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# Neural systems for word meaning modulated by semantic ambiguity

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One important issue in neuroimaging research on language is how the brain processes and represents lexical semantics. Past studies with various paradigms reveal that the left inferior prefrontal and midsuperior temporal regions play a crucial role in semantic processing. Those studies, however, typically utilize words having a precise and dominant meaning as stimuli and have not manipulated lexico-semantic ambiguity, a key feature of human language, as an experimental variable. Here, we used a word generation paradigm to examine whether neuroanatomical networks for meaning are modulated by lexical ambiguity. We found that, compared with semantically precise words, semantically ambiguous words were mediated by strong brain activations in the left dorsal-lateral frontal areas, the anterior cingulate, and the right inferior parietal lobe. Semantically precise words, instead, were associated with the left inferior prefrontal and mid-superior temporal sites. These findings indicate that semantic analysis of written words is a dynamic process involving coordination of widely distributed neural subsystems, which are weighted by semantic ambiguity. © 2004 Elsevier Inc. All rights reserved.

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#### Introduction

A fundamental purpose of language comprehension is the understanding of meanings of words. How does the language system in the brain recognize words with multiple meanings and solve lexical ambiguity? Over the past decade, functional neuroimaging research on brain mechanisms for semantic retrieval has yielded important but contradictory results (see reviews by Bookheimer, 2002; Buckner, 2003; Fletcher and Henson, 2001; Price, 2000). While it has been agreed that the left frontal lobes play a central role in subserving executive aspects of semantic processing involving semantic retrieval, semantic search, and semantic selec-

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tion between concepts in working memory, it remains unclear as to whether subregions within the lateral frontal cortex contribute to different components in semantic memory.

Previous imaging findings reveal that the inferior prefrontal cortex encompassing Brodmann areas (BA) 45/47 and sometimes a portion of 44 mediates goal-driven semantic retrieval in various paradigms (Bokde et al., 2001; Demb et al., 1995; Fiez, 1997; Gabrieli et al., 1998; Gold and Buckner, 2002; Petersen et al., 1989; Poldrack et al., 1999; Roskies et al., 2001; Wagner et al., 2001a,b). In parallel to these findings, the left mid-superior frontal cortex is also implicated in the retrieval of lexical semantics (Scott et al., 2003). In tasks that require subjects to make semantic decisions on words, increased brain activity is often seen in left mid-superior regions (Brunswick et al., 1999; Fletcher et al., 1996; Mummery et al., 1998; Roskies et al., 2001; Scott et al., 2003). For instance, Scott et al. (2003) asked subjects to decide whether a visually exposed English noun could apply to a human ("ambiguous semantic decision") and found that, relative to a syllable judgment on English nouns ("unambiguous phonological decision"), semantic judgments resulted in activity in left superior frontal sites, and this brain activation was dependent on choice reaction time. Thus, these regions seem to be responsible for semantic assessment and meaning selection.

The crucial contribution of left (mid-)superior frontal areas to semantic processing agrees with brain mapping results that show that in a general cognitive system comprising but unlimited to language, the ventrolateral and dorsolateral frontal cortex are assumed to be hierarchically organized. In particular, ventrolateral frontal regions subserve controlled retrieval of representations from posterior cortices and guides active online maintenance and updating of accessed representations (Christoff and Gabrieli, 2000; D'Esposito et al., 1998). Dorsolateral regions, on the other hand, mediate goal-directed selection, manipulation, and monitoring of maintained representations (Fletcher and Henson, 2001). Thus, dorsolateral brain systems operate on the products of ventrolateral cortical areas (Petrides, 2000; Rowe et al., 2000; Smith and Jonides, 1999; Wagner et al., 2001a).

The present study aims to extend this important line of research by manipulating semantic ambiguity of written words with functional magnetic resonance imaging (fMRI). We employed a word generation task in which subjects covertly produced a word that was

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pronunciation:

meanings: clothes, dress; take (medicine); serve; be convinced, obey; be accustomed to; dose; surname.



pronunciation: [ma1]

*meaning:* mother

Fig. 1. Examples of experimental stimuli: semantically ambiguous words (a) and semantically precise words (b). The pronunciation and meaning(s) of each word are illustrated in this figure.

semantically related to a viewed target word. Target words used in our study either had precise meanings ("non-semantic ambiguity") or had several frequently used meanings such that subjects would encounter a difficulty in semantic retrieval and manipulation when performing the generation task ("high semantic ambiguity"). While word generation of the two types of language stimuli requires goaldirected cognitive processes, there are important differences. For words in the non-semantic ambiguity condition, brain activation as indexed by strong BOLD activity will be associated with express and direct semantic retrieval. For words in the high ambiguity condition, there will be a strong demand in semantic retrieval and

### semantic search because meanings of this type of words may compete with one another in the neurocognitive system. Cognitive research on the processing of ambiguous words indicates that several commonly used meanings of words with lexical ambiguity are activated synchronously and context-independent in an autonomous neural network (reviewed by Simpson, 1994). Thus, we assume that compared with the non-semantic ambiguity condition, semantically ambiguous words would recruit mid-superior frontal sites to serve goal-guided meaning manipulation and selection between maintained representations. Conversely, relative to words of high semantic ambiguity, precise-meaning lexical items would allow us to fractionate brain regions involved in rapid and direct semantic retrieval. Our comparisons between the two kinds of words should control for activation due to the visuo-orthographic and phonological processing in the word recognition system (Price et al., 1997).

#### Materials and methods

#### Subjects

Eight male volunteers participated in this study. They gave informed consent in accordance with guidelines set by the University of Texas Health Science Center, San Antonio. All subjects were native Chinese (Mandarin) speakers from mainland China, ranging in age from 29 to 39 and living in the US for no more than 6 years.

All subjects were strongly right handed as judged by the handedness inventory devised by Snyder and Harris (1993). We adopted nine items including unimanual tasks (tasks which can be done by only one hand). A 5-point Liket-type scaled was used, with



## (b) Words without semantic ambiguity minus words with semantic ambiguity



Fig. 2. Functional maps: averaged brain activation provoked by word generation. The functional maps (in color) are overlaid on the corresponding  $T_1$  images (in gray scale). Planes are axial sections, labeled with the height (mm) relative to the bicommissural line. L = the left hemisphere; R = the right hemisphere.

"1" representing exclusive left-hand use, and "5" representing exclusive right-hand use. The items were writing a letter, drawing a picture, throwing a ball, holding chopsticks, hammering a nail, brushing teeth, cutting with scissors, striking a match, and opening a door. The scores on the 9 items were summed for each subject, with the lowest score (9) indicating exclusive left-hand use for all tasks, and the high score (45) indicating exclusive right-hand use. All subjects had scores higher than 40.

#### Apparatus and procedure

The experiment was performed with a 1.9-T GE/Elscint Prestige whole-body MRI scanner (GE/Elscint Ltd., Haifa, Israel) at the Research Imaging Center, University of Health Science Center, San Antonio. All subjects were visually familiarized with the entire procedure and the experimental conditions before the fMRI scans. The subject lay spine on the scanning table and was fitted with plastic ear-canal molds. The subject's head was immobilized by a tightly fitting, thermally molded, plastic facial mask that extended from the hairline to the chin (Fox et al., 1985).

A T<sub>2</sub>\*-weighted gradient-echo echo planar imaging (EPI) sequence was used for fMRI scans, with the slice thickness = 6 mm, in-plane resolution =  $2.9 \times 2.9$  mm, and TR/TE/ $\theta$  = 2000 ms/45 ms/ 90°. The field of view (FOV) was 372 × 210 mm, and the acquisition matrix was 128 × 72. Twenty contiguous axial slices were acquired to cover the whole brain. For each slice, 225 images were acquired in a single run. The anatomical MRI was acquired using a T1-weighted, three-dimensional, gradient-echo pulse-sequence. This sequence provided high-resolution (1 × 1 × 1 mm) images of the entire brain.

#### Materials and behavioral performance

There were two types of stimuli for the present study, words with high semantic ambiguity and words without semantic ambiguity. Fig. 1 shows the examples of experimental materials. The experimental words used here were selected from a published cognitive study in which their semantic imprecision/ambiguity was assessed (Tan et al., 1996). Stimuli were commonly used and had the frequency of occurrences no fewer than 30 per million according to the Modern Chinese Frequency Dictionary (1986). Visual complexity was matched across the two sets of words so that any possible influence of orthographic properties was minimized (Weekes et al., 1998).

The experiment was conducted in a single run, which consisted of three blocks of each of the two types of words. The stimuli were shown through a LED projector system. The subject was asked to silently generate a word that was semantically related to the word they just viewed. Each word was presented for 250 ms, followed by a fixation exposed for 1250 ms. The two experimental conditions were presented in a counter-balanced order.

Subjects continuously performed word generation task (Petersen et al., 1988) during the experiment. We did not specify subjects to generate verbs in this study because it was difficult to categorize Chinese single character words into word classes. The task was demanding because the exposure duration of the visual word was quite brief.

Cognitive experiments using the selected isolated words have reported that the semantic information of the two types of words is activated asynchronously, with semantically precise words accessed first, followed by semantically ambiguous words (Tan et al., 1996). This implies that neural circuits mediating the visual recognition of these stimuli may be different.

#### Data analysis

Matlab (The Math Works, Inc., Natick, MA, USA) and in-house software were used for image data processing (Xiong et al., 1995), which included corrections for head motion and global MRI signal shift. We performed skull stripping of the 3D MRI T<sub>1</sub>-weighted images by using Alice software (Perceptive Systems, Inc., Boulder, CO, USA). These images were spatially normalized to the Talairach brain atlas (Talairach and Tournoux, 1988) using the Convex Hull algorithm (Lancaster et al., 1997, 1999).

Functional images were grouped into semantically ambiguous word and semantically unambiguous (precise) word groups. To minimize the transit effects of hemodynamic responses, we excluded images from the first 8 s of each condition for further data processing. Activation maps were calculated for the two word types, using a Student's group *t* test. Like T<sub>1</sub>-weighted anatomical images, activation maps were also spatially normalized into Talairach space using the Convex Hull algorithm. Two subjects' data were excluded from in-depth statistical analysis due to head motion. The averaged activation maps across subjects with a *t* value threshold of 2.4 (P < 0.005 uncorrected) were overlaid on the

Table 1

Stereotactic coordinates, t values, and corresponding Brodmann areas for regions showing significant activations

Regions activated	BA	X, Y, Z	t
(A) Words with semantic ambiguity –	Words w	ithout semantic ar	nbiguity
Left superior and middle frontal gyri	9	-35, 51, 32	3.50
	10	-10, 60, 26	3.50
	46/9	-45, 41, 26	3.00
Left precentral gyrus	4	-38, -23, 62	2.91
Right superior and middle frontal gyri	6	20, -6, 62	2.77
	46	44, 28, 21	2.99
	10	10, 59, 27	2.98
Right rectal gyrus	11	5, 36, -12	2.86
Right postcentral gyrus	3	33, -22, 44	3.11
Right inferior parietal lobule	40	44, -61, 40	2.94
Left middle occipital gyrus/cuneus	18	-14, -89, 12	2.86
	19	-49, -70, -8	3.00
Right cuneus	19	11, -92, 36	2.99
	17	8, -73, 10	3.15
Right lingual gyrus	18	5, -78, -8	2.70
Anterior cingulate	32	6, 20, -9	3.18
Posterior cingulate	23	4, -32, 25	3.03
(B) Words without semantic ambiguity	– Word.	s with semantic an	nbiguity
Left inferior frontal gyrus	47	-50, 25, -2	3.30
Left insula		-39, 6, -1	3.27
Right postcentral gyrus	2	56, -21, 29	3.03
Left medial frontal gyrus	6	-13, 14, 45	2.93
Right medial frontal gyrus	6	12, -12, 47	2.89
	9	25, 37, 16	3.06
Right inferior frontal gyrus	47	58, 23, -4	2.90
Left inferior temporal gyrus	37	-63, -59, -8	3.64
Left middle temporal gyrus	21	-41, -65, 4	2.88
	39	-32, -59, 17	2.82
Right superior temporal gyrus	22	55, 0, -2	3.29
Right inferior occipital gyrus	18	35, -86, -13	3.62
Right lentiform nucleus		19, -8, 4	2.74

corresponding T<sub>1</sub> images. For each condition, Talairach coordinates of the center-of-mass and volume (mm<sup>3</sup>) of the activation clusters were determined based on the averaged activation maps. Anatomical labels (lobes, gyre) and Brodmann area (BA) designations were applied automatically using a 3D electronic brain atlas (Lancaster et al., 1997). Since dorsal lateral frontal, inferior frontal, and midsuperior temporal cortices in the left hemisphere are assumed to play different roles in the processing of ambiguous and precise words, we selected these areas as regions of interest and compared their mean MR responses to the two types of stimuli. To evaluate the intersubject consistency of brain activation, we applied the binary individual functional map approach to this study (Fox et al., 1996). In this approach, individual variability was determined using a *t* value threshold of 2.4 (P < 0.005) for each subject.

#### Results

Averaged brain activation maps for semantically ambiguous words vs. semantically precise words and semantically precise words vs. semantically ambiguous words are shown in Fig. 2. Table 1 summarizes significant areas of activation for the two comparisons.

Compared with words without lexical ambiguity, semantically ambiguous words provoked very strong brain activity in the left hemispheric sites including mid-superior frontal gyrus (BAs 9, 46, and 10) and the right hemispheric sites involving mid-superior frontal gyri (BAs 46, 9, and 10), inferior parietal lobe (BA 39), and cuneus (BA 17). Anterior cingulate cortex (BA 32) was also strongly activated. Minor brain activities were seen in the left middle occipital gyrus (BA 18 and 19), right lingual gyrus (BA 18), and parahippocampal gyrus.

Brain activations arising from express and direct semantic retrieval, as demonstrated by semantically precise words contrasted with ambiguous words, were found in the left mid-inferior temporal gyri (BA 37 and 21), right temporal cortex (BA 22), bilateral inferior frontal gyri (BA 47), and insula. Right lentiform nucleus was weakly activated.

Averaged MR responses to semantically ambiguous and precise words in left dorsal lateral, inferior frontal, and mid-superior temporal regions were illustrated in Fig. 3. The results showed



Fig. 3. Comparison of mean MR responses to words of ambiguous and unambiguous meaning.

increase of MR signals in dorsal frontal cortex for words of lexical ambiguity and in inferior frontal and mid-superior temporal cortex for words with precise meaning. The individual variability analysis (Fox et al., 1996) indicated that this pattern of results is consistent across all of the subjects we scanned.

#### Discussion

Previous neuroimaging research on cortical mechanisms for the processing of language indicated that a distributed neural network involving the left inferior prefrontal cortex and the left temporal gyrus are relevant to semantic access and organization (Bookheimer, 2002; Fiez, 1997; Price, 2000), though "the differential roles that these areas play in semantic processing is still a matter of debate" (Price, 2000, p. 353). Research showing the contribution of the left mid-superior frontal cortex to semantic memory is meager, despite that the left dorsal lateral frontal lobes are known as a general mechanism in subserving goal-directed search, selection, and manipulation of maintained mental representations (Petrides, 2000; Fletcher and Henson, 2001), which is one of the crucial characteristics of typical lexico-semantic processing.

The present fMRI study has generated important findings that suggest that neural networks responsible for lexical knowledge are modulated by semantic ambiguity. In processing printed words with precise and unambiguous meanings, the left mid-superior temporal and bilateral inferior prefrontal gyri peaked. This pattern of results is consistent with a large body of experimentation with lesion and brain-imaging approaches (see Bookheimer, 2002 and Price, 2000 for review). The coordination of the inferior and posterior brain subsystems leads to rapid and direct processing of lexical semantics in reading. The strong activation in recognizing precise-meaning words was also obtained in the left insula, a brain area which is known to mediate phonological (articulatory) rather than semantic processing previously (Dronkers, 1996; Price, 2000; Wise et al., 1999; Xu et al., 2001). Its particular role in access to word meaning merits further investigation.

More importantly, we found that, in processing written words of high semantic ambiguity that required extensive search and selection of lexical meanings in the word generation task, peak brain activations occurred in left mid-superior frontal cortex, with some involvement of its right homologue. This finding is corroborated by past imaging results that the mid-superior frontal network works as a central executive system of cognition, guiding goal-related search and selection, and operating on the products of ventrolateral frontal sites (D'Esposito et al., 1995, 1998; Fletcher et al., 1996; Petrides, 2000; Wagner et al., 2001a). In word generation, semantically precise words engage a one-to-one mapping process from orthography to meaning, whereas semantically vague linguistic items engage a one-to-many mapping mechanism and are linked to many related words, leading to a chaotic state in the neurocognitive system which comes to be stabilized with competition and selection. Dorsal-lateral-frontal regions are activated in a chaotic state that calls for stabilization.

Recent experiments by Thompson-Schill et al. (1997) suggest that the left inferior prefrontal areas contribute to semantic search and selection rather than semantic processing per se. In the present fMRI study, although we did not vary semantic selection as an experimental variable, the identification of semantically ambiguous words hypothetically involves a higher search and selection load than the identification of semantically precise words. Yet, we found that the left mid-superior, rather than the left inferior, frontal regions subserve words requiring more semantic choices. Our results, thus, are inconsistent with Thompson-Schill et al.'s assumption.

Equally important is our finding of the cortical activity in the anterior cingulate cortex, the right inferior parietal lobe, and the left middle occipital gyrus in processing imprecise-meaning words. Since the anterior cingulate plays a prominent role in the executive control of cognition and the online monitoring and evaluating of performance by detecting cognitive states such as response competition (Carter et al., 1998; Posner and Dehaene, 1994; Tan et al., 2001), greater activation in this area for semantically ambiguous words than for semantically precise words is assumed to stem from the activation of a word's multiple meanings, which compete with one another and lead to a difficulty in semantic selection and manipulation. The right inferior parietal lobe and the left middle occipital gyrus participated in spatial working memory and fine-grained analysis of visuospatial information of words and objects (Haxby et al., 1995; Lepage et al., 2000; Smith and Jonides, 1999; Tan et al., 2001). The semantic ambiguity effect seen in these areas imply that the search and selection of lexical meanings of ambiguous words may be associated with a further analysis of orthographic units of printed words. This proposal is in line with our previous hypothesis that identifying difficult words (e.g., irregular words) requires a double check procedure to verify semantics or phonology against orthographic codes (Tan et al., 2001).

#### Conclusions

Unlike phonological encoding of visual words that recruits a concentrated neuroanatomical system, the processing of meanings of words engages a widely distributed neural network, as assumed by Jobard et al. (2003). This neural network is further complicated when one takes word category and concreteness into account (see Martin and Chao, 2001 and Bookheimer, 2002 for review). Our fMRI findings indicate that the neuroanatomical circuitry for semantic representation and analysis is modulated by lexical ambiguity. In particular, we discovered that, in a word generation paradigm, semantically precise words are associated with the left inferior prefrontal cortex, left mid-inferior temporal regions, and insula. Semantically ambiguous words, however, are associated with the left dorsolateral frontal areas. The heavy involvement of the anterior cingulate and the right inferior parietal lobe in the processing of ambiguous words may be due to an increased demand in meaning manipulation and a double check procedure to verify meanings against orthography. Semantic analysis of visual words is a dynamic process involving coordination of neural subsystems weighted by lexical ambiguity.

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