

Dissociating Frontotemporal Contributions to Semantic Ambiguity Resolution in Spoken Sentences

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Comprehension of sentences containing semantically ambiguous words requires listeners to select appropriate interpretations, maintain linguistic material in working memory, and to reinterpret sentences that have been misinterpreted. All these functions appear to involve frontal cortical regions. Here, we attempt to differentiate these functions by varying the relative timing of an ambiguous word and disambiguating information in spoken sentences. We compare the location, magnitude, and timing of evoked activity using a fast-acquisition semisparse functional magnetic resonance imaging sequence. The left inferior frontal gyrus (LIFG) shows a strong response to sentences that are initially ambiguous (disambiguated by information that occurs either soon after the ambiguity or that is delayed until the end of the sentence). Response profiles indicate that activity, in both anterior and posterior LIFG regions, is triggered both by the ambiguous word and by the subsequent disambiguating information. The LIFG also responds to ambiguities that are preceded by disambiguating context. These results suggest that the LIFG subserves multiple cognitive processes including selecting an appropriate meaning and reinterpreting sentences that have been misparsed. In contrast, the left inferior temporal gyrus responds to the disambiguating information but not to the ambiguous word itself and may be involved in reprocessing sentences that were initially misinterpreted.

Keywords: fMRI, frontal lobes, lexical ambiguity, semantic selection, speech

Introduction

The left inferior frontal gyrus (LIFG) plays a vital role in the combinatorial aspects of sentence comprehension. One clear instantiation of this view is presented in the “unification” account put forward by Hagoort (2005a), which suggests that the role of the LIFG should be characterized in terms of “combinatorial operations (unification) that assemble the basic components into larger structures.” This view accounts for the wide variety of neuroimaging studies that show more activity in LIFG in response to sentences that are made more difficult to understand by introducing either syntactic complexity (see Friederici et al. 2006) or by including words whose meanings or syntactic roles are temporarily ambiguous (see Rodd, Longe, et al. 2010). Despite this emerging consensus, much is still unclear about precisely how the LIFG participates in language comprehension (for a comprehensive review, see Rogalsky and Hickok 2011). Some authors have proposed that the role of the LIFG is to provide a working memory store that can hold in mind any incoming information that cannot be completely integrated into the ongoing representation of the sentence,

that is, because it is currently ambiguous (Caplan et al. 2000; Kaan and Swaab 2002; Fiebach et al. 2005). Other authors have attributed a more active computational role to the LIFG and have emphasized the role of this region in selecting appropriate representations from among competing alternatives (Thompson-Schill et al. 2005; January et al. 2009). Another highly specific claim is that this region serves to reinterpret sentences that were initially misparsed (Novick et al. 2005).

Another relevant proposal regarding the roles of the LIFG in language processing is that tasks that focus on word meanings (i.e., semantics) engage the anterior LIFG (aLIFG), whereas tasks that focus on the word sounds (i.e., phonology) engage more posterior regions (Buckner et al. 1995; Fiez 1997; Poldrack et al. 1999). This view is based largely on functional magnetic resonance imaging (fMRI) studies with single words, although it is also supported by TMS work revealing selective impairment on phonological and semantic tasks using single words after posterior left inferior frontal gyrus (pLIFG) and aLIFG stimulation, respectively (Gough et al. 2005). This view of a semantic-phonological processing gradient within the ventral LIFG has been linked by some authors to a more general “gradient of abstractness” within the frontal cortex as a whole (Badre and D’Esposito 2009; O’Reilly 2010). Under this view, it is the = abstractness of semantic processing relative to phonological processing (which is more closely linked with articulatory processes involving precentral regions) that underlies this processing gradient. A related claim that is more specifically tied to sentence comprehension is made within the unification account of sentence processing (Hagoort 2005a, 2005b), which proposes an anterior-ventral to posterior-dorsal gradient, such that BA 47 and BA 45 are involved in semantic processing; BA 45 and BA 44 contribute to syntactic processing; and finally, BA 44 and parts of BA 6 have a role in phonological processing.

The aim of the current study is to use the phenomenon of semantic ambiguity to specify more precisely the functional roles of the LIFG (and its subregions) during sentence comprehension. Semantic ambiguity is ubiquitous in natural language: at least 80% of the common words in a typical English dictionary have more than one definition and some words have over 40 different possible interpretations (e.g., “an athlete runs,” “a river runs,” “a politician runs”; Parks et al. 1998; Rodd et al. 2002). To understand a sentence containing an ambiguous word, the listener selects the most likely meaning for each word within the sentence on the basis of a range of contextual cues (Twilley and Dixon 2000). In most cases, the listener will select the correct meaning and will be completely unaware of the ambiguity. Occasionally, the listener will select the wrong meaning and may be required to reinterpret part of the sentence.

Recent fMRI studies have consistently highlighted the role of the pLIFG in resolving semantic ambiguities within sentences (Rodd et al. 2005; Davis et al. 2007; Mason and Just 2007; Zempleni et al. 2007; Rodd, Longe, et al. 2010). Rodd et al. (2005) compared spoken sentences that contained several ambiguous words (e.g., the shell was fired toward the tank) with well-matched low-ambiguity sentences (e.g., her secrets were written in her diary). The additional processing required by the high-ambiguity sentences was reflected in a large cluster of activation that included both partes triangularis and opercularis of the LIFG. Subsequent replications have further shown that this ambiguity-related response is attenuated during sedation (Davis et al. 2007) and involves the same portion of the pLIFG as a response to “syntactic” ambiguities (Rodd, Longe, et al. 2010). This semantic ambiguity response is sufficiently robust that it has been used as a marker of preserved speech processing in patients with disorders of consciousness (Coleman et al. 2007, 2009). Similar increases in pLIFG activation are also seen in response to semantic ambiguities in “visually” presented sentences (Mason and Just 2007; Zempleni et al. 2007) and for verbal jokes that depend on semantic ambiguity (Bekinschtein et al. 2011). In some cases, these ambiguity-related responses extend into the inferior portion of the “anterior” LIFG (Mason and Just 2007; Rodd, Longe, et al. 2010), and they have also been observed in the posterior “right” IFG (Rodd et al. 2005; Mason and Just 2007; Zempleni et al. 2007). The proposal that the LIFG plays a critical role in ambiguity resolution in language comprehension is also supported by impaired ambiguity resolution in patients with left frontal lesions (Metzler 2001; Bedny et al. 2007; Vuong and Martin 2010). However, which of the several cognitive operations described above (activation or selection of multiple meanings or reanalysis of misinterpreted sentences) is associated with the LIFG remains unclear.

A second brain region that has been closely associated with semantic disambiguation is the posterior and inferior portion of the left temporal lobe. Ambiguity-related activity has previously been reported in the posterior portion of the left fusiform gyrus as well as the left inferior/middle temporal gyri (Rodd et al. 2005; Davis et al. 2007; Zempleni et al. 2007). Although there is general agreement that this region plays an important role in lexical processing (e.g., Lau et al. 2008), the precise functional roles of these regions in sentence comprehension have yet to be determined.

The aim of the current study is to characterize the nature of the semantic ambiguity response in both the LIFG and in posterior brain regions. In particular, we will assess whether these responses are triggered by the ambiguity itself or the disambiguating information. In order to address hypotheses concerning the time course of neural responses to sentences, without compromising either the quiet listening conditions required for effortless sentence comprehension (Davis and Johnsrude 2003) or sensitivity to activity in critical regions of the inferior temporal lobe (Peelle et al. 2010), we use the interleaved silent steady state (ISSS) sparse imaging protocol (Schwarzbauer et al. 2006). This sequence includes a silent period in which spoken sentences are presented, followed by acquisition of a rapid train of brain images (1-s time resolution) that reveal the time course of the blood oxygen level-dependent response to the preceding sentence (see Davis et al. forthcoming).

The primary analyses focus on high-ambiguity sentences in which an ambiguous word is preceded by a “neutral” context

that does not provide a reliable cue as to which meaning is appropriate: disambiguation occurs “after” the ambiguous word is presented. The critical comparison is between sentences in which the disambiguating information occurs within the next 2 or 3 words after the ambiguous word (“Immediate Disambiguation”; see Fig. 1a) and sentences in which the disambiguation occurs significantly later (Delayed Disambiguation). Neural responses to the ambiguous word will occur at the same time for both types of sentence, but responses associated with disambiguation will occur at different times (Fig. 1c). The contrast between these 2 types of high-ambiguity sentences will therefore allow us to determine whether responses are triggered by the ambiguous words themselves or by their subsequent disambiguation. Based on current psycholinguistic models of ambiguity resolution (Twilley and Dixon 2000), we assume that responses to the ambiguous word reflect the process of selecting a single meaning (based on prior context or meaning frequency), whereas activation that is triggered by disambiguating information reflects reinterpretation of a sentence that was initially misinterpreted.

Based on previous studies (Rodd et al. 2005; Davis et al. 2007; Mason and Just 2007; Zempleni et al. 2007; Rodd, Longe, et al. 2010), we predict that the high-ambiguity sentences will produce more activation than low-ambiguity sentences in both pLIFG and the posterior portion of the temporal lobe but the extent to which these ambiguity-related responses will be triggered by either the ambiguous word itself or the disambiguating word is unclear.

One possible outcome is that ambiguity-related activity within the LIFG will be triggered by the ambiguous word itself. This outcome would be consistent with the idea that when listeners encounter an ambiguity they rapidly select a single appropriate meaning (Twilley and Dixon 2000) and that the LIFG plays a key role in this function of selecting appropriate representations from among competing alternatives (Thompson-Schill et al. 2005; January et al. 2009). This view predicts that ambiguity-related activity should emerge at the same time for both “Immediate” and “Delayed” ambiguities, as the ambiguous word is positioned in same location in these 2 types of sentences. Additionally, this “semantic selection” account predicts that there should be significant ambiguity-related activity for the “Prior” ambiguities in which listeners are required to select the appropriate meaning on the basis of preceding context.

A second possible outcome is that ambiguity-related activity within the LIFG will primarily be triggered by the disambiguating information. This outcome would be consistent with those accounts that emphasize the role of the LIFG in reinterpreting misparsed sentences (Novick et al. 2005). These accounts predict that the ambiguity-related activity for the Immediate and the Delayed sentences should emerge at different points in time. Specifically, there should be an early increase in activity for the Immediate sentences followed by a later increase for the Delayed sentences. Additionally, these accounts predict essentially no ambiguity-related activity for the Prior ambiguities, when listener can immediately select the correct meaning and reinterpretation is required.

A third possible outcome is that the LIFG might show some combination of these effects, suggesting that it plays a role in both the initial selection of a single word meaning and in subsequent sentence reinterpretation. Finally, given that “semantic” and “phonological” functions have been attributed

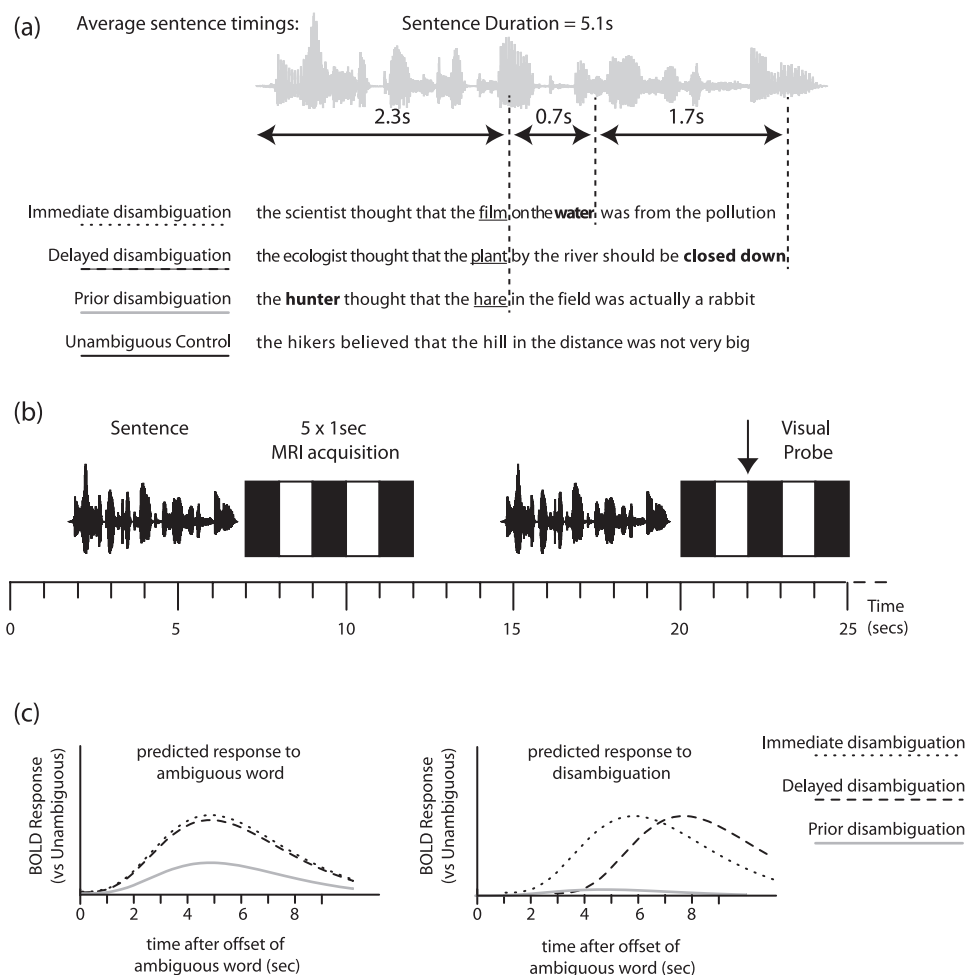


Figure 1. Details of the event timings. (a) Example sentences in the 4 speech conditions (ambiguous word underlined, disambiguation region in bold) together with average timings of the disambiguating information within the Immediate and Delayed sentences relative to the ambiguous words, all timing measured from word offset. (b) ISSS imaging procedure (see Materials and Methods), in which a single stimulus item was presented in the silent period preceding a set of five 1-s scans. The sentences were presented such that there was a 200-ms gap between sentence offset and scan onset. The times at which the ambiguous word and disambiguating context occurred in each sentence were measured in order that scans in the series could be categorized relative to these events. Visual probes occurred at the midpoint of the third of the 5 scans, minimizing sensitivity to the blood oxygen level-dependent (BOLD) effect of the semantic relatedness probe task. (c) Predicting timings of responses to the ambiguous words and disambiguating information. Responses to the ambiguous word are predicted to occur at the same time in all 3 high-ambiguity conditions but are likely to be of smaller magnitude in the Prior disambiguation condition. Responses to the disambiguating information are predicted to occur approximately 1.7 s later in the Delayed condition compared with the Immediate condition.

to the aLIFG and pLIFG, respectively (Buckner et al. 1995; Fiez 1997; Poldrack et al. 1999), the more aLIFG might primarily be recruited during selection of the appropriate meaning of the ambiguous word based on the semantics of the rest of the sentence, whereas the more posterior region might be associated with the phonological memory processes that are necessary for reprocessing sentences that were initially misinterpreted.

Materials and Methods

Materials

Stimuli

The sentences were taken from a recent behavioral experiment (Rodd, Johnsrude, et al. 2010, Experiment 2) and include 3 different types of high-ambiguity sentences in which the relative positions of the ambiguous words and the disambiguating information are varied as well as a matched set of low-ambiguity sentences (see Fig. 1a). There

were 49 sentences in each condition, constructed in quartets (1 sentence for each of the 4 experimental conditions). Sentences within each quartet had similar syntactic structures. The duration of the individual sentences ranged from 3.0 to 7.6 s (mean = 5.1 s). Sentences in the 4 conditions were matched on a range of psycholinguistic variables (see Table 1; Rodd, Johnsrude, et al. 2010).

In 2 sets of sentences, the ambiguous word is preceded by a neutral context and the disambiguating information occurs after the ambiguity. In the Immediate Disambiguation condition, the disambiguation occurs less than a second after the offset of ambiguous word (2–3 words), whereas in the Delayed sentences, the disambiguation occurs on average 2.4 s after the offset of the ambiguous word with several intervening words that do not provide disambiguating information (see Fig. 1a). As shown, there is a 1.7 s difference between the positions of the disambiguating information in these 2 types of sentences, and hence, we predict a delay of nearly 2 s in neural responses to disambiguation. To facilitate fMRI analysis, the position (relative to sentence onset) of the offset of the ambiguous word (and homologous point in the “Unambiguous” sentences) was manually measured for each sentence; these times were matched across sentences of a quartet (see Table 1).

Table 1

Descriptive statistics for sentence materials (SD given in brackets)

Sentence condition	Duration (s)	Words	Syllables	Position of ambiguity (words)	Position of ambiguity (seconds)	Position of disambiguation (words)	Position of disambiguation (seconds)
Immediate	5.1 (0.9)	19.1 (3.3)	25.2 (4.2)	8.0 (2.4)	2.3 (0.7)	10.8 (2.4)	2.95 (0.7)
Delayed	5.1 (0.7)	19.2 (3.3)	25.0 (3.8)	8.0 (2.4)	2.3 (0.7)	18.0 (3.9)	4.75 (0.8)
Prior	5.1 (0.9)	19.1 (3.2)	25.6 (3.9)	8.1 (2.4)	2.3 (0.7)		
Unambiguous	4.9 (0.8)	19.1 (3.3)	25.5 (4.1)	8.0 (2.3)	2.2 (0.6)		

Note: Positions of the ambiguous and disambiguating words were measured from sentence onset. (For the Unambiguous condition, this refers to the matched unambiguous word.).

A sentence completion pretest in which the sentences were cut off immediately after the ambiguous word (for details, see Rodd, Johnsruide, et al. 2010) indicated that for the Immediate and Delayed conditions, participants selected the intended meaning on only 29% (standard deviation [SD] = 24) and 30% (SD = 28) of trials, respectively. Although these sentences contain a mixture of “balanced” ambiguities, which have 2 equally frequent meanings and “biased” ambiguities, which use the subordinate (less preferred) meaning, in neutral contexts such as these, listeners will select the incorrect meaning on about 70% of trials. For the “Prior Disambiguation” sentences, the ambiguous word is preceded by a strongly biasing context that enabled participants to select the appropriate meaning for 96% (SD = 6.1) of sentences in the pretest.

A set of 49 sentences that were not used in the experiment (matched to the experimental sentences for number of syllables, number of words and physical duration, and recorded at the same time by the same speaker) were converted to unintelligible signal-correlated noise (SCN, Schroeder 1968) using Praat software for use as a low-level baseline (Although the amplitude envelope of speech [which is preserved in SCN] can, in theory, provide cues to some forms of prosodic and phonological information [Rosen 1992], such cues are insufficient for the listener to recognize lexical items [Davis and Johnsruide 2003; for an example of this type of stimulus, see http://www.mrc-cbu.cam.ac.uk/~matt.davis/jneurosci/scn_f32.wav]). SCN stimuli have the same amplitude envelope as the original speech, but the amplitude envelope is filled with speech-spectrum noise. They are therefore approximately matched to clear speech on spectral and amplitude profiles but are entirely unintelligible.

For half of the real sentences (randomly selected), a probe word was selected for use in the relatedness judgment task. These probes were taken from our previous study (Rodd, Johnsruide, et al. 2010) and were either strongly related (50% of probes) or unrelated (50% of probes) to the sentence’s meaning. The probes were never related to the unintended meanings of the ambiguous words and were included to ensure participants’ attention to the sentences throughout the experiment (Rodd et al. 2005).

Participants

Fifteen right-handed volunteers (aged 18–40) were scanned. All participants were native speakers of English and declared themselves to be right-handed and to have no history of neurological illness, head injury, or hearing impairment. The study was approved by the Addenbrooke’s Hospital’s Local Research Ethics Committee, and written informed consent was obtained from all participants. All participants were compensated for their time using the standard rate for volunteers from the MRC CBU volunteer panel.

Procedure

We used a semispase imaging technique (ISSS imaging; Schwarzbauer et al. 2006). As with conventional sparse imaging (Hall et al. 1999), acoustic interference from scanner noise is minimized by presenting the sentences in the silent period between image volumes. However, unlike conventional sparse imaging in which only one volume is acquired after each silent period, this technique allows multiple volumes to be taken after each sentence and thereby provides information about the time course of neural responses. Continuous silent slice-selective excitation pulses maintain steady-state longitudinal

magnetization and ensure that signal contrast is constant across successive scans (Schwarzbauer et al. 2006). A single sentence (or noise equivalent) was presented during an 8-s silent period, which was followed by five 1-s scans (Fig. 1b). The sentences were positioned within the silent period such that there was a 200-ms gap between the end of the sentence and the onset of the first scan.

Volunteers were instructed to listen carefully to the sentences. On half of the trials, a visual probe word was presented at the end of the sentence, and volunteers were instructed to make a button press to indicate whether this word was related to the meaning of the sentence or not (right index finger or thumb for related, left index finger or thumb for unrelated). For the baseline noise and silence conditions, the word right or “left” appeared on the screen, and volunteers simply pressed the corresponding button. On the other half of the trials, a fixation cross appeared on the screen, and volunteers were instructed to simply wait for the next trial to begin. These undemanding tasks were included to ensure participants’ attention throughout the experiment. The visual probes appeared at the onset of the second acquisition scan, ensuring that very little of the hemodynamic response to the probe word would be observed in the fMRI data (see Fig. 1b).

The experiment was divided into 6 blocks of 49 trials. Stimulus items were pseudorandomized to ensure that the 4 experimental conditions, noise baseline, and rest scans ($N = 49$) were evenly distributed among the 6 blocks and that each condition occurred equally often after each of the other conditions. One block was administered per scanning run, and block order was counterbalanced across participants. Stimuli were presented to both ears using a high-fidelity auditory stimulus-delivery system incorporating flat frequency-response electrostatic headphones inserted into sound-attenuating ear defenders (Palmer et al. 1998). To further attenuate scanner noise, participants wore insert earplugs. DMDX software running on a Windows 98 PC (Forster KI and Forster JC 2003) was used to present the stimulus items and record button-press responses. Volunteers were given a short period of practice in the scanner with a different set of sentences.

The imaging data was acquired using a Bruker Medspec (Ettlingen, Germany) 3-T MR system with a head gradient set. The following imaging parameters were used: slice thickness, 4 mm; interslice gap, 1 mm; number of slices, 18; slice orientation, axial oblique; field of view, 20 × 20 cm; matrix size, 64 × 64; in-plane spatial resolution 3.1 × 3.1 mm. Acquisition was transverse-oblique, angled away from the eyes, and covered all the brain except the most dorsal and posterior aspect of the parietal lobe in some subjects with larger heads.

fMRI Analysis Method

The fMRI data were preprocessed and analyzed using Statistical Parametric Mapping software (SPM2, Wellcome Department of Cognitive Neurology, London, UK). Preprocessing steps included within-subject realignment, spatial normalization of the structural images (and coregistered functional images) to a standard template (MNI ICBM 152) using smoothly nonlinear warps, and spatial smoothing using a Gaussian kernel of 10-mm full-width at half-maximum (FWHM), suitable for random-effects analysis (Xiong et al. 2000). To assess regional specialization within inferior frontal regions, a second version of normalized data was generated with a smoothing kernel of 6-mm FWHM (Following Xiong et al. (2000), we chose to conduct the main analyses using data smoothed at 10-mm FWHM to optimize the statistical power in the random-effects analyses, which aim to identify those regions that show differences between our

sentences conditions [see Tahmasebi et al. forthcoming]. However, we were concerned that this relatively high level of smoothing might reduce our ability to distinguish neighboring regions of cortex that show different response profiles. The clustering analyses were therefore conducted using data smoothed at 6-mm FWHM). These more lightly smoothed data are only used in clustering and region of interest (ROI) analyses in order to maximize the possibility of fractionating the response profiles of adjacent cortical regions.

In the first stage of the analysis, a single general linear model was constructed for each volunteer in which each scan within each run was coded according to the condition of the preceding stimulus. Given the aim of assessing the time course of the hemodynamic effects in the different conditions relative to the position of the ambiguous word, we constructed single-subject FIR models in which each of the five 1-s scans following each sentence was categorized into 1 of 6 time bins according to its position relative to the ambiguous word. The scans in the first time bin were acquired between 2 and 3 s after the offset of the ambiguous word (or matched unambiguous control), whereas the scans in the final time bin were acquired 7–8 s after the offset of the ambiguous words. Due to the natural variation in sentence lengths and the position of the ambiguities within these sentences, not all the sentences contributed to all the 6 time bins. The percentage of sentences contributing to the 6 time bins were 49%, 92%, 100%, 100%, 95%, and 51%. The 6 scanning runs were modeled within a single design matrix, with additional columns encoding subject movement for each of the 6 runs (as calculated from the realignment stage of preprocessing) as well as a constant term for each run. Images containing the contrasts of parameter estimates for these different conditions were entered into second-level group analyses in which intersubject variation was treated as a random effect (Friston et al. 1999). In this second-level analysis, for whole-brain analyses, we report peak voxels that exceed a significance threshold controlling the rate of false positives across the whole brain (false discovery rate [FDR], $P < 0.05$).

To explore the effects of ambiguity, we first compare the Immediate and Delayed conditions to the Unambiguous sentences and then in a separate set of analyses, we compare the Prior condition to the Unambiguous sentences. This separation reflects the prediction (based on behavioral studies; Twilley and Dixon 2000) that the magnitude of any ambiguity-related activation in the Prior condition will be substantially smaller than the other ambiguous conditions. Accordingly, we consider this condition separately and use the analysis of the Delayed and Immediate conditions to provide a more restricted search volume, thereby increasing our sensitivity to ambiguity-related activity in the Prior condition.

fMRI Analysis Method: Clustering Analyses

To assess whether activation clusters can be reliably fractionated into 2 subregions based on the relative magnitude of responses to the Immediate and Delayed sentences, we used a data-driven k -means clustering analysis (Simon et al. 2004; Davis et al. forthcoming) implemented in Matlab v6.5 (www.mathworks.com). This analysis focuses on the magnitude of the response to each of the Delayed and Immediate sentences relative to Unambiguous sentences in time bin 2 (see fMRI Results).

The algorithm starts by choosing 2 random values for the magnitude of the response to each of the Delayed and Immediate sentences relative to Unambiguous sentences for each of 2 cluster centroids. Active voxels are assigned to the centroid with the most similar response to Delayed and Immediate sentences, and once assigned, the centroids are updated to be the mean of the assigned voxels. These phases are iterated until no voxels are assigned to different clusters in consecutive runs. Since this k -means clustering procedure is sensitive to starting conditions, we repeated this procedure 50 times using different random seeds and the solution that maximized the between-cluster (explained) variance divided by the within-cluster (unexplained) variance was selected. In this way, the clustering algorithm divides the activated region into 2 mutually exclusive subsets, based on the relative magnitude of activation for the Immediate and Delayed conditions in early time bins.

To ensure that voxels were clustered on the basis of the relative magnitude of responses to Immediate and Delayed items and not on the basis of the overall magnitude of the ambiguity response, the condition-specific activation in each voxel was divided by the mean activation in that voxel in the same time bin for both conditions together (relative to unambiguous, for another application of this method, see Davis et al. forthcoming). Because this ratio measure is unstable for voxels with low levels of overall activation, an additional mask was applied such that voxels were only included if either of the 2 ambiguous conditions yielded significantly more activity than the Unambiguous condition at this time bin. In practice, this mask resulted in the exclusion of those voxels that only showed an ambiguity effect in the later time bins.

To assess whether the resulting clusters, which were identified on the basis of activation levels averaged across participants, were significantly different from each other, while avoiding bias caused by using the same data in generating the clusters and in subsequent statistical analysis (cf. Kriegeskorte et al. 2009), we used an iterative, leave-one-out procedure (see also, Davis et al. forthcoming). Clustering is performed on mean data generated from 14 of the 15 participants, and the 2 resulting clusters are then used to extract data from the remaining participant. Data from the 15th participant will therefore come primarily from corresponding locations as in clustering analysis of the entire group of participants (determined using maximal overlap). Importantly, these cluster locations will be independent of the data from the left-out participant. Repeating this procedure for each of the left-out participants thus allows extraction of group data without bias or circularity. We can then conduct statistical analysis on clustered data to test for cluster-by-condition interactions indicative of differential responses to ambiguous words and their disambiguation.

Results

Response-Time Data

The response-time data were only available for 13 of the 15 participants due to a technical error. Responses indicated that participants actively comprehended the sentences throughout the experiment, with low overall error rates (mean = 4.8%, range 0.7–9.0% across participants) and fast response times (mean = 1004 ms, range 577–1453 ms across participants). Since the probe word and subsequent response were present on only 50% of trials and timed to minimize the sensitivity of scans to task effects (see Rodd et al. 2005), we will not consider neural correlates of these response processes in the analysis of our fMRI data.

Speech Versus Noise

To identify the network of brain regions involved in speech comprehension (regardless of ambiguity), we combined the responses to the 4 speech conditions and compared them with the baseline noise condition (collapsed across the 6 time bins). This analysis revealed that large areas of activation centered on the superior and middle temporal gyri bilaterally. In the left hemisphere, this activation cluster extended up into the angular gyrus as well as into the LIFG (partes triangularis and opercularis), and there was also activation in the left fusiform gyrus and left parahippocampal gyrus (Table 2). These activations are consistent with previous studies that include this contrast between spoken sentences and SCN (Davis and Johnsrude 2003; Rodd et al. 2005; Rodd, Longe, et al. 2010).

Immediate and Delayed Versus Unambiguous

Activation in these 3 sentence conditions (each compared with the same baseline SCN condition) was entered into an analysis of variance (ANOVA) with condition (3 levels) and time (6 levels, each corresponding to a single FIR time bin) as the 2

Table 2

All speech conditions versus baseline: all significant activation peaks > 8 mm apart ($P < 0.05$ FDR corrected for multiple comparisons, cluster size > 10 voxels)

Cluster	Voxels	Location	Coordinates	P (uncorrected)	P (FDR)	Z
1	1529	R aSTG	62, -6, -8	0.001	0.001	6.11
		R aSTG	50, 14, -20	0.001	0.001	5.24
		R STS	66, -28, -2	0.001	0.001	4.36
		R STS	56, -32, 0	0.001	0.001	4.34
2	3140	L STS	-62, -16, 0	0.001	0.001	5.82
		L aSTG	-50, 12, 18	0.001	0.001	5.76
		L aMTG	-60, -6, -12	0.001	0.001	5.62
		L STS	-60, -26, -4	0.001	0.001	5.54
		L pMTG	-58, -56, 18	0.001	0.001	4.37
		L IFG (pars orbitalis)	-44, 30, -14	0.003	0.001	3.92
		L IFG (pars triangularis)	-54, 26, 14	0.003	0.001	3.90
		L angular gyrus	-42, -60, 24	0.008	0.001	3.58
3	207	L fusiform gyrus	-26, -36, -18	0.001	0.006	3.72
		L fusiform gyrus	-40, -42, -20	0.001	0.013	3.42
4	16	L parahippocampal gyrus	-30, -6, -26	0.001	0.023	3.19
5	11	L medial SFG	-8, 64, 20	0.001	0.029	3.12

Note: STG, superior temporal gyrus; ITG, inferior temporal gyrus; STS, superior temporal sulcus; IFG, inferior frontal gyrus; IFS, inferior frontal sulcus.

Table 3

Sentence-type by time interaction: all significant activation peaks > 8 mm apart ($P < 0.05$ FDR corrected for multiple comparisons; cluster size > 10 voxels)

Cluster	Voxels	Location	Coordinates	P (FDR)	P (uncorrected)	Z
1	1495	LIFG (pars triangularis)	-52, 22, 18	0.001	0.001	5.08
		LIFG (pars triangularis)	-52, 36, 2	0.001	0.001	4.46
		LIFG (pars triangularis)	-44, 20, 26	0.001	0.001	4.21
		LIFG (precentral gyrus/pars opercularis)	-44, 12, 32	0.001	0.001	4.20
		LIFG (pars orbitalis)	-48, 38, -10	0.003	0.001	3.52
		LIFG (pars orbitalis)	-48, 20, -8	0.017	0.003	2.80
2	514	L pFusiform	-44, -50, -18	0.001	0.001	4.86
		L pMTG	-60, -48, 8	0.001	0.001	4.22
		L ITG	-48, -56, -12	0.002	0.001	4.02
		L pMTG	-54, -44, -8	0.007	0.001	3.29
		L MTG	-52, -38, -2	0.009	0.001	3.22
		L pMTG	-56, -58, 0	0.016	0.002	2.92
		L pMTG	-50, -44, 6	0.025	0.004	2.71
		L pMTG	-62, -50, 10	0.001	0.001	4.15
3	24					
4	12	L fusiform	-32, -38, -18	0.004	0.001	3.59
5	32	L MTG	-56, -26, -6	0.009	0.001	3.21

factors using methods described by Henson and Penny (2003). Several regions showed a main effect of condition (averaged across time) at uncorrected levels of significance, but these clusters did not reach a corrected level of significance (all $P > 0.1$ FDR). This reflects the fact that activation differences show a specific time course reflecting responses to ambiguous words and their subsequent disambiguation. We thus saw a significant Condition-by-Time interaction in several brain regions. To further increase the power of this analysis, it was masked to only include those brain regions that also exhibited a main effect of ambiguity, (i.e., more activation in Delayed and Immediate [combined] compared with Unambiguous, averaged across time $P < 0.05$ uncorrected [This contrast did not reveal any activation that was significant at corrected levels $\{P > 0.05$ FDR corrected}. This reflects the relative insensitivity of this contrast that does not take into account the interaction with time.]). Because the contrast used to create this mask does not include time as a factor, it is orthogonal to the contrast of interest (the Condition-by-Time interaction). This masked interaction analysis yielded 5 significant clusters of activation (Table 3, Fig. 2). These clusters were located in the LIFG, the left inferior temporal gyrus (LITG)/fusiform gyrus (2 clusters), and the middle temporal gyrus (MTG) (2 clusters). The activation in these 5 clusters for each of the 4 speech conditions (relative to SCN, averaged across voxels in the cluster) is shown in Figure 2.

For each of these 5 clusters, we examine activity in 3 key contrasts in order to reveal the critical functional properties of these brain regions. For each of these analyses, activation is averaged across all voxels within the cluster, and the significance of the appropriate contrast is evaluated using MarsBar (Brett et al. 2002). The key contrasts are:

Unambiguous—SCN (Averaged Across Time)

This contrast will reveal whether this brain region is also involved in processing low-ambiguity sentences.

Immediate-Delayed (Time Bin 2)

This time bin includes scans whose onset was 3–4 s after the offset of the ambiguous word. A significant difference on this

contrast will indicate that the response is being triggered (at least in part) by the disambiguating information. In contrast, if these 2 conditions show a similar increase in these 2 conditions (relative to the Unambiguous sentences) then this response is likely to have been triggered by the ambiguous word itself, which occurs at the same time in both sentences (see Fig. 1c). (We do not look in detail at time bin 1 since its onset was only 2–3 s after the offset of the ambiguous word and hence is likely to be too early to show an effect of the ambiguity. Indeed, this time bin showed no clear ambiguity-related response perhaps also due to the reduced amount of data in this time bin [see fMRI Analysis Methods]). This is consistent with previous estimates of hemodynamic responses to auditory stimuli (Hall et al. 2000).

Delayed-Immediate (Time Bin 5)

This time bin includes scans collected 6–7 s after the offset of the ambiguous word. (We do not look in detail at time bin 6 due to the reduced amount of data in this time bin, see fMRI Analysis Methods above.)

Regions in which activity is triggered by the disambiguating information would be expected to show an early increase for Immediate greater than for Delayed disambiguation sentences in earlier time bins but to show the reverse effect at this later time point (see Fig. 1c).

Cluster 1: LIFG

The large cluster of activation within the LIFG (Cluster 1; 1495 voxels) has its peak (-52, 22, 18) in the posterior portion of pars triangularis and extends posteriorly into the pars opercularis and precentral gyrus and anteriorly into the pars orbitalis (Table 3). This region shows no significant difference between Unambiguous sentences and the unintelligible SCN baseline averaged across time (ROI analysis: $t = 1.2$, $P > 0.1$) (There was also no significant interaction between this contrast [Unambiguous—SCN] and time [$t = 1.3$, $P > 0.2$]). Rather, this cluster shows activation increases for both the Immediate and Delayed conditions relative to Unambiguous sentences, with further differences between these 2 ambiguous conditions. In the earlier phase (Fig. 2: Cluster 1), there is more activation for the Immediate condition compared with the Delayed condition

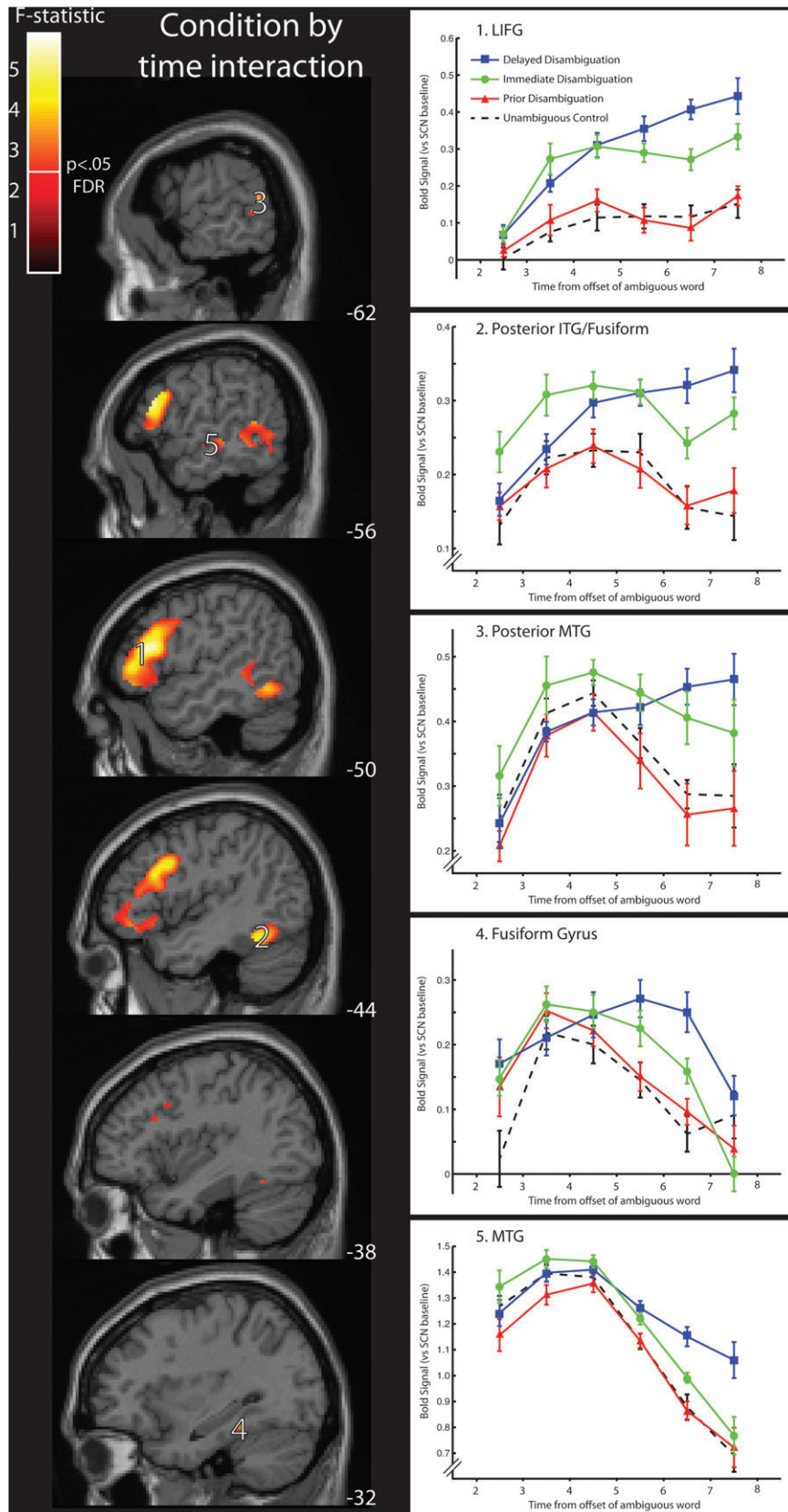


Figure 2. The interaction between sentence-type (Immediate, Delayed, Unambiguous) and time (in 1-s time bins), thresholded at $P < 0.05$ (FDR whole-brain corrected) rendered onto slices of the Montreal Neurological Institute canonical brain image (x -coordinates as shown). Plots show the magnitude of the individual parameter estimates (averaged across all the voxels within each of the 5 significant clusters labeled in slices) for the contrasts between each of the 4 sentence conditions and SCN, plotted against time (average time in seconds from the offset of the ambiguous word or matched control word). Error bars show the standard error of the mean after between-subjects variation is removed, suitable for repeated-measures comparisons.

(ROI analysis: time bin 2, Immediate > Delayed, $t = 2.0$, $P < 0.05$), whereas in the later phase, there is more activation for the Delayed condition (ROI analysis: time bin 5, Delayed > Immediate, $t = 3.8$, $P < 0.001$). So for this cluster, the Condition-by-Time interaction pattern is consistent with this region being sensitive to disambiguation, although it may also be sensitive to the presence of ambiguity.

To assess whether this LIFG cluster can be reliably fractionated into subregions on the basis of the early response to Immediate and Delayed items (a key test for whether activation is triggered by the ambiguity or by disambiguating information), we took 2 approaches.

The first approach was to compare the responses to Immediate and Delayed sentences within 2 ROIs within aLIFG and pLIFG: these regions have been proposed to play different roles (semantic vs. phonological computations) in language tasks (Buckner et al. 1995; Fiez 1997; Poldrack et al. 1999). We selected the coordinates at which TMS has been shown to selectively interfere with these decisions (semantic decisions, aLIFG: -52, 34, -6; phonological decisions, pLIFG: -52, 16, 8; Gough et al. 2005) and created spherical ROIs of 10-mm radius centered on these 2 coordinates (see Fig. 4). The activation within these ROIs was extracted using Marsbar and submitted to the same analyses described before. Both ROIs showed a significant condition $\times$ time interaction (anterior: $F_{10,140} = 4.27$, $P < 0.0001$; posterior: $F_{10,140} = 2.83$, $P < 0.01$). The activation profiles of these 2 ROIs were similar: there was more activity in the Immediate compared with the Delayed condition in time bin 2, but both these conditions were more active than Unambiguous (see Fig. 3). Given the nonsphericity that is expected of time course data, we used a multivariate ANOVA on the difference between the Delayed and Immediate conditions to determine whether there was a significant difference between these 2 ROIs in their responses to the 2 critical conditions (Davidson 1972). This multivariate analysis of variance (MANOVA) showed a significant main effect of time ($F_{5,10} = 3.5$; $P < 0.05$) indicating that the ROIs are involved in disambiguation since these 2 conditions differed only in the timing of disambiguation. The main effect of ROI and the interaction between ROI and time were both nonsignificant ($F_{1,14} < 1$; $F_{5,10} < 1$) indicating no difference in the response of these anterior and posterior IFG regions.

In addition to assessing whether these apriori ROIs showed different response profiles to these 2 critical conditions, we used a data-driven approach to look for functionally different subclusters within this LIFG cluster. As before, we focused on the responses to Immediate and Delayed sentences in time bin 2 (relative to Unambiguous sentences), between 3 and 4 s after the offset of the ambiguous word. The relative sizes of these 2 responses provide a key diagnostic of whether activation is being triggered by 1) the initial ambiguity or 2) the subsequent disambiguating information. Voxels in which activation is primarily triggered by the ambiguity itself will show no difference between these 2 responses, whereas voxels in which activation is primarily triggered by the disambiguating word will show more activation for the Immediate sentences than the Delayed sentences.

We applied a k -means clustering algorithm to the data from time bin 2 in these 2 conditions (see fMRI method). This clustering procedure allowed us to segregate the voxels within the large LIFG cluster into 2 “subclusters,” one of which showed more activation for Immediate than Delayed in time bin 2 and one

of which showed similar responses in both conditions. However, these 2 subclusters are neither unitary nor spatially coherent: voxels belonging to the 2 different subclusters interdigitate across the LIFG and do not respect anatomical constraints. In addition, an ANOVA on the mean response for each participant to the Delayed and Immediate sentences (relative to the Unambiguous), using the leave-one-out procedure (see fMRI method) showed no significant interaction between subcluster and condition ($F_{1,14} < 1$). (The main effects of condition and subcluster were also nonsignificant; $F_{1,14} = 2.45$; $P > 0.1$; $F_{1,14} < 1$). Thus, the results of this algorithm indicate that the each of the 2 response profiles of interest are seen in voxels in both aLIFG and pLIFG and that the precise anatomical localization of these voxels is “not” consistent across participants.

Clusters 2 and 4: Left Inferior Temporal/Fusiform

A second large cluster of activation (Fig. 2, Cluster 2; 514 voxels) has a peak in the left posterior fusiform gyrus (-44, -50, -18) and extends laterally into the left posterior ITG and superiorly into the MTG. There is also a smaller, more anterior, cluster within the fusiform gyrus (Cluster 4; 12 voxels). For both these clusters, there is a significant response to the Unambiguous sentences relative to SCN (ROI analyses: $t = 2.9$, $P < 0.01$; $t = 2.5$, $P < 0.05$). For the larger of these 2 clusters (Cluster 2), there is more activation for the Immediate than for the Delayed sentences in time bin 2 (ROI analysis: $t = 2.1$, $P < 0.05$) and more activation for the Delayed than for the Immediate sentences in time bin 5 (ROI analysis: $t = 3.6$, $P < 0.005$). The activation profile in the smaller cluster (Cluster 4) is less clear. Here, the difference between the Immediate and Delayed sentences in time bin 2 was not significant ($t = 0.8$, $P = 0.2$), although the increase in activation for the Delayed sentences in time bin 5 was significant (ROI analysis: $t = 2.5$, $P < 0.05$).

To confirm that the response profile to the critical Delayed and Immediate conditions in the larger of these 2 temporal lobe clusters (Cluster 2) is significantly different from the earlier LIFG cluster, we conducted a 2-way MANOVA with time and cluster as factors and with the difference between Delayed and Immediate as the dependent variable. This showed a significant interaction between time and cluster ($F_{5,10} = 3.5$; $P < 0.05$). (The main effect of time was significant ($F_{5,10} = 16.9$; $P < 0.001$) but the effect of cluster was not ($F_{1,14} = 2.8$, $P > 0.1$). This confirms that the frontal and temporal lobe show a different temporal profile of responses to ambiguous words and their subsequent disambiguation in spoken sentences.

Clusters 3 and 5: Left MTG

Two small clusters of activation were present for the Time-by-Condition interaction in the posterior portion of the MTG (Cluster 3; 24 voxels) and the middle portion of the MTG (Cluster 5; 32 voxels). In both clusters, activity is greater for the Unambiguous sentences than for SCN (ROI analyses: $t = 4.6$, $P < 0.001$; $t = 9.0$, $P < 0.001$). Although both clusters exhibit an early response to the Immediate sentences and a late response to the Delayed sentences, these effects are not as statistically robust as for the other clusters. The increase for the Delayed condition relative to the Immediate condition in time bin 5 is significant in both clusters ($t = 1.8$, $P < 0.05$; $t = 3.4$, $P < 0.005$), but the increase for the Immediate condition relative to the Delayed condition in time bin 2 is only marginally significant ($t = 1.5$, $P = 0.07$; $t = 1.7$, $P = 0.051$).

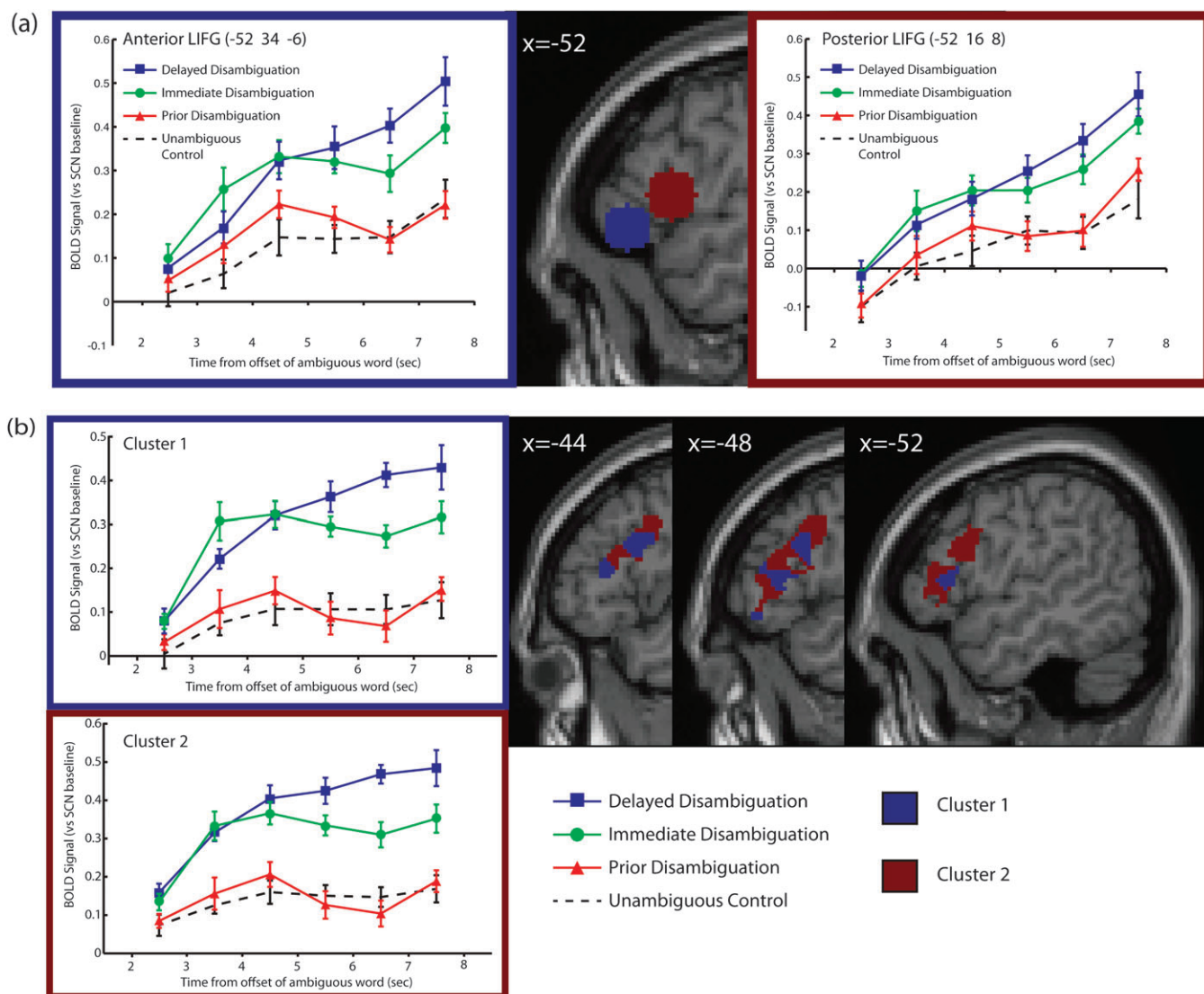


Figure 3. (a) Responses within 2 apriori ROIs within aLIFG and pLIFG (10-mm diameter sphere centered at $-52, 34, -6$ [blue: anterior] and $-52, 16, 8$ [red: posterior]). Plots show the magnitude of the condition-specific blood oxygen level-dependent (BOLD) response against time plotted as in Figure 2 (averaged across all the voxels within each ROI). (b) Results of the *k*-means clustering procedure in which voxels are grouped into clusters defined according to the relative magnitude of the response in time bin 2 to Immediate compared with Delayed sentences. Plots show the magnitude of the condition-specific BOLD response against time for voxels in the corresponding colors, plotted as in Figure 2 (averaged across all the voxels within each subcluster). Although results give the appearance of 2 differentiable subclusters, response differences between these clusters were nonsignificant when cluster locations were defined using a leave-one-out procedure that avoids circularity. Cluster locations are interdigitated over a broad region of the LIFG such that no clear functional or anatomical separation of anterior and posterior regions is shown by this analysis.

Prior Versus Unambiguous

Psycholinguistic studies of stimuli of this type in which the ambiguity is preceded by biasing context indicate that these ambiguities are resolved very rapidly (Twilley and Dixon 2000), and we thus predicted only a transient increase in activity for prior compared with unambiguous sentences, time locked to the ambiguous word. Accordingly, we looked for a main effect of Time in an analysis that included the comparison between the Prior and Unambiguous conditions for each of the 6 different time bins. This main effect of Time did not reach corrected significance in the whole-brain analysis ($P > 0.9$ FDR).

To increase the sensitivity of this analysis, we then reduced the search volume using an ROI based on the responses to Immediate and Delayed ambiguities. To ensure the orthogonality of this mask to the Condition-by-Time interaction, we constructed the ROI mask by selecting only those voxels that

showed significantly more activity for the Immediate and Delayed sentences (combined) compared with the Unambiguous sentences, averaged across the 6 time bins ($P < 0.001$ uncorrected). Because the contrast used to create this mask does not include time as a factor, it is orthogonal to the interaction contrast and hence our test comparing the effect of time in the Prior and the Unambiguous condition is independent under the null hypothesis (cf. Kriegeskorte et al. 2009). This approach produced an ROI of 593 voxels within the LIFG that extended across both partes triangularis and opercularis (with subpeaks in both these regions, see Fig. 4). Within this ROI, the Condition-by-Time interaction for the comparison between Prior and Unambiguous conditions was significant ($F = 3.2, P < 0.05$). The form of this interaction is as shown for the larger LIFG cluster in Figure 2, with small increase for the Prior sentences in the early time bins (1–3; see

Fig. 4). However, the direct contrast between Prior and Immediate conditions in each of the 6 single time bins revealed no significant effect (all $P > 0.1$).

Discussion

The network of inferior frontal and posterior temporal brain regions exhibiting ambiguity-related activity in this study is highly consistent with previous fMRI studies of semantic ambiguity resolution (Rodd et al. 2005; Davis et al. 2007; Mason and Just 2007; Zempleni et al. 2007; Rodd, Lange, et al. 2010) and with deficits in meaning selection for ambiguous words following acquired brain injuries to these regions (Metzler 2001; Bedny et al. 2007; Vuong and Martin 2010). The novel contribution of this experiment was to systematically vary the timing of disambiguating information relative to the ambiguous word within each sentence. In combination with a rapid semisparse imaging sequence (Schwarzbauer et al. 2006), this allows us to assess whether activation in the LIFG and in posterior temporal lobe regions is triggered 1) by the ambiguous word and hence reflects cognitive processes related to meaning selection or 2) by subsequent disambiguating information and hence reflects cognitive processes related to reanalysis. We reasoned that activation triggered by the ambiguity itself would become evident at the same time in both immediate and delayed disambiguation conditions, whereas activation triggered by disambiguating information would occur at different time points depending on when critical disambiguating information occurred in the sentence. A variety of regions, including inferior frontal and inferior temporal regions, exhibited different patterns of sensitivity to experimental conditions over time. We will discuss our results concerning different brain regions in turn.

LIFG Contributions to Sentence Comprehension

The LIFG as a whole shows response increases for both the Immediate and Delayed conditions relative to the Unambiguous condition and significant differences between responses to these 2 types of high-ambiguity sentences. Critically, the Immediate condition elicits significantly more activity than the Delayed condition in the early phase of the response (Fig. 2: Cluster 1), and this pattern is reversed in the later phase. This indicates that the LIFG contributes to the process of reinterpretation, which is required when the listener encounters information that is incompatible with their initial interpretation of the ambiguous word. This result is consistent with the claim that one role of the LIFG in sentence comprehension is to reinterpret sentences that were initially misparsed (Novick et al. 2005).

A key question that arises is whether ambiguity-related activity in the LIFG can be “entirely” explained in terms of a reinterpretation process. Two pieces of evidence suggest this is not the case. First, if activation of the LIFG was triggered only by disambiguating information, we would expect the onset of the response in the Delayed condition to occur significantly later than in the Immediate condition (since disambiguation occurs on average 1.7 s later in the Delayed condition). However, even in time bin 2, which is the earliest bin to show an ambiguity effect, there is a clear response to both the Immediate and Delayed sentences relative to the Unambiguous sentences. This indicates that the ambiguity effect in the Delayed sentences is triggered in part by the ambiguous word itself. Second, the LIFG also shows a small (but significant) response to ambiguous words that were “preceded” by disambiguating information (Prior condition; e.g., “the hunter thought that the hare/hair . . .”) for which no reinterpretation is required. These 2 results indicate that the LIFG activation is not entirely due to a reinterpretation process but that this region is also involved in the initial semantic selection process that is triggered by the ambiguous word.

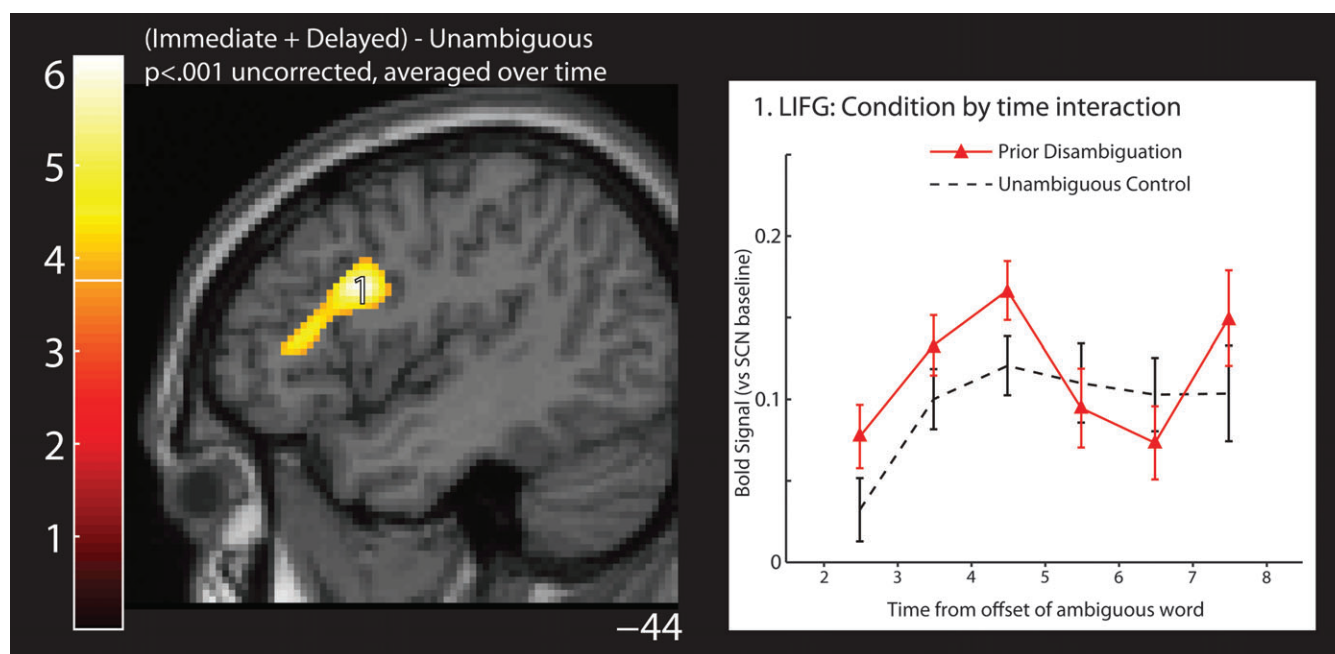


Figure 4. The LIFG ROI used to assess the interaction between sentence-type (Prior vs. Unambiguous) and time. The plot shows the magnitude of the response to these 2 sentence conditions compared with SCN (averaged across all the voxels within this ROI) plotted against time.

The LIFG cluster exhibiting time-dependent condition-specific effects extended over all 3 anatomical subregions (partes orbitalis, triangularis, and opercularis) and posteriorly into precentral gyrus. Given this size, it is likely that it includes regions subserving multiple cognitive functions. This claim is consistent with anatomical evidence dividing the LIFG into a number of subregions that are distinguishable on the basis of their cytoarchitecture and connectivity (Amunts et al. 1999; Petrides and Pandya 2002). We employed 2 different methods to examine the anatomical and functional specialization of different LIFG subregions for semantic selection and reanalysis. The first of these was to use ROIs based on a previous study (Gough et al. 2005) to assess anterior and posterior frontal specialization. However, although both regions appear to contribute to both semantic selection and reanalysis, we saw no evidence for differential responses to one or other process in either region. Since it is hard to rule out the possibility that we selected the wrong ROIs, we also used a leave-one-out *k*-means clustering procedure on data acquired 3–4 s after the occurrence of the ambiguous word. This data-driven method acts to spatially segregate different functional profiles within the LIFG. However, this analysis did not succeed in fractionating the LIFG cluster into 2 spatially separated anatomical subregions nor did the regions discovered show cognitive profiles that were stable across participants.

Thus, although the present study provides evidence for LIFG contributions to both word meaning selection and sentence reinterpretation, these functions did not map directly onto an anterior-ventral and posterior-dorsal functional gradient. Instead, the results of the present study suggest that both anterior and posterior aspects of the LIFG are engaged in both these semantic aspects of sentence processing. A critical aim for future work will be to assess whether consistent functional organization might be revealed by either an alternate characterization of the cognitive processes that contribute to ambiguity resolution or by looking for functional consistency at the level of individual participants. We note that recent results indicate that functional variability in inferior frontal and inferior temporal regions is not closely tied to anatomical macrostructure (Tahmasebi et al. forthcoming). It might therefore be that functional definitions rather than anatomical definitions of critical LIFG regions will be more stable over participants and should be used in future work.

One final issue to be discussed is the role of working memory. Several authors have suggested that the role of the LIFG in sentence comprehension is to provide a working-memory store that can hold in mind any incoming information that cannot be completely integrated into the ongoing representation of the sentence, that is, because it is currently ambiguous (Caplan et al. 2000; Kaan and Swaab 2002; Fiebach et al. 2005). To interpret our results along these lines, however, requires a clear notion of what form of “working memory” is employed in sentence disambiguation (e.g., phonological or semantic maintenance) and under what circumstances. Throughout this paper, we have assumed, on the basis of existing behavioral evidence (Twilley and Dixon 2000), that listeners make a relatively early commitment to a single interpretation and do not maintain multiple sentence interpretations over the multiple words that might intervene between an ambiguous word and subsequent disambiguation. However, even within this framework, working memory is likely to play an important role. Working memory may make

a vital contribution to the process of sentence reinterpretation by allowing the listener to return to earlier parts of the sentence so that this material can be reintegrated in order to produce a single coherent interpretation. According to this view, the cognitive process that is triggered by disambiguating information is “reinterpretation,” but this process is critically dependent on working memory.

In summary, then, it appears that the contribution of the LIFG to the processing of ambiguous words in sentences involves sensitivity both to the ambiguity itself and to subsequent disambiguating information. This finding suggests LIFG involvement in multiple cognitive processes, including selection of an appropriate meaning for an ambiguous word and subsequent reinterpretation of the sentence if the initially selected meaning turns out to be incorrect. This claim is consistent with the data reported by Rodd, Lange, et al. (2010), who found LIFG activation for a set of syntactic ambiguities where reinterpretation was highly likely, as well as for semantic ambiguities where it was not. More generally, it suggests that new methods for assessing functional specialization of inferior frontal regions will be required if we are to make sense of the apparent deficits in ambiguity resolution seen in patients with inferior frontal lesions.

Left Temporal Contributions to Sentence Comprehension

We turn now to discussion of ambiguity responses within the temporal lobe. The largest cluster of temporal lobe activation was focused on the fusiform gyrus but extended into both the LITG and LMTG (Fig. 2, Cluster 2), with an additional small cluster in a more anterior and medial portion of the fusiform gyrus (Cluster 4). These activations correspond well with posterior inferior temporal responses seen in previous fMRI studies of ambiguity resolution for spoken (Rodd et al. 2005; Davis et al. 2007; Rodd, Lange, et al. 2010) and written (Zemleni et al. 2007) sentences. As with these previous studies, our finding that semantic ambiguity resolution activates posterior (and not anterior) temporal cortex is broadly consistent with neurocognitive models of speech comprehension in which posterior temporal regions support “lexical and semantic access in the form of a sound-to-meaning interface” (Hickok and Poeppel 2007; see also Lau et al. 2008). Two additional small clusters of ambiguity-associated activation were also seen within more superior regions of the temporal lobe, including posterior MTG (Cluster 3), and more anterior MTG, directly inferior to primary auditory regions (Cluster 5). Similar superior temporal activations have been seen in previous studies of semantic ambiguity (e.g., Rodd et al. 2005), although they were most apparent in response to syntactically ambiguous sentences that used the nonpreferred interpretation (Rodd, Lange, et al. 2010). One important difference between these temporal-lobe responses (Fig. 2, Clusters 2–5) and the LIFG responses discussed previously is that we also see a significant response to the Unambiguous sentences relative to the unintelligible SCN baseline. Thus, additional activity for ambiguous sentences in the temporal lobe reflects engagement of neural processes that are routinely involved in multiple aspects of speech comprehension. This includes even low-ambiguity sentences, which do not place any specific emphasis on meaning selection for ambiguous words nor involve late reinterpretation.

As in frontal regions, however, the magnitude and timing of differential responses to immediate- and delayed-disambiguation

sentences can distinguish contributions to semantic selection and reinterpretation. For the majority of these temporal-lobe regions (clusters 2, 3, and 5), we see additional activation in the early time bins for Immediate compared with Delayed sentences, whereas later time bins show the reverse pattern. However, unlike the LIFG activation, there is no evidence of an early response to the Delayed sentences nor a response to the Prior condition, relative to the Unambiguous condition. It is this difference that is likely responsible for the significant difference that we see between the response of LIFG and posterior temporal regions to sentences that vary in the timing of disambiguation. This pattern of results confirms that the ambiguity-related activation in the inferior temporal lobe is (unlike in frontal regions) triggered by disambiguating information, suggesting a relatively pure contribution to reanalysis processes. This interpretation is entirely consistent with an earlier finding of posterior temporal activation for a set of syntactically ambiguous sentences where reinterpretation was highly likely but not for a set of semantically ambiguous sentences where no such reinterpretation was required (Rodd, Longe, et al. 2010) and with the observation that LITG activation is observed at sentence offset for another set of materials with delayed ambiguity resolution (Bekinschtein et al. 2011). The response of this inferior temporal region may therefore reflect the reactivation of lexical-semantic representations required when the meaning of a sentence is recomputed during reinterpretation. In this way, ambiguity resolution leads to additional activation in brain regions that are ordinarily engaged during initial sentence comprehension. An alternative interpretation of this result is that reactivation of meaning-based processes during reanalysis is a top-down effect associated with a form of meaning priming, which allows listeners to learn about the relative likelihoods of the different word meanings and which has been shown to follow disambiguation in recent behavioral studies (Rodd et al. under revision). Further studies are clearly needed to assess the relationship between frontal and temporal lobe activity and these and other cognitive processes.

Finally, with respect to both temporal and frontal lobe responses, it is interesting to note that, overall, the magnitude of the responses was usually larger for Delayed than for Immediate sentences. There are several possible explanations for this. First, it is plausible that the greater cognitive “effort” required to reinterpret the Delayed sentences is being driven by the larger number of intervening words between ambiguity and disambiguation, making the reinterpretation process more demanding. Second, the temporal interval between these 2 events may be important: it may be more difficult to integrate information between more temporally distant parts of the sentences. Finally, it is possible that structural distance plays a role: it is perhaps easier to integrate information that is contained within the same linguistic phrase. In the current study, these factors are confounded: for the Delayed sentences compared with the Immediate sentences, the disambiguating information is more distant from the ambiguous word in terms of number of words, temporal distance, and structural distance. Subsequent studies using the current method could potentially disentangle the relative contributions of these factors in determining the ease with which a sentence can be disambiguated and the relative loads that such sentences place on particular brain regions.

In summary, the results presented here help us to refine our account of the functional roles of different regions within the

inferior frontal and posterior temporal network sensitive to semantic ambiguity (Rodd et al. 2005; Zempleni et al. 2007; Rodd, Longe, et al. 2010; and others). The LIFG appears to play a primary role in all aspects of semantic disambiguation: both anterior and posterior portions of the LIFG are involved in the semantic selection process that takes place when an ambiguous word is initially encountered, as well as in subsequent reinterpretation that occurs whenever this initial selection is shown (by subsequent words) to be incorrect. In contrast, activation of posterior temporal regions in response to ambiguities largely reflects reengagement of initial processes involved in sentence comprehension when reanalysis of the meaning of the sentence is required. This reactivation of posterior temporal regions in response to especially challenging ambiguous sentences may reflect demanding top-down processing and perhaps explains the numerous observations of activation of similar temporal-lobe regions during presentation of anomalous or uninterpretable sentences (see Davis and Rodd 2011).

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