positive correlations with fusiform are in the visual system, bilaterally, and extend to include lower-level visual areas not thought to be specialized for word recognition. Other regions positively correlated with left fusiform include frontal regions potentially related to visually encoding the structure of the stimuli – middle frontal gyrus, as well as superior parietal regions implicated in spatial attention (Corbetta, Shulman, Miezin, & Petersen, 1995). Right precentral regions and bilateral insula were also positively correlated with fusiform, perhaps related to motor patterns for how characters are written. Further, strong negative correlations are observed throughout the extent of superior temporal and angular gyri, two regions strongly implicated

in phonological and semantic processing for text (Price, 2000; Booth et al., 2006; Frost et al., 2005).

Discussion

The most striking finding the current study was the "reversed" selectivity to word-likeness in the left fusiform. Word-likeness was manipulated in two ways, first in terms of how "well-structured" the stimuli are as orthographic units, and second via the inclusion of probabilistic sublexical cues to meaning and/or pronunciation. Overall, pseudo-characters were difficult to reject in a lexical decision task, whereas non-characters that violate the statistical regularities of the writing system were very easy to reject. Further, within pseudo-characters, the presence of sublexical cues to meaning and/or pronunciation was related to greater difficulty in the behavioral task, further validating the claim that these stimuli varied parametrically in their word-likeness. Based on the responses of the left fusiform in passive viewing studies, we had predicted that activity in this region would be positively correlated with word-likeness (Vinckier et al., 2007; Binder et al., 2006). The actual results were quite different. The left fusiform was most active for artificial stimuli that were easiest for readers to distinguish from real characters in the lexical decision task, less active for increasingly more word-like pseudo-characters, and least active for real characters. In terms of anatomical specialization within ventral temporal cortex, we found little evidence for the hierarchical organization observed by Vinckier et al. (2007) – the maximal response throughout the region was to artificial stimuli, and there was no clear gradient linking word-likeness to location along the fusiform. Control analyses demonstrated that this was not an artifact of the oneback task difficulty or time-on-task.

Here we consider two possible explanations for the "reversed" pattern of selectivity observed in the current results. First, we address the concern that, although some functional activation patterns in left fusiform are similar between alphabetic writing systems and Chinese, stimulus-driven responses might be slightly different between the two languages. Next, we consider the argument that, irrespective of the writing system, the role of the left fusiform is flexible and task-dependent. Because of its function as a high-level visual area on the ventral stream, and the short-term memory demands of the one-back task, its activity in the current study is related to the dependence on maintaining structured visual representations, which are most important for stimuli that contain no phonological or semantic information.

The left mid-fusiform in studies of Chinese reading

Although there are differences in the neuroanatomy of reading for Chinese relative to alphabetic orthographies, the role of left mid-fusiform appears to be quite similar. Direct comparisons of alphabetic and logographic scripts have demonstrated processing of both stimulus types in this area (Chee et al., 1999; Hu et al., 2010). Further, meta-analyses by Tan et al. (2005) and Bolger et al. (2005) indicate that left mid-fusiform is consistently activated across both alphabetic and logographic writing systems. Few of the studies surveyed in those analyses involved the sort of passive task or control stimuli most commonly used in studies focused on isolating visual word form processing, however. This was recently addressed by C. Liu et al. (2008), who used a size-judgment task with stimulus conditions similar to those used here, including pseudo-characters created by combining radicals in an orthographically legal way (but without any explicit manipulation of sublexical information about sound or meaning) and artificial characters created by rearranging the stroke position of real words. A direct contrast of their pseudo-characters with artificial stimuli was used to localize the VWFA, with results strikingly similar to those in the previous literature. They also found some evidence consistent with the posterior-to-anterior word-likeness gradient described by Vinckier et al. (2007): in contrasts with checkerboard stimuli, a more posterior

portion of the left fusiform was found to be more active for their artificial stimuli, whereas a more anterior portion was more active for words and pseudo-words.

Thus, under task conditions that bias bottom-up stimulus processing and have limited working memory demands, left fusiform responses to Chinese stimuli are quite similar to what has been observed previously for English. This suggests that the effects observed here are not idiosyncratic to differences between the Chinese and English writing systems, although it will be important in future research to demonstrate that the current stimulus set produces the expected results under task demands that more closely approximate studies that have found word selectivity in alphabetic writing systems.

Activity in left mid-fusiform is modulated by task demands

Although it is clearly activated by words and word-like stimuli in passive paradigms, there is a good deal of evidence that visual presentation of words is not a necessary condition for activation of the left mid-fusiform. A number of recent studies have explored the role of the putative VWFA in tasks that do not involve the visual presentation of words. Notably, this region is consistently observed in contrasts between auditory rhyme judgment and a variety of control tasks (Booth et al., 2006; Cone, Burman, Bitan, Bolger, & Booth, 2008; Yoncheva, Zevin, Maurer, & McCandliss, 2010). These results are consistent with behavioral findings demonstrating a role for orthographic similarity in rhyme judgments (even when stimuli are carefully designed to unconfound orthographic and phonological similarity, Seidenberg and Tanenhaus (1979)). That is, it is thought that activity in this region during rhyme judgment is a neural correlate of activating the written forms of words. There are also a number of studies in which activity in this region is observed during tasks that are more difficult to relate to visual word processing, however, such as object naming (see Price & Devlin, 2003, 2004, for review). Strikingly, McCrory, Mechelli, Frith, and Price (2005) provided evidence that not only was left fusiform active for picture and word naming, but reduced activity in this region was observed for both stimulus classes in dyslexics. Taken together, these studies indicate that while stimulus-driven response properties are an important part of the characterization of left fusiform, it is clear that activation in this region is modulated – and in some cases driven entirely – by task constraints.

In a small number of studies, null or reversed selectivity has been observed in left fusiform under particular task conditions. For example, Xue and Poldrack (2007) used a challenging same-different task with rapidly presented stimuli, and introduced visual noise to reduce performance differences between stimulus types. They found no difference between unfamiliar Korean words and English words in the middle fusiform, and in fact found that activity to Korean stimuli in this area decreased after visual word form training on those stimuli. Reinke, Fernandes, Schwindt, O'Craven, and Grady (2008) also showed greater activity to Hebrew than English in a one-back task with English speakers naïve to Hebrew orthography. Both studies suggest a complex relationship among task, stimulus structure and familiarity. In particular, they suggest that stimuli drawn from an unfamiliar orthography can serve as the "best stimulus" for left fusiform under task demands that emphasize visual processing. This is potentially consistent with the neuronal recycling hypothesis (Dehaene, 2005), in particular, the notion that writing systems take advantage of visual properties that are particularly felicitous for activating the putative visual word form area.

Left fusiform is active both when top-down task demands engage the reading system in the absence of visual stimuli and when task demands are biased toward visual processing of unfamiliar stimuli. Interestingly, when task demands most closely resemble those involved in reading, as in silent reading (Vigneau et al., 2005; Kronbichler et al., 2004), results are quite inconsistent – Vigneau et al. (2005) found no difference between words and

pseudowords, whereas Kronbichler et al. (2004) found a reversed pattern of selectivity, similar to what was found in the current study. In another study using a modified lexical decision task, Kronbichler et al. (2007) observed greater activity to pseudohomophones (e.g., the nonword "taksi") than real words ("taxi") in this region. In this case, the task demands may have also played an important role: participants were asked to determine not whether stimuli were real words, but whether they could be pronounced to rhyme with real words. This may have encouraged more intensive orthographic processing of the less familiar forms.

Reconsidering one-back as a "localizer" task—The current results also have consequences for the use of the one-back task as a "localizer" for visual word form area (e.g., Baker et al., 2007); it is, on its face, well-suited to this application because it requires (and provides a behavioral index of) attention to the stimuli, and has nominally similar task demands across a wide variety of stimulus classes. Further, use of one-back as a "bottom-up" localizer is well-supported by EEG studies that compare the N170 (an early, visual evoked response to print Bentin, Mouchetant-Rostaing, Giard, Echallier, & Pernier, 1999) across stimulus conditions similar to those used in the current study. Interestingly, those studies routinely show larger evoked responses to words and word-like stimuli than to symbols or unfamiliar scripts (Maurer, Brandeis, & McCandliss, 2005; Maurer, Brem, Bucher, & Brandeis, 2005; Maurer et al., 2006; Maurer, Zevin, & McCandliss, 2008). A number of these studies localize the left-lateralized N170 to print as arising from the left mid-fusiform (Tarkiainen et al., 1999; Rossion, Joyce, Cottrell, & Tarr, 2003; Maurer, Brem, et al., 2005). One possibility is that the responses observed here are later-evolving than the initial evoked responses measured early in the EEG to print. That is, it may be that the specificity of the response in this region evolves over time, with early stimulus-driven responses reflecting a selectivity for print, but later, endogenously generated responses reflecting more general visual processes and task demands.

There is abundant evidence for late-evolving responses in the EEG literature itself. For example, a one-back study using Japanese pseudohomophones (Maurer et al., 2008) found no effect of lexicality on the N170, but did find later, more sustained responses that distinguished these stimuli from both the real word and non-word stimuli. It may be that the time course of designs such as those employed in the current study, in which each stimulus is presented long enough to be processed fully and must be held in memory, favor metabolic responses driven by later, longer-lasting feedback processes over the rapidly evoked early responses observable as the N170 in electrophysiological measures. Interestingly, the presentation rate in the Vinckier et al. (2007) study was quite rapid (200ms/item), which may have contributed to their ability to observe fine-grained selectivity throughout ventral temporal cortex. Further studies combining EEG and fMRI will be necessary to disentangle the dynamics of reading system over time. Nonetheless, it is important to consider whether the observed specificity (or lack therein) of left fusiform responses is related not only to task constraints, but also to the timing with which it is evoked and measured.

Conclusions

The results reported here highlight the difficulty of predicting how a region will respond to task demands by its "best stimulus." If we draw the analogy to receptive fields further, this is not so unexpected: it is now clear that receptive fields in primary visual cortex are highly context-dependent (David, Vinje, & Gallant, 2004) and there is evidence for short-term task-dependent tuning of receptive fields in primary auditory cortex (Fritz, Elhilali, & Shamma, 2005). In this context, it is clear that the current results cannot be interpreted as refuting stimulus selectivity in the left fusiform. Rather, they suggest that the role of this region is flexible and task-dependent. Under task demands that emphasize visual working memory,

the pattern of selectivity that implicates this region as a visual word form area reverses, and it "hangs together" more with the visual system than with parts of the reading network that are engaged in other forms of processing (phonological and semantic). The results suggest that the canonical pattern of selectivity in this region is at least in part due to the very superficial level of processing required by tasks used to assess its function, and that its role during reading may be difficult to guess based on sole consideration of its "best stimulus" response properties.

Acknowledgments

The authors would like to thank Guoqing Xu and Guangzhen Jia's work on the data collection. This research was supported by Program for Changjiang Scholars and Innovative Research Team in University (IRT0710), NSF of China 30870758, NSF of Beijing 7092051(HS) and NIH R21-DC0008969 (JDZ)

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O: 𠂇 𠂇 𠂇 𠂇
S: 𠂇 𠂇 𠂇 𠂇
PS: 𠂇 𠂇 𠂇 𠂇

[illegible]

Examples of Chinese Components (A) and materials in current study (B). A) Components can contain only orthographic information (O), probabilistic information about semantics (S), or probabilistic information about phonology and semantics (PS). B) Combining two of three categories of components forms eight conditions varying in word-likeness: Real PS, OS, OO; Pseudo PS, OS, OO; RR and NN.

Figure 2.
Behavioral performance on a lexical decision task collected outside the scanner (Panel A),
and the one-back task performed during the imaging experiment (Panel B).

Figure 3. Different classes of stimuli (Real, Pseudo and Artificial) activated a very similar brain network as shown in (A) side-by-side comparisons of activation maps and (B) an overlap map.

Figure 4.
Direct contrasts among three super-conditions stimuli ($p < .05$, corrected)

Figure 5.

Beta weights for three regions (Angular Gyrus, AG; Superior/Middle Temporal Gyrus, STG/MTG; Supramarginal Gyrus, SMG) identified as "activated" in the Real > Artificial contrast depicted in Figure 4.

Figure 6.

A) Beta weights and impulse response functions (as percent signal change) for three super-conditions (Real words, Pseudocharacters, and Artificial stimuli) in left fusiform. B) Beta weights for all eight conditions in the same region, * = $p < .05$, corrected.)

Figure 7. Analyses of the topography of sensitivity in left ventral temporal cortex following Vinckier et al., (2007). A) Gradient maps representing the proportion of activation of the *least* wordlike stimuli. B) Beta weights for three super-conditions varying in wordlikeness (from greatest to least) across six ROIs from anterior to posterior ventral temporal cortex.

Figure 8.
Functional connectivity of left fusiform gyrus ($p < .05$, corrected).

Table 1

Brain regions observed in the Task > Rest contrast, and percentage overlap in conjunction analysis for each.

Regions	BA	Voxels	Coordinates				Percentage(%)						
			Z	x	y	z	RPA	RP	RA	PA	R	P	A
Left Hemisphere													
SPL	7	1591	6.10	-27	-65	46	73.4	0.1	1.0	21.1	0.0	0.2	4.3
FuG	37	1268	6.37	-39	-55	-8	78.7	2.7	2.8	9.0	2.1	0.8	2.8
PrG	6/9	1204	5.55	-43	3	32	77.4	4.7	2.2	8.5	1.0	1.9	3.4
SFG	6	1156	6.08	-5	7	50	67.4	12.5	0.9	13.6	1.6	2.0	1.9
IFG	45	460	5.48	-27	23	8	79.4	4.4	2.4	5.0	2.4	0.9	4.1
FuG	20	206	4.63	-39	-15	-24	59.7	12.1	2.9	3.4	1.0	13.1	6.8
Right Hemisphere													
FuG	37	1402	6.65	45	-53	-12	65.3	2.6	4.6	17.8	1.0	1.4	6.5
SPL	7	1274	6.70	25	-55	42	61.0	0.0	0.6	32.7	0.0	0.2	5.4
PrG	6/9	617	5.52	43	3	32	59.3	0.2	3.9	24.2	0.3	0.5	11.0
IFG	45	556	5.89	35	23	4	70.3	2.0	5.2	12.6	0.9	2.3	4.1
MFG	6	377	5.99	31	-5	50	66.8	2.9	3.5	20.2	0.3	1.3	4.5
Cg	24	91	5.89	5	1	28	0.0	0.0	0.0	79.1	0.0	2.2	16.5

Note: BA = Brodmann's Area; Volume is given in number of voxels ($2 \times 2 \times 2 \text{ mm}^3$); T = peak value of inferential test for Task than Fixation; Coordinates (x,y and z) for the most active voxel in each cluster are given with reference to the Talairach atlas. RPA = Real + Pseudo + Artificial; RP = Real + Pseudo; RA = Real + Artificial; PA = Pseudo + Artificial; SPL, Superior parietal gyrus; FuG, Fusiform gyrus; MFG, middle frontal gyrus; IFG, inferior frontal gyrus; PrG, Precentral Gyrus including part of MFG and IFG; SFG, superior frontal gyrus; Cg, Cingulate cortex.

Table 2

Brain regions highly correlated with left fusiform gyrus

Regions	BA	Voxels	Z	Coordinates		
				x	y	z
Positive Correlation						
Bilateral						
Superior Parietal Lobule, Precuneus, Fusiform Gyrus, Middle Occipital Gyrus						
Medial Frontal Gyrus	6	644	10.41	-3	11	46
Left Hemisphere						
Middle FusiformGyrus	6	759	7.66	-25	-9	44
Insula	45	240	7.83	-25	29	6
Medial Temporal Pole	38	61	5.62	-29	5	-30
Right Hemisphere						
Inferior Frontal Gyrus	9	334	8.35	45	3	30
Precentral Gyrus	6	303	7.65	31	-7	48
Insula	45	303	11.08	29	25	4
Negative Correlation						
Bilateral						
Medial Frontal Gyrus						
Precuneus, Posterior Cingulate		8908	-15.47	9	57	18
Left Hemisphere						
Middle Temporal Gyrus	21/22	1515	-9.59	-59	-21	-8
Angular Gyrus	39/40	1440	-14.88	-53	-59	32
Inferior Frontal Gyrus (Orbital)	45	596	-7.83	-35	57	0
Inferior Frontal Gyrus (Triangular)	44/45	69	-6.74	-49	21	20
Precentral Gyrus	4	89	-6.09	-47	-15	38
Precuneus	7	70	-5.46	-11	-53	60

Regions	BA	Voxels	Z	Coordinates		
				x	y	z
Right Hemisphere						
Middle Temporal Gyrus	21/22	1671	-11.28	63	-27	-4
Angular Gyrus	39/40	1115	-13.61	51	-57	34
Inferior Frontal Gyrus (Orbital)	45	766	-9.84	47	37	-2
Insula	13	206	-6.8	43	-11	12
Superior Parietal Lobule	7	196	-10.68	25	-45	60

Note: BA = Brodmann's Area; Volume is given in number of voxels ($2 \times 2 \times 2mm^3$); Z = peak value of correlation Z; Coordinates (x,y and z) for the most correlated voxel in each cluster are given with reference to the Talairach atlas.