

An Event-Related fMRI Investigation of Implicit Semantic Priming

Jesse Rissman¹, James C. Eliassen, and Sheila E. Blumstein

Abstract

■ The neural basis underlying implicit semantic priming was investigated using event-related fMRI. Prime-target pairs were presented auditorily for lexical decision (LD) on the target stimulus, which was either semantically related or unrelated to the prime, or was a nonword. A tone task was also administered as a control. Behaviorally, all participants demonstrated semantic priming in the LD task. fMRI results showed that for all three conditions of the LD task, activation was seen in the superior temporal gyrus (STG), the middle temporal gyrus (MTG), and the inferior parietal lobe, with greater activation in the unrelated and nonword conditions than in the related condition. Direct comparisons of the

related and unrelated conditions revealed foci in the left STG, left precentral gyrus, left and right MTGs, and right caudate, exhibiting significantly lower activation levels in the related condition. The reduced activity in the temporal lobe suggests that the perception of the prime word activates a lexical-semantic network that shares common elements with the target word, and, thus, the target can be recognized with enhanced neural efficiency. The frontal lobe reductions most likely reflect the increased efficiency in monitoring the activation of lexical representations in the temporal lobe, making a decision, and planning the appropriate motor response. ■

INTRODUCTION

The lexical processing system is a critical component of language. It provides the means by which arbitrary symbols convey meaning, and it provides a framework for the organization of the lexical-semantic system. A great deal of recent neuroimaging research has focused on the neural systems underlying processing of word meaning. Although it has been shown that posterior brain structures, including the superior temporal gyrus (STG) and middle temporal gyrus (MTG) are involved in lexical-semantic processing (Price, Moore, Humphreys, & Wise, 1997; Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996; Demonet et al., 1992; Wise et al., 1991), considerable attention has been focused on anterior brain structures and, in particular, the inferior frontal gyrus in such processing (Roskies, Fiez, Balota, Raichle, & Petersen, 2001; Wagner, Pare-Blagoev, Clark, & Poldrack, 2001; Poldrack et al., 1999; Gabrieli, Poldrack, & Desmond, 1998; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997; Petersen, Fox, Posner, Mintun, & Raichle, 1988). It has been suggested that while long-term conceptual knowledge may be represented in the lateral temporal cortices, it is the frontal regions that are involved in the retrieval, selection, and recovery of word meaning.

In those studies focusing on the role of the inferior frontal gyrus in semantic processing, the experimental

tasks have required the participants to make an overt decision about the semantics of the lexical entry. They either have to compare the meanings of words and make a decision about that comparison (Spitzer et al., 1996), categorize a word in terms of a semantic attribute (Binder et al., 1997; Gabrieli et al., 1996; Kapur et al., 1994; Demonet et al., 1992), or generate a word given another according to some semantic or lexical feature (Frith, Friston, Liddle, & Frackowiak, 1991; Petersen et al., 1988). What is less clear is whether the lexical processing system relies so heavily on the inferior frontal gyrus when subjects do not have to explicitly make a semantic decision about a lexical entry, but where there is nonetheless a semantic relationship between lexical items. It is one of the goals of the current research to explore this question.

In both the normal and aphasia literature, there has been a great deal of research exploring the nature of lexical processing by investigating implicit access to semantic information. One of the paradigms used is a lexical decision (LD) semantic priming paradigm. In this task, subjects are required to make a LD to a target stimulus. Normal subjects display semantic priming in a LD task. That is, they show faster LD latencies when a target word is preceded by a semantically or associatively related word than when it is preceded by a semantically unrelated word or a nonword. These results are consistent with the view that the presentation of a word influences the activation of that word's representation, as well as its lexical-semantic network. Thus, a prime word like "cat,"

Brown University

will not only activate the lexical representation for “cat,” but it will also partially activate its lexical–semantic network, including “dog.” It has been hypothesized that it is this partial activation of the semantically related word that accounts for the shorter reaction time (RT) latencies in the LD task.

Results of a series of studies with aphasic patients exploring lexical processing suggest that, contrary to the classical lesion models, the lexical processing system is a distributed network including both posterior brain structures (temporal and parietal) and anterior brain structures (inferior frontal gyrus). Although both Broca’s and Wernicke’s aphasics show semantic priming in a LD task (Blumstein, Milberg, & Shrier, 1982; Milberg & Blumstein, 1981), they show “pathological” patterns of semantic priming when the prime stimuli are phonologically or phonetically altered (Utman, Blumstein, & Sullivan, 2001; Milberg, Blumstein, & Dworetzky, 1988b), or when they are semantically ambiguous (Milberg, Blumstein & Dworetzky, 1987). Of importance, these patterns suggest that both Broca’s and Wernicke’s aphasics have deficits that lie in the processes of lexical activation, but that the nature of the deficit for these two groups of patients is different (see Blumstein & Milberg, 2000). Taken together, lesion-based studies suggest that both anterior and posterior brain structures contribute to lexical–semantic processing, but in different ways.

Several neuroimaging investigations have explored the neural systems underlying lexical processing using the LD semantic priming paradigm. These studies have investigated two processes contributing to semantic priming: one, automatic processing, which is thought to reflect implicit access to semantic information, and the other, controlled processing, which is thought to reflect voluntary or strategic access to semantic information. To investigate this issue, stimulus parameters were manipulated that in behavioral studies appear to contribute differentially to these two processes. These parameters include the proportion of related prime–target pairs (Mummary, Shallice, & Price, 1999) and the interstimulus interval (ISI) between the prime and target (Rossell, Bullmore, Williams, & David, 2001). Controlled processes are thought to be invoked when there is a high proportion of related prime–target pairs or when there are longer time intervals between prime–target pairs. In either case, participants appear to more likely use strategies in “guessing” the target given the prime. Mummary et al.’s PET study showed a decrease in anterior temporal lobe activation (BA 38) as the proportion of related words increased (except in the highest proportion condition when activation increased) and a decrease in the activation of the anterior cingulate with increased proportion of related prime–target pairs. Rossell et al. showed some differences in the activation patterns of long and short SOAs affecting particularly bilateral MTG (BA 21/38), the putamen and hippocampus (BA 35), and the right supramarginal

gyrus (BA 40). Nonetheless, because these studies used a block design, neither study was able to directly investigate whether there were differences in the neural activation of semantically related prime–target pairs and semantically unrelated prime–target pairs.

The current study will examine the neural correlates underlying implicit lexical–semantic processing. To this end, we will use event-related fMRI to investigate semantic priming in an auditory LD task. We will compare the activation patterns and time course of activation of real word targets that are semantically related or semantically unrelated to the real word prime, as well as to nonword targets preceded by a real word prime. We will explore the processes involved in implicit lexical–semantic access by having a short ISI between prime–target pairs (50 msec) and by having a relatively low proportion of semantically related prime–target pairs (25%). These parameters make it difficult for subjects to benefit from the use of strategies (e.g., explicitly generating an expectancy set), increasing the likelihood that any facilitation of related targets will reflect automatic processing. In addition, we will compare the activation patterns of the LD task to a tone task, which includes auditory and motor response components absent of any lexical–semantic processing.

We hypothesize that the related, unrelated, and nonword prime–target pairs will activate similar neural structures, because all three conditions require the same underlying processing mechanisms. However, we expect that small differences will emerge when the activation patterns of semantically related and unrelated word pairs are directly contrasted, reflecting the neural correlates of the behavioral priming effect. Because the subject is not required to overtly retrieve or analyze the semantic content of the stimuli, we do not anticipate that this task will strongly engage the frontal lobes. We will also test whether there will be differences in activation when pairs with real word targets are compared with nonword targets, although any such effect will necessarily be tempered by the fact that in both cases the target is immediately preceded by a real word prime. We expect that nonword and real word targets will activate similar neural structures although some areas may show a greater magnitude of activation for word targets given that unlike nonwords they lexically match a stored phonological representation and they have semantic content. By contrasting the LD task with a simple tone task, we will be better able to determine the brain areas involved in lexical–semantic processing while controlling for lower-level auditory and motor response components of the LD task.

RESULTS

Behavioral Results

Behavioral results, including RT latencies and performance accuracy, are shown in Table 1. Only correct

Table 1. Mean RT in Milliseconds and Mean Accuracy with Standard Deviations (*SD*) for the LD Task (*N* = 15)

	<i>Related</i>	<i>Unrelated</i>	<i>Nonword</i>
Mean RT	890	1051	1139
<i>SD</i>	137	116	201
% Correct	97	89	81
<i>SD</i>	3.7	6.6	10.1

responses were included in the RT analysis. Each of the 15 participants exhibited semantic priming, that is, faster RTs to semantically related targets than unrelated targets. Both the RT and accuracy measures were submitted to a one-way repeated-measures analysis of variance (ANOVA) with the only factor being stimulus condition (related vs. unrelated vs. nonword). The ANOVA on the RT data revealed a significant effect of stimulus condition, $F(2,28) = 33.6, p < .0001$. Post hoc pairwise comparisons showed that each stimulus condition was significantly different from all others. The ANOVA on the accuracy data also revealed a significant effect of stimulus condition, $F(2,28) = 32.2, p < .0001$. Similar to the RT data, post hoc tests showed all means to be significantly different from each other.

fMRI Results

Figure 1 provides an assessment of the activation patterns that emerged across the three conditions of the LD task, as well as the tone task. These maps represent mean unscaled fit coefficients indicating the goodness of the least-squares fit of the measured fMRI signal data to the reference waveform of each stimulus condition (cf. Harrington et al., 2000). Active voxels at a significance level of $p < .0001$ are shown. Inspection of these statistical maps allows for a qualitative assessment of the similarities and differences between the conditions. In all three conditions of the LD task, activation emerged in the STG, the MTG, and the inferior parietal lobe. The LD con-

ditions elicited substantial activation of the STG bilaterally in contrast to the tone task that showed more focal activation. Although the anterior-to-posterior extent of this activation was similar across the LD conditions, activation was noticeably broader in the unrelated and nonword conditions compared to the related condition. In addition to the STG, a posterior MTG region was activated in both the related and unrelated conditions, but not in the nonword condition. Similar to the findings for the STG, the extent of MTG activation was greater in the unrelated than in the related condition. The pattern of activation in the MTG appeared to be different in the two hemispheres. In the left hemisphere, activation of the MTG was clearly differentiated from the STG activation, whereas in the right hemisphere, there was continuous extension of the STG activation into the MTG. For all conditions of the LD task, there was activation of the left inferior parietal lobule. Finally, at the threshold level of $p < .0001$, only the unrelated and nonword conditions showed activation in the left precentral gyrus.

Statistical Comparisons of Experimental Conditions

A summary of the results of the analysis of variance showing those regions in which significant differences emerged between conditions based on a corrected significance of $p < .05$ are summarized in Table 2.

Unrelated Greater than Related

There were five statistically significant clusters that emerged in which there was greater activation in the unrelated condition compared to the related condition (see the top panel of Figure 2). These areas included the left STG, the left precentral gyrus, the middle frontal gyrus bilaterally, and the right caudate. No clusters were found to show significantly greater activation for semantically related pairs compared to unrelated pairs.

Figure 1. Statistical activation maps for the four stimulus conditions (semantically related word pairs, unrelated word pairs, pairs with nonword targets, and tone control pairs). Active voxels are significant to $p < .0001$, and their color intensity represents the relative magnitude of the fit coefficients.

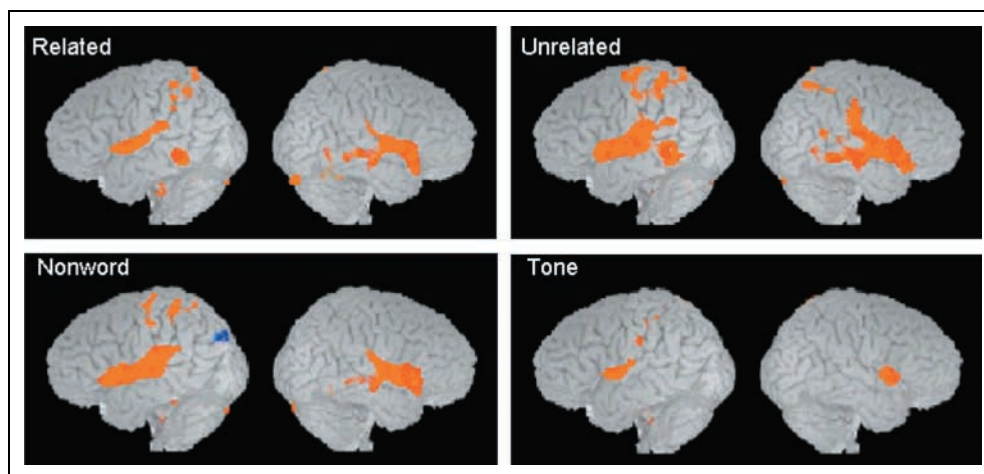


Table 2. Regions Exhibiting Significant Differences in BOLD Signal Intensity between Conditions

<i>Region</i>	<i>BA</i>	<i>x</i>	<i>y</i>	<i>z</i>	<i>Number of Voxels</i>	<i>Max t Value</i>
<i>Unrelated>Related</i>						
L superior temporal gyrus	21/22	-57	-12	-1	47	3.29
L precentral gyrus	6	-31	-11	62	52	4.29
L middle frontal gyrus	46/9	-45	22	35	57	3.46
R middle frontal gyrus	46/9	36	15	22	42	4.43
R caudate	-	4	3	11	124	4.50
<i>Words>Nonwords</i>						
L middle temporal gyrus	21/37	-61	-44	-7	111	6.44
L anterior cingulate	32/10	-2	48	5	134	3.48
L precuneus	7	-3	-57	42	43	2.84
L angular gyrus	39	-34	-66	34	340	4.25
R angular gyrus	39	47	-63	30	111	3.31
<i>LD>Tones</i>						
L superior temporal gyrus	22	-58	-24	5	200	5.79
L superior temporal gyrus	38	-35	11	-19	50	4.65
L cerebellum/fusiform gyrus	37	-31	-62	-27	376	5.71
L cerebellum (culmen)	-	-7	-53	-5	55	4.07
L claustrum/insula	-	-24	23	14	80	4.99
L lentiform nucleus/putamen	-	-23	-4	-6	75	4.86
R superior temporal gyrus	22	53	31	5	157	5.14
R cerebellum (declive)	-	21	-67	-17	74	5.58
R parahippocampal gyrus	-	21	-17	-7	59	4.09
<i>Incorrect>Correct</i>						
L inferior frontal gyrus	44/45	-45	17	10	669	6.82
L superior frontal gyrus	9	-30	48	27	62	3.99
L cingulate gyrus	32	-1	22	41	554	7.53
L cerebellum (culmen)	-	-38	-49	-28	95	4.01
L cerebellum	-	-25	70	-38	54	5.10
R inferior frontal gyrus	44/45	44	16	16	476	6.53
R middle frontal gyrus	46/10	43	47	7	58	3.67
R superior frontal gyrus	10	17	62	-2	58	3.26

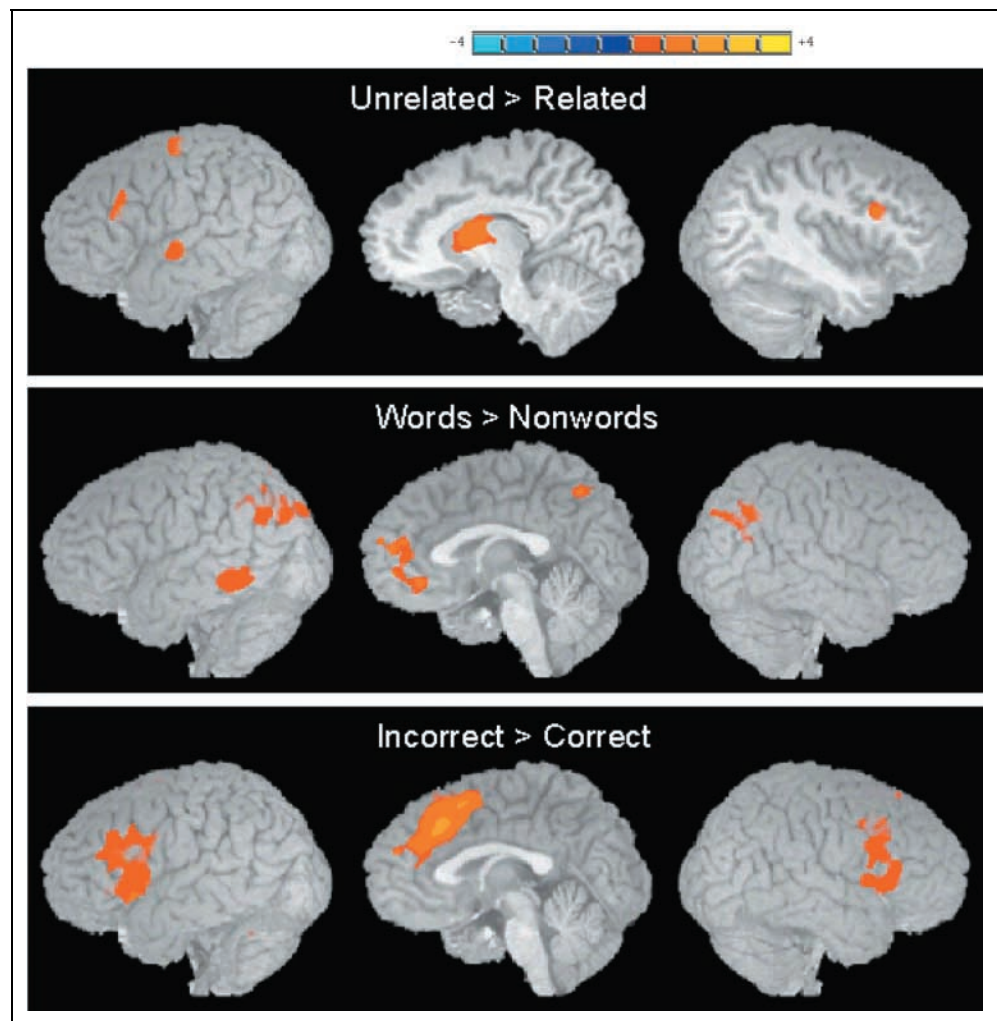
Stereotaxic coordinates are given according to Talairach and Tournoux's atlas space and refer to the center of mass of each cluster. The max *t* value corresponds to the voxel exhibiting the highest significance level for that cluster.

Words Greater than Nonwords

Five statistically significant clusters that showed greater activation for stimulus pairs with word targets than for

stimulus pairs with nonword targets were identified. These are shown in the center panel of Figure 2. These regions include the left MTG, left anterior cingulate, and left precuneus. There was also greater activation

Figure 2. Regions demonstrating significant differences in activation level for three contrasts of interest. Only those clusters visible at the cortical surface or perisagittal ($x = 0$) section are shown, with the exception of the Unrelated > Related comparison (top panel), which shows the right caudate cluster at $x = 10$ and the right MFG cluster at $x = 40$.



for words than nonwords in the angular gyrus bilaterally, but this was due to negatively correlated activation (deactivation) for the nonwords. This finding of deactivation in the left angular gyrus can be seen in Figure 1. No clusters that showed greater activation for nonwords than for words were found. Two additional analyses comparing the real word conditions (related and unrelated) separately to those of the nonwords were conducted. Results paralleled the findings of the word-nonword analysis, with significant differences emerging in the five clusters described above. No other significant effects emerged.

Lexical Decision Greater than Tones

The comparison of LD task to the tone task revealed much greater activation for LD across a multitude of brain regions as shown in Table 2. Large clusters emerged for the LD task in the STGs bilaterally with a larger number of voxels activated on the left than on the right. The LD task also showed more activation than the tone task in bilateral cerebellar and subcortical structures. No regions showed more activation for tones than for LD.

Incorrect Greater than Correct

Analysis of incorrect responses in comparison to correct responses revealed greater activation, as well as substantially larger cluster sizes in bilateral prefrontal cortical regions and the anterior cingulate gyrus (BA 32). Also, smaller regions in the left cerebellum showed more activation for incorrect responses.

The analysis comparing incorrect and correct responses was limited to only those regions that showed greater activation for incorrect responses than for correct responses. There were, in fact, several areas where there was greater activation for correct than incorrect responses, but consideration of this finding is beyond the scope of this investigation.

Time Course of the Hemodynamic Response

In order to investigate in more detail the nature of the difference between the related and unrelated conditions, we explored the time course of the hemodynamic response functions in those cortical regions that showed statistical differences between the two conditions (see

Figure 3. The time course of the average hemodynamic response function for the related and unrelated conditions in regions exhibiting a significant activation difference between these two conditions. Each data point represents the percent change of the fMRI signal from baseline averaged across all of the voxels in the cluster and across 15 participants. Error bars indicate standard error.

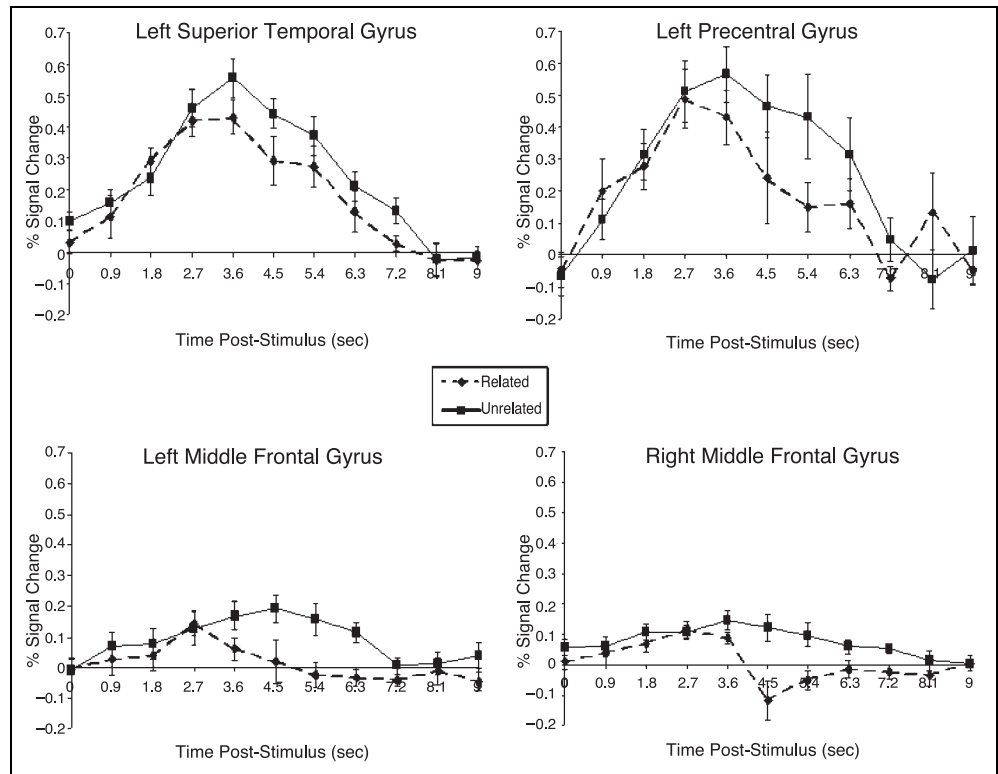


Figure 3). These regions included the left STG, the left precentral gyrus, and the middle frontal gyrus bilaterally. Each of the areas showed a significantly higher peak of activation in the unrelated condition than in the related condition. As Figure 3 shows, in the left STG cluster, although the peak activation level was reached at the same time point in the two conditions, the related condition approaches its maximum level earlier, plateaus, and then tapers off, maintaining a lower activation level than the unrelated until it reaches baseline. The left precentral cluster showed both a later and higher peak for the unrelated condition, as well as a slower rate of decay. The two frontal clusters showed relatively weak activation as indexed by their low percent signal change. In these clusters, the related condition reached its peak earlier and returned to the baseline earlier than did the unrelated condition, which showed a broader hemodynamic response.

Although we found a significant cluster in the left MFG differentiating the unrelated and related conditions that bordered on the IFG, we did not show significant differences between the two conditions in the left IFG *per se*. Nonetheless, because of the focus of the IFG in semantic tasks reported in the literature, we decided to investigate its hemodynamic time course to see if it exhibited any evidence of semantic priming effects. To that end, we selected the left IFG (BA 44–45) as defined in the TT atlas data set from AFNI (Lancaster et al., 2000). The results can be seen in Figure 4. As the graph shows, the hemodynamic response functions for the related and

unrelated conditions in the left IFG follow a similar time course as that observed in the left and right middle frontal gyri. In particular, these frontal regions all have relatively weak activation in both the related and unrelated conditions, as indexed by their low percent signal change. However, the unrelated condition did show more activation than the related condition, peaking higher and later and returning to the baseline more gradually than the related condition.

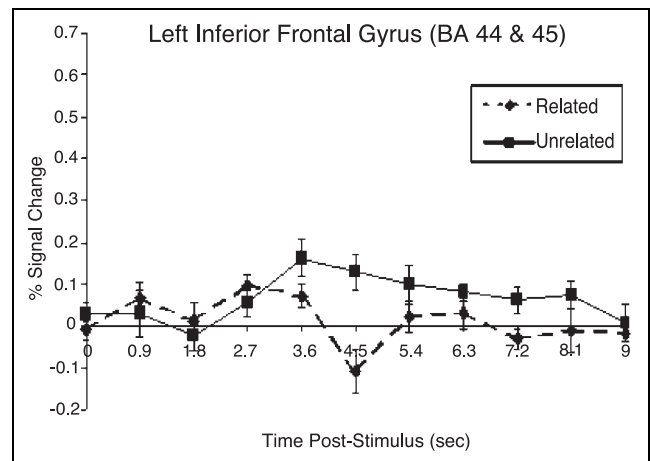


Figure 4. The time course of the average hemodynamic response function for the related and unrelated conditions in the left inferior gyrus (BA 44 and 45). Each data point represents the percent change of the fMRI signal from baseline averaged across all of the voxels in the cluster and across 15 participants. Error bars indicate standard error.

DISCUSSION

The results of this study suggest that the neural correlates underlying semantic priming involve a distributed system including both anterior and posterior brain structures. As the activation maps for the related, unrelated, and nonword conditions show, similar neural systems appear to be activated across these conditions with differences emerging in the extent and magnitude of activation rather than in the areas of activation.

Behavioral Findings

The behavioral results replicated the pattern of results in the lexical processing literature showing semantic priming in a LD task. Namely, participants showed faster RT latencies to real word targets when they were preceded by semantically related words than when they were preceded by semantically unrelated words. Moreover, there were fewer errors in the related than in the unrelated condition. Finally, the nonword targets showed the slowest RT latencies and the greatest number of errors.

Comparison of Lexical Decision and Tone Tasks

The comparison of the activation patterns for LDs (including the related, unrelated, and nonword conditions of the LD task) and tones showed a number of important differences. Despite the fact that the cognitive demands of the two tasks were different, they had certain features that were similar. Both tasks involved auditory input of a pair of stimuli that had similar duration and presentation parameters, and both tasks involved a motor response requiring the pressing of one of the two response buttons. As the results showed, the activation map of the tones was more narrowly focused, activating fairly focal regions of the primary and secondary auditory cortices of the STG bilaterally. In contrast, the activation map of the LD task showed a broad network encompassing the STG and MTG, the angular gyrus, and subcortical and cerebellar structures. Statistically reliable differences between the two tasks emerged in the STG bilaterally (with a larger group of activated voxels on the left than the right), the left claustrum/insula and lentiform nucleus/putamen, the right parahippocampal gyrus, and bilateral cerebellar structures (Table 2).

Semantic Priming: Related, Unrelated, and Nonword Conditions

The activation maps of the three conditions (related, unrelated, and nonword) in the LD task showed greater activation in the unrelated and nonword conditions

compared to the related condition. Results of both the cluster analysis and the assessment of the hemodynamic time course confirmed this observation. In particular, there was greater activation in the unrelated condition compared to the related condition in the left STG, the left precentral gyrus, the middle frontal gyrus bilaterally, and the right caudate. As the time course graphs showed (Figure 3), the unrelated condition peaked later and at a greater magnitude than the related condition, and it also decayed slower. Of interest, neurophysiological findings are consistent with these neuroimaging results. In particular, using a LD paradigm, semantically unrelated words elicited a significantly larger N400 than semantically related words (Bentin, McCarthy, & Wood, 1985; cf. Kutas & Van Petten, 1994). Additionally, while it is not possible to localize the exact neural source of the electrode sites, the locus of this effect was predominantly over posterior scalp locations.

At first blush, it might seem counterintuitive to find less activation for semantically related words than for unrelated words. After all, one might expect to see more activation as the system is being more “selective.” However, these results are compatible both with hypotheses about the functional architecture of the lexical processing system, as well as with recent neuroimaging results showing reductions in activation under conditions of repetition priming. In particular, current models of lexical access propose that the presentation of a word activates not only the lexical representation of the word candidate but also its lexical–semantic network. Hence, when the first word is presented, a set of semantic features is automatically activated, and the neural representations of semantically or associatively related lexical entries also become weakly activated. When the second word is presented, the decision of its lexicality can be executed with greater neural efficiency, because it requires less neural activity for its representation to be activated above the recognition threshold.

The reduction in activation for semantically related versus unrelated word pairs appears to be analogous to the findings of reduced activation under conditions of repetition priming. Results of a series of studies involving both perceptual and conceptual priming have shown that the previous presentation of a stimulus results in decreases in activation in neural areas related to the task requirements (for reviews, see Schacter & Buckner, 1998, and Buckner et al., 1995; Buckner et al., 1998; Raichle et al., 1994). These findings emerge in different modalities (Buckner, Koutstaal, Schacter, & Rosen, 2000), with single or repeated presentations (Demb et al., 1995), with items that are perceptually different exemplar across repetitions (Koutstaal et al., 2001), and appear to be both task and process specific (Wagner, Koutstaal, Maril, Schacter, & Buckner, 2000; Demb et al., 1995). Similar to studies of repetition priming, the current study showed priming-induced reductions in activation in anterior and posterior brain

regions (Buckner et al., 2000; Thompson-Schill, D'Esposito, & Kan, 1999). Nonetheless, in contrast to these studies of repetition priming, the current study showed a reduction in activation under conditions of semantic relatedness in the absence of stimulus repetition. These semantically related stimulus pairs differed in both their sound shape and their meaning, for instance, "trapeze-circus".

As shown in a number of earlier neuroimaging studies of word reading (Herbster, Mintun, Nebes, & Becker, 1997; Price, Wise, & Frackowiak, 1996; Fiez, Balota, Raichle, & Petersen, 1995), nonwords, also called pseudowords, activate a similar neural system as real words. In the current study, we observed a similar phenomenon with stimuli presented in the auditory modality. The fact that many brain regions respond similarly to real and nonword stimuli is consistent with behavioral studies of lexical processing demonstrating that nonwords do indeed activate the lexicon. In particular, nonword stimuli such as "gat" and "wat" prime "dog," although to a lesser extent than "cat" (Milberg, Blumstein, & Dworatzky, 1988a; cf. also Connine, Titone, Deelman, & Blasko, 1997). These results suggest that activation of the lexicon is graded and that the degree of activation is influenced by the phonological distance of a nonword stimulus to a lexical entry. Consistent with these findings are behavioral and modeling data showing that lexical access is influenced by the degree to which the phonetic structure of the input matches word candidates (see McNellis & Blumstein, 2001; Luce & Pisoni, 1998). The similar areas of activation in the nonword condition compared to the related and unrelated conditions (Figure 1) can likely be attributed to the fact that these pseudowords automatically activate a set of phonologically similar lexical representations.

Although nonwords appear to activate similar neural systems to words, differences in the magnitude of activation emerged in the current study, with greater activation for word targets than for nonword targets in the left MTG, the left anterior cingulate, and the left precuneus. There was also greater activation for words than nonwords in the angular gyrus bilaterally, but this was due to deactivation for the nonwords. Similar patterns of activation and deactivation have been reported by Henson, Price, Rugg, Turner, and Friston (2002) using a visual LD task and by Schulman et al. (1997) in a variety of visual language tasks. The reasons for the deactivation in the angular gyrus are unclear, but warrant further study given that similar results have been reported.

Most studies comparing word and nonword processing have explored word reading and have shown greater activation for nonwords than for words. These differences have been attributed largely to processes of grapheme-to-phoneme conversion (Price, 1998; Herbster et al., 1997; Rumsey et al., 1997). Only a few studies have investigated auditory word and nonword process-

ing (Newman & Tveig, 2001; Binder et al., 1994). Although all of these studies have found that words and pseudowords activate similar neural systems, a number of them have found no significant differences in the amount of activation between words and pseudowords (Hirano et al., 1997; Binder et al., 1994; Wise et al., 1991).

In contrast, Newman and Tveig (2001) showed greater activation for nonwords than for words in the posterior STG and the inferior parietal regions. These results are in conflict with the current findings that showed similar activation maps for the unrelated and nonword conditions, and significantly greater activation for words than for nonwords in the left MTG, the left anterior cingulate, and the left precuneus. It is difficult to resolve the reasons for the different findings owing to the differences among the studies in terms of tasks, experimental design and analysis methods. A few suggestions, however, may be worth considering. In the Newman and Tveig (2001) study, word and nonword stimuli were presented in blocks and participants performed a phoneme monitoring task on each stimulus. Thus, in the case of the nonword stimuli, participants needed to actively make use of the phonological representation of the nonword to make their phoneme monitoring decision, presumably invoking the phonological buffer and inferior parietal lobe structures. In contrast, the random presentation of the test stimuli in the LD task in the current study did not hold such requirements. Participants did not need to actively segment out the phonological properties of the stimulus to make a decision, but rather only had to determine whether there was a "match" to a lexical representation. The greater activation for words compared to nonwords in the MTG could be due to the success of the matching process of the auditory input with an existing stored phonological and meaning representation for words compared to nonwords. Finally, it is worth noting that the nonword target stimuli in the current study were preceded by real word primes. Thus, the activation pattern for nonwords encompassed not only responses to the nonword targets but also the contextual influence of the preceding real word primes.

The Role of Posterior versus Anterior Brain Structures

The results of the current study suggest that posterior brain structures including the STG and MTG and the angular gyrus play a crucial role in lexical-semantic processing. Based on the current findings, it appears that their functional role is to house stored semantic representations and the lexical-semantic network. Moreover, the posterior structures do not appear to be a "static" storehouse of semantic representations that require the recruitment of anterior brain structures

for building up or establishing semantic relations. Rather, these posterior structures appear to be actively involved in the recovery of meaning and in the implicit processing of semantic relationships.

That the reduced activation in the related condition occurred in the left STG may seem surprising, because studies of lexical–semantic processing have typically shown activation in the MTG and reported to a lesser degree activation in the STG (see Binder & Price, 2001 for a review). One possibility is that the STG subserves functions involved in the coactivation of distributed semantic representations (Mesulam, 1998). Because semantically related pairs may share semantic codes, the processing demands on the STG are reduced resulting in the modulation of activation shown for semantically related prime–target pairs compared to semantically unrelated prime–target pairs. In contrast to most other studies of lexical–semantic processing in the current experiment, subjects did not have to explicitly attend to the meanings of the words or the semantic relationship between the prime–target pairs in order to make a decision about lexicality. Thus, activation in the STG may reflect the differential modulation resulting from the automatic activation of shared semantic representations. That the left STG was modulated by semantic properties of the stimuli does not necessarily imply that the semantic representations themselves are housed within this brain structures or that the modulation of the activated semantic codes occurs within the STG. It may be the case that the role of the STG in semantic processing is to serve as a relay to/from other temporal lobe structures. Further research is needed to better understand this issue. Another possibility is that the modulation of activation seen in the STG reflects greater processing resources required for words that are semantically unrelated compared to those that are related. Nonetheless, if this were the case, the locus of the source of this modulation would still need to be identified.

In contrast to the activation patterns of the STG, the MTG showed significantly greater activation for words than nonwords, but failed to show any modulatory effects of semantic priming, that is, $U > R$. This pattern of results suggests that the activation of the MTG is sensitive to the LD requirements of the task and reflects the success of the matching process of the auditory input with an existing stored lexical–semantic representation for words.

The role of the frontal structures is less clear. Although the middle frontal gyri showed significant differences in activation between the related and unrelated conditions, the time course graphs (Figure 3) showed that the signal level detected in the MFG was, overall, quite weak. Consistent with studies implicating the MFG in high-level executive processing (see D'Esposito, Postle, & Rypma, 2000), we propose that the MFG effects probably reflect the processes of monitoring the activa-

tion of lexical representations in the temporal lobes and using these graded activation patterns to make a LD.

The modulatory effects that emerged for semantically related prime–target pairs in the left precentral gyrus, which falls in the premotor area (BA 6), may reflect the faster and more efficient planning of the appropriate motor response in the related condition. This finding is consistent with fMRI and ERP results demonstrating priming effects in the motor areas contralateral to the hand that responded to the target stimuli in a visual masked priming task (Dehaene et al., 1998). As for the signal reduction in the right caudate, we do not, at this point, have any hypothesis concerning its role in the semantic priming phenomenon.

The inferior frontal gyrus, the focus of a number of previous neuroimaging studies of word meaning, did not emerge as a significant cluster in the analysis of the priming conditions. Moreover, the time course function for the left inferior frontal gyrus showed overall weak activation levels. Thus, it appears that significant activation in the inferior frontal gyrus emerges consistently in those tasks that require explicit decisions about the semantic content of the stimuli. Spitzer et al. (1996) showed that overt judgments of semantic relatedness using pairs of words that were semantically related, indirectly semantically related, or unrelated resulted in activation primarily in left frontal areas. In contrast, the current study showed that using pairs of words that were semantically related or unrelated in a LD task resulted in activation primarily in left posterior areas. It is of interest that the neuroimaging studies investigating the role of automatic and controlled processing in semantic priming also did not report activation in the inferior frontal gyrus for semantic priming (Rossell et al., 2001; Mummery et al., 1999).

These findings then raise the question whether the inferior frontal gyrus is invoked only in those tasks requiring explicit retrieval, selection, or recovery of word meaning for decisions about the semantic content of the stimuli. That is one possibility. Another is that the inferior frontal gyrus is invoked in accessing word meaning even in implicit semantic priming tasks but only under conditions of increased processing difficulty. In particular, a series of studies with aphasic patients has shown deficits in the patterns of semantic priming, as the relationship between prime–target pairs has become more complex. Broca's patients with anterior brain damage typically including the inferior frontal gyrus have shown “pathological” patterns of semantic priming when semantically ambiguous words are a part of the prime stimuli (Milberg, Blumstein, Katz, Gershberg, & Brown, 1995). They have also shown impairments when the prime stimulus was manipulated phonologically (Milberg et al., 1988b), and also phonetically under conditions of lexical competition (Utman et al., 2001). Given these results from lesion studies, it may be that neuroimaging studies with normal participants will show

increased activation in the inferior frontal gyrus under similar conditions.

Analysis of Errors

Comparison of the activation patterns for errors compared to correct responses revealed significantly greater activity bilaterally in prefrontal cortices (BA 44, 45, 47) and a region encompassing the anterior cingulate and medial frontal gyrus. These findings are consistent with recent work suggesting that the anterior cingulate and the lateral prefrontal cortices are part of a circuit that, irrespective of modality, detects errors and behavioral conflict (Gehring & Knight, 2000; Kiehl, Liddle, & Hopfinger, 2000). It has also been proposed that the anterior cingulate is activated not simply when errors occur but under conditions of response competition. In this view, as task difficulty increases, response competition also does (Carter et al., 1998). Thus, increased anterior cingulate activity has been shown in tasks that have a high degree of response conflict but low error rates, for example, the Stroop task (MacDonald, Cohen, Stenger, & Carter, 2000; Pardo, Pardo, Janer, & Raichle, 1990) and the verb generation task (Barch, Braver, Sabb, & Noll, 2000). Although results of the current experiment suggest that there is greater ACC activity when errors are made, it is worth noting that most errors occurred in the nonword target condition (19% vs. 11% in the related and 3% in the unrelated priming conditions). The nonword stimuli are not only the most likely to result in errors, but they are also the most likely to produce response conflict because they presumably activate a large set of competing lexical candidates.

Conclusion

The results of this study demonstrate that the cognitive processing required to make a decision on the lexical status of an auditory stimulus engages primarily posterior brain structures including the STG, MTG, and regions of the inferior parietal lobule. Most importantly, we have shown that the neural correlates of the semantic priming phenomenon can be seen in both the frontal and temporal lobes, where semantically related word pairs showed consistently less activation than unrelated pairs. The left temporal lobe appears to be involved in the implicit processing of the meanings of words, as well as in the recovery of semantic relationships between and among them. That signal reductions in this region emerged in the absence of stimulus repetition suggests that the semantic representations of words are organized in terms of a lexical–semantic network sharing a common substrate. The priming induced modulations of areas of the frontal lobe more likely reflect the enhanced efficiency with which subjects are able to make the LD and map it to the appropriate motor response.

METHODS

Participants

Fifteen participants (8 women, 7 men) were recruited on a voluntary basis from the Brown University community. The ages of the participants ranged from 18 to 44 years, with a mean of 22.9 ± 6.5 years. All participants were strongly right-handed, as confirmed by the administration of the Edinburgh Handedness Inventory (Oldfield, 1971). By self-report, all had normal neurological function and did not have any bodily ferromagnetic materials. Each participant gave written informed consent according to guidelines established and approved by the Human Subjects Committees of both Brown University and the Memorial Hospital of Rhode Island. Participants received modest monetary compensation for their time and effort.

Tasks

Participants were scanned while performing a LD task or a tone control (TC) task. Each participant performed seven runs of experimental trials, the order of which was held constant across participants (TC, LD, LD, TC, LD, LD, TC). Trials consisted of pairs of auditory stimuli presented binaurally over sound attenuating air conduction headphones (Resonance Technologies[®], Northridge, CA). The sound level was adjusted as needed for each participant to ensure that stimuli were heard comfortably during the scanning against the background noise of the scanner gradients.

The stimuli for the LD task consisted of pairs of real words and nonwords in which the first member of the pair was the prime and the second member of the pair was the target (see Appendix). There were three stimulus conditions. In the related condition, a real word target was preceded by a semantically related prime, for example, “trapeze–circus.” In the unrelated condition, a real word target was preceded by a semantically unrelated prime that shared neither a semantic or associative relationship with the target, for example, “pollute–circus.” In the nonword condition, a nonword target was preceded by a real word prime chosen from two arbitrarily grouped lists of words, for example, “couple–veekle.” The nonwords followed English phonotactic constraints and were created by substituting a single phoneme or cluster in a set of real words.

There were a total of 40 real word and 40 nonword targets. Each target stimulus occurred twice during the course of the experiment preceded by a different prime, always in nonadjacent runs. For the real word targets, half of the targets occurred with their related prime first, and half occurred with their unrelated prime first. The particular prime–target pairs used in this experiment were chosen based on pilot work in our laboratory indicating that these pairs exhibited robust semantic priming effects. The related and unrelated primes, as

well as the primes preceding the nonwords, were all multisyllabic and matched for stimulus duration and lexical frequency, confirmed by nonsignificant one-way ANOVAs [duration: $F(3,156) = .377$; lexical frequency: $F(3,156) = .192$] and post hoc pairwise comparisons. The duration of the related primes was 541 msec and the unrelated primes was 542 msec. The real word and nonword target stimuli were similarly matched for duration (537 vs. 533 msec). The ISI between prime and target pairs was 50 msec. The stimuli were recorded by a phonetically trained male speaker and were digitized at a sampling rate of 22,050 Hz to produce 16-bit digital sound files.

The TC task consisted of a single stimulus, a 400-Hz sine wave tone with a duration of 540 msec. This duration was chosen in order to closely approximate the average duration of the speech stimuli. Similar to the design of the LD task, the tone stimuli were presented in pairs separated by a 50-msec ISI (see Image Collection for details about the intertrial interval).

In the LD task, participants were instructed that they would hear a pair of speech stimuli and their task was to decide whether or not the second stimulus in the pair was a real word in English. They were to indicate their response as quickly and accurately as possible by pressing one of two handheld buttons with their index finger, which rested in-between the two buttons while they waited for each new trial. For all participants, the two-button unit was held comfortably in their right hand. A press of the right button indicated that they thought the target was a real word; a press of the left button indicated a nonword response. Responses were transmitted to an apparatus in the control room via fiber optic cables, and this information was relayed to the laptop computer (IBM Thinkpad), where responses were registered for both accuracy and RT. The RT latencies were measured from the onset of the target stimulus.

In the TC task, participants were instructed that they would hear a pair of tones. They were instructed to make a button press after hearing the second tone of each pair, alternating between the right and left buttons in consecutive trials.

In sum, each participant performed seven runs of experimental trials with 40 trials per run in the LD task and 16 trials per run in the tone task.

MRI Procedures

Image Collection

Anatomical and functional MR images were acquired with a Symphony Magnetom MR system (Siemens Medical Systems, Erlangen, Germany) equipped for echo-planar imaging and operating at 1.5 T. Participants lay supine on an automated gurney for insertion into the MR system bore. The head rested within a circularly

polarized quadrature head coil. Each participant's head was roughly centered in the magnetic field of the MR system by aligning the nasion with a laser cross-hair projection before transport into the MR system bore. Head movement was minimized by cushioning and mild restraint, and participants were instructed to refrain from moving the head and speaking during MR imaging. In order to reduce eye movement artifacts and activation of visual areas, participants were instructed to keep their eyes closed during the functional runs of the experiment and the room lights were dimmed.

We acquired a three-dimensional, high-resolution anatomical data set (Siemens' magnetization prepared rapid acquisition gradient echo [MPRAGE] sequence, TR = 1900 msec, TE = 4.15 msec, TI = 1100 msec, 1 mm isotropic voxels, 256 mm FoV). Echo-planar images (EPIs) were acquired in a transverse plane using blood-oxygenation-level-dependent (BOLD) imaging (Kwong et al., 1992). Forty-five slices were sampled from the superior convexity to inferior regions of the cerebellum. Images were acquired from inferior to superior in interleaved fashion. Each slice was 3 mm thick and encompassed a field of view of 192 mm with a 64 mm² image matrix. Voxels had an in-plane resolution of 3 × 3 mm and a volume of 27 mm³. The imaging sequence for the functional runs used a TR = 3600 msec and a TE = 38 msec.

In order to capture better the temporal profile of the hemodynamic response, we employed a design in which stimuli were presented at intervals of TR/4 resulting in an effective sampling rate of 900 msec (cf. Price, Veltman, Ashburner, Josephs, & Friston, 1999; Josephs, Turner, & Friston, 1997). The interval elapsing between trial events (trial onset asynchrony [TOA]) was also varied systematically to improve the efficiency of our design in estimating the shape of the hemodynamic response (cf. Miezen, Maccotta, Ollinger, Petersen, & Buckner, 2000; Dale, 1999; Glover, 1999; Dale & Buckner, 1997). The timing of stimulus events was jittered according to a uniform distribution of eight distinct TOA values ranging from 2700 to 9000 msec in 900-msec steps. The average TOA was thus 5850 msec. The eight TOA values were pseudorandomized across our trial list using a Latin Squares procedure (see Hagberg, Zito, Patria, & Sanes, 2001), such that the first eight trials had a random ordering of the eight TOA values, the next eight trials had a different random ordering, and so forth.

Data Analysis

The processing of the MR images was carried out on a Silicon Graphics Origin 2000 and analyzed using AFNI (Cox, 1996; Cox & Hyde, 1997; <http://afni.nimh.nih.gov/afni/>). A total of 366 echo-planar volumes were acquired during the experiment in sets of either 30 (TC Task) or

69 volumes (LD Task). The first four volumes (14.4 sec) in each measurement were censored from analysis due to T1 saturation effects. Volumes acquired in successive runs were concatenated into a single EPI data set of 366 volumes. Each participant's MPRAGE and EPI image series were coregistered using the positioning coordinates from the scanner system. The MPRAGE anatomical image was normalized to the standardized space of Talairach and Tournoux (1988) as implemented in AFNI. Each participant's EPI images were coregistered to the first EPI volume in the experiment using a six-parameter rigid body transformation (Cox & Jesmanowicz, 1999). Following this motion correction procedure, the EPI image set was transformed to standardized space by adoption of the landmarks defined in the MPRAGE data set. The normalized EPI data set was then spatially smoothed using a 6-mm Gaussian kernel. This normalized and smoothed EPI data set was then analyzed as described below to obtain functional brain activation maps.

Deconvolution Analysis

The EPI time series of each participant was submitted to deconvolution to estimate the hemodynamic response during performance of each stimulus condition. Deconvolutions were performed separately on each participant's EPI data on a voxel by voxel basis. Unlike correlation analysis, deconvolution allows the simultaneous estimation of contributions from multiple input stimulus functions, or reference waveforms. The first four reference waveforms were specified by the stimulus conditions (related word targets, unrelated word targets, nonword targets, tones). For each of these four stimulus conditions, a vector that listed the time of onset of each target stimulus in that condition was created. These trial timing vectors were then adjusted for each individual participant so that they only referenced those trials for which the participant responded correctly. Any trial that elicited an erroneous response for a given participant was listed in a separate vector containing the target onset times of all targets that participant responded to incorrectly. This resulted in the creation of a fifth stimulus condition representing response errors. Because the TC task only required an alternating button press response, the behavioral data from this task was not analyzed, and the same timing vector was used for all participants when creating the reference waveform for the tone condition.

To turn these vectors consisting of target onset times into reference waveforms to be used as covariates in the deconvolution analysis, we convolved each vector with a gamma-variate function obtained from AFNI. The gamma function is thought to provide an approximation of a canonical hemodynamic response (Cohen, 1997). We then down-sampled the temporal resolution of the resulting waveform, such that values were

specified only at intervals of the TR (every 3.6 sec). In this manner, we created waveforms for each participant for each condition. The output parameters of the motion correction algorithm, x , y , and z translation and roll, pitch, and yaw rotations served, as six additional reference waveforms that were entered into the deconvolution analysis.

Intersubject Analysis

The raw fit coefficients from the deconvolution analysis were submitted to a two-factor ANOVA using stimulus condition (fixed effect) and participant (random effect) as independent variables. Mean statistical activation maps were calculated for each of the five conditions. In addition, three contrasts were specified in order to examine differences between particular groupings of these categories. These groupings included: Related versus Unrelated, Words versus Nonwords, and LD versus Tone. At this point, we performed several thresholding procedures on the statistical maps.

To determine which brain regions exhibited reliable differences in activation between contrasting conditions, we looked for the clustering of activated voxels (Forman et al., 1995; Xiong, Gao, Lancaster, & Fox, 1995). It has been suggested that activation across broader regions is more powerfully detected using less stringent voxel-level thresholds and more stringent cluster size thresholds (Friston, Worsley, Frackowiak, Mazziota, & Evans, 1994). As a consequence, we chose a voxel-level threshold of $p < .02$ and a cluster threshold of 42 contiguous voxels, which, based on our Monte Carlo simulations, achieved a corrected significance level of $p < .05$.

Time Course of the Hemodynamic Response

To explore the shape of the hemodynamic response functions evoked by trials of various types in those brain regions identified in the preceding analyses, we performed a new set of deconvolution analyses on each participant's normalized and spatially smoothed EPI data set. Instead of inputting reference waveforms constructed with the assumption of a canonical gamma-shaped hemodynamic response, we created binary stimulus functions for each condition with 1's at those time points where a stimulus of that condition occurred, and 0's at all remaining time points. However, since our stimuli were not presented at discrete intervals of the TR, but rather at intervals specified by $TR/4$, we created these stimulus functions as if our EPI data set contained four time points per TR, or a total of 1464 time points. By adjusting the parameters of AFNI's 3dDeconvolve program accordingly, we were able to model a series of scaling coefficients for each reference function at 11 lag values ranging from 0 to 9 sec poststimulus, in steps of 900 msec.

Acknowledgments

This work was supported in part by the Ittleson Foundation and NIH grant DC00142. Many thanks to Jerome Sanes, for his advice at all stages of this research, and to William Heindel, for many helpful discussions.

Reprint requests should be sent to Sheila E. Blumstein, Department of Cognitive and Linguistic Sciences, Brown University, Box 1978, Providence, RI 02912, USA, or via e-mail: Sheila_Blumstein@brown.edu.

The data reported in this experiment have been deposited in The fMRI Data Center (<http://www.fmridc.org>). The accession number is 2-2003-113Y6.

Note

1. Now at the University of California, Berkeley, USA.

REFERENCES

- Barch, D. M., Braver, T. S., Sabb, F. W., & Noll, D. C. (2000). Anterior cingulate and the monitoring of response conflict: Evidence from an fMRI study of overt verb generation. *Journal of Cognitive Neuroscience*, *12*, 298–309.
- Bentin, S., McCarthy, G., & Wood, C. C. (1985). Event-related potentials associated with semantic priming. *Electroencephalography and Clinical Neurophysiology*, *60*, 343–355.
- Binder, J., & Price, C. J. (2001). Functional neuroimaging of language. In R. Cabeza & A. Kingstone (Eds.), *Handbook of functional neuroimaging* (pp. 187–251). Cambridge: MIT Press.
- Binder, J. R., Frost, J. A., Hammeke, T. A., Cox, R. W., Rao, S. M., & Prieto, T. (1997). Human brain language areas identified by functional magnetic resonance imaging. *Journal of Neuroscience*, *17*, 353–362.
- Binder, J. R., Rao, S. M., Hammeke, T. A., Yetkin, Y. Z., Jesmanowicz, A., Bandettini, P. A., Wong, E. C., Estkowski, L. D., Goldstein, M. D., Haughton, V. M., & Hyde, J. S. (1994). Functional magnetic resonance imaging of human auditory cortex. *Annals of Neurology*, *35*, 662–672.
- Blumstein, S. E., & Milberg, W. P. (2000). Language deficits in Broca's and Wernicke's aphasia: A singular impairment. In Y. Grodzinsky, L. Shapiro & D. Swinney (Eds.), *Language and the brain: Representations and processing* (pp. 167–184). New York: Academic Press.
- Blumstein, S. E., Milberg, W. P., & Shrier, R. (1982). Semantic processing in aphasia: Evidence from an auditory lexical decision task. *Brain and Language*, *17*, 301–315.
- Buckner, R. L., Goodman, J., Burock, M., Rotte, M., Koutstaal, W., Schacter, D. L., Rosen, B., & Dale, A. (1998). Functional-anatomic correlates of object priming in humans revealed by rapid presentation event-related fMRI. *Neuron*, *20*, 285–296.
- Buckner, R. L., Koutstaal, W., Schacter, D. L., & Rosen, B. R. (2000). Functional MRI evidence for a role of frontal and inferior temporal cortex in amodal components of priming. *Brain*, *123*, 620–640.
- Buckner, R. L., Petersen, S. E., Ojemann, J. G., Miezin, F. M., Squire, L. R., & Raichle, M. E. (1995). Functional anatomical studies of explicit and implicit memory retrieval tasks. *Journal of Neuroscience*, *15*, 12–29.
- Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science*, *280*, 747–749.
- Cohen, M. (1997). Parametric analysis of fMRI data using linear systems methods. *Neuroimage*, *6*, 93–103.
- Connine, C. M., Titone, D., Deelman, T., & Blasko, D. (1997). Similarity mapping in spoken word recognition. *Journal of Memory and Language*, *37*, 463–480.
- Cox, R. W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research*, *29*, 162–173.
- Cox, R. W., & Hyde, J. S. (1997). Software tools for analysis and visualization of fMRI data. *NMR in Biomedicine*, *10*, 171–178.
- Cox, R. W., & Jesmanowicz, A. (1999). Real-time 3D image registration for functional MRI. *Magnetic Resonance in Medicine*, *42*, 1014–1018.
- Dale, A. M. (1999). Optimal experimental design for event-related fMRI. *Human Brain Mapping*, *8*, 109–114.
- Dale, A. M., & Buckner, R. L. (1997). Selective averaging of rapidly presented individual trials using fMRI. *Human Brain Mapping*, *5*, 329–340.
- Dehaene, S., Naccache, L., Le Clec'H, G., Koechlin, E., Mueller, M., Dehaene-Lambertz, G., van de Moortele, P.-F., & Le Bihan, D. (1998). Imaging unconscious semantic priming. *Nature*, *395*, 597–600.
- Demb, J. B., Desmond, J. E., Wagner, A. D., Vaidya, C. J., Glover, G. H., & Gabrieli, J. D. E. (1995). Semantic encoding and retrieval in the left inferior prefrontal cortex: A functional MRI study of task difficulty and process specificity. *Journal of Neuroscience*, *15*, 5870–5878.
- Demonet, J. F., Chollet, F., Ramsay, S., Cardebat, D., Nespoulous, J. L., Wise, R., Rascol, A., & Frackowiak, R. S. J. (1992). The anatomy of phonological and semantic processing in normal subjects. *Brain*, *115*, 1753–1768.
- D'Esposito, M., Postle, B. R., & Rypma, B. (2000). Prefrontal cortical contributions to working memory: Evidence from event-related fMRI studies. *Experimental Brain Research*, *133*, 3–11.
- Fiez, J., Balota, D. A., Raichle, M. E. & Petersen, S. E. (1999). Effects of lexicality frequency, and spelling-to-sound consistency on the functional anatomy of reading. *Neuron*, *24*, 205–218.
- Forman, S. D., Cohen, J. D., Fitzgerald, M., Eddy, W. F., Mintun, M. A., & Noll, D. C. (1995). Improved assessment of significant activation in functional magnetic resonance imaging (fMRI): Use of a cluster-size threshold. *Magnetic Resonance in Medicine*, *33*, 636–647.
- Friston, K. J., Worsley, K. J., Frackowiak, R. S., Mazziotta, J. C., & Evans, A. C. (1994). Assessing the significance of focal activations using their spatial extent. *Human Brain Mapping*, *1*, 210–220.
- Frith, C. D., Friston, K. J., Liddle, P. F., & Frackowiak, R. S. (1991). A PET study of word finding. *Neuropsychologia*, *29*, 1137–1148.
- Gabrieli, J. D. E., Desmond, J. E., Demb, J. B., Wagner, A. D., Stone, M. V., Vaidya, C. J., & Glover, G. H. (1996). Functional magnetic resonance imaging of semantic memory processes. *Psychological Science*, *7*, 278–283.
- Gabrieli, J. D. E., Poldrack, R. A., & Desmond, J. E. (1998). The role of the left prefrontal cortex in language and memory. *Proceedings of the National Academy of Sciences, U. S. A.*, *95*, 906–913.
- Gehring, W. J., & Knight, R. T. (2000). Prefrontal-cingulate interactions in action monitoring. *Nature Neuroscience*, *3*, 516–520.
- Glover, G. H. (1999). Deconvolution of impulse response in event-related BOLD fMRI. *Neuroimage*, *9*, 416–429.
- Hagberg, G. E., Zito, G., Patria, F., & Sanes, J. N. (2001). Improved detection of event-related functional MRI signals using probability functions. *Neuroimage*, *14*, 193–205.

- Harrington, D. L., Rao, S. M., Halland, K. Y., Bobholz, J. A., Mayer, A. R., Binder, J. R., & Cox, R. W. (2000). Specialized neural systems underlying representations of sequential movements. *Journal of Cognitive Neuroscience*, *12*, 56–77.
- Henson, R. N. A., Price, C. J., Rugg, M. D., Turner, R., & Friston, K. J. (2002). Detecting latency differences in event-related BOLD responses: Application to words versus nonwords and initial versus repeated face representations. *Neuroimage*, *15*, 83–97.
- Herbster, A. N., Mintun, M. A., Nebes, R. D., & Becker, J. T. (1997). Regional cerebral blood flow during word and nonword reading. *Human Brain Mapping*, *5*, 84–92.
- Hirano, S., Naito, Y., Okazawa, H., Kojima, H., Honjo, I., Ishizu, K., Yenokura, Y., Nagahama, Y., Fukuyama, H., & Konishi, J. (1997). Cortical activation by monaural speech sound stimulation demonstrated by positron emission tomography. *Experimental Brain Research*, *113*, 75–80.
- Josephs, O., Turner, R., & Friston, K. J. (1997). Event-related fMRI. *Human Brain Mapping*, *5*, 243–248.
- Kapur, S., Rose, R., Liddle, P. F., Zipursky, R. B., Brown, G. M., Stuss, D., Houle, S., & Tulving, E. (1994). The role of the left prefrontal cortex in verbal processing: Semantic processing or willed action? *NeuroReport*, *5*, 2193–2196.
- Kiehl, K. A., Liddle, P. F., & Hopfinger, J. B. (2000). Error processing and the rostral anterior cingulate: An event-related fMRI study. *Psychophysiology*, *37*, 216–223.
- Koutstaal, W., Wagner, A. D., Rotte, M., Maril, A., Buckner, R. L., & Schacter, D. L. (2001). Perceptual specificity in visual object priming: Functional magnetic resonance imaging evidence for a laterality difference in fusiform cortex. *Neuropsychologia*, *39*, 184–199.
- Kutas, M., & Van Petten, C. K. (1994). Psycholinguistics electrified. In M. A. Gernsbacher (Ed.), *Handbook of psycholinguistics* (pp. 83–143). New York: Academic Press.
- Kwong, K. K., Belliveau, J. W., Chesler, D. A., Goldberg, I. E., Weisskoff, R. M., Poncelet, P. B., Kennedy, D. N., Hoppel, B. E., Cohen, M. S., & Turner, R. (1992). Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proceedings of the National Academy of Sciences, U. S. A.*, *89*, 5675–5679.
- Lancaster, J., Woldorff, M., Parsons, L., Liotti, M., Freitas, C., Rainey, L., Kochunov, P., Nickerson, D., Mikiten, S., & Fox, P. (2000). Automated Talairach atlas labels for functional brain mapping. *Human Brain Mapping*, *10*, 120–131.
- Luce, P. A., & Pisoni, D. B. (1998). Recognizing spoken words: The neighborhood activation model. *Ear and Hearing*, *19*, 1–36.
- MacDonald, A. W., Cohen, J. D., Stenger, V. A., & Carter, C. S. (2000). Dissociation of the role of the dorsolateral prefrontal and anterior cingulate cortex in cognition control. *Science*, *288*, 1835–1838.
- McNellis, M., & Blumstein, S. E. (2001). Self-organizing dynamics of lexical access in normals and aphasics. *Journal of Cognitive Neuroscience*, *13*, 151–170.
- Mesulam, M. M. (1998). From sensation to cognition. *Brain*, *121*, 1013–1052.
- Miezen, F. M., Maccotta, L., Ollinger, J. M., Petersen, S. E., & Buckner, R. L. (2000). Characterizing the hemodynamic response: Effects of presentation rate, sampling procedure, and the possibility of ordering brain activity based on relative timing. *Neuroimage*, *11*, 735–759.
- Milberg, W. P., & Blumstein, S. E. (1981). Lexical decision and aphasia: Evidence for semantic processing. *Brain and Language*, *14*, 371–385.
- Milberg, W. P., Blumstein, S. E., & Dworetzky, B. (1987). Processing of lexical ambiguities in aphasia. *Brain and Language*, *31*, 138–150.
- Milberg, W. P., Blumstein, S. E., & Dworetzky, B. (1988a). Phonological factors in lexical access: Evidence from an auditory lexical decision task. *Bulletin of the Psychonomic Society*, *26*, 305–308.
- Milberg, W. P., Blumstein, S. E., & Dworetzky, B. (1988b). Phonological processing and lexical access in aphasia. *Brain and Language*, *34*, 279–293.
- Milberg, W. P., Blumstein, S. E., Katz, D., Gershberg, & Brown, T. (1995). Semantic facilitation in aphasia: Effects of time and expectancy. *Journal of Cognitive Neuroscience*, *7*, 33–50.
- Mummery, C. J., Shallice, T., & Price, C. J. (1999). Dual-process model in semantic priming: A functional imaging perspective. *Neuroimage*, *9*, 516–525.
- Newman, S. D., & Tweig, D. (2001). Differences in auditory processing of words and pseudowords: An fMRI study. *Human Brain Mapping*, *14*, 39–47.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, *9*, 97–113.
- Pardo, J. V., Pardo, P. J., Janer, K. W., & Raichle, M. E. (1990). The anterior cingulate cortex mediates processing selection in the Stroop attentional conflict paradigm. *Proceedings of the National Academy of Science, U. S. A.*, *87*, 256–259.
- Petersen, S. E., Fox, P. T., Posner, M. I., Mintun, M., & Raichle, M. E. (1988). Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature*, *331*, 585–589.
- Poldrack, R. A., Wagner, A. D., Prull, M. W., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. E. (1999). Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. *Neuroimage*, *10*, 15–35.
- Price, C. J. (1998). The functional anatomy of word comprehension and production. *Trends in Cognitive Science*, *2*, 281–288.
- Price, C. J., Moore, C. J., Humphreys, G. W., & Wise, R. J. S. (1997). Segregating semantic from phonological processes during reading. *Journal of Cognitive Neuroscience*, *9*, 727–733.
- Price, C. J., Veltman, D. J., Ashburner, J., Josephs, O., & Friston, K. J. (1999). The critical relationships between the timing of stimulus presentation and data acquisition in blocked designs with fMRI. *Neuroimage*, *10*, 36–44.
- Price, C. J., Wise, R. J. S., & Frackowiak, R. S. J. (1996). Demonstrating the implicit processing of visually presented words and pseudowords. *Cerebral Cortex*, *6*, 62–70.
- Raichle, M. E., Fiez, J. A., Videen, T. O., MacLeod, A. M., Pardo, J. V., Fox, P. T., & Petersen, S. E. (1994). Practice-related changes in human brain functional anatomy during nonmotor learning. *Cerebral Cortex*, *4*, 8–26.
- Roskies, A. L., Fiez, J. A., Balota, D. A., Raichle, M. E., & Petersen, S. E. (2001). Task-dependent modulation of regions in the left inferior frontal cortex during semantic processing. *Journal of Cognitive Neuroscience*, *13*, 829–843.
- Rossell, S. L., Bullmore, E. T., Williams, S. C. R., & David, A. S. (2001). Brain activation during automatic and controlled processing of semantic relations: A priming experiment using lexical-decision. *Neuropsychologia*, *39*, 1167–1176.
- Rumsey, J. M., Horwitz, B., Donohue, B., Nace, K., Maisog, J. M., & Andreason, P. (1997). Phonological and orthographic components of word recognition: A PET-rCBF study. *Brain*, *120*, 739–759.
- Schacter, D. L., & Buckner, R. L. (1998). Priming and the brain. *Neuron*, *20*, 185–195.

- Schulman, G. L., Fiez, J. A., Corbetta, M., Buckner, R. L., Miezen, F. M., Raichle, M. E., & Petersen, S. E. (1997). Common blood flow changes across visual tasks: II. Decreases in cerebral cortex. *Journal of Cognitive Neuroscience*, *9*, 648–663.
- Spitzer, M., Bellemann, M. E., Kammer, T., Guckel, F., Kischka, U., Maier, S., Schwartz, A., & Brix, G. (1996). Functional MR imaging of semantic information processing and learning-related effects using psychometrically controlled stimulation paradigms. *Cognitive Brain Research*, *4*, 149–161.
- Talairach, J., & Tournoux, P. (1988). *A co-planar stereotaxic atlas of a human brain*. Stuttgart, Germany: Thieme.
- Thompson-Schill, S. L., D'Esposito, M., Aguirre, G. K., & Farah, M. J. (1997). Role of left inferior prefrontal cortex in retrieval of semantic knowledge: A reevaluation. *Proceedings of the National Academy of Sciences*, *94*, 14792–14797.
- Thompson-Schill, S. L., D'Esposito, M., & Kan, I. P. (1999). Effects of repetition and competition on activity in left prefrontal cortex during word generation. *Neuron*, *23*, 513–522.
- Utman, J. A., Blumstein, S. E., & Sullivan, K. (2001). Mapping from sound to meaning: Reduced lexical activation in Broca's aphasia. *Brain and Language*, *79*, 444–472.
- Vandenberghe, R., Price, C., Wise, R., Josephs, O., & Frackowiak, R. S. J. (1996). Functional anatomy of a common semantic system for words and pictures. *Nature*, *383*, 254–256.
- Wagner, A. D., Koutstaal, W., Maril, A., Schacter, D. L., & Buckner, R. L. (2000). Task-specific repetition priming in left inferior prefrontal cortex. *Cerebral Cortex*, *10*, 1176–1184.
- Wagner, A. D., Pare-Blagoev, E. J., Clark, J., & Poldrack, R. A. (2001). Recovering meaning: Left prefrontal cortex guides controlled semantic retrieval. *Neuron*, *31*, 329–338.
- Wise, R. J. S., Chollet, F., Hadar, U., Friston, K., Hoffner, E., & Frackowiak, R. (1991). Distribution of cortical neural networks involved in word comprehension and word retrieval. *Brain*, *114*, 1803–1817.
- Xiong, J., Gao, J., Lancaster, J. L., & Fox, P. T. (1995). Clustered pixels analysis for functional MRI activation studies of the human brain. *Human Brain Mapping*, *3*, 287–301.

APPENDIX

<i>Real Word Target</i>			<i>Nonword Target</i>		
Prime			Prime		
Related	Unrelated	Target	Group A	Group B	Target
country	appease	town	tower	detest	depleve
pencil	public	lead	shaky	hotel	aben
pilot	culture	plane	pity	tackle	drooz
teacher	pony	student	admit	soccer	darl
cattle	carbon	cow	return	poker	kunner
coffee	compare	tea	kitten	second	booch
cousin	perform	uncle	cocoon	castle	consool
tunnel	collect	dark	content	topic	glucher
tiger	parent	lion	pursuit	cotton	akend
turtle	token	shell	taxi	money	telect
jacket	coupon	coat	tangle	supper	sheck
paper	patrol	pen	picnic	cable	preak
happy	total	sad	chicken	today	meab
package	naked	box	tiny	polite	chiddel
ticket	pecan	movie	detain	yesterday	krink
racket	dinner	tennis	arcade	taboo	betch
protect	opaque	guard	target	cushion	drom
puppy	pastel	dog	command	forbidden	frass
zipper	rapid	pants	butter	puppet	inbrect
confine	consent	cage	party	thicken	grav
permit	pollen	allow	worker	argue	keetch
police	picture	cop	croquet	lucky	bling
cartoon	canoe	comic	appear	puzzle	freen
collapse	liquor	fall	carpet	temper	milut
petite	construct	small	depict	control	jettel
perfume	cancel	smell	rocket	retain	conforp
bouquet	complaint	flowers	person	weapon	kibb
raccoon	applause	skunk	career	engine	heint
trapeze	pollute	circus	repel	pepper	serg
attempt	cannon	try	peanut	locate	bainuh
cocaine	title	drug	account	prepare	jeenuv
occur	motel	happen	concern	routine	aproom
decay	locker	rot	pedal	tycoon	boip
oppose	choppy	against	table	convict	absire
repair	tourist	fix	marker	finished	gaig
depart	temple	leave	kitchen	diaper	chell
pretend	protest	fake	poppy	pocket	drime
copper	constant	brass	attach	timber	plew
guitar	persuade	strings	maker	couple	veekle
technique	blockade	style	compete	tattoo	foop