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fMRI correlates of cortical specialization and generalization for letter processing

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The present study used functional magnetic resonance imaging to examine cortical specialization for letter processing. We assessed whether brain regions that were involved in letter processing exhibited domain-specific and/or mandatory responses, following Fodor's definition of properties of modular systems (Fodor, J.A., 1983. The Modularity of Mind. The MIT Press, Cambridge, MA.). Domain-specificity was operationalized as selective, or exclusive, activation for letters relative to object and visual noise processing and a baseline fixation task. Mandatory processing was operationalized as selective activation for letters during both a silent naming and a perceptual matching task. In addition to these operational definitions, other operational definitions of selectivity for letter processing discussed by [Pernet, C., Celsis, P., Demonet, J., 2005. Selective response to letter categorization within the left fusiform gyrus. NeuroImage 28, 738–744] were applied to the data. Although the left fusiform gyrus showed a specialized response to letters using the definition of selectivity put forth by [Pernet, C., Celsis, P., Demonet, J., 2005. Selective response to letter categorization within the left fusiform gyrus. NeuroImage 28, 738–744], this region did not exhibit specialization for letters according to our more conservative definition of selectivity. Instead, this region showed equivalent activation by letters and objects in both the naming and matching tasks. Hence, the left fusiform gyrus does not exhibit domain-specific or mandatory processing but may reflect a shared input system for both stimulus types. The left insula and some portions of the left inferior parietal lobule, however, did show a domain-specific response for letter naming but not for letter matching. These regions likely subserve some linguistically oriented cognitive process that is unique to letters, such as grapheme-to-phoneme translation or retrieval of phonological codes for letter names. Hence, cortical specialization for letters emerged in the naming task in some peri-sylvian language related cortices, but not in occipito-temporal cortex. Given that the domain-specific response for letters in left peri-sylvian regions was only present in the naming task, these regions do not process letters in a mandatory fashion, but are instead modulated by the linguistic nature of the task.

Introduction

Alphabetic systems are a relatively recent development from an evolutionary perspective, having first emerged around 1500 BC (Driver, 1976). Because cortical specializations for reading and other modern-day cognitive capacities have not had enough time to evolve (Tooby and Cosmides, 2000), the capacity for recognizing letter forms may have exploited neural circuitry that was already in place for recognizing object form (Joseph et al., 2003). Moreover, given that alphabetic systems emerged from pictographic systems (Driver, 1976) the same neural substrates that recognize objects (e.g., the fusiform gyrus) may extend to recognizing highly stylized symbols that now compose alphabetic systems. However, it is entirely possible that a brain region (or a cortical network) becomes specialized for letter processing due to experience with the domain (Polk and Farah, 1998; Polk et al., 2002).

The neuroimaging evidence to date seems to support a specialized letter processing region in the left fusiform gyrus or in left extrastriate cortex. This general region is consistently activated for single letters or non-pronounceable letter strings as compared with other categories (Cohen et al., 2002; Dehaene et al., 2002; Flowers et al., 2004; James et al., 2005; Jessen et al., 1999; Longcamp et al., 2003; Pernet et al., 2005; Polk and Farah, 1998; Polk et al., 2002; Price et al., 1996; Puce et al., 1996; Sergent et al., 1992; Tagamets et al., 2000). Cohen and colleagues (Cohen et al., 2002; Dehaene et al., 2002) have referred to a left fusiform region as the visual word form area (VWFA) based on the finding that alphabetic strings activate the region more strongly than do checkerboard patterns. They have demonstrated that activation in this region is not driven by low-level visual information nor is it retinotopically organized. In fact, this region does not appear to be sensitive to letter case, implying that it processes abstract letter form (but see Gauthier et al., 2000). In addition, the response in this region is modulated by task demands. As an example, Gros et al. (2001) showed that the left fusiform gyrus showed an adaptation response to an ambiguous stimulus (e.g., a shape that could be perceived as either a circle or the letter "O") only when it was primed by letters but not when primed by shapes. Hence, the

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left fusiform gyrus responded to an abstract representation of letter form that was driven by top-down information about the visual category rather than driven by low-level visual information in a bottom-up fashion. Importantly, this body of work has outlined factors that may modulate VWFA responses, but the question still remains as to whether VWFA processing is unique to letters or whether the processing in this region is shared with other visual categories.

Joseph et al. (2003) showed no letter-selective activation in the fusiform gyrus during passive viewing and silent naming of individual letters in an fMRI study. Instead, the left fusiform gyrus was equally activated by letter and object naming, as revealed by a type of conjunction analysis (Joseph et al., 2002; Nichols et al., 2005). Joseph et al. (2003) suggested that this region does indeed process abstract representations of form as suggested by others (Cohen et al., 2002; Dehaene et al., 2002; Gros et al., 2001; Pernet et al., 2005), but such representations are not unique to letters. Additional support for this conclusion is suggested by studies showing no differential activation when words are compared with objects (Jessen et al., 1999; Joseph et al., 2003; Price et al., 1996; Sergent et al., 1992; Tagamets et al., 2000).

The goal of the present study is to examine whether brain regions that appear to respond specifically to visual letters encapsulate processing that is unique to letters. The present analysis will use two properties of modularity proposed by Fodor (1983) as a starting point to shape an operational definition of cortical specialization. The property of domain specificity emerges when a particular type of input (e.g., human speech or face recognition) makes special processing demands that cannot be accommodated by existing input systems. Domain specific systems only represent a narrow range of properties from the environment and they require specialized computations to process that narrow range of input. The property of mandatory processing implies that a module will automatically process the information to which it is specifically tuned in a bottom-up or data driven fashion. In other words, the module will process the specific domain regardless of other task demands. These two properties are considered by some (Garfield, 1987) to be essential to the concept of modularity.

In the present study, we isolate a number of different response profiles using a conservative hypothesis testing approach (Joseph et al., 2002) and use these profiles as operational definitions for domain specificity and mandatory processing (Fig. 1). We suggest that *selective* responses (Fig. 1A) provide the strongest evidence for domain-specificity. Selective activation for letter processing is defined as a statistically significant response for letters relative to all other conditions (objects, visual noise and a baseline task of visual fixation), but no statistically significant response among objects, noise and baseline. Hence, selective activation reflects processing that is unique to letters and not shared by other visual categories manipulated in a given study. With a selective response, some of the comparisons are required to be statistically equivalent and others are required to be statistically non-equivalent. However, statistical equivalence of certain conditions must co-occur with statistical non-equivalence of another subset of conditions in the same voxel. Hence, a single test of no differences is not sufficient in the logical combination tests, but is only part of a larger prediction that includes positive results. Specifically, these individual comparisons are only valid in the context of a significant main effect or interaction, much like conducting post hoc comparisons.

A selective response can be contrasted with a *preferential* response, in which the experimental condition of interest yields a greater response than at least one other control condition and/or baseline in a given brain region. *Graded* responses (described in Appendix) are similar to preferential responses, but slightly more stringent. With both preferential and graded responses, the control condition(s) could yield a greater-than-baseline signal, which does not occur with selective responses (see Fig. 1b); consequently, the region subserves some type of processing that is shared by both conditions, but to varying degrees.

We also isolate a *conjoined* response for letters and objects in which letters and objects produce a statistically greater response than fixation and noise, but objects and letters are statistically equivalent (Fig. 1c). The statistical equivalence of two conditions implies that the region is equally recruited in both conditions and likely subserves some form of processing that is shared by both conditions (see Friston et al., 2005; Joseph et al., 2002; Nichols et al., 2005; Price and Friston, 1997 for discussions of conjunction analysis). Again, statistical equivalence is only valid in the context of a main effect of condition, as discussed above. A conjoined response provides evidence for cortical generalization rather than specialization.

The property of mandatory processing for letters has also been addressed previously. Pernet et al. (2005) and Pernet et al. (2004) describe a response in which a brain region responds to the preferred category in two different tasks (Fig. 1D), which we refer to as a *task-independent* response. In this example, letters produce a greater response than noise and baseline in both a naming (gray bars) and a matching task (white bars). A task-independent response embodies both domain-specificity and mandatory processing in that the response is specific to the domain of interest (preferential) and is automatic whenever the information is presented regardless of the task (mandatory). The present analysis will also modify the definition of task-independence to use selective rather than preferential responses as a more restrictive test of domain-specificity. This *selective* + *task-independent* response is shown in Fig. 1E.

Pernet et al. (2005) defined another response profile that isolates domain-specific responses that are not mandatory. Here, the preferred category induces a response in only one task (Fig. 1F). Pernet et al. (2005) termed this activation pattern as "selective," but to avoid confusion with Joseph et al.'s, (2002) use of the term, we adopt the term *task-dependent*. A task-dependent response does not guarantee that the region would be specialized for letter processing because the definition implies that other categories can activate the region greater than baseline. In addition, even if a letter-preferential response does not emerge in the matching task, it is possible that the matching task significantly activates the region above baseline in a non-preferential manner. Hence, those regions in which matching activation is significantly greater than baseline would need to be excluded before concluding that a region is involved in letter naming specifically. Fig. 1g illustrates a *selective* + *task-dependent* response, in which the response to letters in the naming task is selective and the matching task does not activate the region greater than the baseline condition.

The present study combines the data of Joseph et al. (2003) with a new dataset that uses the same stimuli (i.e., letters, objects, visual noise and a visual fixation baseline), but employs a perceptual matching task instead of passive viewing and silent naming. The analysis will apply the various definitions of cortical specialization (Figs. 1D–G) and generalization (Fig. 1C) to this

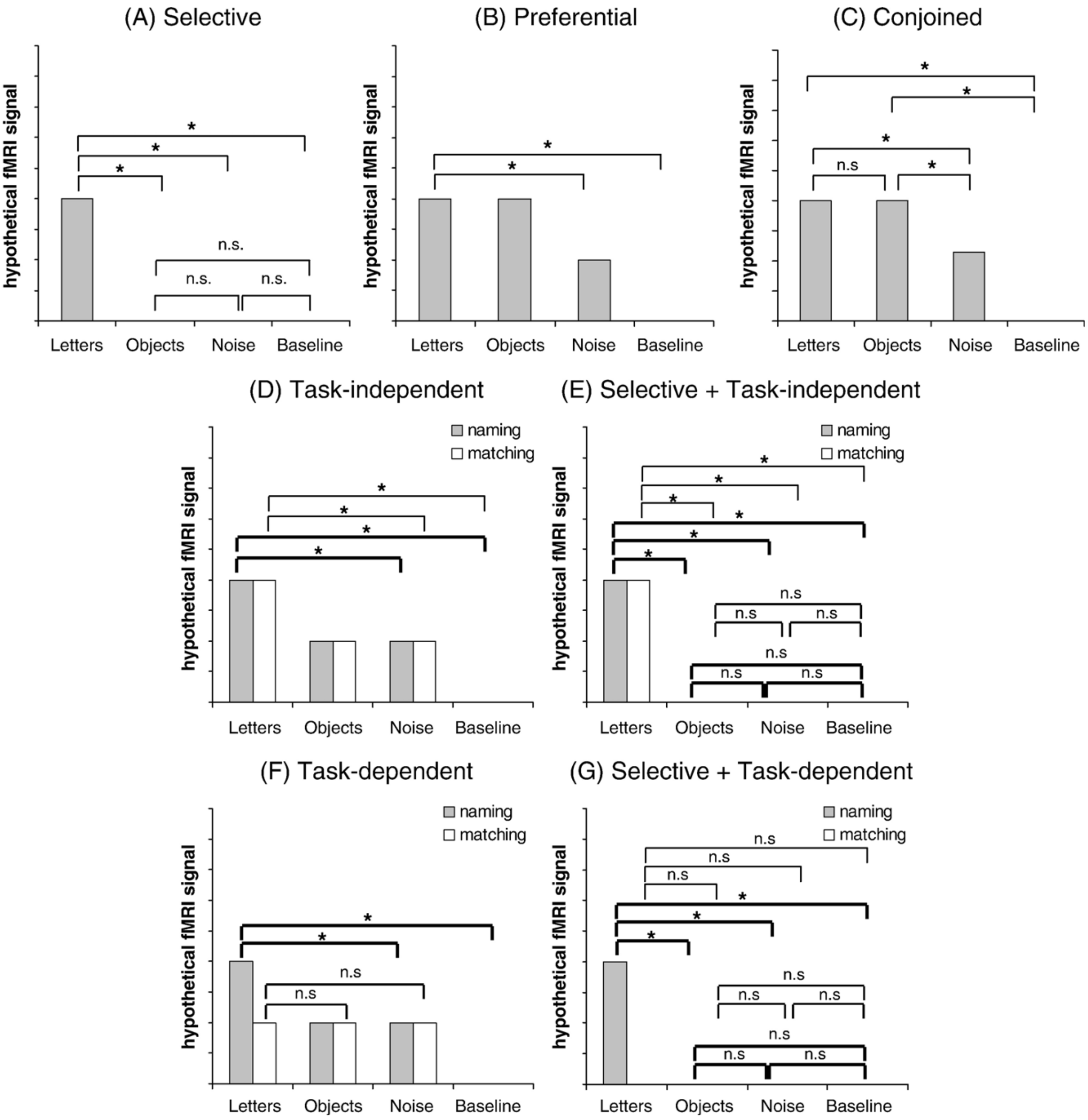

Fig. 1. Operational definitions in the present study. Hypothetical fMRI signal is plotted on the y axis for different categories or conditions (objects, letters, visual noise and baseline) and two different tasks—naming (grey bars), and matching (white bars). For each operational definition, the expected significant differences among categories are indicated with "*" and the expected non-significant differences are indicated with "n.s." Expected differences/non-differences for naming are indicated with darker bars. If a comparison is not labeled with "*" or "n.s" this implies that it is not tested as part of the definition. (A) Selective activation for letters requires an exclusive response by letters such that the letter condition produces more activation than all other conditions but the other conditions are not different from each other. (B) Preferential activation for letters occurs when letters produce a greater response than baseline and a greater response than at least one other category. (C) Conjoined activation refers to statistically significant responses by two or more categories relative to baseline. In this example, letters and objects produce more activation than baseline and visual noise, but equivalent activation relative to each other. (D) Task-independent responses require a preferential response to the category of interest across both naming and matching tasks. (E) Selective + task-independent responses require a selective response to the category of interest across both naming and matching tasks. (F) Task-dependent responses require a preferential response in just the naming task. (G) Selective + Task-dependent responses require a selective response in just the naming task, and no significant activation above baseline in the matching task.

combined data set. Although the focus is on the left fusiform gyrus throughout this analysis given its proposed role as a letter processing region, we also report on any other regions that satisfy the different definitions of cortical specialization or generalization.

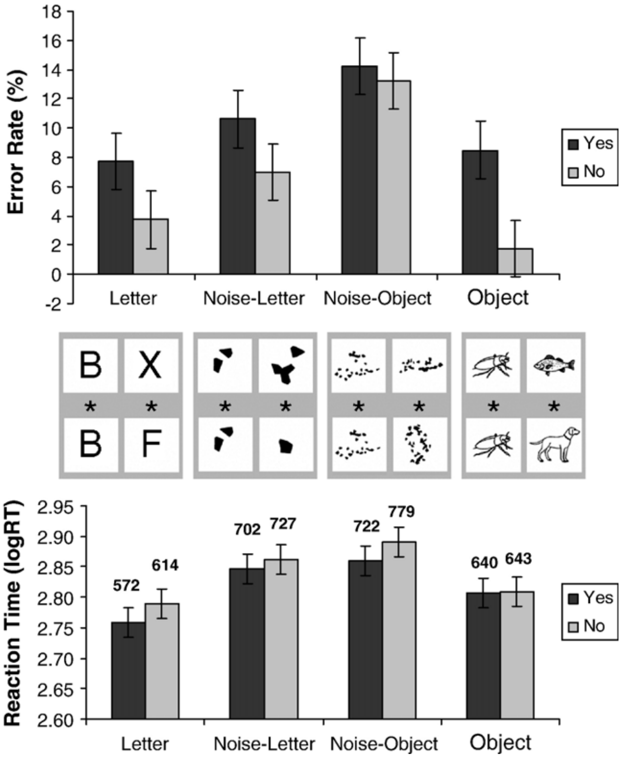

Fig. 2. Sample stimuli and behavioral results for the matching task. The center panel illustrates sample pairs for experimental conditions that correspond to bars in the graphs. (A) error rate, (B) log-transformed RT. Error bars reflect within-subjects confidence intervals (Loftus and Masson, 1994). Value labels indicate RT in ms before log transformation.

Materials and methods

Full details on the matching task are provided below, but details of the naming experiment (Joseph et al., 2003) are reiterated here when necessary.

Subjects

Eleven paid adult volunteers were scanned, but data from one female and one male were omitted due to excessive head motion. The remaining sample consisted of five males and four females (mean age of 27.6 years). All participants were right-handed with normal or corrected-to-normal vision and native English speakers. No participants had a history of medical, neurological, or psychiatric illness. Participants gave written consent, in accord with the guidelines of the University of Kentucky Institutional Review Board.

Stimuli

The 26 letter (L) stimuli were from the Latin alphabet. Each letter was displayed in upper case Arial font only for the matching task, but for the naming task, each letter was displayed in both upper and lower case. Object (O) stimuli were 26 line drawings of animals from previously published picture sets (Joseph, 1997; Snodgrass and Vanderwart, 1980) with mean name agreement of 77% (SD = 15.03%) and mean word frequency was 12.9 (SD = 21.1%) (Kucera and Francis, 1967). For the 26 visual noise (N) stimuli, 13 upper case letter stimuli and 13 object stimuli were pixelated using Photoshop (Adobe Systems Incorporated, San Jose, CA). See Fig. 2 for examples of stimuli.

In the naming task, all letter and object stimuli were pixilated to create all noise stimuli. The visual fixation condition (F) consisted of a single black asterisk. Stimuli were projected onto an 83 × 82 cm screen through an Epson LCD projector connected to a Dell computer running E-Prime software (Psychology Software Tools, Pittsburgh, PA). Each stimulus was presented singly in black centered on a white background (approximate visual angle of 6.7°), surrounded by a black background. For the matching task, stimuli were presented in pairs, one stimulus on top of the other, with an asterisk in the center. Stimulus pairs were centered on a gray background surrounded by a black background. Single stimuli were randomly paired together to create twenty-six match pairs and 26 non-match pairs for all three stimulus types.

fMRI design

In the matching task, a functional run consisted of nine task blocks (three each of letters, objects, and noise in pseudorandom order) interleaved with nine fixation blocks (12 s each). Within each task block for the matching experiment, 22 randomly ordered stimuli were presented for 400 ms each, followed by a fixation asterisk for 1600 ms. (In the naming experiment, 21 randomly ordered stimuli were presented for 200 ms each, followed by 1800 ms of fixation. A shorter duration was used when presenting single pictures in the naming experiment to reduce saccadic eye movements. However, a duration of 200 ms was not long enough to perform the matching task, based on pilot testing). For each functional run 33 match trials and 33 non-match trials were distributed throughout the three task blocks of each stimulus so that within an individual block a given match or non-match pair would not occur more than once. The three task blocks for each stimulus either had 9, 11, or 13 match pairs with 13, 11, or 9 non-match pairs, respectively.

Procedure

For the matching task, each subject was introduced to the experiment through a short training session that consisted of three task blocks (one for each type of stimulus) and three fixation blocks. A single task block was comprised of 6 stimulus pairs interleaved with fixation presented at the same rate as the experiment. During training, the subject was instructed to decide whether the two pictures on a given trial were the same or different. They were asked to make their decision as quickly and as accurately as possible by pressing the button under their index finger (“same”) or middle finger (“different”). A response was accepted either during stimulus presentation or the fixation period. For the naming task, participants were instructed to passively view five experimental stimuli from each of the three categories (letters, objects, noise) and brief fixation epochs during their training session.

Following the training session, the subjects were taken to the MRI for their functional scan. The stimuli were presented on a screen at the foot of the MRI scanner bed, and reflected through a mirror attached to the head coil at a specific angle so the subject could see both pictures. Each subject completed three functional runs (8.4 min per run in the matching experiment and 9.1 min per run in the naming experiment) followed by an anatomical scan that lasted approximately ten min. The experimental task for the matching experiment was identical to that during training. For the naming task, however, participants were instructed to passively view the stimuli in functional Runs 1 and 2. In Run 3, they were instructed to silently name the objects and letters and silently repeat the word "blob" each time a noise stimulus was present. Because most participants reported silently naming the stimuli in all three runs, we combined the three runs to increase statistical power.

fMRI data acquisition

A Siemens Vision 1.5 T magnet equipped with a quadrature head coil for whole-brain imaging and a T2*-weighted gradient echo sequence was used to collect functional brain images (40 ms echo time, 64 × 64 matrix, 228 mm field of view, 4-s repetition time, 44 3-mm slices with a 0.6 mm gap acquired in interleaved order, which provided whole brain coverage with 3.6-mm cubic voxels). Eleven whole-brain volumes were collected per task epoch, and three whole-brain volumes were collected per fixation epoch. Image acquisition parameters were similar for the naming task (Joseph et al., 2003).

fMRI data analysis

Preprocessing

MEDx software (Sensor Systems, Sterling, VA) was used for fMRI data analysis. After discarding the first three fixation volumes of each time series, the time series was phase shifted by 3 TRs to account for the hemodynamic lag. The remaining 123 volumes were realigned to the mean intensity image of the time series using a 6-parameter rigid body model and the 3D scanline chirp-Z algorithm with a least-squares cost function for resampling (Woods et al., 1992). Three-dimensional spatial filtering (Gaussian FWHM = 6 × 6 × 6 mm, kernel size = 9 × 9 pixels) and global intensity normalization (ratio-normalized to a mean of 1000 per volume) were applied to the motion-corrected time series. High-pass filtering using a period of 112 s was also applied to each time series. We visually inspected the amount of head movement before and after motion correction using the center-of-intensity as an estimate of head motion in three dimensions. Cases where the center of intensity was extremely variable across the functional run or not corrected to within 0.2 mm relative to the first time point were discarded. Two functional runs (one each from two of the nine subjects) were discarded based on this criterion. For spatial normalization, each subject's mean intensity image for a time series was warped to the ICBM152 template using AIR and the transformations were saved. Four condition mean images for the four experimental conditions (O, L, N, F) within a functional run were computed for each subject–one for the baseline condition and one each for objects, letters and noise–which reflected the fractional signal changes for that condition collapsed across all time points. The four condition means for each subject and each run were then spatially normalized using the saved transformations described above. This resampling yielded condition mean images with 2 × 2 × 2 mm resolution and anatomic axes. The stereotactic coordinates presented here are based on the ICBM152 template, but labels for regions were derived by converting these coordinates into Talairach space (Brett et al., 2002; Talairach and Tournoux, 1988; http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml). The spatially normalized condition mean images were then averaged across all of the usable runs for a subject, yielding four condition mean images per subject. Using paired t tests (converted into z scores) with subjects as a random effect, twelve group statistical maps that reflected the 12 unique pair-wise contrasts (O > F, O > N, O > L, L > F, L > N, L > O, N > F, N > O, N > L, F > N, F > O, F > L) were computed. The logical combination approach (Joseph et al., 2002) was then applied to these contrasts to isolate seven different response profiles: letter-selective, letter-graded, letter-preferential, OLN-conjoined, ON-conjoined, OL-conjoined and LN-conjoined. Additional details of the logical combination approach are outlined in Appendix. The logical combination approach yielded 81 clusters in the naming task and 23 clusters in the matching task, which served as regions-of-interest (ROIs) submitted to additional analyses described below.

Regions-of-interest analysis

The logical combination approach operates at the level of z maps by combining z maps using logical operators. However, the logical combination approach is not an inferential statistical technique; therefore, additional random effects analyses were performed within each of the clusters isolated above. The fractional signal change value within each cluster was calculated for each

Table 1
Task-dependent regions (bolded t values are significant)

Anatomical	Profile	Size^{a}	x	y	z	F value	Naming task t values					
Region (BA)						Task × Category	L > F	N > F	O > F	L > N	L > O	O > N
L FG (37)	OL-conjoined	15	−40	−44	−17	4.8^{b}	**6.6**^{c}	**4.9**^{c}	**5.2**^{c}	**5.0**^{c}	0.25	**4.8**^{c}
L FG (37)	OL-conjoined	5	−43	−65	−13	3.9^{b}	**4.6**^{c}	**3.5**^{c}	**4.7**^{c}	**5.1**^{c}	1.4	**3.2**^{d}
L SPL (7)	Letter-selective	9	−38	−50	+48	2.7^{b}	**5.2**^{c}	1.7	2.2	**3.9**^{c}	**3.3**^{c}	0.10
L SMG (40)	Letter-selective	25	−39	−38	+37	9.3^{b}	**6.8**^{c}	2.0	0.70	**6.2**^{c}	**5.3**^{c}	−0.90
L IPL (40)	Letter-selective	80	−52	−35	+43	11.0^{b}	**7.2**^{c}	2.0	1.8	**8.2**^{c}	**6.3**^{c}	−0.60
L Insula	Letter-selective	12	−37	+8	−5	7.4^{b}	**4.7**^{c}	2.0	1.7	**4.4**^{c}	**5.1**^{c}	0.70
L IFG (6/9)	OL-conjoined	19	−47	+5	+27	11.6^{b}	**4.6**^{c}	**3.3**^{c}	**4.9**^{c}	**4.0**^{c}	−0.29	**4.7**^{c}

Note—BA, Brodmann's Area; x, medial–lateral coordinate; y, anterior–posterior coordinate; z, inferior–superior coordinate; L, left; FG, fusiform gyrus; IPL, inferior parietal lobule; SPL, superior parietal lobule; SMG, Supramarginal gyrus; IFG, inferior frontal gyrus.

[a] Cluster size is expressed in voxels after transformation into standardized space in which each voxel is 2 mm^3.

[b] $P < 0.008$.

[c] $P < 0.01$.

[d] $P < 0.05$.

Table 2
Selective +Task-Dependent regions for letters (bolded t values are significant)

Anatomical	Size[a]	x	y	z	F value task t values	Naming task t values						Matching		
Region (BA)					Task × Cat	L > F	N > F	O > F	L > N	L > O	O > N	L > F	N > F	O > F
L SPL (7)	9	−38	−50	+48	2.7[b]	**5.2**[c]	1.7	2.2	**3.9**[c]	**3.3**[c]	0.10	**2.4**[b]	**2.5**[b]	**2.4**[b]
L SMG (40)	25	−39	−38	+37	9.3[b]	**6.8**[c]	2.0	0.70	**6.2**[c]	**5.3**[c]	−0.90	1.9	1.9	2.0
L IPL (40)	80	−52	−35	+43	11.0[b]	**7.2**[c]	2.0	1.8	**8.2**[c]	**6.3**[c]	−0.60	**2.9**[b]	**2.8**[b]	**2.4**[b]
L Insula	12	−37	+8	−5	7.4[b]	**4.7**[c]	2.0	1.7	**4.4**[c]	**5.1**[c]	0.70	0.90	0.90	0.0

Note. BA, Brodmann's Area; x, medial–lateral coordinate; y, anterior–posterior coordinate; z, inferior–superior coordinate; T, Task; Cat, Category; L, left; IPL, Inferior parietal lobule; SPL, Superior parietal lobule; SMG, Supramarginal gyrus.

[a] Cluster size is expressed in voxels after transformation into standardized space in which each voxel is 2 mm^3.

[b] $P < 0.008$.

[c] $P < 0.05$.

subject and each of the experimental conditions (O, L, N, F) and submitted to a scalar, one-way, repeated measures ANOVA with experimental condition as the independent variable and fractional signal change as the dependent variable. Post hoc t tests with Bonferroni correction were conducted for each cluster to determine whether the pair-wise differences among experimental conditions were significant or not significant, as required by each of the five profile types (see Appendix). For example, the profile for letter-selective activation requires that the letter condition produce a statistically greater response than the object, noise and fixation conditions, and that the pair-wise comparisons among the object, noise and fixation conditions are not significant. This requires six post hoc comparisons, which yields an adjusted alpha-level of 0.0083. For OL-conjoined activation, five post hoc comparisons were required, yielding an alpha-level of 0.01. Only those clusters that showed a significant main effect, as well as the predicted pattern of pair-wise differences (or non-differences) outlined in Appendix are reported and discussed.

A final set of analyses was conducted to determine, within each ROI, whether category (object, letter, noise, fixation) or task (matching, naming) effects were more prominent or whether the two factors interacted. Testing for an interaction is critical for defining task-independent, selective + task-independent, task-dependent and selective + task-dependent responses. The category variable was manipulated within-subjects, but the task variable was between-subjects (9 subjects performed the matching task and 11 subjects performed the naming task). To control for potential differences in the two subject groups in terms of overall levels of activation, we applied the ROIs isolated in the matching task to both sets of subjects, and applied the ROIs isolated in the naming task to both sets of subjects. The data were then submitted to 3 (category) × 2 (task) repeated-measures ANOVAs with fractional signal change value as the dependent variable. In these random-effects analyses, both between- and within-subject variability are taken into account, and the main effects of category and task (as well as the interaction) are assessed relative to the pooled variance of both subject groups. The results of these ANOVAs are provided in Tables 1 and 2.

Results

Behavioral results

The naming task involved passive viewing and silent naming of pictures so no overt responses were recorded and analyzed. For the matching task, both reaction time (RT) on correct trials and errors were analyzed. To meet the assumptions of normality for the multivariate approach to repeated-measures analysis of variance (ANOVA; O'Brien and Kaiser, 1985) log transformed RTs were used to normalize the RT distribution. In addition, to address the issue of potential violations of homogeneity of variance (in the analysis of behavioral data and in the regions-of-interest analyses below), we used the guidelines outlined by Hertzog and Rovine (1985) to determine whether sphericity assumptions were violated (i.e., when Mauchly's tests of sphericity revealed that the Greenhouse–Geisser epsilon was less than 0.75). We report results from the multivariate tests when sphericity assumptions were violated; however, we report the univariate results when sphericity holds. During matching, subjects responded more slowly and made more errors when presented with noise stimuli (Fig. 2). These trends were confirmed by a main effect of category for both errors, $F(3, 5) = 14.6$, $P < 0.007$, and RT, $F(3, 5) = 97.2$, $P < 0.001$. Post hoc paired comparisons (using a corrected $P < 0.0083$) revealed that the noise conditions were more difficult than either the object or letter conditions, and the object condition was more difficult than the letter condition for RT. In terms of errors, however, the noise conditions were more difficult than letters, but no other differences were significant. Participants responded to "same" pairs significantly faster than to "different" pairs, $F(1, 7) = 7.4$, $P < 0.03$, but did not produce more errors, $F(1, 7) = 0.37$, $P = 0.56$.[1]

fMRI results

Of the numerous brain regions that were activated in both the naming and matching tasks, we first present those regions that passed the tests for task-independent and task-dependent processing, as defined in Figs. 1d and f, respectively. Task-independent regions will show a preferential/graded response in both naming and matching tasks, whereas task-dependent regions will show a preferential/graded response in only one task. We then incorporate the more conservative criterion for selectivity (rather than preferential/graded responses) into the definition for task-independent and task-dependent responses to

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[1] We do not analyze brain responses separately for the two different noise conditions, nor do we separate out effects of "same" v. "different" response because these conditions were not separable with the present fMRI block design.

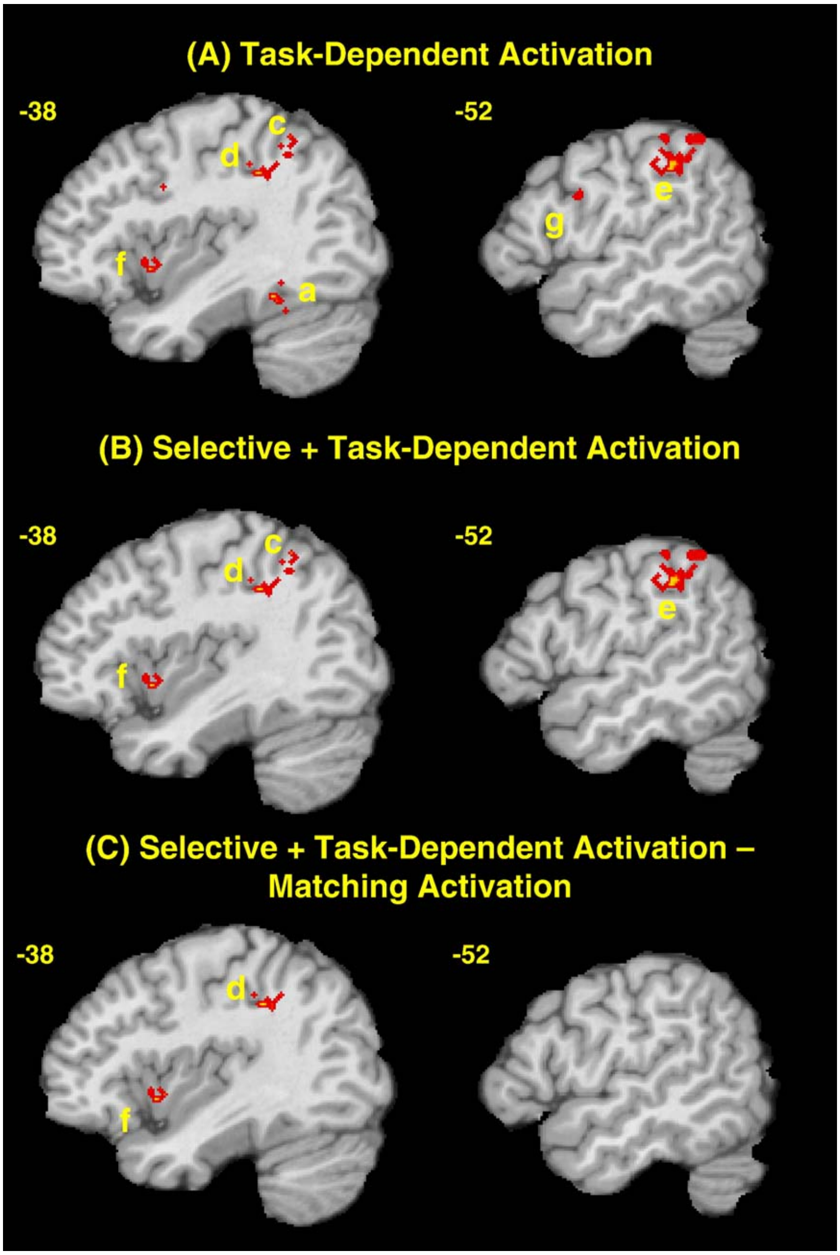
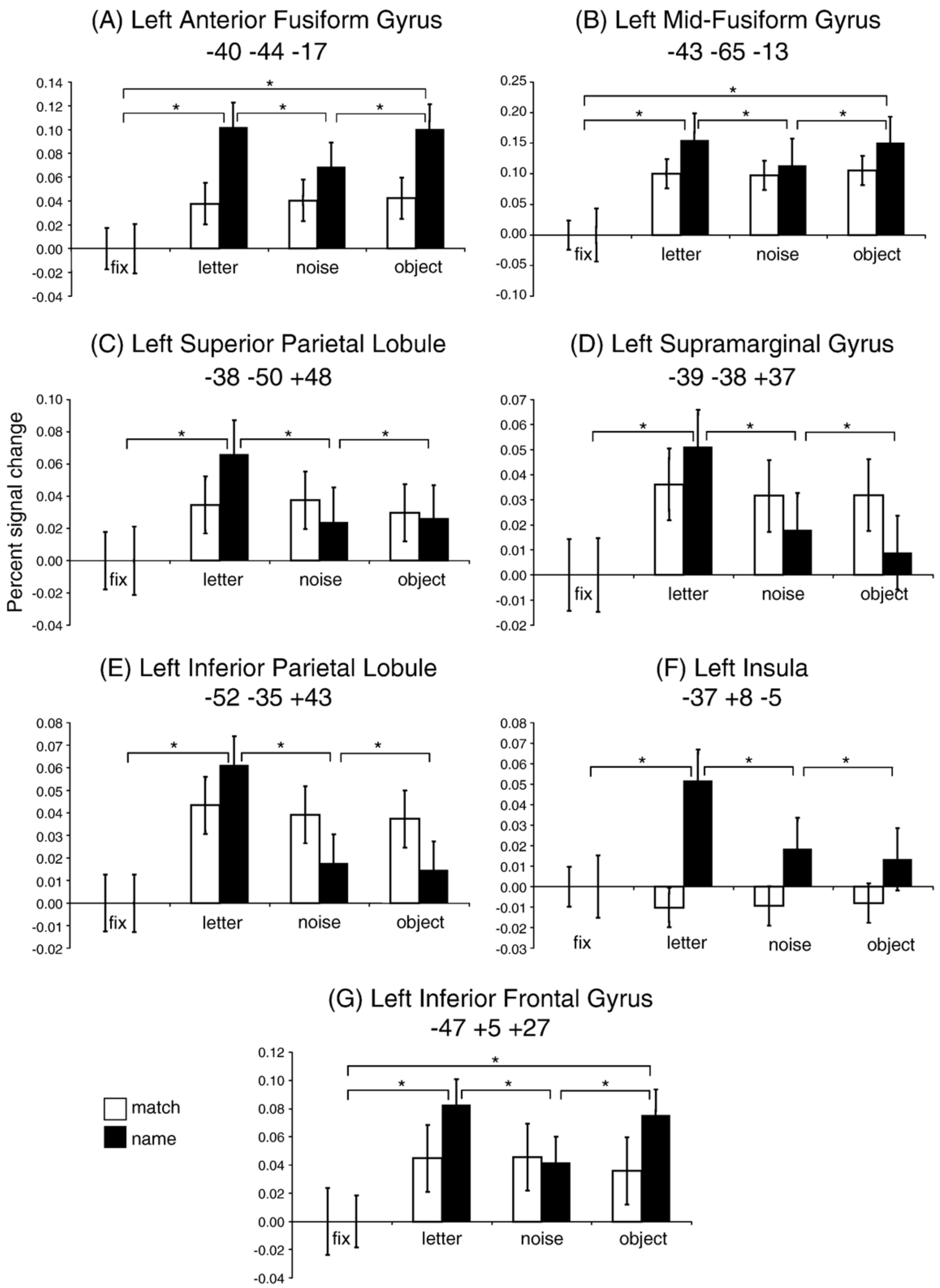


Fig. 3. fMRI results for Task-dependent and Selective + Task-dependent responses. (A) Task-dependent activation for letter naming emerged in the left anterior fusiform gyrus, the inferior parietal lobule, the left inferior frontal cortex and the left insula. (B) When the more stringent definition of letter-selective activation was applied, the left anterior fusiform gyrus and left inferior frontal activation does not survive. (C) When the additional constraint of excluding significant

isolate candidate regions that meet the criteria for selective + task-independent (Fig. 1E) and selective + task-dependent (Fig. 1G). However, within the selective + task-dependent regions, we also eliminate those regions in which the non-selective task produces significant activation relative to baseline. Because the selective + task-dependent regions are not selective for matching

Fig. 4. Response profiles for the task-dependent regions listed in Table 1. Percent signal change is plotted as a function of experimental condition, including the baseline fixation task (fix) because the hypothesis-testing approach relies on post hoc comparisons of various experimental conditions relative to baseline. Significant post hoc comparisons for naming are indicated by an asterisk for each region, but the non-significant post hoc tests for naming are not indicated (see Table 1 for that information). Although all regions showed task-dependent responses, as indicated by a significant Task × Category interaction, the regions showed different response profiles during the naming task, according to the logical combination approach: (A) Left Anterior Fusiform Gyrus (−40 −44 −17) showed an OL-conjoined response, (B) Left Mid-Fusiform Gyrus (−43 −65 −13) showed an OL-conjoined response, (C) Left Superior Parietal Lobule (−38 −50 +48) showed a letter-selective response, (D) Left Supramarginal Gyrus (−39 −38 +37) showed a letter-selective response (which was also selective +task-dependent), (E) Left Inferior Parietal Lobule (−52 −35 +43) showed a letter-selective response, (F) Left Insula (−37 +8 −5) showed a showed a letter-selective response (which was also selective +task-dependent), (G) Left Inferior Frontal Gyrus (−47 +5 +27) showed a showed an OL-conjoined response.

in the example in Fig. 1G, there is no guarantee that the matching task will not activate the region above baseline. This final exclusion leaves only those regions that show selective + task dependent responses that are not mandatory (Fig. 1G). Finally, we also report those regions that showed three- and two-way conjoined responses as a test for domain generality. When we refer to different aspects of the fusiform gyrus, we will adopt the following terms: anterior fusiform refers to those aspects in which the standardized anterior–posterior (*y*) coordinate is within 50 mm of the plane of the anterior commissure; mid-fusiform refers to those aspects in which the *y* coordinate is between −51 and −70 mm; posterior fusiform refers to those aspects in which the *y* coordinate is 71 mm or more from the plane of the anterior commissure.



Task-independent responses for letters

As outlined in Fig. 1d, task-independent activation requires a preferential or graded response to letters in both the naming and matching tasks. Such a pattern would index both domain specific and mandatory processing of letters and would support a specialized input system for letters that is automatically activated when letters are presented as input. In the present experiment, we used the logical combination approach to isolate letter-graded brain regions, but none emerged for either task. We also used logical combination to isolate letter-preferential responses (see Appendix). Although some brain regions showed a letter-preferential response, no regions showed letter-preferential responses across both tasks. Consequently, no regions satisfied the definitions of task-independent or selective + task-independent activation.

Task-dependent responses for letters

The definition of task-dependent responses for letters in Fig. 1F (and Pernet, et al.'s 2005 definition) requires a significant Task (naming, matching) × Category (L, O, N, baseline) interaction and a preferential or graded response for letters in one of the tasks, according to post hoc comparisons. Such a pattern would indicate domain-specific but not mandatory processing of letters because only one task (most likely naming, based on Pernet, et al.'s finding) leads to the domain specific response. Several regions satisfied this definition (see Table 1 and Fig. 3) and all showed a preferential response during the naming but not the matching task. Importantly, two regions of the left fusiform gyrus satisfied task-dependency, in keeping with other studies reporting activation for letter processing or word form processing in similar regions (e.g., Pernet, et al.). Left inferior parietal and left inferior frontal regions also satisfied the criteria for task-dependency.

Selective + task-dependent responses for letters

The criteria for selective rather than preferential activation were applied to the task-dependent regions in Table 1 to further isolate those regions that were selective + task-dependent (Fig. 1G). Letter-selective responses indicate that a brain region responds exclusively to the domain of letters and that other categories do not produce responses that are different from baseline. But the additional constraint of task-dependency requires that this letter-selective response only occur for one task. Selective + task-dependent responses differ from task-dependent responses in that the latter responses allow for the non-letter conditions to be different from baseline, whereas selective + task dependent responses do not allow this. Among those regions that showed the critical Task × Condition interaction in Table 1, letter-selectivity was assessed for each task separately and was defined as a simple main effect of category (O, L, N, baseline) and significant post hoc comparisons showing that letters activate the region more than objects, noise and baseline and insignificant post hoc comparisons showing that objects, noise and baseline are statistically equivalent (all using a corrected alpha level of 0.0083; see Appendix). The results for the simple main effect of the naming task and the post hoc comparisons are shown in Table 1. None of the simple main effects was significant for the matching task. When this more conservative definition of selectivity is applied, only some of the task-dependent regions survive. The surviving regions are in the left inferior parietal cortex and left insula (Table 2), whereas the regions that do not meet the criterion of selectivity are the left fusiform and left inferior frontal cortices (see Fig. 3). The left inferior parietal regions and the left insula, however, only show a selective response during letter naming, and not during letter matching (see Fig. 4). Hence, the letter selectivity presently demonstrated is task-dependent selectivity rather than task-independent selectivity. In other words, left inferior parietal regions and the left insula show a domain-specific response to letters that is not mandatory because the selective response emerges only during naming.

Of those regions that showed a main effect of condition only for naming in Table 2 (in other words, a Task × Condition interaction), any regions in which the matching task also significantly activated the region relative to baseline, albeit in a non-preferred manner, were excluded. To assess this, we determined whether activation for letter, object or noise matching was greater than baseline using post hoc comparisons and an alpha level of 0.05 given that only one of these comparisons needed to be significant to demonstrate significant activation during matching. As shown in Table 2, two of the left parietal regions that had shown task-dependent responses for letters also showed significant activation for letter, object or noise matching. These regions were eliminated because matching of objects or visual noise activated the regions above baseline, which can be seen in Figs. 4C and E. The regions that do survive this additional requirement of no activation during matching are the supramarginal gyrus (Fig. 4D) and the left insula (Fig. 4F). In these regions, the matching task does not activate these regions greater than the baseline task. [The activation levels for the matching task in the left supramarginal gyrus appear to be greater than baseline according to Fig. 4D. However, according to Table 2, these activation levels fell short of significance ($P < 0.097$)].

Conjoined regions

Numerous brain regions showed conjoined responses to letters, objects, and visual noise for both matching and naming tasks. Much of the conjoined activation emerged in the fusiform gyrus (Fig. 5), parietal cortex and the inferior and middle frontal gyri bilaterally (Tables 3 and 4). These regions showed an equivalent response to letters, objects, and noise relative to baseline (OLN-conjoined) or to some subset of the three categories (ON- and OL-conjoined) relative to baseline. Importantly, the left anterior fusiform gyrus showed an OL-conjoined response during naming and a marginally significant OLN-conjoined response during matching (Fig. 4A). The letter versus object contrast failed to reach significance in both tasks, implying that this region is recruited equally for letter and object processing. The left mid-fusiform gyrus showed a similar pattern (Fig. 4B): an OLN-conjoined response during matching and a letter-preferential response during naming. However, during naming, letters did not activate this region more than did objects. For this reason, the region cannot be classified as specialized for letter processing.

Comparison with "letter areas" and the "visual word form area" in the fusiform gyrus

The present analysis did not implicate the left fusiform gyrus as specialized for letters. Potentially, single letters are not an optimal stimulus for inducing left fusiform activation. Had pseudowords, letter strings or words been used, the present study may have isolated letter specialized regions. However, as Fig. 5 shows, the

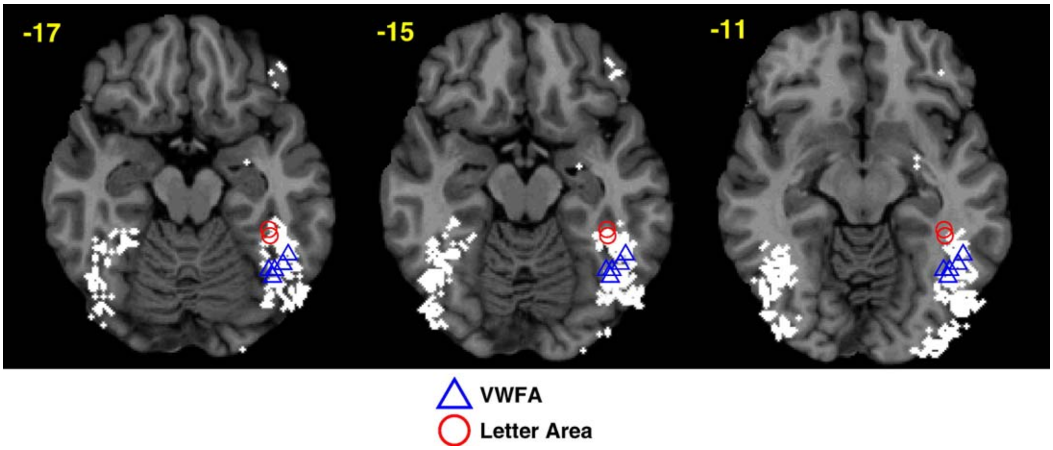


Fig. 5. Conjoined activation for the naming task. Three axial slices show the three types of conjoined activation (white voxels) listed in Table 3—OLN-conjoined, OL-conjoined and ON-conjoined. Letter areas, as reported by Polk et al. (2002) and James et al. (2005) are depicted as red circles and are projected through all three slices. Visual Word Form Areas (VWFAs), as reported by Cohen, et al. (2002; two foci), Dehaene et al., (2002), James et al. (2005) and Pernet et al. (2005) are depicted as blue triangles and are projected through all three slices. The conjoined activation overlaps with VWFAs and letter areas reported in other studies.

left (and right) fusiform gyrus was strongly recruited for the naming task, indicating that single letters induce robust fusiform activation. Nevertheless, single letters may recruit separate regions from the VWFA (James et al., 2005), so we next examined whether the conjoined activation in the left fusiform gyrus was co-localized with left fusiform activation reported in other studies of letter processing. We overlaid the reported standardized coordinates from other studies describing a letter area (James et al., 2005; Polk et al., 2002) onto three axial slices showing conjoined activation in the present study (Fig. 5, red circles)[2]. Likewise, we overlaid reported standardized coordinates from other studies describing the VWFA (Cohen et al., 2002; Dehaene et al., 2002; James et al., 2005; Pernet et al., 2005) onto three axial slices showing conjoined activation in the present study (Fig. 5, blue triangles). In all cases, the letter areas and VWFA overlap with some form of conjoined activation, implying that these regions are recruited equally for letters and objects or for letters, objects and visual noise patterns during naming. Although we did not use pseudowords, words, or letter strings in the present study, the left fusiform activation elicited by single letters was similar to the left fusiform activation normally associated with the VWFA or with a letter area. Importantly, however, the left fusiform activation in the present study was not specialized for letters, but was shared with other categories.

Discussion

The present study has replicated a frequently reported finding of letter-selective activation in the left fusiform gyrus using a definition of selectivity put forth by Pernet et al. (2005), which we referred to as task-dependent activation (Fig. 1f). This response pattern is characterized by a differential response to letters as compared with other stimulus categories, but only in a single task (naming). However, the present study also illustrated that when a more stringent definition of selectivity proposed by Joseph et al. (2002) is applied (selective + task-dependent activation, Fig. 1g), the left fusiform gyrus does not exhibit selective activation for letter naming. Both definitions require a differential response to letters than to the other categories only in the naming task, as indexed by a Task × Category interaction. However, the two definitions differ from each other in two important ways. Selective + task dependent responses require the non-letter conditions to be equivalent to baseline in the selective task whereas task-dependent responses do not. In addition, task-dependent responses only require a main effect of letters during naming but do not require that each post hoc comparison between letters and the other conditions be significant, as required by selective + task-dependent responses. It is for this latter reason that the left fusiform gyrus did not exhibit letter specialization. Instead, the left fusiform was activated equally by object and letter naming, implying that this region subserves a cognitive process that is shared by both letters and objects. As Joseph et al. (2003) have suggested, the shared activation by letters and objects in the fusiform gyrus may reflect the more recent letter system using existing input systems for object processing. Specifically, the left fusiform gyrus is involved in access to and representation of abstract form descriptions for both letters and objects. This conclusion overlaps with suggestions by Cohen and colleagues (Cohen et al., 2002; Dehaene et al., 2002) that abstract letter form is represented in the left fusiform gyrus. However, the present finding of equivalent activation by letters and objects suggests that this region does not represent letter forms exclusively.

The present finding of conjoined activation for letters and objects in the left fusiform gyrus is also consistent with other literature findings of no differential activation for letters when the

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[2] In the two studies the describe letter areas (James et al., 2005; Polk et al., 2002), the coordinates are reported as "Talairach" coordinates but no information is available as to the template used for spatial normalization. In general, Talairach coordinates tend to differ from MNI coordinates (which is the template used in Fig. 5)—especially in fusiform regions (http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml). The coordinates reported by James, et al. and Polk et al. tended to fall in the white matter of the temporal lobe in MNI space rather than in the fusiform gyrus. When we converted those reported coordinates into MNI space (http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml), they tended to fall more in the fusiform gyrus. The range of reported coordinates in the inferior–superior dimension (z coordinate) from individual subjects in these two studies (after conversion) was −15 to −3, which overlaps with the conjoined regions reported in the present study.

Table 3
Conjoined regions for naming (bolded t values are significant)

Anatomical Region (BA)	Profile	Size[a]	x	y	z	Naming task t values LvF	NvF	OvF	LvN	LvO	OvN
R MOG (19)	OLN-conjoined	1045	+39	−71	−12	**5.1**[b]	**4.5**[b]	**6.0**[b]	−1.0	−0.70	0.10
L MOG (19)	OLN-conjoined	1356	−43	−70	−11	**7.4**[b]	**7.3**[b]	**7.4**[b]	0.70	−1.5	−1.8
L FG (37)	OL-conjoined	15	−40	−44	−17	**6.5**[c]	**4.9**[b]	**5.2**[c]	**4.8**[c]	0.20	**4.8**[c]
L FG (37)	OL-conjoined	5	−43	−65	−13	**4.6**[b]	**3.5**[b]	**4.7**[b]	**5.1**[b]	1.4	**3.2**[c]
L FG (19)	ON-conjoined	15	−38	−71	−18	2.0	**5.3**[b]	**4.1**[b]	**−4.0**[b]	**−4.3**[b]	−1.2
R FG (37)	ON-conjoined	12	+35	−41	−23	2.6	**7.3**[b]	**6.4**[b]	**−4.5**[b]	**−6.5**[b]	−1.5
L IPL (7)	OLN-conjoined	78	−39	−59	+55	**3.8**[b]	**5.4**[b]	**7.0**[b]	0.30	−0.10	0.80
L SPL (7)	OLN-conjoined	24	−29	−53	+41	**6.2**[b]	**5.7**[b]	**7.7**[b]	1.1	0.90	0.10
R IPL (7)	OLN-conjoined	29	+33	−57	+46	**5.3**[b]	**4.7**[b]	**9.1**[b]	0.70	−0.30	0.70
R PostCG (1)	OLN-conjoined	17	+28	−37	+71	**5.0**[b]	**6.5**[b]	**8.5**[b]	−0.20	−0.10	1.2
L PreCG (4)	OLN-conjoined	29	−27	−28	+74	**6.1**[b]	**4.6**[b]	**8.6**[b]	0.20	−2.4	1.4
L PostCG (3)	OLN-conjoined	23	−43	−22	+65	**6.0**[b]	**5.2**[b]	**8.1**[b]	0.10	−0.10	1.1
R STG (22)	OLN-conjoined	22	+65	−44	+8	**5.4**[b]	**4.8**[b]	**6.7**[b]	−0.20	−1.3	1.2
L MTG (21)	OLN-conjoined	15	−67	−34	−5	**8.2**[b]	**5.1**[b]	**9.8**[b]	0.0	−0.60	0.50
L Amygdala	OLN-conjoined	53	−28	−1	−22	**7.7**[b]	**6.2**[b]	**12.9**[b]	−0.30	−0.50	0.20
L IFG (6)	OLN-conjoined	15	−41	+2	+32	**5.1**[b]	**4.5**[b]	**5.6**[b]	1.4	−0.10	1.3
L MFG (6)	OLN-conjoined	82	−55	+6	+42	**4.9**[b]	**5.0**[b]	**7.8**[b]	1.4	0.80	0.30
L IFG (9)	OLN-conjoined	49	−49	+10	+29	**5.5**[b]	**5.5**[b]	**7.9**[b]	1.6	0.80	1.0
L IFG (45)	OLN-conjoined	23	−48	+24	+25	**3.5**[b]	**4.6**[b]	**8.0**[b]	0.70	−0.10	0.80
L IFG (44)	OL-conjoined	19	−47	+5	+27	**5.9**[c]	**3.3**[b]	**5.1**[c]	**6.6**[c]	0.80	**4.3**[c]
L MFG (11)	OLN-conjoined	38	−43	+41	−12	**9.1**[b]	**6.0**[b]	**9.1**[b]	0.10	−0.80	1.8
L IFG (45)	OLN-conjoined	14	−33	+31	+9	**−7.0**[b]	**−6.5**[b]	**−6.5**[b]	−0.80	0.0	−1.1

Note. BA, Brodmann's area; x, medial–lateral coordinate; y, anterior–posterior coordinate; z, inferior–superior coordinate; MOG, Middle occipital gyrus; FG, Fusiform gyrus; IPL, Inferior parietal lobule; SPL, Superior parietal lobule; PostCG, Postcentral gyrus; PreCG, Precentral gyrus; STG, Superior temporal gyrus; MTG, Middle temporal gyrus; IFG, Inferior frontal gyrus; MFG, Middle frontal gyrus.

[a] Cluster size is expressed in voxels after transformation into standardized space in which each voxel is 2 mm^3.

[b] $P < 0.008$.

[c] $P < 0.01$.

comparison category is familiar and meaningful as with words or objects (Jessen et al., 1999; Joseph et al., 2003; Price and Friston, 1997; Price et al., 1996; Sergent et al., 1992; Tagamets et al., 2000). Most studies that have isolated the VWFA or a letter area have not compared words or letters to objects (e.g., Cohen et al., 2002; Dehaene et al., 2002; James et al., 2005; Polk and Farah, 1998; Polk et al., 2002). The present study suggests that when objects are the comparison category the VWFA or letter area may not emerge. However, a letter area typically emerges when single letters or letter strings are contrasted with single digits or digit strings (James et al., 2005; Polk and Farah, 1998; Polk et al., 2002), which are familiar and meaningful entities. One possibility for this is that the more anterior letter area is activated in order to differentiate the visually similar digits and letters. Such a mechanism has been proposed in the object recognition literature (Damasio et al., 1996; Gauthier et al., 1999; Joseph and Gathers,

Table 4
Conjoined regions for matching (bolded t values are significant)

Anatomical Region (BA)	Profile	Size[a]	x	y	z	Matching task t values LvF	NvF	OvF	LvN	LvO	OvN
L FG (19)	OLN-conjoined	1785	−39	−73	−14	**13.8**[b]	**13.2**[b]	**11.8**[b]	0.90	−0.30	0.60
R FG (19)	OLN-conjoined	3435	+28	−70	−14	**12.6**[b]	**13.1**[b]	**13.6**[b]	0.20	−0.30	0.80
L SPL (7)	OLN-conjoined	130	−27	−64	+45	**7.1**[b]	**6.6**[b]	**6.4**[b]	−0.30	0.50	0.70
R IPL (7)	OLN-conjoined	325	+30	−59	+42	**9.7**[b]	**9.0**[b]	**8.9**[b]	−0.60	0.30	−0.90
L PostCG (1)	OLN-conjoined	1444	−48	−21	+52	**9.7**[b]	**9.6**[b]	**9.0**[b]	1.4	1.5	0.20
R MFG (6)	OLN-conjoined	43	+32	−2	+49	**6.4**[b]	**6.1**[b]	**6.1**[b]	0.40	0.30	0.10
R IFG (44)	OLN-conjoined	80	+47	+7	+28	**8.5**[b]	**7.5**[b]	**6.7**[b]	−0.90	1.0	−1.5
L MFG (6)	OLN-conjoined	58	−5	+11	+49	**7.4**[b]	**6.0**[b]	**6.1**[b]	0.20	2.6	1.6
L IFG (45)	OLN-conjoined	34	−31	+23	+6	**10.8**[b]	**10.8**[b]	**11.1**[b]	0.60	−0.10	0.80
R IFG (11)	OLN-conjoined	53	+25	+37	−20	**7.4**[b]	**7.3**[b]	**7.2**[b]	0.70	0.60	0.10
R MFG (46)	OLN-conjoined	22	+49	+37	+28	**5.9**[b]	**6.1**[b]	**5.6**[b]	−0.60	0.0	1.8

Note. BA, Brodmann's Area; x, medial–lateral coordinate; y, anterior–posterior coordinate; z, inferior–superior coordinate; FG, Fusiform gyrus; IPL, Inferior parietal lobule; SPL, Superior parietal lobule; PostCG, Postcentral gyrus; IFG, Inferior frontal gyrus; MFG, Middle frontal gyrus.

[a] Cluster size is expressed in voxels after transformation into standardized space in which each voxel is 2 mm^3.

[b] $P < 0.008$.

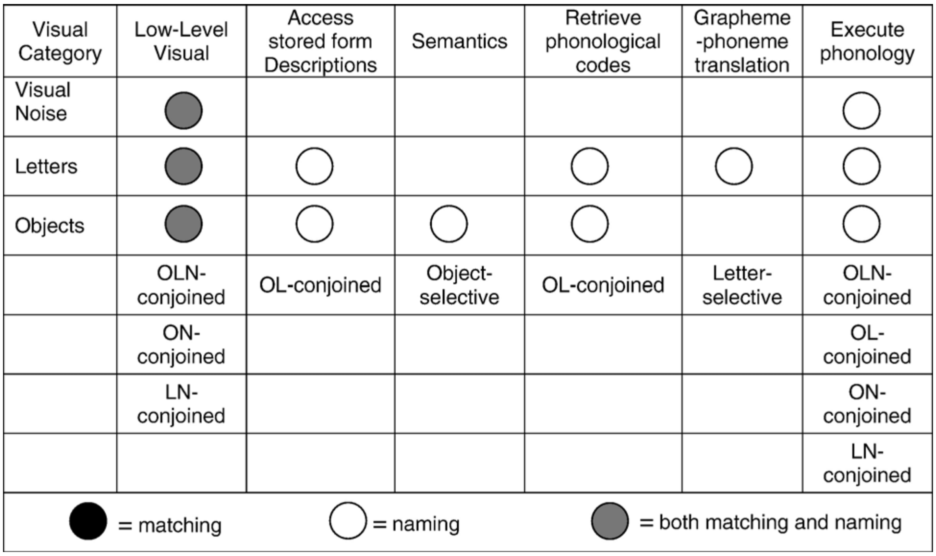
2003; Rogers et al., 2005; Tranel et al., 1997), but would need to be explicitly tested for letters.

Two potential alternative explanations for the present finding of no letter selective activation in the left fusiform gyrus need to be discussed. First, single letters may not be the optimal stimulus and letter strings may be more effective. However, James et al. (2005) recently showed that single letters (as compared with single digits and single Chinese characters) robustly activate the left fusiform gyrus. In addition, within the VWFA single letters showed more activation than single digits, but in the more anterior letter area there were no differences among letter strings, digit strings and Chinese character strings. They suggested that single letters may be a more optimal stimulus than letter strings for studying early processing of letters.

Second, highly familiar and simple stimuli like letters may be quickly processed and, in turn, induce a lower fMRI response, as reported by Pernet et al. (2005) in the right and left fusiform gyrus. In the present analysis approach, such a response would be reflected by ON-conjoined activation in which letters produce a significantly lower response than objects and noise. ON-conjoined activation occurred in the right anterior fusiform gyrus ($x = +35$, $y = -41$, $z = -23$) and the left posterior fusiform gyrus ($x = -38$, $y = -71$, $z = -18$) during naming but not during matching (Tables 3 and 4). The left fusiform region is more posterior than the region reported by Pernet, et al. as letter-selective, but it does show a reduced response for letters. We presently interpret this ON-conjoined response as reflecting low-level visual processing during naming (Fig. 6). A recent relevant finding from James et al. (2005) showed that single letters and digits were processed equally fast, but there was still greater activation in the left fusiform gyrus for single letters as compared with single digits. Nevertheless, the issue as to whether letter specialization should be reflected in a greater response for letters relative to other categories or a reduced response due to adaptation is currently unresolved-applying fMR-adaptation paradigms (e.g., Gros et al., 2001) will be able to answer this question more definitively.

In addition to exploring a category manipulation, the present study also examined the influence of task–naming or matching–on cortical specialization and generalization for letters. A naming task emphasizes linguistic processing, whereas a matching task emphasizes perceptual processing. Not surprisingly, activation in the naming task was more left-sided than in the matching task, which was more bilateral. In addition, the naming task induced letter-selective activation in the left hemisphere, whereas no letter-selective activation emerged during matching. Previous studies have shown top-down influences on the VWFA by linguistically oriented tasks (e.g., Gros et al., 2001; Pernet et al., 2005). In the present study, an equivalent response to letters and objects but not to visual noise (an OL-conjoined response) in the left fusiform gyrus emerged only during the naming task. During the matching task, the left fusiform gyrus responded equally to letters, objects and visual noise (an OLN-conjoined response). In accord with previous suggestions in the literature (Cohen et al., 2002; Dehaene et al., 2002; Gros et al., 2001; Pernet et al., 2005), this top-down modulation likely reflects the need to process abstract representations of letter form.

Fig. 6 outlines the cognitive structure of the tasks and manipulations in the present study. Similar to an analysis by Price and Friston (1997), each row indicates a visual category and each column represents a proposed cognitive process. This is not intended to be an exhaustive list of processes, but rather, a working model to help interpret the present findings. A circle in any given cell means that the particular visual category is associated with the process indicated in the column. Processes that are specific to naming are indicated by white circles, matching processes are indicated by black circles and processes engaged during both tasks are indicated by gray circles. In this conceptualization, no processes are unique to matching; instead, processes for matching are also shared by those for naming so only gray and white circles are present. Hence, the matching task is not expected to yield selective activation for any category. This indeed occurred in the present study. Note that not all processes are obligatory for a given task, such as grapheme-to-phoneme translation for letter naming,



Visual Category	Low-Level Visual	Access stored form Descriptions	Semantics	Retrieve phonological codes	Grapheme -phoneme translation	Execute phonology
Visual Noise	◍					○
Letters	◍	○		○	○	○
Objects	◍	○	○	○		○
	OLN-conjoined	OL-conjoined	Object-selective	OL-conjoined	Letter-selective	OLN-conjoined
	ON-conjoined					OL-conjoined
	LN-conjoined					ON-conjoined
						LN-conjoined

● = matching ○ = naming ◍ = both matching and naming

Fig. 6. Working model for the cognitive processes involved in the naming and matching tasks in the present study. Each of the top three rows represents a single category that was manipulated (visual noise, letters and objects) and each column represents a purported cognitive process that is involved in matching (black circles), naming (white circles) or both matching and naming tasks (grey circles). Below each column are listed the response profiles that would reflect the cognitive process represented in that column. For example, access to stored form descriptions is involved in both matching and naming of all three categories and this shared processing would be reflected in an OLN-conjoined response profile.

but letters are more likely to engage such a process than are the other manipulated categories. Likewise, semantic processing for objects could occur during matching, but naming is more likely to engage this process. The bottom rows of the figure indicate which response profile would reflect the cognitive structure of a particular task-category combination.

Only one process is unique to letters in this conceptualization-grapheme-to-phoneme translation. Consequently, brain regions that show letter-selective activation (left insula and left inferior parietal cortex) potentially could be involved in this process. However, grapheme-to-phoneme translation is not required either during naming of single letters or for matching. Another possibility is that letter-selective activation reflects retrieval of simple phonological codes. Letter names are mono-syllabic whereas object names are often multi-syllabic. Although both letter and object naming require access to phonological descriptions, the simpler phonological codes associated with letter naming may recruit different brain regions than the codes used for object naming. Left inferior parietal activation is often reported in the same studies that report left fusiform/extrastriate activation for letters (James et al., 2005; Jessen et al., 1999; Longcamp et al., 2003; Pernet et al., 2004; Price et al., 1996; Puce et al., 1996; Sergent et al., 1992; Tagamets et al., 2000). In addition, left insula activation is often reported in studies that involve phonological retrieval (Price and Friston, 1997) and phonological processing as assessed with rhyme judgment or generation (Joseph et al., 2001). Consequently, the left insula and left inferior parietal cortex may cooperatively interact to support an output module for the retrieval of phonological codes.

In conclusion, the input system for letters (the left fusiform gyrus) is not domain-specific because objects produce equivalent activation in this region. Instead, cortical specialization for letters emerged in the left inferior parietal cortex and the left insula, and these regions may collectively represent an output module for the retrieval of phonological codes for letter names. The goal of future research will be to characterize the more precise role of these regions in letter processing and whether such regions might participate in an interactive network of regions that collectively support the reading process (Price and Devlin, 2003).

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Appendix A. Logical Combination Approach Used in the Present Study

To test for selective and conjoined brain activation using the logical combination approach (Joseph et al., 2002) each of the twelve group statistical z-maps was thresholded at a *z* score of 1.644, which corresponds to an uncorrected probability of 0.05 for a one-tailed test. The thresholded z-maps were then converted into binary masks, with any *z* score above the threshold associated with the value 1 and any *z* score below the threshold value associated with the value 0. The binary masks derived from the thresholded z-maps were then combined using logical operators in the image calculator of MEDx to yield seven different response profiles: (a) letter-selective, (b) letter-graded, (c) letter-preferential, (d) object–letter–noise conjoined (OLN-conjoined), (e) object–letter conjoined (OL-conjoined), (f) object–noise conjoined (ON-conjoined) and (g) letter–noise conjoined (LN-conjoined). Letter-graded activation could be defined in several different ways and we tested all possible versions of letter-graded activation that included all four of the experimental conditions. None of the definitions of graded activation yielded any clusters of activation; therefore, we only describe one of these graded profiles. Table A1 shows the logical combinations used for each profile. We performed separate logical combinations for naming and matching tasks.

After logically combining the z-maps to create the four profiles for each task, cluster detection was performed ($z > 2.33$) for each profile to yield 81 regions of interest (ROIs) for naming and 23 ROIs for matching. Scalar, repeated-measures ANOVAs were then conducted in each of these ROIs to confirm a main effect of condition (O, L, N, F) on fractional signal change values. It is essential to compare the fractional signal change values rather than percent signal change values expressed relative to the fixation task because the statistical contrasts with fixation are a necessary component of logical combination. Percent signal change does not allow for statistical comparison of the experimental or control conditions with the baseline fixation condition. Scalar post hoc comparisons with Bonferroni correction were then conducted within each ROI that showed a main effect of condition to confirm that the pattern of significant contrasts outlined in Table A2 for each profile type. As an example, the letter-selective profile requires that the letter condition produces significantly greater activation than objects, noise and fixation, but that the pair-wise comparisons of objects, noise and fixation not be significant at the 0.0083 alpha-level. For the two-way conjoined profiles (OL- and ON-conjoined) only five post hoc comparisons are needed because the relationship between the third condition (e.g., the N condition for OL-conjoined) and baseline is not constrained.

Table A1 Logical combinations for each profile

Profile	Logical combination
(a) Letter-selective	(L > F) and (L > N) and (L > O) and ∼ (O > F) and ∼ (O > N) and ∼ (N > F) and ∼ (N > O) and ∼ (F > N) and ∼ (F > O)
(b) Letter-graded	(L > F) and (L > O) and (L > N) and (O > F) and (O > N) and ∼ (N > F) and ∼ (F > N)
(c) Letter-preferential	(L > F) and [(L > O) | (L > N)]
(d) OLN-conjoined	(O > F) and (L > F) and (N > F) and ∼ (O > L) and ∼ (O > N) and ∼ (L > O) and ∼ (L > N) and ∼ (N > O) and ∼ (N > L)
(e) OL-conjoined	(O > F) and (L > F) and (O > N) and (L > N) and ∼ (O > L) and ∼ (L > O)
(f) ON-conjoined	(O > F) and (N > F) and (O > L) and (N > L) and ∼ (O > N) and ∼ (N > O)
(g) LN-conjoined	(L > F) and (N > F) and (L > O) and (N > O) and ∼ (L > N) and ∼ (N > L)

Note. F, fixation; L, letter; N, visual noise; O, object; and , logical AND; ∼, logical NOT; \| logical OR.

Table A2 Post hoc comparisons performed for each profile

Profile	Post hoc comparisons	Alpha
(a) Letter-selective	L > F, L > N, L > O, O = F, O = N, N = F	0.0083
(b) Letter-graded	L > F, L > O, L > N, O > N, O > F, N = F	0.0083
(c) Letter-preferential	L > F, L > O—or—L > F, L > O	0.025
(d) OLN-conjoined	O > F, L > F, N > F, O = L, O = N, L = O	0.0083
(e) OL-conjoined	O > F, L > F, O > N, L > N, O = L	0.01
(f) ON-conjoined	O > F, N > F, O > L, N > L, O = N	0.01
(g) LN-conjoined	L > F, N > F, L > O, N > O, L = N	0.01

Note. F, fixation; L, letter; N, visual noise; O, object; >, refers to statistical significance; =, refers to statistical non-significance at the specified alpha level.

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