◆ **Human Brain Mapping 7:15–28(1999)** ◆

Auditory and Visual Word Processing Studied With fMRI

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Abstract: Brain activations associated with semantic processing of visual and auditory words were investigated using functional magnetic resonance imaging (fMRI). For each form of word presentation, subjects performed two tasks: one semantic, and one nonsemantic. The semantic task was identical for both auditory and visual presentation: single words were presented and subjects determined whether the word was concrete or abstract. In the nonsemantic task for auditory words, subjects determined whether the word had one syllable or multiple syllables. In the nonsemantic task for visual words, subjects determined whether the word was presented in lower case or upper case.

There was considerable overlap in where auditory and visual word semantic processing occurred. Visual and auditory semantic tasks both activated the left inferior frontal (BA 45), bilateral anterior prefrontal (BA 10, 46), and left premotor regions (BA 6) and anterior SMA (BA 6, 8). Left posterior temporal (middle temporal and fusiform gyrus) and predominantly right-sided cerebellar activations were observed during the auditory semantic task but were not above threshold during visual word presentation. The data, when averaged across subjects, did not show obligatory activation of left inferior frontal and temporal language areas during nonsemantic word tasks.

Individual subjects showed differences in the activation of the inferior frontal region while performing the same task, even though they showed similar response latency and accuracy. *Hum. Brain Mapping 7:15–28, 1999.* © 1999 **Wiley-Liss, Inc.**

Key words: functional magnetic resonance imaging; semantic processing; lexical processing; frontal cortex; supplementary motor area

INTRODUCTION

Noninvasive imaging of the brain with positron emission tomography and blood oxygen level-dependent (BOLD) contrast functional magnetic resonance imaging (fMRI) provides us with powerful tools to understand how the brain deciphers words. The use of different experimental paradigms with the intention of probing similar processes has resulted in topographically different brain activations [Binder et al., 1997a; Demb et al., 1995; Demonet et al., 1992; Howard et al., 1992; Petersen et al., 1988; Shaywitz et al., 1996; Wise et al., 1991]. Variations in results have been attributed to differences in processing demands of the task [Howard et al., 1992; Shaywitz et al., 1996], choice of control task

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Contract grant sponsor: Glaxo-Wellcome/Academy of Medicine, Singapore; Contract grant sponsor: NMRC, Singapore.

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Received for publication 18 November 1997; accepted 16 June 1998

[Wise et al., 1991], word class difference between conditions [Shaywitz et al., 1996], and rate of word presentation [Price et al., 1994; Raichle et al., 1994]. As it is difficult to isolate single cognitive processes, even in the course of performing simple tasks on single words, it is desirable to collect and review data from several different word-based experiments before drawing firm conclusions about where and how language processing occurs.

We chose a word classification task which has been previously shown by fMRI to activate semantic (word meaning) processing [Demb et al., 1995; Desmond et al., 1996] in order to further our knowledge on the following issues: Does semantic processing of auditory and visually presented words occur in common or distinct areas? What are the relative contributions of the left temporal and frontal areas? What other areas are activated during semantic processing of single words? What are the intersubject variations in brain activation with respect to single word tasks?

Specifically, we extended earlier fMRI studies by having subjects perform multiple classification tasks in both the auditory and visual modalities and these tasks to a low-level control task (fixation). The favorable signal-to-noise characteristics of fMRI allowed us to examine data from individual subjects as well as from averaged subject groups. This addresses the criticism that functional imaging studies using only averaged data sets fail to take into account the individual variability in language processing [Steinmetz and Seitz, 1991] demonstrated using electrical stimulation [Ojemann et al., 1989].

METHODS

Eight right-handed volunteers between ages 22–38 years were studied. Right-handedness was established by the Edinburgh handedness inventory [Oldfield, 1971]. All had English as their first language, no history of neurological disorder, and at least a college level education. All 5 men and 3 women gave informed consent.

Auditory and visual words were presented separately. For each form of word presentation, subjects performed two tasks: one semantic, and one nonsemantic. The semantic task (Abstract/concrete) was identical for both auditory and visual presentation: subjects determined whether the word presented was concrete or abstract. In the nonsemantic task for auditory words (Syllable), subjects determined whether the word had one syllable or multiple syllables. In the nonsemantic task for visual words (Case), subjects determined whether the word was presented in lower case or upper case.

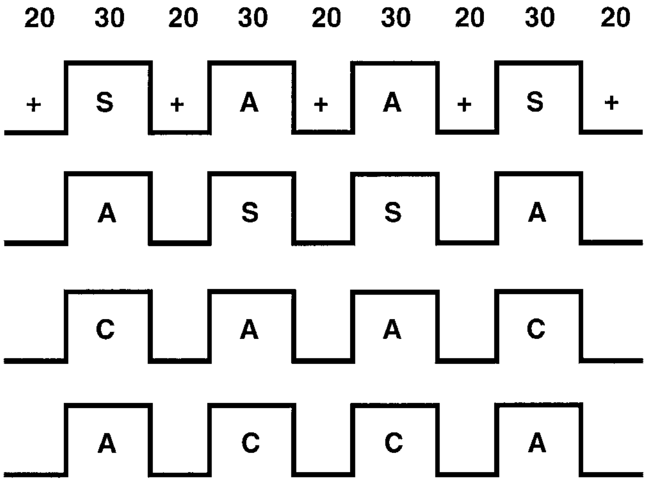


Figure 1.
Experimental paradigm. Numbers above square waves represent time in seconds. +, fixation; A, Abstract/concrete; S, Syllable; C, Case.

The words used were taken from a set used by Demb et al. [1995]. Words were arranged in blocks of 15 and the tasks were interleaved with periods of fixation. During fixation, subjects were told to focus their entire attention on the cross-hair and not look elsewhere. Performance of an active task lasted 30 sec and fixation intervals lasted 20 sec. Balanced numbers of abstract and concrete words with equal numbers in upper case and lower case were used, and the order of task presentation was counterbalanced to minimize order effects (Fig. 1). Auditory or visual stimuli were delivered in separate runs. Subjects received practice on the tasks 30 min prior to scanning. During scanning, a 1-sec cue appeared prior to stimulus presentation, giving information about the task and reminding the subject of the button press required. Visual stimuli were projected using an LCD projector. Auditory stimuli (words lasting about 1 sec, read by a single speaker and digitized) were delivered through modified headphones attached to semirigid tubes which in turn were connected to an MR-compatible sound transducer. Reaction time and accuracy of response data were collected using a custom-made magnet-compatible key-press system.

Imaging was performed on a General Electric 1.5T Signa scanner, using a quadrature, gradient head coil system (Advanced NMR, MA). In 6 subjects, a bite-bar was utilized to reduce head motion. A sagittal localizer scan covering the entire brain was obtained using an SPGR sequence. Sixty slices, 2.8 mm thick, were obtained. This served as the structural scan for transformation of the brains into the stereotaxic atlas space of Talairach and Tournoux [1988]. Shimming according to a procedure devised by Reese et al. [1995] was performed to optimize B_0 homogeneity. SPGR T1-weighted flow-compensated oblique axial images were obtained to provide anatomical information for Talairach transformation. Further anatomical information was collected in an echo-planar inversion recovery scan (TR = 25 sec, TI = 1,200 msec). Whole-head axial scans were oriented parallel to the intercommissural plane and comprised 16 slices 7 mm thick, with a 1-mm gap between slices. The in-plane resolution of these anatomical images was 1.57 mm. Functional images were obtained using an asymmetric spin echo (ASE) sequence with TR = 2,000 msec and TE = 50 msec, with a 180° refocusing pulse offset by -25 msec. The resultant functional images had an in-plane resolution of 3.125 mm. One hundred and ten images per slice were collected over a period of 220 sec in each of eight runs.

Images were motion-corrected using an algorithm developed by Jiang et al. [1995], based on automated image registration (AIR) [Woods et al., 1992].

The experimental paradigm placed images into one of four categories: "fixation," "A," "S," or "C." This grouping of data was shifted by two images to take into account the anticipated 4-sec delay between brain activation and changes in BOLD signal [Buckner et al., 1996]. The functional data as originally collected were smoothed in-plane using a one-pixel-wide Hanning filter. Kolmogorov-Smirnov (KS) statistical maps were generated. The data from the KS statistic were represented in pseudocolor and overlaid onto corresponding structural MR images. Regions of activation were inspected. We found one subject (G.O.C.) exhibiting "mirror-image" activation of language-related brain areas in the right hemisphere and excluded his data from the average. His data are discussed separately.

Functional and anatomic images of each subject were then transformed into Talairach space [Talairach and Tournoux, 1988] and resliced in the coronal orientation over 57 slices with voxel dimensions of x = 3.125, z = 3.125 by y = 3 mm. The data from 7 subjects were then averaged. This formed the basis for our analysis of activations.

Regions of significant activation were noted visually from the KS maps and activation peaks, using an automated program [Bush et al., 1996]. A conservative threshold of $P < 1 \times 10^{-5}$ was used. The program was used to detect peak activations (in terms of statistically most significant pixels) as well as to compute the volume of brain activated.

TABLE I. Behavioral data*

Task	Number of responses (mean)	Percentage correct (mean)	Reaction time (mean; msec)
Auditory: abstract/concrete	118.0	85.0	1,250
Auditory: syllable	119.5	94.8	1,000
Visual: abstract/concrete	119.7	92.6	850
Visual: case	120.0	96.7	580

* Paired t-test between auditory abstract/concrete and syllable reaction times: t = 6.188, $P < 0.01$; between visual abstract/concrete and syllable reaction times: t = 6.40, $P < 0.01$.

From Kolmogorov-Smirnov maps of semantic vs. nonsemantic comparisons, regions of peak activation were examined to ascertain how MR signal modulated across semantic, nonsemantic, and fixation tasks. We reordered the raw activation data to account for the counterbalanced order of presentations across runs and averaged the results of four runs into one display. A moving average of five time points was overlaid onto the time course curve to allow both visualization of the raw time course as well as visualization of the temporally smoothed time course. The time courses were inspected to ensure that activation followed the experimental paradigm, as a secondary measure of guarding against false positives.

Additional analysis was performed for 3 subjects whose activations were particularly clear. We performed pairwise Kolmogorov-Smirnov tests on time courses obtained from voxels in the inferior frontal region (IFR). We determined if differences in MR signal during semantic, nonsemantic, and fixation periods were statistically significant. Alpha of 0.05 was corrected for three comparisons, giving a threshold of significance of 0.017 for these comparisons.

RESULTS

Behavioral data

Table I presents the summary of behavioral data. The increase in reaction times (RT) in the semantic compared to the nonsemantic tasks in both modalities was statistically significant. This, as well as the greater number of incorrect responses in the semantic condition, reflected the additional processing load in the semantic vs. the nonsemantic tasks. The visual words appeared in their entirety at the instant of presentation, whereas it took a variable period of time to present the spoken words. Therefore, reaction times in the audi-

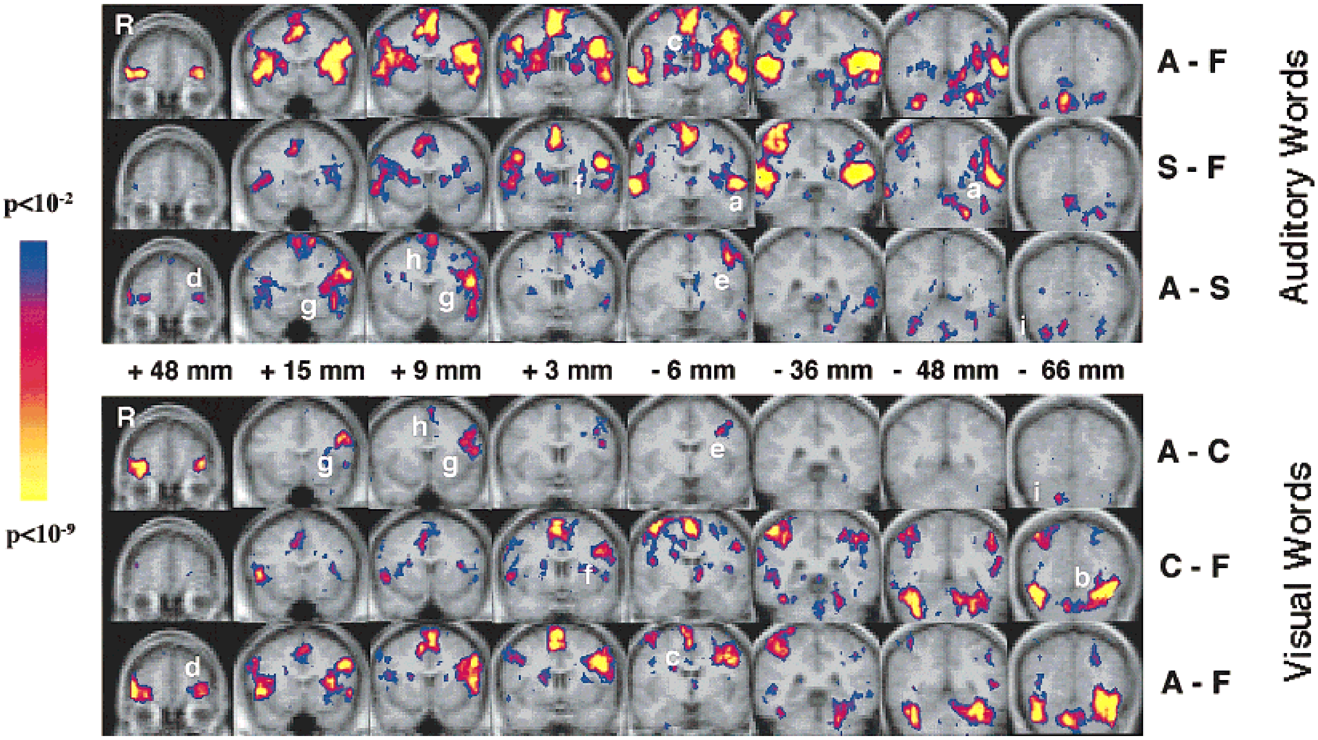


Figure 2.

Kolmogorov-Smirnov (KS) maps of brain activations in selected regions. Numbers represent distance along the anterior-posterior direction in Talairaich space. Letters to right of the KS maps refer to comparisons between tasks. F, fixation; A, Abstract/concrete; S, Syllable; C, Case; a, superior temporal gyrus; b, extrastriate cortex; c, posterior SMA; d, anterior prefrontal region; e, left premotor area; f, insula, posterior inferior frontal gyrus; g, left inferior frontal region; h, anterior SMA; i, right cerebellar hemisphere.

tory and visual word experiments are not directly comparable.

Activation data across subjects

Activations related to nonsemantic tasks

Performance of Syllable in comparison with fixation showed bilateral activation of the superior temporal gyrus with greater posterior extension on the left (Table II). The anterior posterior extent of this was from $y = 0$ mm to $y = -42$ mm (Talairach coordinates) on the right side, and $y = 0$ to $y = -48$ mm on the left side. There was activation of the left angular gyrus (Fig. 2, slice at $x = -48$ mm). Case vs. fixation showed bilateral extrastriate activation, principally in the posterior fusiform gyrus. Bilateral activation of the superior parietal lobules was present.

Midline region activations seen in both Syllable and Case in contrast to fixation were in the posterior portion of the supplementary motor area (SMA) (peak centered at Talairach coordinates 6, -9, 62 for auditory words and 3, -6, 56 for visual words) and the anterior cingulate gyrus. Bilateral activation was present in the premotor cortex (BA 6), posterior inferior frontal gyrus, insula (BA 44), the inferior parietal lobules (BA 40), and the cerebellar hemispheres.

Activations related to semantic tasks

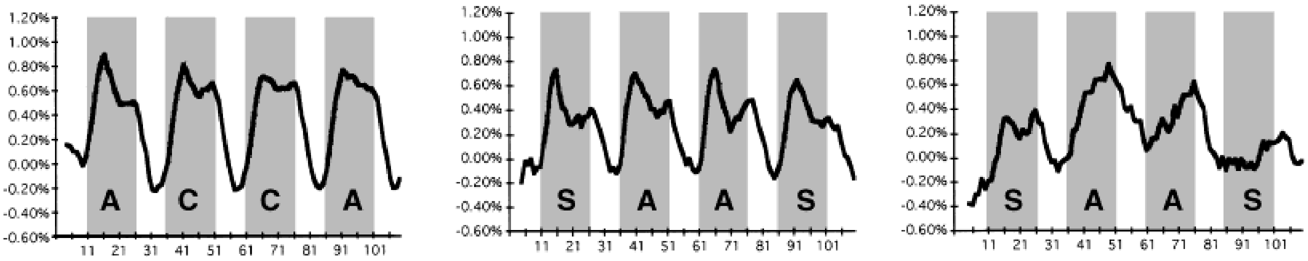
Comparing activations during the semantic vs. the nonsemantic task, four frontal regions showed more pronounced activation. These were the anterior portion of the SMA (BA 6, 8), the left premotor region (BA 6), and the anterior prefrontal regions bilaterally (BA 10, 46) (Figs. 2, 3; Tables III, IV).

Bilateral IFR activation was seen when either auditory or visual word semantic tasks were compared to fixation. When compared to their respective nonsemantic tasks, markedly asymmetric left-IFR activation remained. This was similar in location across auditory and visual word presentations, but activations in the auditory word task were more extensive. Peak activations were located at the superior end of the inferior

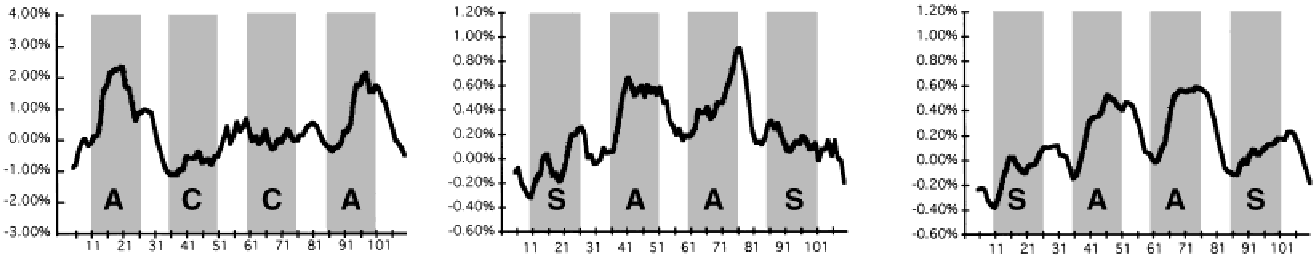
TABLE II. Brain activation during nonsemantic tasks vs. fixation*

	Syllable vs. fixation					Case vs. fixation				
			Talairach coordinates (peak activations)					Talairach coordinates (peak activations)		
Brain region	*P*-value	Volume (mm^3)	x, L-R	y, A-P	z, S-I	*P*-value	Volume (mm^3)	x, L-R	y, A-P	z, S-I
Frontal lobe										
R, IFG (BA 44, 45)	2.10E-07	2,400	34	18	15	2.90E-08	4,100	46	15	6
L, IFG (BA 44)						1.80E-05	800	−31	6	18
R dorsolateral prefrontal (BA 9)						1.30E-05	1,600	46	24	37
L posterior inferior frontal / precentral gyrus (BA 6, 44)	4.30E-14	5,700	−43	3	28	4.30E-12	4,000	−43	3	26
R premotor area (BA 6)	3.10E-09	5,000	50	−3	31	4.30E-08	3,500	53	0	40
L premotor area (BA 6)	1.10E-10	2,800	−46	−3	18	5.10E-07	2,900	−56	0	21
L primary motor area (mouth)						2.80E-06	1,100	−43	0	6
R primary motor area (hand)	4.20E-13	21,600	34	−27	53	2.70E-20	19,900	43	−21	56
Supplementary motor area (SMA)	1.30E-13	12,200	6	−9	62	4.90E-11	12,500	3	−6	56
Supplementary motor area (SMA)	3.30E-08	600	−18	−15	62					
Anterior cingulate (BA 32)	6.70E-09	2,000	3	12	40	7.20E-08	2,700	9	12	46
Temporal lobe										
R superior temporal gyrus (BA 22)	1.60E-28	28,400	59	−18	9	3.10E-05	1,600	59	−42	18
R superior temporal gyrus (BA 22)	1.00E-24	11,200	62	−33	12					
L superior temporal gyrus (BA 22)	1.50E-28	42,600	−46	−21	12	2.60E-06	500	−53	−48	21
R middle temporal gyrus (BA 21)	4.60E-19	1,300	59	−30	3	2.60E-06	1,300	50	−30	3
L middle temporal gyrus (BA 21)	1.50E-14	1,800	−59	−45	6					
R inferior temporal gyrus (BA 37)	2.70E-08	600	62	−48	−6					
Parietal lobe										
R primary somatosensory area	1.10E-13	3,600	37	−33	65	5.90E-14	3,700	−40	−33	50
R inferior parietal lobule (BA 40)						4.40E-08	4,700	40	−57	46
(supramarginal gyrus)						1.20E-10	3,300	53	−42	50
L inferior parietal lobule (BA 40)	2.50E-10	4,300	−50	−36	46	3.30E-07	3,100	−37	−39	40
(supramarginal gyrus)						3.40E-08	3,000	−46	−51	43
						1.40E-07	2,900	−34	−54	37
R superior parietal lobule (BA 7)	5.00E-08	2,300	40	−48	62	1.30E-10	2,500	28	−75	46
						2.00E-07	2,700	43	−66	50
R supramarginal gyrus	1.90E-07	3,400	46	−60	43					
Occipital lobe										
R extrastriate cortex						1.30E-19	12,600	21	−81	−15
R extrastriate cortex						1.50E-14	7,600	40	−66	−18
L extrastriate cortex						4.60E-21	12,700	−25	−84	−15
Cerebellum										
R cerebellar hemisphere						4.80E-07	1,300	9	−63	−28
L cerebellar hemisphere	6.70E-10	3,000	−25	−48	−25	9.20E-12	5,600	−18	−42	−21
L cerebellar hemisphere	8.60E-09	1,000	−40	−51	−12	6.50E-15	3,800	−21	−54	−18
Midline cerebellum	3.20E-07	2,100	−3	−54	−12	2.70E-08	4,500	−3	−63	−21
Subcortical structures										
Basal ganglia	3.70E-05	1,400	15	6	12					
Basal ganglia	2.80E-05	500	−18	9	9					

* IFG, inferior frontal gyrus; MFG, middle frontal gyrus; L-R, Left-right; A-P, anterior-posterior; SI, superior-inferior.



Right extrastriate cortex **Posterior SMA (y= -9mm)** **Left mid. temporal gyrus**



Right anterior prefrontal **Anterior SMA (y= +15 mm)** **Left inferior frontal region**

Figure 3.

Time courses from Regions of Interest (ROI) in the averaged data set. The y-axis shows MR signal in the ROI in terms of percent change relative to the mean MR signal during fixation for that slice. The x axis shows image number. The time course line depicts a five-point moving average and therefore commences at image 3. Shaded bars indicate periods where tasks were performed. A, Abstract/concrete; S, Syllable; C, Case.

frontal gyrus and middle frontal gyrus. This was anterior and superior to "Broca's area."

The supplementary motor area (BA 6) and pre-SMA (BA 8) extending from y = -12–+24 showed anterior-posterior differences in activation. The posterior portion of the SMA was equally active during the Syllable and Abstract/concrete tasks, whereas the anterior SMA and pre-SMA (anterior to y = +9 mm) were active only during the Abstract/concrete task. A similar trend was observed for visual words, but there were far fewer activated pixels.

When activations associated with the nonsemantic task were accounted for, right cerebellar hemisphere activation during the auditory semantic task was noted. This activation was marginal during visual word presentation.

Activations of the left temporal region were seen during auditory word presentation but not visual word presentation. The more prominent activations were in the left posterior middle temporal gyrus and left fusiform gyrus (basal temporal language area). The left supramarginal gyrus was equally active in the semantic and nonsemantic tasks and was not activated above threshold in the comparison between the two.

Negative activations

Areas more active during fixation relative to any of the four active tasks were located in the medial frontal gyrus, parts of the anterior cingulate, right parietal region, and midline precuneus and cuneus. The lateral, anterior, and midline superior frontal and temporal regions did not show negative activations in any combination of comparisons (Fig. 4).

Inferior frontal and posterior temporal activations in individual subjects

Six of the 7 subjects who had left hemisphere-dominant language showed varying degrees of activations of the IFR in the Abstract/concrete vs. Syllable and Abstract/concrete vs. Case comparisons (Table Va). The single nonactivator showed behavioral evi-

TABLE III. Brain activations in semantic tasks vs. fixation*

	Auditory abstract / concrete vs. fixation					Visual abstract / concrete vs. fixation				
			Talairach coordinates (peak activations)					Talairach coordinates (peak activations)		
Brain region	*P*-value	Volume (mm^3)	x, L-R	y, A-P	z, S-I	*P*-value	Volume (mm^3)	x, L-R	y, A-P	z, S-I
Frontal lobe										
R anterior prefrontal (BA 10)	5.00E-13	4,500	40	48	6	3.90E-10	3,600	40	51	3
	3.20E-13	2,300	25	57	6	2.00E-10	1,800	25	54	3
L anterior prefrontal (BA 10)	4.40E-12	4,300	−28	57	0	1.20E-07	3,100	−31	51	0
R dorsolateral prefrontal MFG (BA 46)	8.40E-08	1,500	43	39	21	2.60E-09	3,100	40	27	31
R dorsolateral prefrontal MFG (BA 46)	3.20E-08	1,100	34	45	34					
R insula	8.40E-08	8,100	25	6	21					
L insula	4.80E-07	500	−31	−6	0	1.10E-10	7,200	−28	18	18
R inferior frontal IFG (BA 45)	1.70E-14	27,500	37	18	6	2.40E-08	3,600	53	30	21
R inferior frontal IFG (BA 44)						8.50E-10	3,200	50	15	3
L inferior frontal IFG MFG (BA 44, 45)	9.90E-18	11,200	−31	18	12	1.20E-11	16,200	−46	9	31
	2.70E-11	5,500	−46	27	25	9.30E-09	4,900	−46	12	18
						8.30E-11	4,800	−40	33	12
L inferior frontal IFG (BA 6, 44)	1.10E-17	19,000	−43	3	28	1.10E-13	10,900	−43	3	28
L premotor area (BA 6)	7.80E-15	9,000	−40	−6	46	1.10E-11	4,300	−40	−6	56
R primary motor area	3.40E-18	15,000	37	−24	59	3.60E-13	14,700	34	−27	53
Supplementary motor area (SMA)	1.10E-17	19,700	9	3	53	3.70E-13	6,900	6	3	65
Supplementary motor area (SMA)	6.30E-13	6,500	3	−9	59	2.90E-11	6,400	6	3	53
Supplementary motor area (SMA)	3.00E-12	2,200	−21	−9	65	3.40E-08	800	−3	21	62
Supplementary motor area (SMA)	2.70E-07	1,400	34	0	68	2.80E-09	600	−2	−9	65
Temporal lobe										
R superior temporal gyrus (BA 42)	2.30E-32	24,000	59	−18	9					
R superior temporal gyrus (BA 22)	5.70E-32	12,500	62	−33	12					
L superior temporal gyrus (BA 42)	5.40E-28	52,600	−59	−18	15					
L fusiform gyrus (BA 37)	1.10E-11	5,600	−37	−54	−9					
Parietal lobe										
R primary somatosensory area	4.00E-23	4,300	37	−33	65					
L inferior parietal lobule (BA 40)	1.80E-06	500	−46	−42	53	2.60E-08	1,700	−43	−45	43
L inferior parietal lobule (BA 40)	2.40E-07	200	−43	−54	53	4.50E-07	600	−37	−42	34
Occipital lobe										
R extrastriate cortex						1.30E-13	18,500	40	−60	−21
R extrastriate cortex						5.30E-15	13,000	21	−81	−15
L extrastriate cortex						7.40E-23	24,300	−34	−60	−12
L extrastriate cortex						1.20E-22	16,400	−25	−84	−15
Cerebellum										
R cerebellar hemisphere	3.50E-09	9,900	3	−54	−15	2.40E-10	7,000	9	−69	−28
R cerebellar hemisphere	4.00E-10	6,500	34	−48	−31	5.90E-08	1,300	0	−51	−31
R cerebellar hemisphere	1.20E-08	3,600	9	−66	−25	5.40E-09	4,000	−18	−42	−25
L cerebellar hemisphere	2.90E-14	15,000	−25	−51	−21	3.20E-21	3,000	−18	−78	−18
Midline cerebellum	7.60E-08	400	0	−27	−31	9.60E-19	2,800	−21	−54	−18
Subcortical structures										
Basal ganglia						9.30E-05	400	18	6	21
Caudate	3.90E-09	2,800	−6	0	21					

* IFG, inferior frontal gyrus; MFG, middle frontal gyrus.

TABLE IV. Brain activation in semantic vs. nonsemantic tasks*

	Abstract / concrete vs. syllable					Abstract / concrete vs. case				
			Talairach coordinates (peak activations)					Talairach coordinates (peak activations)		
Brain region	*P*-value	Volume (mm^3)	x, L-R	y, A-P	z, S-I	*P*-value	Volume (mm^3)	x, L-R	y, A-P	z, S-I
Frontal lobe										
R anterior prefrontal (BA 10)	8.30E-07	2,200	31	54	3	2.30E-11	6,000	31	51	3
L anterior prefrontal (BA 10)						3.30E-10	4,200	−34	48	3
R dorsolateral prefrontal MFG (BA 46)	4.10E-05	600	53	42	6					
L dorsolateral prefrontal MFG (BA 46)	1.60E-06	1,800	−43	42	0					
L dorsolateral prefrontal (BA 9)	6.30E-06	1,700	−40	36	15					
R insula	4.10E-07	7,900	34	18	−3					
L insula	7.70E-10	6,100	−28	18	15	1.20E-05	1,400	−31	21	15
	9.40E-08	4,400	−37	15	−3					
R inferior frontal IFG (BA 45)	2.00E-07	500	50	36	−6					
L inferior frontal IFG (BA 44, 45)	8.30E-07	2,500	−46	30	0	3.20E-06	5,500	−43	33	9
L inferior frontal IFG (BA 44, 45)						9.40E-08	11,500	−40	15	31
L inferior frontal IFG (BA 44, 45)	3.30E-10	10,400	−46	18	34	2.00E-07	5,300	−37	27	0
L inferior frontal IFG (BA 44)	3.50E-12	5,500	−46	9	21	1.80E-09	2,100	−25	33	0
L premotor area (BA 6)	2.00E-08	4,800	−40	−6	46	1.10E-09	3,500	40	−6	56
Supplementary motor area (SMA)	9.20E-09	11,400	−6	9	65	6.30E-06	800	−3	9	62
Supplementary motor area (SMA)	4.10E-07	10,900	−6	24	43					
Supplementary motor area (SMA)	1.20E-05	500	−28	6	50					
Anterior cingulate	4.10E-07	1,800	−15	3	34					
Temporal lobe										
L middle temporal gyrus (BA 21)	1.20E-05	800	−56	−36	0					
L middle temporal gyrus (BA 21)	6.30E-06	400	−59	−6	−15					
L fusiform gyrus (BA 37)	6.30E-06	700	−37	−54	−9					
Cerebellum										
R cerebellar hemisphere	4.40E-08	5,500	28	−57	−37	2.30E-05	600	12	−63	−37
R cerebellar hemisphere	4.10E-09	2,100	15	−30	−28					
R cerebellar hemisphere	3.20E-06	3,800	15	−69	−34					
L cerebellar hemisphere	2.00E-07	2,700	−34	−45	−21					
L cerebellar hemisphere	1.60E-06	1,100	−25	−60	−31					
L cerebellar hemisphere	9.40E-08	1,500	−18	−30	−31					

* IFG, inferior frontal gyrus; MFG, middle frontal gyrus; STG, superior temporal gyrus.

dence that he was performing the tasks correctly. Four subjects showed left posterior temporal activations (Table Vb). If a subject showed strong activations in the frontal regions during the auditory Abstract / concrete task compared to fixation, there were also roughly equivalent activations during visual Abstract / concrete processing. Poor activators activated poorly in response to both visual and auditory words. This set of correlations was most clearly seen in the comparison between semantic and fixation in the data from individuals.

Inferior frontal activations across semantic and nonsemantic tasks in individual subjects

To evaluate individual differences in brain activation according to task, we defined regions around significant voxels within the IFR in the Abstract / concrete vs. Syllable KS maps and examined the associated time courses (Table VI, Fig. 5). Among the 7 subjects, 4 showed activation patterns that were of interest. In subject J.G., significant activation of the left IFR was only seen in the Abstract /

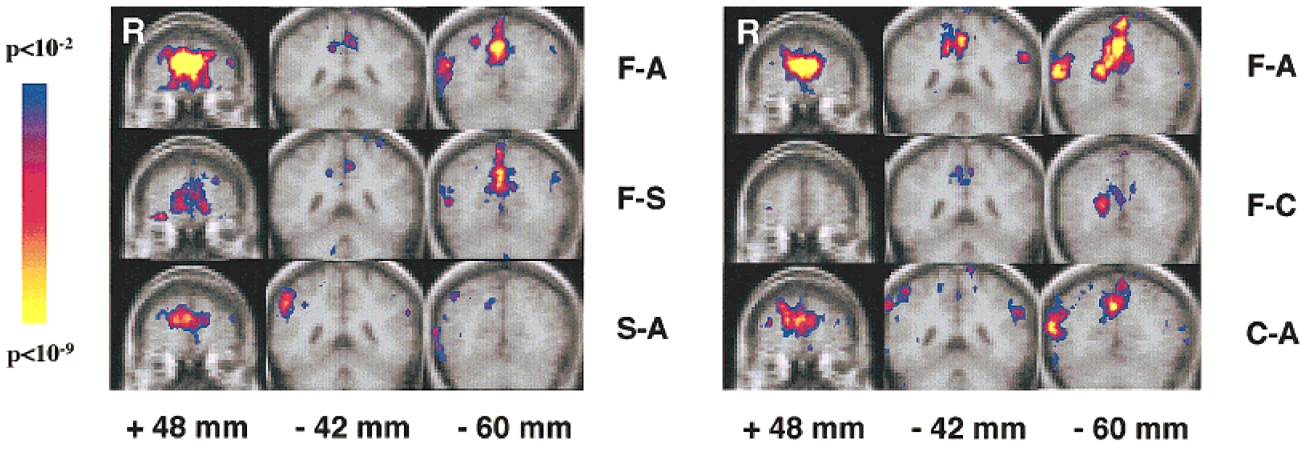


Figure 4.

KS maps of regions more active during fixation compared to active tasks. F, fixation; A, Abstract/concrete; S, Syllable; C, Case. Numbers represent distance along the anterior-posterior direction in Talairaich space.

concrete vs. fixation but not in the Syllable vs. fixation condition. Subject H.C., on the other hand, showed clear activations in the Abstract/concrete vs. fixation as well as Syllable vs. fixation. There was no significant difference in the level of activation between Abstract/concrete and Syllable in both the visual and auditory modality (data shown only for the auditory modality). In subject M.S., there were three levels of activation corresponding to Fixation, Syllable, and Abstract/concrete.

Finally, subject G.O.C. (who was excluded from pooled analysis) showed "mirror" activation of the right IFR (Fig. 6). There was no a priori reason to expect him to have right hemisphere-dominant language. He underwent a repeat visual word test in a separate session which replicated the findings. In addition, a word-stem completion test also showed right hemisphere-dominant activation. Word-stem completion has previously been shown to have strong left-lateralized activation activation at the group and individual subject level [Buckner et al., 1995b, 1996].

All 4 subjects showed similar behavioral responses, even though their activation patterns were different.

DISCUSSION

A common semantic network for auditory and visual words

Our findings suggest a common semantic network for the processing of auditory and visual words involving the left inferior frontal region, the anterior prefrontal regions, bilaterally, the anterior SMA, the left premotor area, and the cerebellum. The overlap of areas involved with semantic processing, whether one is presented auditory words or visual words, could account for why the majority of patients with left hemisphere lesions who lose language function do so in all modalities of word presentation. Visual words and pictures activate a common semantic system [Vandenberghe et al., 1996] involving the inferior frontal, posterior temporal region, and angular gyrus. Face and proper name semantics [Gorno Tempini et al., 1997], as well as different auditory and visual word tasks [Binder et al., 1997b], activate common semantic networks. While the precise components of the "common semantic network" vary somewhat with experimental design, it appears that the knowledge of concrete items, irrespective of sensory modality, is stored and/or retrieved from overlapping regions in the left cerebral hemisphere.

Activations related to the nonsemantic tasks

Activation of the lateral extrastriate cortex by the Case task is consistent with previous studies where visual words were presented [Petersen et al., 1990; Price et al., 1996; Pugh et al., 1996]. Activations in the superior temporal and extrastriate regions did not appear in the semantic vs. nonsemantic comparisons; these findings are in agreement with those of Petersen

TABLE Va. Individual subject activation in left IFR at coronal slice y = 9 mm (y = 12 mm for G.O.C.)*

Subject	A-F	S-F	A-S	V-F	C-F	V-C
M.S.	384	213	86	194	59	0
H.C.	250	243	0	270	115	64
J.G.	119	0	119	143	0	123
E.J.L.	0	0	0	0	0	0
M.N.	88	0	0	81	50	14
J.R.	0	0	4	0	0	0
R.J.	108	40	80	74	15	41
G.O.C.[a]	165	0	39	110	0	98

* Figures represent number of significantly activated pixels. A, auditory, abstract/concrete; V, visual abstract/concrete; S, syllable; C, case; F, fixation.

[a] Mirror regions in the right hemisphere were activated in this subject.

et al. [1988] that these areas are active in the early processing of auditory and visual word stimuli, but do not support the notion that marked modulations of these perceptual regions occur via task demands, at least to a level detectable by our fMRI procedures.

The key-press response contributes to activation of the SMA and bilateral premotor areas. However, activation of the posterior inferior frontal gyrus and the insula region bilaterally is unlikely to be related to finger movement, as this is close to the mouth primary motor area. Both visual word and auditory word presentation produced comparable activations when compared to fixation.

TABLE Vb. Individual subject activations in left posterior temporal region at approximately y = −36 mm or −39 mm, z = 0–4*

Subject	A-S	V-C
M.S.	37	27
H.C.	49	0
J.G.	0	0
E.J.L.	0	0
M.N.	0	0
J.R.	21	0
R.J.	74	0
G.O.C.[a]	0	0

* This corresponds to the middle temporal gyrus/superior temporal sulcus. Figures represent number of significantly activated pixels. A, auditory abstract/concrete; V, visual abstract/concrete; S, syllable; C, case; F, fixation.

[a] G.O.C. did not show activation of either temporal lobe.

Activations related to the semantic task

Left inferior frontal region

Activation of the left IFR included areas anterior and superior to "Broca's area" in the middle frontal gyrus and the middle third of the inferior frontal gyrus. This region is activated by a number of word-processing tasks as well as by object and face working memory. Word-processing tasks activating the left IFR include semantics [Demb et al., 1995; Petersen et al., 1988], phonologic processing [Zatorre et al., 1992], and short-term storage of auditory information [Paulesu et al., 1993]. Since we seek to determine if access to auditory and visual word semantics activates common brain areas, it is important to show that this accounts for a significant portion of the activation seen in the contrast between our semantic and nonsemantic tasks. The use of identical word stimuli in the pair of tasks contrasted

TABLE VI. Pairwise comparisons performed on activated pixels in the inferior frontal region at slice y = +12, using the KS statistic*

Subject	Abstract/concrete vs. fixation	Syllable vs. fixation	Abstract/concrete vs. syllable
J.G.	$P < 0.0001$	$P = 0.41$ (NS)	$P < 0.0001$
H.C.	$P < 0.0001$	$P < 0.0001$	$P = 0.39$ (NS)
M.S.	$P < 0.0001$	$P = 0.0002$	$P < 0.0001$
Averaged data	$P < 0.0001$	$P = 0.48$ (NS)	$P < 0.0001$

* Alpha 0.05, significance threshold $P < 0.017$.

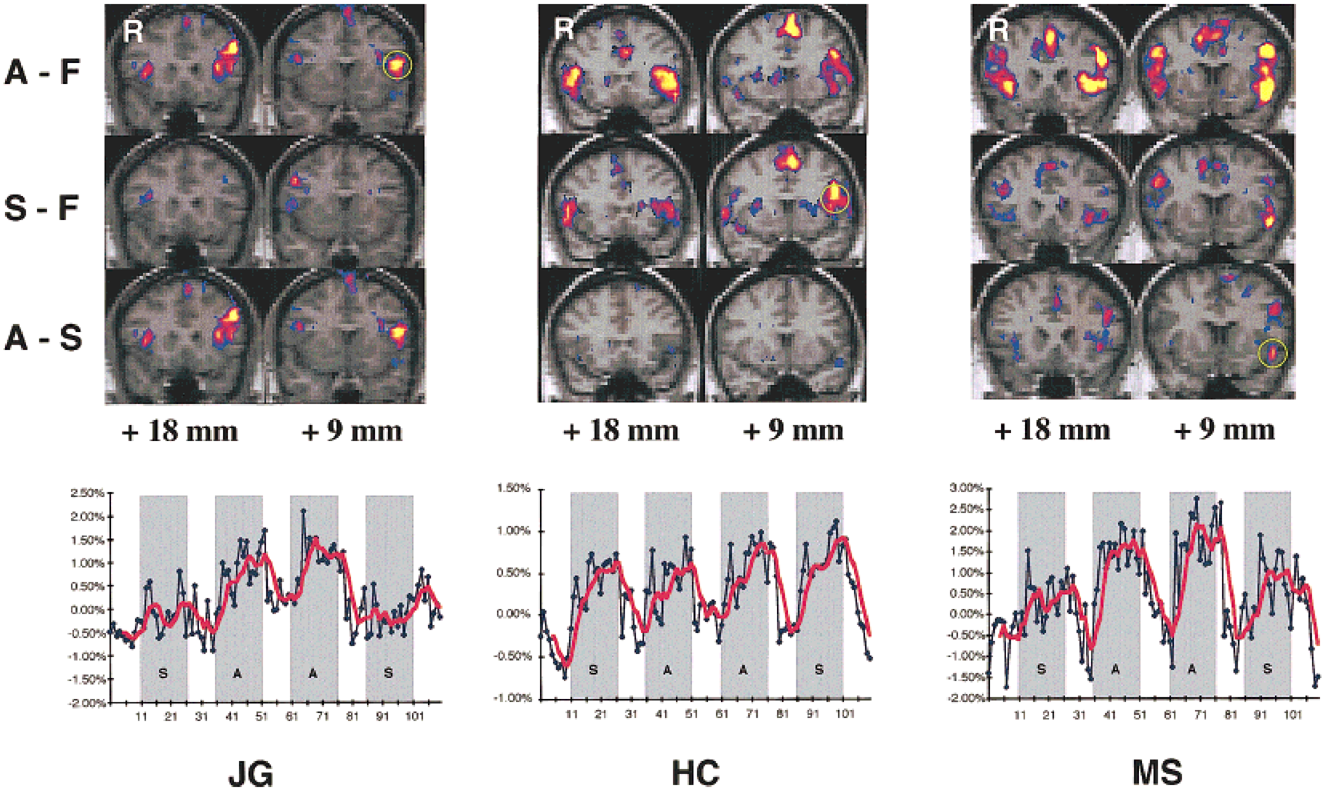


Figure 5.

KS maps and corresponding time courses of 3 subjects, showing variations in activation of the left inferior frontal region according to task. The y-axis shows MR signal in the ROI in terms of percent change relative to the mean MR signal during fixation for that slice. Circles indicate the region from which time course information was obtained. Activation is dichotomous in J.G., equivalent across tasks in H.C., and graded according to task in M.S.

should remove activations common to processing of word stimuli, leaving task difficulty / working memory load or semantic demands as the cognitive tasks most likely to be responsible for activation of the left IFR. Demb et al. [1995] showed that left IFR activation was present when the Abstract/concrete task was contrasted to two nonsemantic tasks of greater and lesser difficulty. In the present study, residual activity in the left IFR in the Abstract/concrete vs. Syllable comparison suggests that the semantic demands of word classification are greater than phonologic ones.

Supplementary motor area

The supplementary motor area [Penfield and Welch, 1951]is not one homogenous area. Rizzolatti et al. [1996] described a posterior "SMA proper," termed F3, and an anterior "pre-SMA," termed F6. These areas differ cytoarchitecturally and functionally. Whether cessation of speech results from interference with motor function or "higher" language functions has not been clarified by electrical stimulation [Lim et al., 1996].

We observed a functional distinction between the anterior and the posterior SMA whereby the anterior SMA was active in the semantic task but not the nonsemantic task. Buckner et al. [1995b] found that the anterior SMA (y = + 13 mm) was activated by picture and auditory word recall tasks vs. repetition, but not by word repetition compared to rest. In contrast, the posterior SMA (y = -1) was active in the recall conditions as well as repetition when compared to rest. Fiez et al. [1996] showed that greater SMA activation was found in a verbal working memory task than in a silent rehearsal task. Binder et al. [1997a] demonstrated anterior SMA activation in a semantic word task. If anterior SMA activation is a result of "inner speech" [Wise et al., 1991], we would expect it to be active in the nonsemantic tasks. This did not occur, even though

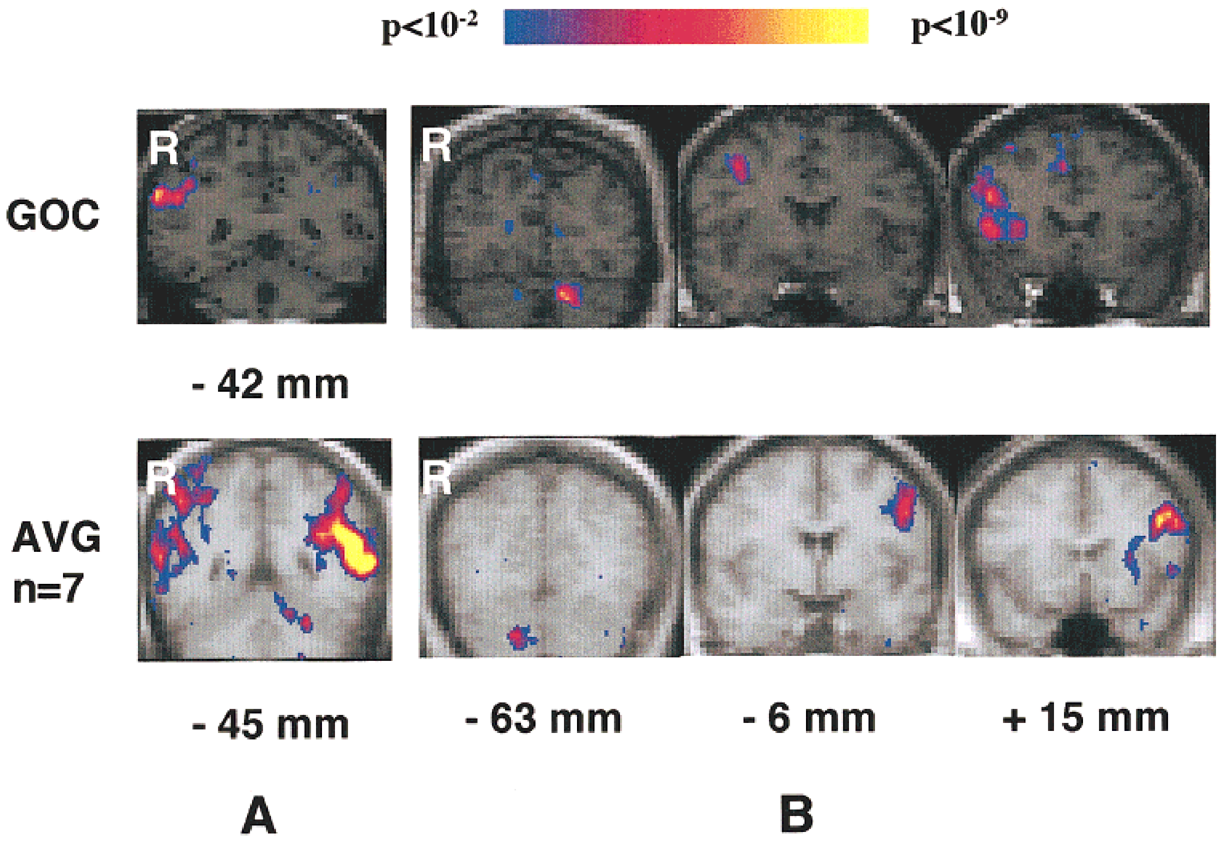


Figure 6.
KS maps show auditory Syllable vs. fixation **(A)** and visual Abstract/concrete vs. Case **(B)** comparisons in G.O.C. (upper panels) and averaged data from 7 other dextrals (lower panels). Activations in the posterior temporal, inferior frontal, prefrontal, and cerebellar regions in G.O.C. are contralateral to those seen in the other subjects. Numbers represent distance relative to the anterior commissure in the A-P direction.

mouth motor activation was present during nonsemantic tasks. Anatomic support for a language/cognitive role for the anterior SMA lies in the observation that F6 has rich connections to the anterior prefrontal and inferior frontal regions [Rizzolatti et al., 1996], areas known to be involved in higher-level cognitive processes. In contrast, F3 has greater connectivity to motor areas.

Left premotor, anterior prefrontal areas, and cerebellum

Activation of the left inferior frontal gyrus in the semantic task extended anteriorly almost into the frontal pole. The left anterior prefrontal region in BA 9, 10, 46, and 47 participates in semantic retrieval [Buckner and Petersen, 1996], and activation of this region was expected. Activation of the right anterior prefrontal area, an area associated with episodic recall [Buckner et al., 1995a], was less expected as we did not ask our subjects to keep track of what words they were exposed to. The left premotor cortex in BA 6 is thought to be related to working memory from lesion studies in primates [Weinrich and Wise, 1982]. It was activated during short-term maintenance of verbal information [Fiez et al., 1996], and its activation as part of extensive activation of the dorsolateral prefrontal cortex was also observed in a semantic task [Binder et al., 1997a].

A greater awareness of the cognitive role of the cerebellum is emerging [Fiez, 1996], and cognitive deficits have been reported with cerebellar damage [Fiez et al., 1992]. Activation of the right cerebellar hemisphere has been observed with word-stem completion [Buckner et al., 1995a] as well as a semantic task not requiring word generation [Binder et al., 1997a].

Left posterior temporal areas

Extensive activation of the posterior temporal area relative to the inferior frontal was expected on the basis of aphasia studies [Hart and Gordon, 1990]. Some functional imaging studies reiterated the importance of this region in semantic processing [Demonet et al., 1992; Pugh et al., 1996; Wise et al., 1991], whereas others consistently demonstrated activation of the left IFR in semantic tasks (Demb et al., 1995; Petersen and Fiez, 1993; Petersen et al., 1988; Raichle et al., 1994] and weaker or nonexistent posterior temporal activation.

The choice of probe and control task [Warburton et al., 1996] is an important determinant of the pattern of ''language activations'' seen. As knowledge of concrete words may be category-specific [Warrington and Shallice, 1984] and may reside in particular parts of the temporal lobes [Damasio et al., 1996; Martin et al., 1996], repeated access to a particular class of words may account for why some experiments result in greater left temporal activation than others. For example, naming pictures of animals has been linked to the inferior and midtemporal cortex. Demonet et al. [1992], using a semantic task which required the matching of an animal name and ''positive'' attributes, obtained activations of the left inferior temporal area. A variant of this task where the animal had to be ''native to the USA'' and ''commonly used by people'' to qualify for an affirmative response also elicited left inferior temporal gyrus activation in addition to left ''posterior polymodal areas'' [Binder et al., 1996]. Verb-generation or the abstract-concrete task we used, in contrast, may not strongly activate this area because the word categories accessed keep shifting.

Intersubject differences in activation

We found a pair of subjects who showed contrasting patterns of the IFR: one showed equal activation of the left IFR during semantic and nonsemantic tasks across both auditory and visual word modalities, whereas the other showed left IFR activation only during the semantic task.

Since the former subject, like the others, took longer to perform the semantic task compared to the nonsemantic task, a possible explanation for her pattern of left inferior frontal activation is that following each nonsemantic response, additional (presumably semantic) processing occurred and filled up the remaining time until the next word appeared on-screen.

Our subject with mirror-image right hemisphere language illustrates the usefulness of screening individual subjects before averaging data. Exclusively right hemisphere language dominance in dextrals without structural brain abnormalities is rare and is seen in 2% or fewer of patients undergoing workup for epilepsy surgery [Loring et al., 1990].

These examples show that differences in brain activation may occur when individuals appear to be performing the same task. While Fiez et al. [1996] suggested that differences in performance may be contributory, we show that even with comparable intersubject performance, variations in topography of brain activation may occur. These variations can disappear in grouped data or may ''contaminate'' it. Data from single subjects are therefore complementary to information gleaned from pooled observations. There may be good biological reasons for why particular brain regions are consistently activated in different individuals while performing the same task. If so, this information is evident only from looking at data from multiple subjects. Further, weak activations that may be of biological significance may only be evident from pooled data.

ACKNOWLEDGMENTS

M.W.L.C. was supported by a Glaxo-Wellcome/Academy of Medicine of Singapore Traveling Fellowship and an NMRC Senior Medical Research Fellowship award. We thank Anthony Wagner and John Gabrieli for providing stimuli lists, and Randy L. Buckner for providing invaluable assistance in the design and critique of this work.

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