

# Neural Correlates of Lexical Access during Visual Word Recognition

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## Abstract

■ People can discriminate real words from nonwords even when the latter are orthographically and phonologically word-like, presumably because words activate specific lexical and/or semantic information. We investigated the neural correlates of this identification process using event-related functional magnetic resonance imaging (fMRI). Participants performed a visual lexical decision task under conditions that encouraged specific word identification: Nonwords were matched to words on orthographic and phonologic characteristics, and accuracy was emphasized over speed. To identify neural responses associated with activation of nonsemantic lexical information, processing of words and nonwords with many lexical neighbors was contrasted with processing of items with no neighbors. The fMRI data showed robust differences in activation by words and word-like nonwords, with stronger word activation occurring in a distributed, left hemisphere

network previously associated with semantic processing, and stronger nonword activation occurring in a posterior inferior frontal area previously associated with grapheme-to-phoneme mapping. Contrary to lexicon-based models of word recognition, there were no brain areas in which activation increased with neighborhood size. For words, activation in the left prefrontal, angular gyrus, and ventrolateral temporal areas was stronger for items *without* neighbors, probably because accurate responses to these items were more dependent on activation of semantic information. The results show neural correlates of access to specific word information. The absence of facilitatory lexical neighborhood effects on activation in these brain regions argues for an interpretation in terms of semantic access. Because subjects performed the same task throughout, the results are unlikely to be due to task-specific attentional, strategic, or expectancy effects. ■

## INTRODUCTION

The content words of a language are symbols that refer to knowledge about the world. To understand and formulate language, the brain must carry out mappings between the perceptual representations of words and this associated knowledge. This use of word meaning, or semantic processing, has been the subject of many functional neuroimaging studies based on word or sentence comprehension tasks. In some of these experiments, attempts were made to isolate the semantic component of these tasks by comparison with a matched control condition that did not require semantic access. While these studies are beginning to converge on a common set of candidate brain regions involved in some way in retrieving word meaning, several potential confounds in these experiments are notable and limit their interpretability.

Semantic processing demands were manipulated in these studies by varying the tasks subjects performed. For example, in many instances, a contrast was made between a task requiring access to word meaning, such as semantic categorization or a semantic relatedness

judgment, and a control task requiring only access to perceptual or phonologic information, such as letter case matching, size discrimination, phoneme detection, syllable counting, or rhyme judgment (Roskies, Fiez, Balota, Raichle, & Petersen, 2001; Binder et al., 1999; Poldrack et al., 1999; Mummery, Patterson, Hodges, & Price, 1998; Price, Moore, Humphreys, & Wise, 1997; Pugh et al., 1996; Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996; Demb et al., 1995; Démonet et al., 1992). An objection to this general approach is that there remains the possibility that the tasks being compared differ in ways other than semantic demands, thereby producing brain activation differences unrelated to semantic processing. For example, semantic tasks might unavoidably make greater demands on general mechanisms involved in memory search, selection, and decision than do control tasks (Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997; Démonet, Wise, & Frackowiak, 1993). Semantic and control tasks might require very different levels of arousal and attention. Although task performances can be matched on accuracy and processing time, this does not guarantee that subjects use the same strategies or attentional resources to achieve these matched performances.

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Other potential problems concern the choice of stimuli for the control condition. In some cases, the control items were nonwords (Binder et al., 1999; Poldrack et al., 1999; Pugh et al., 1996; Démonet et al., 1992). A concern with this approach is that words and nonwords can differ not only in terms of meaning but also in terms of perceptual qualities such as familiarity of phonologic and orthographic form, and these properties were not strenuously matched in prior studies. Another objection to this approach, according to some theorists, is that words engage an internal lexicon prior to semantic access, while nonwords do not. Thus, comparisons between words and nonwords could potentially cause differential activation of several processing systems or representational levels unrelated to word meaning. To avoid these confounds, some investigators have used word stimuli for both semantic and control conditions, varying only the task performed (Roskies et al., 2001; Poldrack et al., 1999; Mummery et al., 1998; Price et al., 1997; Pugh et al., 1996; Vandenberghe et al., 1996; Demb et al., 1995). While this design eliminates stimulus differences between conditions, a different problem arises because of uncertainty over the extent to which word meaning is processed “automatically” in the control condition. Evidence from priming and interference experiments suggests that some access to word meaning occurs in a relatively obligatory, automatic manner (Glaser, 1992; Neely, 1991), which might greatly reduce the contrast between semantic and control conditions in studies using real word control items.

A solution to some of these problems is to compare responses to words and closely matched nonwords under the same instructional conditions. The underlying premise of such a comparison is that, if cognitive task demands are held as constant as possible, differences in brain activation can be attributed mainly to differences in the degree of semantic access induced by the stimuli. An obvious candidate task for such an approach is the lexical decision paradigm, in which subjects are asked to categorize stimuli as words or nonwords. Several previous neuroimaging studies of reading used a visual lexical decision task (Rumsey et al., 1997; Price et al., 1994). In these studies, however, brain responses to words and nonwords were combined during image acquisition, preventing a direct comparison between word and nonword conditions. Event-related functional magnetic resonance imaging (fMRI) overcomes this difficulty, allowing responses to words and nonwords to be segregated. To minimize differences in attentional set or processing strategy between stimulus types, words and nonwords can be presented in random order and with random interstimulus interval durations. Thus, the only remaining difference between word and nonword tasks would involve the categorization response given for each stimulus type.

Because words and nonwords can differ along several dimensions, however, lexical decision is a complex

process that can be performed using any of several decision criteria (Grainger & Jacobs, 1996; Stone & Van Orden, 1993; Posner & Carr, 1992; Seidenberg & McClelland, 1989; Waters & Seidenberg, 1985; Balota & Chumbley, 1984; Shulman, Hornak, & Sanders, 1978; James, 1975). If nonword items contain relatively uncommon letter combinations (e.g., consonant strings or strings comprised of uncommon bigrams), lexical decisions might be made solely on the basis of orthographic familiarity without the need to access phonologic, lexical, or semantic codes. For example, James (1975) reported faster responses to concrete than to abstract words during lexical decision when using very word-like nonwords, indicating that subjects made use of semantic information to categorize the items. This effect disappeared when the nonwords were changed to orthographically unfamiliar letter strings. Similarly, increasing the orthographic similarity between words and nonwords results in the emergence of spelling-to-sound regularity effects, indicating greater use of word-specific phonologic information (Waters & Seidenberg, 1985). These data suggest that matching word and nonword items on orthographic familiarity forces subjects to access specific word information during lexical decision. Because such information is only available in the case of real words, comparing brain activation by the word items with activation by the nonword items under these conditions should enable identification of these word-specific processes.

Stronger responses to words, however, could be interpreted as the result of either access to word meaning or to activation of presemantic word codes. Many models of word recognition posit the existence of an internal lexicon comprised of specific word codes separate from representations of word meaning (McClelland & Rumelhart, 1981; Coltheart, Davelaar, Jonasson, & Besner, 1977; Morton, 1969). According to such models, the successful discrimination of words from word-like nonwords during lexical decision reflects the activation, above some criterion level, of the presented item’s word code. Assuming that word codes are activated relatively little by nonwords, the presentation of real words should produce higher levels of activation in the internal lexicon than the presentation of nonwords. The extent to which word codes are activated by nonwords, however, remains a matter of some uncertainty. Some models explicitly assume that word-like nonwords partially activate word codes that they resemble (e.g., MAVÉ activates HAVE and MOVE). An influential connectionist model of word recognition, the interactive activation model of McClelland and Rumelhart (1981), even predicts that summed activity across all word code units should be approximately equal for words and word-like nonwords. This follows from an assumption in the model that activation of the target word node during word presentation causes inhibition of other word nodes, keeping the summed activity level in the lexicon

relatively constant. During processing of nonwords, many word nodes are partially activated but no single node becomes strongly active, keeping the summed activity level relatively constant. This idea has received support from several functional neuroimaging studies of word and word-like nonword reading, which showed either no significant differences in activation between words and nonwords or stronger activation from nonwords (Paulesu et al., 2000; Fiez, Balota, Raichle, & Petersen, 1999; Rumsey et al., 1997; Price, Wise, & Frackowiak, 1996; Petersen, Fox, Snyder, & Raichle, 1990). If this model is correct, then any differences in brain activation that favor words over word-like nonwords during lexical decision are likely to reflect semantic access rather than word code activation.

Because of this potential ambiguity between word-level and semantic-level processing, we tested activation of word codes more explicitly by manipulating the “neighborhood” statistics of the test items used for lexical decision. Nonwords and words may or may not closely resemble other words. Words that share all but one letter with another stimulus are the “orthographic neighbors” of the stimulus, making HOUSE an orthographic neighbor of HORSE and of POUSE (Coltheart et al., 1977). Some words, such as SHAVE, have many such neighbors (e.g., SLAVE, STAVE, SUAVE, SHEVE, SHOVE, SHADE, SHAKE, SHALE, SHAME, etc.), while others, such as GEESE, have none. Like words, nonwords can also have many word neighbors or few. Studies show that the number of neighbors a stimulus has affects processing time during visual lexical decision tasks. In general, nonwords with many neighbors are

categorized more slowly than nonwords with few neighbors (Forster & Shen, 1996; Grainger & Jacobs, 1996; Sears, Hino, & Lupker, 1995; Andrews, 1989, 1992; Coltheart et al., 1977). In contrast, neighbors often have a facilitatory effect on recognition of low-frequency (but not high-frequency) words (Carreiras, Perea, & Grainger, 1997; Forster & Shen, 1996; Huntsman & Lima, 1996; Sears et al., 1995; Andrews, 1989, 1992). The standard interpretation of these effects is that the orthographic neighbors of a stimulus (or, more precisely, the neural representations of these neighbors) are partially activated when the stimulus is presented. In the case of nonwords, activation of these neighbor representations slows categorization of the stimulus as a nonword. In the case of words, activation of the orthographic neighborhood speeds acceptance of the stimulus as a word (Andrews, 1989).

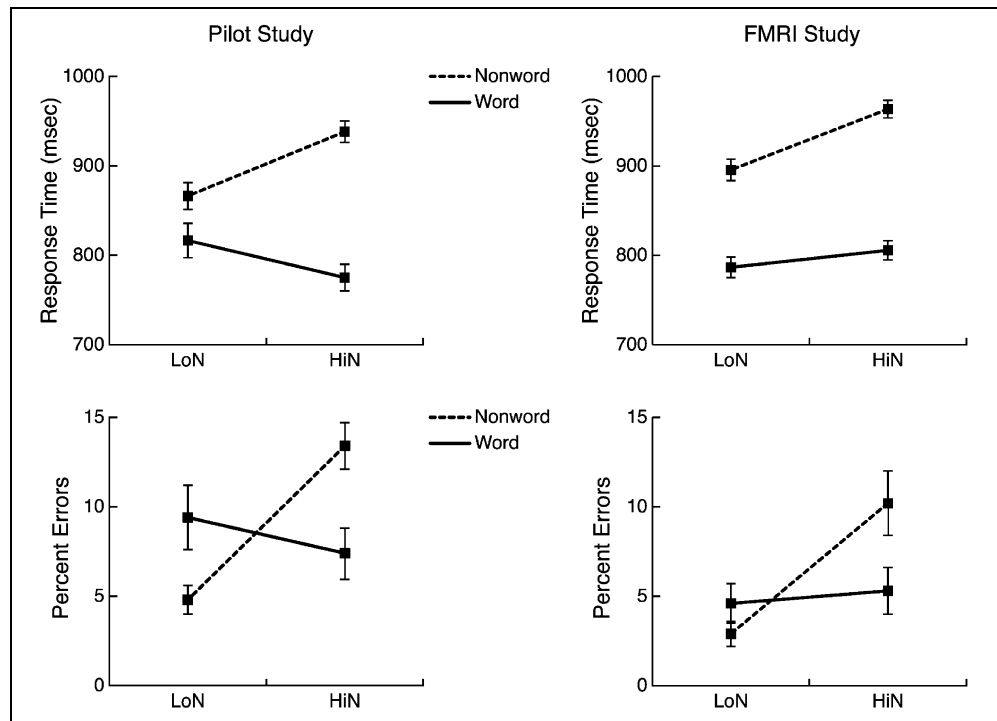
If neighborhood size is correlated with activation of lexical representations, and if activation of these representations is associated with neural activity, then it is reasonable to expect differences in brain activation for stimuli with large compared to small neighborhoods, regardless of whether the stimuli are words or nonwords. A contrast between stimuli with many compared to few neighbors should, according to this scenario, identify brain activity corresponding to activation of word codes and help to distinguish this activity from processing of semantic codes. Thus, our hypotheses were: (i) words should produce stronger activation than word-like nonwords in many of the same brain regions previously identified in studies comparing semantic to nonsemantic tasks, and (ii) a subset of these regions

**Table 1.** Summary Statistics and Lexical Decision Performance Data for the Four Stimulus Sets, including Mean Letter Length, Orthographic Frequency per million words (OF), Mean Positional Bigram Frequency (MPBF) per million words, Orthographic Neighborhood Size (ONS), Phonological Neighborhood Size (PNS), Percent Error (%Error), and Response Time in milliseconds (RT) in the Pilot Study, and Percent Error and Response Time in the fMRI Study

	# Letters	OF	MPBF	ONS	PNS	Pilot Study		fMRI Study	
						% Error	RT	% Error	RT
<i>Words</i>									
HiWord	5.3 (0.5)	3.8 (2.5)	1455 (776)	7.3 (1.7)	11.1 (4.4)	7.4 (9.9)	775 (105)	5.3 (9.3)	806 (81)
LoWord	5.3 (0.5)	3.6 (2.8)	603 (748)	0.0 (0.0)	2.8 (2.4)	9.4 (12.4)	816 (135)	4.6 (7.9)	787 (76)
All	5.3 (0.5)	3.7 (2.7)	1029 (871)	3.7 (3.9)	7.4 (6.8)	8.4 (11.2)	796 (122)	5.0 (8.6)	796 (79)
<i>Nonwords</i>									
HiNon	5.1 (0.4)	0.0 (0.0)	1353 (765)	8.2 (1.8)	10.3 (5.4)	13.4 (9.1)	938 (85)	10.2 (12.4)	963 (84)
LoNon	5.2 (.04)	0.0 (0.0)	431 (353)	0.0 (0.0)	1.1 (2.5)	4.8 (6.0)	866 (107)	2.9 (4.8)	896 (70)
All	5.2 (0.4)	0.0 (0.0)	719 (605)	4.1 (4.3)	5.7 (5.8)	9.1 (8.8)	902 (103)	6.5 (10.0)	930 (84)
<i>p</i> (W–N)	<i>ns</i>	<.0001	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>	<.0001	<i>ns</i>	<.0001
<i>p</i> (Hi–Lo)	<i>ns</i>	<i>ns</i>	<.0001	<.0001	<.0001	<.05	<i>ns</i>	<.005	.0001

Numbers in parentheses are standard deviations. The *p* values are given for comparisons on each measure between words and nonwords (W–N) and between Hi and Lo neighborhood items (Hi–Lo). See Appendix 1 for details on calculation of OF, MPBF, ONS, and PNS.

**Figure 1.** Response times and error rates in the four conditions of the pilot study (left) and the fMRI study (right). Error bars represent *SEM*.



should show stronger responses to items with many lexical neighbors, indicating activation of presemantic word codes.

We explored these hypotheses using fMRI during visual lexical decision (see Methods). Subjects were asked to categorize written words and nonwords according to lexical status. Words and nonwords were matched on visual, orthographic, and phonologic characteristics (Table 1). Word and nonword sets were each evenly divided between stimuli with no orthographic neighbors and stimuli with many ( $\geq 5$ ) neighbors. All items were tested in pilot studies to confirm the expected effects of lexicality and neighborhood size on response time and error rates (Table 1). Brain responses to words were contrasted with responses to nonwords to identify potential neural correlates of lexical and semantic processing. Brain responses to large neighborhood stimuli were contrasted with responses to neighborless stimuli to identify activity corresponding to processing of word-level codes. Results were compared to previous functional imaging studies of word and nonword processing.

## RESULTS

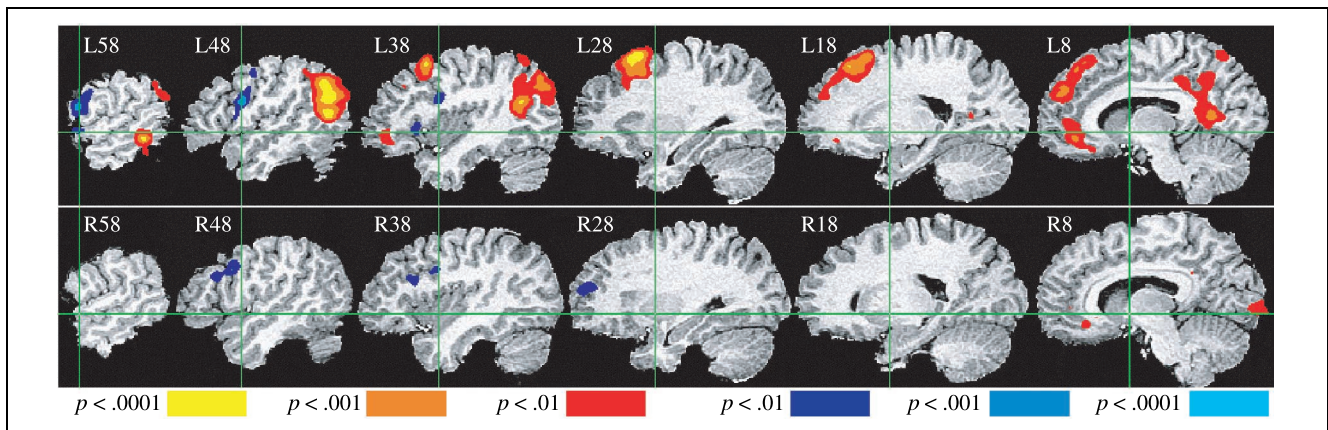
### Task Performance

Response times and error rates from each participant were submitted to two-factor analysis of variance (ANOVA) for the item analyses ( $F_1$ ) and for the subject analyses ( $F_2$ ). Response times less than 200 msec or more than 3000 msec were removed from the response latency data. A total of 22 observations (0.5% of the data)

were removed by this procedure. The overall error rate was 5.8%, and the overall response time was 863 msec. Compared to the pilot study, there were fewer errors overall ( $t = -5.33, p < .0001$ ) and longer response times ( $t = 2.13, p < .05$ ), reflecting the greater emphasis placed on accuracy in the fMRI study (see Methods). Means for each condition are given in Table 1 and depicted graphically in Figure 1.

Analysis of the response time data showed a main effect of lexicality in both the item analysis,  $F_1(1,196) = 146.52, p < .001$ , and the subject analysis,  $F_2(1,23) = 23.46, p < .001$ , due to faster responses for words. There was a main effect of neighborhood size in the item,  $F_1(1,196) = 15.50, p < .001$ , but not in the subject analysis,  $F_2(1,23) = 2.49, p > .1$ , due to faster responses for items with no neighbors. These effects were qualified by a Lexicality  $\times$  Neighborhood size interaction in the item,  $F_1(1,196) = 4.92, p < .05$ , but not in the subject analysis,  $F_2(1,23) = 0.75, p > .1$ . As shown in Figure 1, the interaction is due to a larger inhibitory effect of neighborhood size on nonword responses than on word responses. These effects were investigated using planned-comparison Bonferroni/Dunn tests, which confirmed a difference between nonwords with many neighbors (HiNon) and nonwords with no neighbors (LoNon) (corrected  $p < .001$ ). There was no difference between HiWord and LoWord items ( $p > .1$ ).

Analysis of the error rate data showed no main effect of lexicality,  $F_1(1,196) = 1.55$  and  $F_2(1,23) = 2.39$ ; both  $p > .1$ . There was a main effect of neighborhood size on error rate in both the item analysis,  $F_1(1,196) = 9.87$ ,



**Figure 2.** Word–nonword contrast. The thresholded, group-average activation map is superimposed in color on serial sagittal slices from a representative brain. The color scale refers to uncorrected  $p$  values. Positive values are shown in red–yellow and indicate stronger activation by words. Negative values are shown in blue–cyan and indicate stronger activation by nonwords. Left–right ( $x$ ) stereotaxic coordinates are given at the upper left of each slice. Green lines indicate the stereotaxic anterior–posterior ( $y$ ) and inferior–superior ( $z$ ) axes.

$p < .01$ , and the subject analysis,  $F_2(1,23) = 15.23$ ,  $p < .001$ , due to lower error rates for items with no neighbors. These effects were qualified by a Lexicality  $\times$  Neighborhood size interaction in both the item,  $F_1(1,196) = 6.51$ ,  $p < .05$ , and the subject analyses,  $F_2(1,24) = 10.05$ ,  $p < .01$ . As with the response time data, the interaction is due to a larger inhibitory effect of neighborhood size on nonword responses than on word responses. Planned comparisons confirmed a difference between HiNon and LoNon conditions (corrected  $p < .001$ ), but no difference between HiWord and LoWord conditions ( $p > .1$ ).

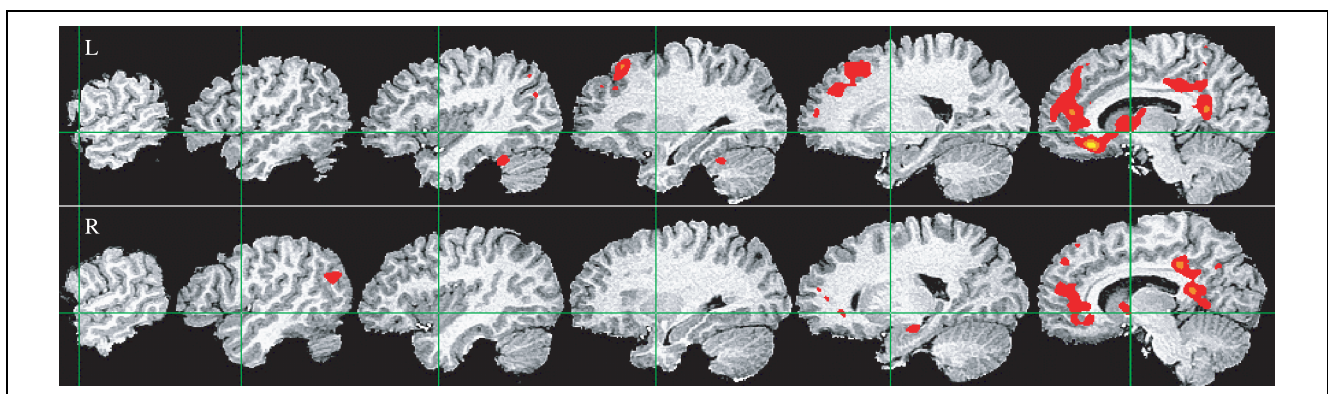
These results closely replicate those of the pilot study, confirming significantly slower responses to nonwords than to words and greater difficulty responding correctly to items with many orthographic neighbors. As in the pilot study, the neighborhood size manipulation interacted with lexicality such that increases in neighborhood size were clearly inhibitory only for nonwords. A subtle but notable difference between the pilot and fMRI data is that increasing neighborhood size was slightly facilitatory for words in the pilot study

but slightly inhibitory for words in the fMRI study. This difference likely reflects the greater emphasis placed on accuracy in the fMRI study (Grainger & Jacobs, 1996), as will be discussed below.

### fMRI Data

#### Words versus Nonwords

Lexicality effects were assessed by contrasting the brain responses for words (HiWord + LoWord) to the brain responses for nonwords (HiNon + LoNon). A group of brain areas, located almost exclusively in the left hemisphere, showed stronger responses to words than to nonwords (Figure 2 and Table 2). In roughly descending order of size, these included the left angular gyrus (Brodmann’s area [BA] 39), the left dorsal prefrontal cortex in the middle (BA 6, 8) and superior (BA 6, 8, 9) frontal gyri, the left rostral–ventral cingulate gyrus (BA 32, 24), the left posterior cingulate gyrus and precuneus (BA 23, 29–31, 7), and the junction of the left posterior middle temporal and inferior temporal gyri (BA 21, 37). Smaller foci were observed in the left pars



**Figure 3.** Neighborhood contrast with formatting as in Figure 2. There were no foci with stronger activation by large neighborhood items. Positive values (red–yellow) indicate stronger activation by items with no neighbors.

orbitalis of the inferior frontal gyrus (anterior IFG, BA 47), the left anterior hippocampus and entorhinal cortex (not shown), and the right occipital pole (BA 17/18). Stereotaxic coordinates for the main activation peaks are given in Table 2.

A second set of areas, located exclusively in the frontal lobes, showed stronger responses to nonwords (blue areas in Figure 2). These included the cortex along the ventral precentral sulcus bilaterally (BA 6), with extension into the left pars opercularis and pars triangularis (posterior IFG, BA 44/45) and the right inferior frontal sulcus (BA 44/9); the supplementary motor area (SMA), and pre-SMA bilaterally (BA 6, not shown); and the right anterior middle frontal gyrus (BA 10/46).

### Neighborhood Size Effects

Neighborhood effects were assessed by contrasting the brain responses for items with many neighbors (HiWord + HiNon) to the brain responses for items with no neighbors (LoWord + LoNon). A number of areas showed stronger responses for items with no neighbors (Figure 3 and Table 3). These included the left dorsal prefrontal cortex in the superior (BA 8–10) and middle (BA 6, 8) frontal gyri, the rostral anterior cingulate gyrus and adjacent ventromedial prefrontal cortex bilaterally (BA 32, 33, 24), and the posterior cingulate gyrus and adjacent precuneus bilaterally (BA 23, 29–31, 7). Smaller foci were observed in the angular gyrus bilaterally (BA 39), the head of the caudate nucleus bilaterally, the left anterior thalamus, and the left cerebellum.

These results were unanticipated in two ways. First, none of the neighborhood size effects were in the expected direction. That is, all of these areas responded more strongly to items with no neighbors than to items with many neighbors. This was unexpected both because of the hypothesis, stated in the Introduction, that activation of neighbor representations might be associated with greater neural activation, and because of the longer response times to nonwords with many neighbors, which might be expected to reflect a longer duration of neural activity for these items. A second unanticipated aspect of these results was that many of the affected regions were near the midline and bilateral, and therefore not brain areas classically associated with orthographic or lexical processes. Some of these regions had also shown effects of lexicality in the word–nonword contrast (Figure 2), raising the possibility that some factor other than lexicality or neighborhood size, but common to both contrasts, could be responsible for the observed patterns.

To investigate these phenomena further, an interaction contrast ( $[\text{HiWord} - \text{LoWord}] - [\text{HiNon} - \text{LoNon}]$ ) was carried out to determine whether neighborhood effects on brain activation were different for words and nonwords, as was the case for the accuracy and response

time data. Several foci showed significant interactions (Table 4).

Follow-up contrasts were performed to assess neighborhood effects separately for nonwords (HiNon – LoNon) and words (HiWord – LoWord). Results for the HiNon–LoNon contrast are shown in Figure 4 and Table 4. Neighborhood effects for nonwords were observed almost exclusively in midline structures, including the posterior cingulate gyrus and the precuneus bilaterally and the ventromedial prefrontal cortex bilaterally. Very small foci appeared in the head of the left caudate nucleus and rostral superior frontal gyrus (BA 9) bilaterally. As with the main neighborhood contrast (Figure 3), all of these neighborhood effects were due to stronger responses for the items with no neighbors (LoNon > HiNon).

Neighborhood effects on word processing, shown in Figure 5 and Table 4, occurred in a strikingly different pattern from those observed with nonwords. These areas were more left-lateralized and involved nonmidline regions to a much greater extent, including many that had shown lexicality effects in the word–nonword contrast. As with the other neighborhood analyses, all of the affected areas showed stronger responses to items with no neighbors than to items with many neighbors. These areas included the left dorsal prefrontal cortex in the middle and superior frontal gyri, the left angular gyrus, the left middle temporal gyrus, and the bilateral rostral anterior cingulate gyrus. Smaller foci appeared in the posterior cingulate gyrus bilaterally, the right angular gyrus, the left cerebellum, and the bilateral anterior thalamus and caudate nucleus. Areas of overlap between the neighborhood effect maps for words and nonwords were identified by creating a composite of the maps in stereotaxic space. The only common areas showing neighborhood effects for both words and nonwords were a few scattered, small foci in the posterior cingulate gyrus and rostral anterior cingulate gyrus.

### DISCUSSION

The results indicate significant differences in the way the brain processes words and word-like nonwords, and complex effects of “neighbor” word representations on the processing of words and nonwords. The main findings were robust differences in brain activation by words and nonwords even when the task instructions were constant across all stimuli and random ordering of the test items gave subjects no opportunity to change processing strategies or stimulus expectations prior to stimulus presentation. Because the task was designed to encourage access to whole-word knowledge (rather than orthographic or phonologic form) as a means of discriminating words from nonwords, we believe the differences in brain activation favoring words, which occurred almost exclusively in the left hemisphere, reflect the successful activation

**Table 2.** Activation Coordinates of Local Maxima in Standard Stereotaxic Space from the Word–Nonword Contrast

<i>Locations</i>	<i>Cluster Size</i>	<i>BA</i>	<i>x</i>	<i>y</i>	<i>z</i>	<i>p</i>
<i>Word &gt; Nonword Activations</i>						
<b>L superior and middle frontal g.</b>	26,708					
L superior frontal s.		6	–25	15	55	<.00001
L superior frontal g.		8	–16	30	48	<.00001
L superior frontal g.		9	–7	49	27	<.0001
L middle frontal g.		6/8	–35	9	47	<.0001
L middle frontal g.		8/9	–31	21	34	<.01
<b>Anterior cingulate s.</b>						
Anterior cingulate s.		32/10	0	46	13	<.0001
Anterior cingulate s.		32	–1	47	2	<.0001
<b>Gyrus rectus</b>						
L gyrus rectus		32	–9	40	–5	<.0001
Gyrus rectus		11/32	1	28	–12	<.001
<b>L pars orbitalis</b>	590	47	–38	38	–5	<.01
<b>L angular g.</b>	17,247					
L angular g.		39	–50	–64	26	<.00001
L angular g.		39	–38	–74	40	<.0001
L angular g.		39	–41	–76	27	<.0001
<b>L supramarginal g.</b>		40	–51	–48	43	<.01
<b>L middle temporal g.</b>		37	–50	–65	14	<.00001
<b>L angular g.</b>	407	39	–38	–62	52	<.01
<b>L inferior temporal g. and s.</b>	1559					
L inferior temporal s.		21/37	–59	–47	–5	<.00001
L inferior temporal g.		37	–59	–49	–15	<.01
<b>Posterior cingulate g. and precuneus</b>	10,097					
Posterior cingulate g.		23/31	–1	–38	35	<.00001
L posterior cingulate g.		23/30	–9	–60	12	<.00001
L precuneus		7	–5	–58	41	<.0001
L subparietal s.		31	–4	–54	27	<.01
Posterior cingulate g.		31	1	–25	39	<.01
<b>L precuneus</b>	807	7	–7	–68	56	<.001
<b>R calcarine s.</b>	608	17	7	–93	4	<.01
<b>L anterior hippocampus</b>	443	–	–23	–10	–14	<.01
<i>Nonword &gt; Word Activations</i>						
<b>L precentral g.</b>	4894					
L precentral g.		6	–43	–1	24	<.00001
L precentral g.		6	–55	1	18	<.00001
L precentral g.		6	–51	–8	43	<.001



**Table 2.** (Continued)

<i>Locations</i>	<i>Cluster Size</i>	<i>BA</i>	<i>x</i>	<i>y</i>	<i>z</i>	<i>p</i>
<b>R inferior frontal lobe</b>	2544					
R precentral s.		6	44	5	33	<.0001
R inferior frontal s.		44/9	44	20	29	<.01
<b>SMA and pre-SMA</b>		2159				
SMA		6	-1	3	51	<.0001
Pre-SMA		6	0	13	45	<.001
<b>R middle frontal g.</b>	948	10/46	27	49	19	<.001
<b>L pars triangularis</b>	581	45	-40	17	2	<.01

Maxima falling within the same cluster are grouped together, with the cluster size ( $\mu$ l) given on the first line of each group. Abbreviations in this and following tables: BA = approximate Brodmann's area, L = left, R = right, g. = gyrus, s. = sulcus. Numbers in the last column refer to the uncorrected  $p$  value at each voxel coordinate.

of this knowledge. In the discussion that follows, this interpretation is presented in greater detail, and the results of the present study are compared with prior functional imaging studies of word and nonword processing. Of considerable importance in interpreting these word–nonword effects are the concurrent comparisons made between items with and without lexical neighbors. As we will argue below, these neighborhood effects on both brain activation and behavioral performance, interpreted within the context of recent accounts of the lexical decision task, suggest that the observed differences in brain activation by words and nonwords reflect semantic access rather than lexical or sublexical processes.

### Visual Word Recognition and Lexical Decision

Before embarking on a detailed discussion of the fMRI findings, the task performance data will be discussed in the context of prior experimental investigations of visual word recognition. Central to most theories of word recognition is the idea that processing of words and word-like stimuli involves the activation of multiple, relatively distinct representations or codes (Carr & Pollatsek, 1985). Processing visual words, for example, may involve computation of orthographic, phonologic, and semantic representations. Although activation of these various codes is thought to be, at least to some degree, obligatory, there may also be an element of strategic control over the extent to which these codes are accessed, depending on the task and the context in which a response must be made (Grainger & Jacobs, 1996; Stone & Van Orden, 1993; Posner & Carr, 1992; Seidenberg & McClelland, 1989; Waters & Seidenberg, 1985; Balota & Chumbley, 1984; Shulman et al., 1978; James, 1975). The object for subjects in a lexical decision experiment is to discriminate real words from nonwords. Though this task might intuitively seem to require access to specific word knowledge, this need

not be the case when the word and nonword items can be distinguished on the basis of more general characteristics. As mentioned earlier, for example, subjects in lexical decision experiments may or may not use phonologic and semantic information, depending on whether or not word and nonword items are orthographically distinguishable (Waters & Seidenberg, 1985; Shulman et al., 1978; James, 1975). The reason for this variability in strategy lies in the relatively longer time needed to compute phonologic and semantic codes for visually presented items compared to visual codes. When subjects must respond as quickly and accurately as possible, the more rapidly accessed orthographic code will be used as the basis for responding, provided that this information reliably distinguishes word from nonword items.

A similar principle applies to the use of information about orthographic neighbors during lexical decision. An unresolved issue is whether the existence of such neighbors facilitates or inhibits processing of words, with empirical data showing facilitation under some conditions and inhibition under others (Pollatsek, Perea, & Binder, 1999; Andrews, 1989, 1997; Grainger, O'Regan, Jacobs, & Segui, 1989; Grainger & Jacobs, 1996; Sears et al., 1995; Johnson & Pugh, 1994; Snodgrass & Mintzer, 1993; Stone & Van Orden, 1993). At least three variables seem to determine the direction of neighborhood effects on word processing during lexical decision. The first and perhaps most robust is the orthographic composition of the nonword set. When the nonwords are orthographically unfamiliar (i.e., composed of unusual letter combinations), increasing neighborhood size is facilitatory for the word items (i.e., responses are faster for items with larger neighborhoods). This pattern suggests that under these circumstances subjects rely on orthographic familiarity to distinguish words from nonwords. Because words with many neighbors are more orthographically familiar than words with few neighbors, these items are accepted



**Table 3.** Coordinates of Local Maxima from the Hi–Lo Neighborhood Contrast

<i>Location</i>	<i>Cluster Size</i>	<i>BA</i>	<i>x</i>	<i>y</i>	<i>z</i>	<i>p</i>
<i>Hi &gt; Lo Activations</i>						
None						
<i>Lo &gt; Hi Activations</i>						
<b>Superior frontal g. and s.</b>	33,339					
L superior frontal g.		8	–23	27	44	<.00001
L superior frontal g.		8	–15	40	30	<.0001
L superior frontal g.		9/10	–14	54	15	<.001
L superior frontal g.		8	–14	30	49	<.001
L superior frontal g.		8/6	–16	18	45	<.01
L superior frontal g.		10	–3	57	11	<.01
L superior frontal g.		8	–3	38	31	<.01
L superior frontal s.		8	–22	27	34	<.01
R superior frontal g.		9	13	52	17	<.001
<b>Anterior cingulate g. and s.</b>						
anterior cingulate s.		32	–1	42	15	<.00001
Anterior cingulate g.		32	0	44	0	<.001
<b>L subcallosal g.</b>		32	–7	29	–9	<.00001
<b>Anterior callosal s.</b>		33	1	29	9	<.01
<b>Basal ganglia and capsule</b>						
L internal capsule		–	–5	1	4	<.001
L caudate nucleus		–	–7	15	–3	<.01
R caudate nucleus		–	7	5	5	<.01
L anterior thalamus		–	–4	–7	11	<.01
<b>R angular g.</b>	1052	39	45	–70	28	<.001
<b>L angular g.</b>	745	39	–42	–65	37	<.01
<b>Posterior cingulate g. and precuneus</b>	17,503					
R posterior cingulate g.		23/31	2	–37	35	<.00001
R retrosplenial cortex		26/29	4	–45	16	<.00001
Posterior cingulate g.		23/31	–1	–51	25	<.00001
L posterior cingulate g.		23/30	–7	–55	17	<.0001
R precuneus		31/7	3	–67	38	<.001
<b>L precuneus</b>	382	7	–4	–55	62	<.01
<b>L superior cerebellum</b>	888	–	–35	–46	–21	<.001

as words more quickly. In the present experiment, words and nonwords were closely matched in terms of orthographic and phonologic familiarity, preventing reliance on orthographic processing for making the lexical decision. Consistent with this model, no facilitatory effect of neighborhood size on word processing was observed.

A second modulating variable is the relative emphasis placed by investigators on accuracy relative to speed. When speed is emphasized, increasing neighborhood size tends to facilitate word responses, whereas this effect can be reversed when accuracy is emphasized. This pattern suggests that subjects rely on the more rapidly accessed orthographic code under conditions

emphasizing speed, resulting in faster responses for more orthographically familiar words (those with more neighbors). In contrast, when accuracy is emphasized, subjects can afford to wait until specific word identification has occurred through activation of lexical and/or semantic codes. Because subjects are in essence ignoring orthographic familiarity, no facilitation occurs from increasing neighborhood size. Consistent with this

**Table 4.** Coordinates of Local Maxima Showing Neighborhood Effects for Either Nonwords (LoNon > HiNon) or Words (LoWord > HiWord), for Regions Showing Significant Lexicality × Neighborhood Interactions

<i>Region</i>	<i>BA</i>	<i>x</i>	<i>y</i>	<i>z</i>
<b>L middle frontal g.</b>				
LoWord > HiWord	10/9	-21	39	32
LoWord > HiWord	8	-26	26	45
LoWord > HiWord	8	-37	17	38
LoWord > HiWord	6	-30	9	46
LoWord > HiWord	6	-27	12	56
<b>R middle frontal g.</b>				
LoWord > HiWord	8/6	36	14	45
<b>Anterior cingulate s.</b>				
LoWord > HiWord	32/8	1	16	42
<b>L subcallosal g.</b>				
LoNon > HiNon	32/11	-7	29	-10
<b>L angular g.</b>				
LoWord > HiWord	39	-51	-52	29
LoWord > HiWord	39	-43	-66	41
LoWord > HiWord	39	-50	-63	30
LoWord > HiWord	39	-48	-51	30
<b>L middle temporal g.</b>				
LoWord > HiWord	21	-58	-21	-11
<b>L inferior temporal g.</b>				
LoWord > HiWord	20/21	-53	-13	-20
<b>L posterior cingulate g.</b>				
LoNon > HiNon	23/31	-9	-56	17
LoNon > HiNon	23/31	-1	-51	24
<b>R posterior cingulate and retrosplenial</b>				
LoNon > HiNon	23/31	3	-35	36
LoNon > HiNon	29/30	3	-47	15
LoNon > HiNon	30	6	-54	6
LoWord > HiWord	23/31	1	-40	31
LoWord > HiWord	31	1	-52	31

model, we observed a trend toward a facilitatory effect of neighborhood size on word responses in the pilot study ( $p = .06$ ), in which the instruction was to “respond as quickly and accurately as possible,” whereas neighborhood size showed no facilitation in the fMRI study, in which the instruction was changed to “respond as quickly as possible without making errors” (Figure 1).

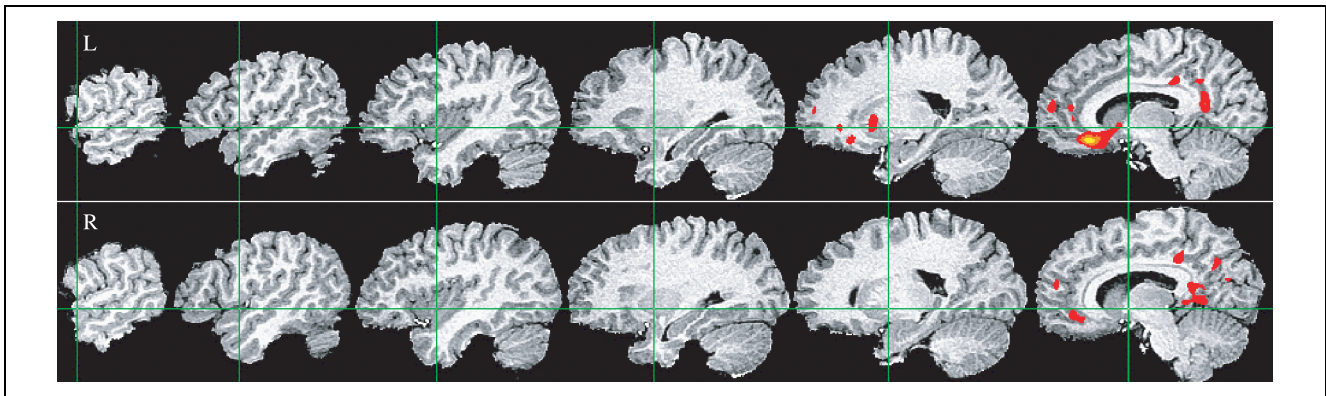
A third important variable is the word frequency of the neighbors. Grainger and Jacobs (1996) and Grainger et al. (1989) have argued that activation of neighbor words can be inhibitory when these neighbors have a higher frequency than the test item itself. This claim is based on an interactive activation model with mutually inhibitory connections between lexical nodes. According to this model, activated neighbors send inhibitory input to other word nodes. Because word frequency determines the resting level of activation of word nodes in the model, nodes representing high-frequency neighbors of a word are initially more strongly activated than the target word node itself and so produce very potent inhibition, slowing activation of the target node. Because this effect is based on slowing specific word identification, it would emerge in lexical decision experiments only when subjects are relying on lexical and/or semantic access, that is, when words and nonwords are matched on orthographic familiarity and accuracy is emphasized over speed. This model is consistent with the small, though non-significant, increase in response time we observed for the large neighborhood versus small neighborhood words in the fMRI study (806 vs. 787 msec). Because increasing neighborhood size also increased the likelihood of higher-frequency neighbors, access to target lexical and/or semantic information was likely to have been slower for the items with more neighbors (Pollatsek et al., 1999; Carreiras et al., 1997; Grainger et al., 1989; Grainger & Jacobs, 1996; Huntsman & Lima, 1996).

In summary, prior lexical decision studies suggest that orthographic neighbors have a facilitatory effect on word responses when task conditions encourage subjects to use an orthographic familiarity criterion. The fact that these conditions did not hold in the present study, and that increasing the orthographic neighborhood size (ONS) produced no facilitatory effect in the fMRI study, suggests that subjects relied primarily on specific word identification to perform the task. The contrast between word and nonword conditions (Figure 2, Table 2) demonstrates the neural correlate of this access to specific word information.

### Lexicality Effects on Brain Activation

#### Activations Favoring Words

Several brain regions showed stronger activation by words than nonwords. These areas were almost all in

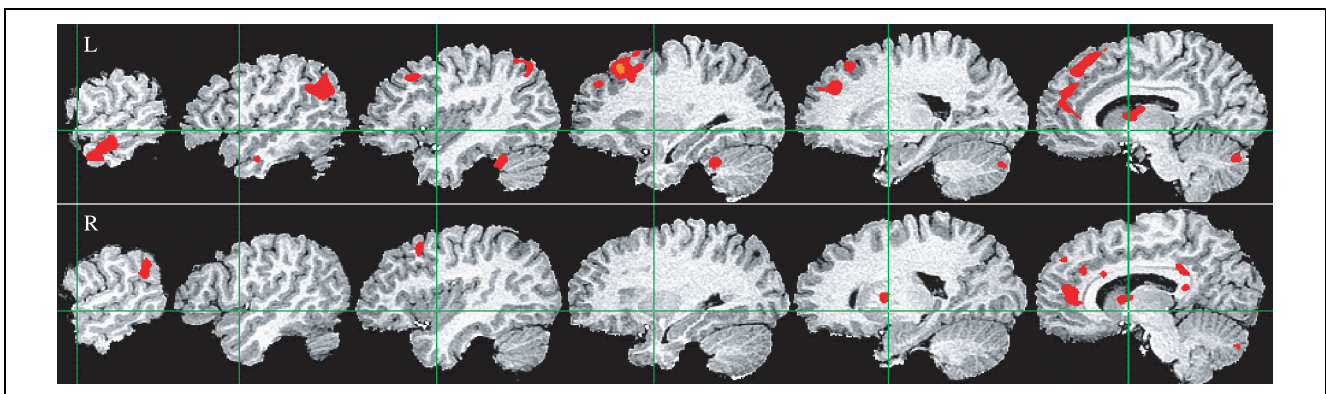


**Figure 4.** Neighborhood contrast for nonwords with formatting as in Figure 2. There were no foci with stronger activation by large neighborhood items. Positive values (red–yellow) indicate stronger activation by items with no neighbors.

the left hemisphere and included the angular gyrus, the dorsal prefrontal cortex, the rostral and ventral anterior cingulate gyrus, the posterior cingulate gyrus, the middle temporal and posterior inferior temporal gyri, the pars orbitalis, and the hippocampus/parahippocampus. It should be emphasized that activation differences in these areas cannot be ascribed to differences in task instructions, task strategies, attentional level, or stimulus expectations. On the other hand, we do not claim that the task requirements were entirely identical for words and nonwords, because positive responses were required for words while negative responses were required for nonwords. It is likely that there are different mechanisms involved in the generation of positive and negative responses, and these different mechanisms might account for some of the differences in activation. For example, negative responses likely require more effortful and extensive “search” to exclude a possible matching lexical–semantic representation. Supporting this assumption are the behavioral measures, which clearly indicate that nonwords were more difficult and took longer to process, as in many previous lexical decision studies (Grainger & Jacobs, 1996; Forster & Shen, 1996; Sears et al., 1995; Andrews, 1989, 1992;

Coltheart et al., 1977). Scott, Holmes, Friston, and Wise (2000) observed increased brain activation when subjects classified filtered speech sounds as nonspeech relative to when they classified the same sounds as speech, providing further support for this idea. Yet the main fMRI results we observed indicate stronger activation by words, which could not be explained as an effect of response difficulty. It thus seems likely that the activation by words in these regions results from the fact that words elicit activation of associated representations. The marked left-hemisphere lateralization of these areas is further evidence that their activation represents access to linguistic information.

But what is the nature of this information? What is accessed when a word is uniquely and specifically identified? Some theories of word recognition posit specific phonologic and orthographic word codes that comprise a mental word list or lexicon. An alternative view is that word identity is inextricably linked to word meaning. For example, some connectionist accounts of word recognition consist of pathways by which distributed orthographic, phonologic, and semantic representations are mapped onto each other, but there are no specific word nodes or other representations that stand for word



**Figure 5.** Neighborhood contrast for words with formatting as in Figure 2. There were no foci with stronger activation by large neighborhood items. Positive values (red–yellow) indicate stronger activation by items with no neighbors.

entities (Plaut, McClelland, Seidenberg, & Patterson, 1996; Hinton & Shallice, 1991; Seidenberg & McClelland, 1989). In these models, presentation of an orthographic or phonologic pattern consistent with a known word produces activation in the network that spreads automatically to intermediate nodes and then to semantic nodes, eventually resulting in activation above threshold of the semantic representations corresponding to the meaning of the word. Thus, access to specific word information (i.e., word identification or lexical access) is represented in these models by activation of a specific pattern of semantic codes. Although presentation of word-like nonwords might result in partial, transient activation of semantic codes for words that resemble the nonword, activation of these codes would be much weaker in the case of nonwords because of the much weaker connections between nonword orthographic patterns and semantic patterns.

We believe the word–nonword results are more compatible with activation of semantic codes than orthographic or phonologic word codes. A problem for an interpretation based on activation of word codes is that there is no reason why activation of such codes should be stronger for words than for nonwords in the current experiment. In models based on localist word codes, the main determinant of the summed word node activation level for any given item is its neighborhood size. Because this factor was matched for words and nonwords, summed word node activation level should not have differed greatly for words and nonwords. Even at later stages of processing a word, when word identification has been achieved through very strong activation of the target word node, the overall level of word node activation should not greatly differ between words and nonwords. This follows from the assumption of lateral inhibition, which states that as the target word node becomes more activated, it inhibits other word nodes, with little or no net change in the overall summed activation level (Grainger & Jacobs, 1996; McClelland & Rumelhart, 1981). According to this view, the summed word node activation level depends on the number of neighbors the target item has, but not on whether word identification has been achieved.

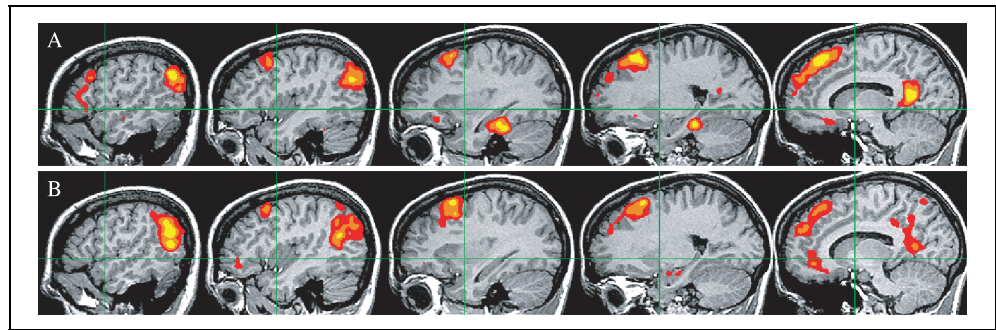
What is needed to explain the word–nonword activation differences is a representational level that is activated more strongly when a word has been specifically identified. We propose that the semantic level meets this criterion. Through experience with real words and their meanings, the word recognition network establishes strong connections between unique word input patterns and their semantic representations. Presentation of an unfamiliar input in the form of a nonword produces activation of orthographic and phonologic codes to approximately the same level as with words, but little activation of semantic representations because the mapping from intermediate to semantic codes does not exist for nonwords.

We return to this issue later in discussing the results of the neighborhood size comparisons. Before leaving the word–nonword activation contrast, however, it is important to compare these results with those from other studies in which words were contrasted with nonwords, and to look for patterns of divergence and convergence across studies. Many of these experiments involved contrasts between orthographically legal items (words or pronounceable pseudowords) and orthographically illegal items (unpronounceable strings of consonants) (Bavelier et al., 1997; Indefrey et al., 1997; Price et al., 1994; Howard et al., 1992; Petersen et al., 1990). Because the word–nonword contrasts in these studies likely emphasized differences in orthographic and phonologic processing, the results are not comparable to the present word–nonword contrast in which orthographic and phonologic processing demands were matched as closely as possible. Other investigators used word–nonword contrasts to identify brain activation related to semantic processing (Binder et al., 1999; Poldrack et al., 1999; Pugh et al., 1996; Démonet et al., 1992; Démonet, Price, Wise, & Frackowiak, 1994). In these studies, semantic categorization tasks performed on words were compared with phonologic tasks performed on pronounceable pseudowords. For example, Binder et al. (1999) described averaged brain activation patterns in 30 normal subjects during performance of an auditory word semantic decision task (decide if named animals are “found in the United States and used by people”) and a phoneme detection task (decide if a pseudoword contains the phonemes /b/ and /d/). Results of the semantic–phonologic contrast, shown in Figure 6, demonstrate greater activation during the semantic task in several left hemisphere regions, including the angular gyrus, the dorsal prefrontal cortex, the posterior cingulate gyrus, and the fusiform gyrus/parahippocampus. As can be seen from Figure 6, the overall results are strikingly similar to the word–nonword contrast in the present experiment. This replication is remarkable given that the tasks and stimuli were quite different in the two experiments, including differences in the sensory modality of stimuli.

In addition to these word–pseudoword comparisons, other investigations were designed to identify semantic processing systems by contrasting semantic and phonologic tasks performed on visually presented words (Roskies et al., 2001; Poldrack et al., 1999; Mummery et al., 1998; Price et al., 1997). In these studies, subjects made a category decision in the semantic condition, such as deciding whether the word represents a living or nonliving entity, and a phonologic decision in the control condition, such as deciding whether the word contains a target number of syllables. In most cases, the left angular gyrus, the left dorsal prefrontal cortex, the left posterior cingulate gyrus, and the left ventral temporal lobe showed greater activation in the semantic condition. Figure 7 shows the location of activation



**Figure 6.** Comparison of left hemisphere activations associated with (A) performance of a semantic task compared with a phonologic task in the study by Binder et al. (1999), and (B) word > nonword activation in the current study. Formatting is as in Figure 2, except that slice locations begin at L50 and proceed in 10-mm steps to L10.

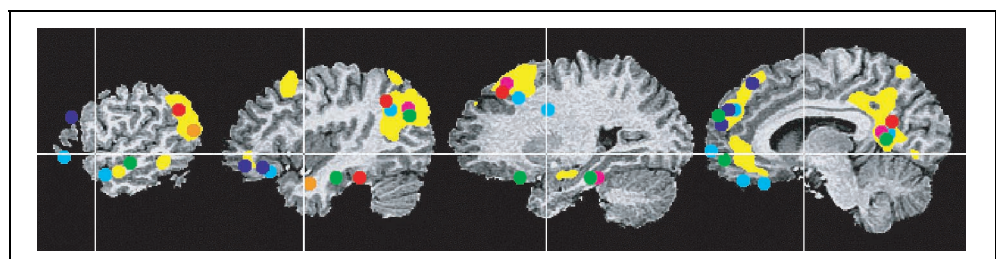


peaks from all these studies, together with peaks from previous word–pseudoword comparisons, superimposed on the word–nonword contrast from the present study. The strong convergence of results from these seven experiments lends further support to the claim that the word–nonword activation differences observed in the present study represent differences in the degree to which semantic codes were evoked by words and pronounceable pseudowords.

The functional neuroimaging data thus reveal a left hemisphere frontal–temporal–parietal network associated with retrieval of word meaning, although the specific processes carried out by the nodes of this distributed network are still largely unknown. Several extensive reviews have discussed the possible roles of these brain regions (Binder & Price, 2001; Binder, 2002; Grabowski & Damasio, 2000). In brief, lesions in the left angular gyrus, the middle temporal gyrus, the inferior temporal gyrus, the fusiform gyrus, and the inferior frontal gyrus have all been reported to cause deficits in spoken and written language comprehension without impairments of phonologic processing (“transcortical sensory aphasia”), suggesting a supramodal role in semantic processing (Otsuki et al., 1998; Chertkow, Bub, Deaudon, & Whitehead, 1997; Damasio, Grabowski, Tranel, Hichwa, & Damasio, 1996; Rapcsak & Rubens, 1994; Schäffler, Lüders, Dinner, Lesser, & Che-

lune, 1993; Hillis & Caramazza, 1991; Sirigu, Duhamel, & Poncet, 1991; Hart & Gordon, 1990; Alexander, Hiltbrunner, & Fischer, 1989; Silveri & Gainotti, 1988; Warrington & Shallice, 1984; Benson, 1977, 1979; Geschwind, 1965; Nielsen, 1938). Isolated lesions of the left dorsal prefrontal cortex produce the “transcortical motor aphasia” syndrome, in which propositional speech output is diminished with relative preservation of comprehension and phonologic processing (Rapcsak & Rubens, 1994; Alexander, Benson, & Stuss, 1989). The latter pattern suggests that the left dorsal prefrontal cortex may function as an intermediary between semantic knowledge stores and motor response systems, perhaps by directing attention to or “selecting” task-relevant information needed for response formulation. The left posterior cingulate cortex, activated in five of six studies shown in Figure 7, has been linked with a variety of cognitive processes, including episodic memory encoding (Vogt, Finch, & Olson, 1992; Rudge & Warrington, 1991; Valenstein et al., 1987), monitoring of the environment (Raichle et al., 2001), and emotion processing (Maddock, 1999). Depth of processing is known to modulate storage of episodic memories ( Craik & Lockhart, 1972). Thus, posterior cingulate activation, as well as left anterior hippocampus and parahippocampus activation observed in some semantic studies, may be due in part to stronger episodic memory encoding

**Figure 7.** Summary of seven neuroimaging studies of semantic processing. Yellow regions represent areas of word > nonword activation during lexical decision in the current study. Colored dots represent the principal activation peaks from six previous studies in which semantic tasks were contrasted with phonologic tasks. Red = Démonet et al. (1992); orange = Price et al. (1997); green = Mummery et al. (1998); magenta = Binder et al. (1999); dark blue = Poldrack et al. (1999); light blue = Roskies et al. (2001).



during semantic processing relative to nonsemantic processing. Finally, the ventromedial prefrontal cortex, activated in three of seven studies shown in Figure 7, has been linked to reward obtainment and emotion processing (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001; Simpson, Snyder, Gusnard, & Raichle, 2001; Bechara, Damasio, & Damasio, 2000). Conceivably, the greater activation by semantic conditions in these three studies could be due to processing of emotional aspects of word meaning. Some of the items in our word set have undeniable emotional valence or could be associated with pleasant or unpleasant situations (e.g., BULLY, CHICK, NOOSE, ADDICT, HAVOC, VIRUS), so an account of this sort seems reasonable. Future studies could test this hypothesis by comparing activation by neutral and emotional words during lexical decision.

### *Activations Favoring Nonwords*

Several frontal lobe areas showed stronger responses to nonwords than to words (Table 2, Figure 2), reminiscent of similar results from previous word–pseudoword comparisons. For example, in several word naming studies, pseudowords produced greater activation of left IFG and premotor cortex than did words with regular spelling–sound correspondences (Paulesu et al., 2000; Fiez et al., 1999; Hagoort et al., 1999; Herbster, Mintun, Nebes, & Becker, 1997). In some of these studies, words with irregular pronunciations (e.g., DEBT, GAUGE) also produced greater activation of these areas compared to regular words, prompting the investigators to postulate a role for the left posterior IFG in grapheme-to-phoneme mapping (Fiez et al., 1999; Herbster et al., 1997). This account is based on the idea that mapping from grapheme to phoneme codes develops as a result of experience with particular grapheme–phoneme correspondences (Seidenberg & McClelland, 1989). Performance on a particular grapheme string improves with repeated exposure to the grapheme–phoneme pairing (the frequency effect), particularly when the constituent graphemes are consistently mapped to particular phonemes (the consistency effect). Thus, mapping is slower for grapheme combinations never before encountered (nonwords) and for items with inconsistently mapped graphemes (exception words). Though we did not manipulate grapheme–phoneme consistency in our word sets, nearly all of the word items had regular pronunciations (the notable exceptions were SWABS, ALGAE, and YACHT). Thus, our results could also be explained in terms of less efficient grapheme-to-phoneme mapping in the case of the nonwords. This interpretation is also supported by the posterior frontal and premotor locations of the nonword activations, which closely resemble locations reported in previous studies.

A potential problem with this interpretation is the bilateral location of the nonword activations. Previous

nonword > word activations ascribed to grapheme-to-phoneme mapping processes have been lateralized to the left hemisphere, and the strong association between left hemisphere lesions and phonologic reading disorders leaves little reason to expect this processing system to be bilateral (Fiez & Petersen, 1998).

One alternative account is that greater activation by nonwords simply reflects a decision mechanism. We refer here to a mechanism that receives available information about a stimulus and maps this onto an appropriate response. If activation of this mechanism is assumed to cease once a response is selected, then its activity integrated over time would vary with response latency. Because response times were longer for nonwords, such a mechanism would show higher levels of activation for nonwords than for words. A problem with this account is that it predicts greater activation for large neighborhood nonwords than for nonwords without neighbors, as response times for the former were significantly longer than the latter. Though this effect was not observed in the thresholded HiNon–LoNon group map (Figure 4), this could reflect a relative lack of sensitivity due to the smaller response time difference associated with the large versus small neighborhood nonword contrast (67 msec) compared to the response time difference between nonwords and words (134 msec). To test this possibility further, we used a much more liberal threshold ( $p < .05$ ) on the HiNon–LoNon contrast map to detect small differences between conditions. Even at this lower threshold, however, none of the frontal regions identified in the word–nonword contrast showed any trend toward stronger activation by large neighborhood nonwords. This negative result argues against an interpretation based solely on a decision mechanism.

Another possibility is that the posterior inferior frontal regions showing stronger activation by nonwords perform an attentional function when word-like nonwords cannot be identified. Specifically, activation of a large number of neighbors might result in a signal that biases the subject to respond “word.” If no word representation then becomes sufficiently activated, as occurs with large neighborhood nonwords, this conflicting information may cause the frontal cortex to generate an attentional signal. The purpose of such a signal would be to enhance processing of the stimulus by the word recognition system in order to optimize detection of any semantic activation. Like the decision mechanism account, however, this attentional account predicts higher levels of activity when processing large neighborhood nonwords than neighborless nonwords. As noted above, however, we saw no evidence for such an effect in the HiNon–LoNon contrast map. We conclude that the most likely interpretation of the stronger activation by nonwords is that the regions showing this pattern are involved in some way in mapping between orthography and phonology, a process that

requires more neural activity when unfamiliar mappings are involved.

### Effects of Neighborhood Size on Brain Activation

Manipulation of neighborhood size had the expected effect on response times for nonwords: Responses were slower for nonwords with more neighbors. The standard interpretation of this effect is that the codes representing the word neighbors of the nonword are partially activated when the nonword is presented, biasing the system toward a positive response and slowing categorization of the item as a nonword. Manipulation of neighborhood size also produced robust effects on brain activation, though these were in an unanticipated direction. Nearly all of the areas that showed an effect of neighborhood size were more strongly activated by the items with no neighbors than by the items with many neighbors. These effects cannot be due to differences in word code activation, which would have produced effects in the direction opposite to those observed. Two issues arise from this paradox: (i) What is the explanation for the observed brain activation differences, which favored the small neighborhood conditions? (ii) Why were no differences observed in the expected direction?

Different brain areas were sensitive to the neighborhood size manipulation depending on whether the stimuli were words or nonwords (Figures 4 and 5). In the case of words, these areas were predominantly in the left hemisphere and included many of the same regions that had shown stronger responses to words in the word–nonword contrast, such as the angular gyrus, the dorsal prefrontal cortex, and the middle temporal gyrus (Figure 5). As noted, these regions have been implicated in semantic processing in many previous studies (Figure 7). This pattern suggests that the level of activation in the semantic system was higher for words with no neighbors. This result is consonant with the findings of Pollatsek et al. (1999), Carreiras et al. (1997), Grainger et al. (1989), Grainger and Jacobs (1996), Huntsman and Lima (1996) that the presence of neighbors—particularly higher-frequency neighbors—slows identification of the target word. Thus, specific word identification, that is, activation of semantic representations associated with the word, is more rapid in the case of words that have no competing neighbors. Response times were not significantly faster for small neighborhood words, however, suggesting that subjects' responses to these items may have been slowed somewhat by the relative lack of orthographic familiarity of these items. Thus, in the case of small neighborhood items, subjects seem to require more extensive semantic access to compensate for the fact that these items are less orthographically word-like. In contrast, the high degree of orthographic familiarity of the large neighborhood items biases the subject initially

toward a positive response, and relatively little semantic activation is needed to complete the response selection. It is this difference in the level of activation of target semantic information that could explain the pattern of brain activation differences observed in the HiWord–LoWord contrast (Figure 5). This pattern is similar to that observed in the word–nonword contrast because the underlying mechanism—differences in the level of activation of target semantic information—is the same in both cases.

This account also explains why neighborhood size effects were not observed in these brain areas when using nonwords (Figure 6). In the case of nonwords, there is relatively little activation of semantic information, regardless of neighborhood size. The contrast between large and small neighborhood nonword items thus does not produce differential activation of semantic representations.

A different account is needed to explain the neighborhood size effects in the ventromedial prefrontal cortex and the posterior cingulate cortex. The posterior cingulate cortex showed higher activation levels for small neighborhood items compared to large neighborhood items whether these were words or nonwords, and also showed higher activation levels for words than nonwords. The ventromedial prefrontal cortex showed a similar pattern except that the neighborhood size manipulation produced no effect for words. Activation in these regions appears to be roughly inversely correlated with response time. That is, activation is lowest in the case of large neighborhood nonwords, which produced the longest response times, higher for small neighborhood nonwords, which produced somewhat faster responses, and higher still for words, which produced still faster responses. Indeed, the small difference in response time between large and small neighborhood words did not reach significance, a pattern mirrored in the much smaller neighborhood size effects seen in posterior cingulate and ventromedial prefrontal cortices with words. Why should brain activity in a region be inversely correlated with response time? One possibility is that these areas are “tonically active” during resting states and become relatively less active when the brain is engaged in an attentionally demanding task. Several prior studies have drawn attention to such “task-induced deactivation,” and ventromedial prefrontal and posterior cingulate cortices are among the most consistent areas to show this phenomenon (McKiernan, Kaufman, Kucera-Thompson, & Binder, 2003; Mazoyer et al., 2001; Raichle et al., 2001; Binder et al., 1999; Shulman et al., 1997). Thus, the pattern of activation in these two regions supports the idea that active processing of a stimulus can cause suspension of tonic activation in some brain regions, and that the magnitude of this deactivation is correlated with the amount of time spent on task-related processing (McKiernan et al., 2003).



The second issue concerning neighborhood size effects is why no effects were observed in the “expected” direction. If items with larger neighborhoods produce activation of a larger number of word codes, then why were there virtually no brain areas with higher levels of activation for large neighborhood items? One possibility is that there simply is no one-to-one relationship between unique word codes and specific neurons or groups of neurons in the brain. Our a priori hypothesis concerning the neighborhood size manipulation was based on a model portraying words as unique nodes, but this “localist” schema is not the only one possible. An alternative is that word representations are highly distributed, such that all lexical items are coded as different patterns of activity across the same population of neurons (Plaut et al., 1996; Hinton & Shallice, 1991; Seidenberg & McClelland, 1989). This scenario includes the possibility that activation of many “word codes” does not entail more neural activity than activation of fewer codes, but simply a different pattern of activity over a distributed network. If so, the neighborhood size manipulation used in the present experiment would not have had any effect on the global activation signal in this network. Rather, the activation differences we observed in the neighborhood size contrasts were due to other phenomena, such as differences in the level of semantic processing or differences in the level of activation of “tonically active” systems, and not to differences in the number of activated word codes.

### **Behavioral Measures as Predictors of Blood Oxygenation Level Dependent (BOLD) Signal**

A final point that seems worthy of note is that response time and accuracy were not related in any simple way to brain activation level as measured by BOLD signal. It is often assumed that task “difficulty” is a major predictor of brain metabolism, following the assumption that more difficult tasks require longer processing time and thus greater energy expenditures. Although this principle may apply in some task situations or in particular brain areas, we observed here robust activation differences that clearly argue against the generality of the principle. For example, the main finding consisted of stronger activation by words than by nonwords in a number of large brain areas, despite the fact that response time and error rate were greater in the nonword condition. Within many of these regions, there were also effects of the neighborhood size manipulation for the word conditions, despite the fact that this manipulation had no effect on behavioral performance for words. Other brain areas were more strongly activated by nonwords, potentially consistent with a “difficulty” effect, yet these areas showed no neighborhood effects in the nonword conditions, despite the fact that this manipulation had a strong effect on the speed and accuracy

of nonword processing. Thus, the main findings would not have been predicted from an examination of the behavioral data alone. The only regions in which activation appeared to be related to task difficulty were the posterior cingulate gyrus and the ventromedial frontal cortex, yet activation in these regions paradoxically “decreased” with increasing difficulty level (see preceding discussion). We are therefore led to question the validity of any general connection between behavioral measures of overall processing load and brain activation. Like many previous investigators, however, we found the performance data to be a useful indication of the underlying processing strategies adopted by our participants in solving the lexical decision problem.

### **Summary**

Visual word processing can involve activation of orthographic, phonologic, and semantic codes. This experiment incorporated nonwords that were orthographically and phonologically word-like, requiring subjects to access specific word information in order to respond correctly during lexical decision. A set of left hemisphere brain regions showed stronger activation by words than by nonwords during this task, suggesting a neural correlate for specific word identification. Activation in these regions was not enhanced by increasing the neighborhood size of word items, suggesting that the activation was not related to processing at a presemantic “word code” level. On the contrary, many of these regions showed stronger activation by words with no neighbors than by words with many neighbors. Because words with many neighbors can often be correctly classified on the basis of their orthographic code alone, the task makes a greater demand on semantic access when processing words with no neighbors. Thus, the pattern of results is consistent with the claim that this large-scale left hemisphere network is involved in processes underlying semantic access. This interpretation was supported by a review of six previous neuroimaging studies designed to isolate semantic processes, which revealed a strong convergence of results concordant with the present study. Key regions implicated by these studies include the left angular gyrus, the left dorsal prefrontal cortex, the left middle and inferior temporal gyri, and the left fusiform gyrus. Variability of activation of ventral temporal and ventromedial frontal cortices across studies may reflect variation in the semantic category, concreteness, and emotional valence of the test items used in different studies.

Increasing the number of word neighbors of an item did not produce enhanced activation in any brain regions. This finding is difficult to explain using models that employ localist word representations and assume that representations of the word neighbors of an item are

partially activated by the item itself. An alternative view is that word representations are distributed over a common population of neurons, allowing “neighbor” activations to be encoded in the pattern of activity, rather than the magnitude of activity, across the network.

## METHODS

### Stimuli

Stimuli were printed words and nonwords. A two-factor (Lexicality  $\times$  Neighborhood size) design was used. Orthographic frequency (OF) and neighborhood counts for these items were derived from the CELEX database (Baayen, Piepenbrock, & Gulikers, 1995). Word items consisted of 100 nouns. Half of these had at least five orthographic neighbors (HiWord), and half had no orthographic neighbors (LoWord). We define “neighbors” of an item as those entries in the CELEX dictionary that are exactly one letter different, by substitution only, from the item (Coltheart et al., 1977). HiWord and LoWord sets were matched on mean length and orthographic word frequency, but not on bigram frequency or phonologic neighborhood size (PNS), which are strongly linked to ONS (see Table 1 and Appendix 1). Nonword items consisted of 100 pronounceable pseudowords, half of which had at least five orthographic neighbors (HiNon) and half of which had no orthographic neighbors (LoNon). Nonwords were generated using a second-order (pairwise) Markov chaining procedure, followed by elimination of poorly pronounceable items. HiNon and LoNon sets were matched on mean length. The 100 words and 100 nonwords (collapsing across neighborhood size) were matched on length, mean positional bigram frequency (MPBF), ONS, and PNS.

### Pilot Study

Pilot testing was conducted to confirm that the neighborhood size manipulation would produce expected effects on response latency during lexical decision. Twenty-five healthy, right-handed undergraduates from the University of Windsor participated for partial course credit. The participants were instructed to “decide as quickly and accurately as possible” whether randomly presented single items were real English words. The items were presented one at a time on a computer screen, and subjects responded with key presses to the computer keyboard using the dominant hand for “yes” responses and the nondominant hand for “no” responses (using the “?” and “z” keys). The order of presentation was randomized across item conditions. In every trial a 50-msec blank screen was followed by a 250-msec fixation cross that appeared at the center of the computer display. Following the fixation cross, the item appeared and remained on the screen until a response was made. Response times and error rates

from each participant were submitted to two-factor ANOVA for the item analyses ( $F_1$ ) and for the subject analyses ( $F_2$ ).

Response times less than 200 msec or more than 3000 msec were removed from the response latency data. A total of 55 observations (1.1% of the data) were removed by this procedure. The overall error rate was 8.7%, and the overall response time was 841 msec. Means for each condition are given in Table 1 and depicted graphically in Figure 1. Analysis of the response time data showed a main effect of lexicality in both the item analysis,  $F_1(1,196) = 47.22, p < .001$ , and the subject analysis,  $F_2(1,24) = 19.83, p < .001$ , due to faster responses for words. There was no main effect of neighborhood size in the item analysis,  $F_1(1,196) = 0.96, p > .1$ , but there was in the subject analysis,  $F_2(1,24) = 7.27, p < .05$ , due to faster responses for items with no neighbors. These effects were qualified by a Lexicality  $\times$  Neighborhood size interaction in both the item analysis,  $F_1(1,196) = 13.32, p < .001$ , and the subject analysis,  $F_2(1,24) = 21.95, p < .001$ . As shown in Figure 1, the interaction is due to large inhibitory effects of neighborhood size on nonword response time but slightly facilitatory effects on word responses. These effects were investigated using planned-comparison Bonferroni/Dunn tests, which confirmed a difference between HiNon and LoNon items (corrected  $p < .001$ ). The difference between HiWord and LoWord items showed a trend toward significance ( $p = .06$ ).

Analysis of the error rate data showed no main effect of lexicality,  $F_1(1,196)$  and  $F_2(1,24)$  both less than 1. There was a main effect of neighborhood size on error rate in both the item analysis,  $F_1(1,196) = 5.80, p < .05$ , and the subject analysis,  $F_2(1,24) = 8.02, p < .01$ , due to lower error rates for items with no neighbors. These effects were qualified by a Lexicality  $\times$  Neighborhood size interaction in both the item analysis,  $F_1(1,196) = 15.02, p < .001$ , and the subject analysis,  $F_2(1,24) = 20.07, p < .001$ . As with the response time data, the interaction is due to large inhibitory effects of neighborhood size on nonword accuracy but slightly facilitatory effects on word accuracy. Planned comparisons confirmed a difference between HiNon and LoNon items (corrected  $p < .001$ ). The difference between HiWord and LoWord items was not significant ( $p > .1$ ).

To summarize these effects, words are responded to more quickly than nonwords, and the neighborhood size manipulation interacts with the lexicality manipulation such that increases in neighborhood size are inhibitory for nonwords but weakly facilitatory for words. These results are consistent with many previous studies of lexical decision (Grainger & Jacobs, 1996; Andrews, 1989; Coltheart et al., 1977). As discussed above, the relatively weak facilitatory effect of neighborhood size on word processing is likely due to the use of very word-like nonwords (Grainger & Jacobs, 1996).

## fMRI Study

### *Subjects*

Participants in the fMRI study were 24 healthy, right-handed volunteers (15 women) with no history of neurologic disease or neurologic symptoms. All spoke English as a first language. The mean age was 25.2 years (range 18–49), mean handedness laterality quotient on a modified version of the Edinburgh inventory (Oldfield, 1971) was 86.2 (range 62–100), and mean duration of formal education was 15.7 years (range 12–24). All subjects signed a written informed consent approved by the Medical College of Wisconsin Institutional Review Board. Subjects were paid a small hourly stipend for participating.

### *Task Procedures*

Stimuli in the fMRI task were computer generated using PsyScope software (Cohen, MacWhinney, Flatt, & Provost, 1993), which also recorded accuracy and response time data. A liquid crystal display projector was used to rear-project the stimuli onto a screen located near the subject's feet, which subjects viewed through prism lenses. Stimuli were presented in white lowercase Geneva font on a black background and subtended an average horizontal visual angle of 3°.

The four stimulus types—HiWord, LoWord, HiNon, and LoNon—were presented in random order for lexical decision. A fixation cross appeared in the center of the screen between trials, and subjects were asked to fixate this stimulus when it was present. Trials began with disappearance of the fixation cross and presentation of the stimulus for 1000 msec, followed by reappearance of the fixation cross. Interstimulus intervals could be 2, 4, 6, or 8 sec. Timing of trials was precisely controlled by triggering each trial with an external pulse generator that provided pulses at 1-sec intervals with microsecond accuracy. Responses were made by operating a keypad with the left hand, pressing one key to indicate “word” and another to indicate “nonword.” After the subject was positioned in the scanner, instructions and 12 practice trials were given prior to scanning. Because of the relatively high error rates obtained in the pilot study, instructions were adopted that placed greater emphasis on accuracy. Subjects were instructed to “respond as quickly as possible without making errors.” No subject missed more than one item on the practice trials.

### *MRI Acquisition*

MRI data were acquired on a GE Signa 1.5 Tesla scanner (GE Medical Systems, Milwaukee, WI) using a three-axis, whole-head, local gradient coil with a built-in transmit–receive RF coil (Medical Advances, Milwaukee, WI). High-resolution, T1-weighted anatomic reference images were acquired as a set of 124 contiguous sagittal

slices ( $0.9375 \times 0.9375 \times 1.2$  mm) using a spoiled gradient-echo sequence (“SPGR,” GE Medical Systems). Functional imaging used a gradient-echo echo-planar sequence with the following parameters: 40 msec echo time, 2 sec repetition time, 24 cm field of view,  $64 \times 64$  pixel matrix, in-plane voxel dimensions  $3.75 \times 3.75$  mm, and 19 contiguous sagittal slice locations covering the entire brain. Slice thickness was either 7 or 7.5 mm depending on brain width. Four sets of time-series echo-planar imaging runs were acquired, each composed of 136 whole-brain image volumes collected at 2-sec intervals. Lexical decision trials began at 16 sec into each run and continued throughout.

### *fMRI Data Analysis*

All image analysis was done with the AFNI software package (available at <http://afni.nimh.nih.gov/afni>) (Cox, 1996). Motion artifacts were minimized by within-subject registration of all raw echo-planar image volumes to the first steady-state volume (fifth volume in the first run). Estimates of the three translation and three rotation movements at each point in each time-series were computed during registration and saved. The first four images of each series, during which spin relaxation reaches an equilibrium state, were discarded, and the mean and linear trends across time were removed on a voxel-wise basis from the remaining 132 image volumes of each series.

Deconvolution analysis of the combined image time-series (528 volumes) in each subject was performed using the “3dDeconvolve” module of AFNI. Hemodynamic impulse response functions were estimated at six 2-sec time lags (0–12 sec) after stimulus presentation for each of the four stimulus conditions (HiWord, LoWord, HiNon, and LoNon). These estimates produced magnitude, variance, and *t*-statistic parameters (relative to the interstimulus interval baseline) at each time lag, which were used to perform contrasts between conditions under a general linear model. Translation and rotation movement parameters estimated during image registration were included in the deconvolution model to remove residual variance associated with motion-related changes in voxel signal. Trials on which error responses occurred were treated as a separate condition and did not contribute to the impulse response function estimates for the four main conditions.

Contrasts were performed at the subject level to identify differences in hemodynamic response magnitude between words and nonwords ([HiWord + LoWord] – [HiNon + LoNon]), differences between stimuli with many versus no orthographic neighbors ([HiWord + HiNon] – [LoWord + LoNon]), and interactions between lexicality and neighborhood size ([HiWord – LoWord] – [HiNon – LoNon]). The resulting statistical parametric maps of *t*-deviates were linearly resampled in standard stereotaxic space to a voxel size of  $1 \text{ mm}^3$  and spatially

smoothed with a 4-mm root-mean-square (5.4-mm full width half maximum) Gaussian kernel to compensate for intersubject variance in anatomic structure. The smoothed maps for each contrast were then averaged across subjects to generate group maps. Probability values associated with these average *t*-deviates were estimated by repeating the entire analysis after randomly reassigning trials to the four conditions. Fifty such randomization analyses were performed, and the probability density function of average *t*-deviates produced by combining these analyses was used to estimate the likelihood of a given value occurring by chance. Group maps were then thresholded at a voxel-wise, uncorrected, two-tailed probability of  $p < .01$  ( $|\text{average } t\text{-deviate}| \geq 0.36$ ). Monte Carlo simulation with the “AlphaSim” module of AFNI was then used to estimate the chance probability of spatially contiguous clusters of voxels passing this threshold. Clusters smaller than 300 voxels in the group maps were removed, resulting in a corrected two-tailed probability threshold of  $p < .05$  for each group map.

## APPENDIX 1

The following is a brief description of how the stimulus measures were computed. All measures are based on a dictionary derived from the CELEX database. For words, all are available online at <http://www.wordmine.org>, where further details are also provided.

**Orthographic frequency (OF):** The OF of the item per million words of text. This was computed by summing the OFs of all entries for the word form in the word-form dictionary. Thus, for example, the OF of the word “walk” reflects the sum of the respective frequencies of two entries with that orthography: one for the noun and one for the verb.

**Mean positional bigram frequency (MPBF):** MPBF is the product of the controlled bigram neighborhood sum (CONBG-SUM) and the mean controlled bigram neighborhood frequency (CONBG-NFREQ), divided by the number of bigrams in the item. CONBG-SUM is a count of the number of words in the dictionary that are of the same length as the item and that contain an overlapping bigram in the same position as the item (these are the “controlled bigram neighbors” of the item). For example, CAN is a controlled bigram neighbor of CAT because it is of the same length and contains CA in the same position as CAT. Words of the same length that have overlapping bigrams with the target word in more than one position are counted once for each overlapping bigram. CONBG-NFREQ is the mean OF of all the controlled bigram neighbors of the item. MPBF thus expresses how often, on average, one would encounter a given bigram from the item, in exactly the same position in which it occurs in the item, if one read one million words of text.

**Orthographic neighborhood size (ONS):** The total number of entries in the dictionary that are exactly one letter different, by substitution only, from the target item. This measure (also known as Coltheart’s *N*) collapses entries that appear more than once in the dictionary, and excludes the item itself. For example, the orthographic neighbors of the word “talk” includes only a single entry for “walk,” though there are two entries for the word in the dictionary: one for the noun, and one for the verb.

**Phonologic neighborhood size (PNS):** The total number of entries in the dictionary that are exactly one phoneme differ-

ent, by substitution only, from the target item. Like ONS, this measure collapses entries that appear more than once in the dictionary, and excludes the item itself.

## APPENDIX 2

List of the stimuli.

<i>HiWord</i>	<i>LoWord</i>	<i>HiNon</i>	<i>LoNon</i>
banker	addict	barls	abink
boxing	algae	blace	absen
braces	aroma	bling	addig
brake	arrow	bolly	adift
bully	atlas	brack	adook
chick	attic	burge	balum
couch	banjo	chals	buraf
crane	bugle	cleck	burim
dancer	buyer	clight	butrit
ditch	cactus	conds	buzza
diver	chalk	coose	cafid
fiddle	chisel	couse	calake
grape	cocoon	crade	calip
greed	crayon	crose	convy
grove	crumb	dender	drion
hanger	denim	dorse	dwarce
hound	donor	fints	eaket
latch	eagle	frick	eakete
lather	fungi	fross	entle
lease	geese	haming	ettle
lever	havoc	hanter	fulpt
litter	icing	hults	golarm
miner	magnet	mangs	grolke
mints	maple	mards	guend
moose	ozone	minge	hamink
mower	pecan	mobble	holak
noose	photo	pards	ickle
paste	pizza	plack	ildin
peach	plasma	pland	incon
puddle	raisin	pluts	inize
riddle	razor	poose	lockle
rocket	rodent	scake	nuced
scout	scuba	scall	nylia
shack	stereo	sellow	obley
shave	syrup	shing	ockel

siding	theft	shink	ockey
singer	trophy	shint	pepra
slacks	tulip	sline	perna
sling	twist	slint	plury
snack	typist	solts	porak
spade	ulcer	sping	prefl
spice	venom	spint	respy
spike	virus	stabes	salub
spool	vodka	stard	scrok
stack	wagon	steet	sigag
stalk	walrus	stook	sinan
stall	width	twing	splur
strap	yacht	vicks	taxop
swabs	zebra	vords	unimp
wager	zenith	woose	urtle

## Acknowledgments

This research was supported by National Institute of Neurological Diseases and Stroke grant R01 NS33576, National Institute of Mental Health grant P01 MH51358, and National Institutes of Health General Clinical Research Center grant M01 RR00058. Pilot studies were funded by the Natural Science and Engineering Research Council of Canada. We thank T. Prieto, B. D. Ward, A. Moths, and D. Sabsevitz for technical assistance.

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The data reported in this experiment have been deposited in The fMRI Data Center (<http://www.fmridc.org>). The accession number is 2-2002-11385.

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