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An examination of regional cerebral blood flow during object naming tasks

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Abstract

The purpose of this study was to examine regional cerebral blood flow using positron emission tomography (PET) during the performance of tasks related to visual confrontation naming. Ten healthy, young participants were scanned twice in each of 5 conditions; blood flow was measured using standard PET [^{15}O]-water technology. Two major findings have replicated previous studies. First, the naming of visually presented objects, whether covert or overt, requires a region of the left inferior cortex including the fusiform gyrus. Second, during overt naming, there is an increase in activity in the inferior or frontal cortex and insula as a consequence of generating speech code. These data are consistent with other studies demonstrating the importance of the inferior temporal regions for semantic processing, and the frontal cortex for word form generation. (*JINS*, 1998, *4*, 160–166.)

Keywords: Fusiform gyrus, Object naming, Positron emission tomography, Visual processing

INTRODUCTION

Current techniques in neuroimaging permit *in vivo* studies of the functional organization of the human brain that allow for the identification of specific changes in focal regions in response to cognitive demands (Fox et al, 1985; Mintun et al., 1989). This has led to a series of studies investigating certain basic cognitive processes such as object knowledge (Bookheimer et al., 1995; Martin et al., 1996). Indeed, several recent studies have examined the neural correlates of visual confrontation naming: the act of giving a specific name to a visually presented target, usually in the form of a two-dimensional line drawing (Bookheimer et al., 1995; Martin et al., 1996). Data from these studies, as well as the array of more traditional neuropsychological studies (e.g., Farah, 1990) are consistent on several points, and emphasize that the act of naming involves the interaction of several cognitive and anatomical systems. Indeed, it is possible to track the advancement of visual information as it moves through a hierarchically organized system from the primary visual areas through ventral occipital and temporal regions (Ungerleider & Mishkin, 1982).

Although the anatomy of the visual pathways is well known, the opportunity to study the function of these brain regions *in vivo* presents a difficult challenge. As has been recently pointed out (Vitouch & Gluck, 1997), there are serious statistical limitations to functional imaging studies that involve relatively few participants. As such, replication becomes even more important to the advancement of the field, since this permits the identification of consistent activations, and allows for caution in interpreting novel findings. Given the importance of between-center replication (e.g., Becker et al., 1994) the present study was an attempt to determine those brain regions whose activity covaried with specific aspects of visual naming. Thus, the purpose of this study was to develop a protocol to examine the neuroanatomical correlates of naming based on the results of existing protocols. Specifically, the development of the scanning protocol was greatly influenced by the work of Bookheimer (Bookheimer et al., 1995) and Martin (Martin et al., 1996), and their colleagues. While not a direct replication of either study, the present protocol shows many of the activation conditions specified in these two studies, and this permits conclusion about the generalization of the findings.

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METHODS

Research Participants

There were 10 participants (3 men, 7 women), 26.2 years of age (range: 19–30), with 17.1 years of education (range: 13–20). All were healthy (no history of neurological or psychiatric disorders), right-handed, and English was their native language. Informed consent was obtained prior to the start of the scanning session. Each of the female volunteers had a negative serum pregnancy test on the day of the PET scan. This research had been reviewed and approved by the Institutional Review Board of the University of Pittsburgh Medical Center.

PET Procedures

Each was scanned 10 times measuring relative cerebral blood flow (relCBF) using [^{15}O]-water with standard laboratory procedures (Becker et al., 1994). The participants were placed in the supine position on the Siemens 951R/31 PET scanning table. The scanner collects 31 parallel planes over a 10.8-cm axial field of view. An antecubital intravenous catheter was placed in the left arm for radiopharmaceutical injection. The head was positioned within the head holder and a softened thermoplastic mask fitted over the face, molded to the patient's facial contours, and fastened to the head holder (Fox et al., 1985). The PET gantry was rotated and tilted such that the lowest imaging plane was parallel to, and at the canthomeatal line. Using a system of three laser lines the face was marked with washable ink in five places to allow checks for movement of the patient during the study and to allow for positioning of the patient's head if necessary. Transmission scanning was done in all PET studies prior to radiopharmaceutical injection using three rotating rod sources of ^{68}Ge/^{68}Ga. Following this scan, the septa were retracted to permit three-dimensional acquisition of data.

The participant was instructed to lie motionless on the scanning table. The head was positioned in a head holder and a customized mask (with cutouts for the eyes and ears) was fitted over the face and fastened to the head holder. An intravenous catheter was placed in the left arm for radiopharmaceutical injection.

Measurements of relCBF were made after an intravenous bolus injection of 5–7 mCi of H_2[^{15}O]-water in 5 to 7 ml of saline. Beginning approximately 5 s after the point when activity began to enter the brain (to allow for partial clearance of the H_2[^{15}O] from vascular structures), we began a 60-s sampling frame, which was used as the qualitative map of cerebral blood flow (Fox & Mintun, 1989). Data were acquired and reconstructed in full three-dimensional mode (Townsend et al., 1991).

The collected PET images from each patient were centered (left–right), vertically aligned to correct for movement in the transverse and coronal planes, and coregistered to one another to correct for slight head movement during the scan (Miroshima et al., 1992; Woods et al.,1992). The rest of the PET scans collected on the subject were mathematically registered to the first scan by PET-to-PET alignment (Woods et al., 1992). These processes centered the images and oriented them in the same coordinate system for later processing.

The statistical analysis of the data was carried out using Statistical Parametric Mapping program (SPM95; Friston et al., 1991) in PRO MATLAB (Mathworks Inc., Sherborn, MA). The scans were spatially normalized using linear transformation, which removed individual subject variability and transformed each brain into a standard Talairach and Tournoux brain atlas (Talairach & Tournoux, 1988). We did this to avoid loss of information at the top- and bottom-most scans, which can occur with SPM95's default nonlinear transformation. The scans were then smoothed with a three-dimensional Gaussian filter of 16 mm full-width half maximum (inplane) to suppress noise and minimize the effects of normalization errors by increasing the sensitivity of the signal.

Differences in global activity within and between participants were removed by analysis of covariance (ANCOVA) on a voxel-by-voxel basis with global counts as covariate and regional activity across subjects for each task as treatment. The ANCOVA was used for the comparison of tasks, with each individual being studied in all conditions. Comparisons of the means across selected conditions were made on a voxel-by-voxel basis using the *t* statistic. The resulting values constituted a statistical parametric map (Friston et al., 1991). The critical level of alpha was set at .001 for all comparisons, except as noted. Pixel locations correspond to peak *z* scores, and relCBF values were recorded from images after smoothing and thus represented a weighted average similar to the size of the Gaussian filter (i.e., 16 $\times$ 16 $\times$ 12 mm) centered over the voxel location.

Behavioral Task Procedures

Instructions and test material were presented using PsyScope© (Cohen et al., 1993) *via* a Macintosh computer with a video monitor above the participant's head in the PET scanner. Nonobject stimuli were taken from the corpus formulated by Kroll and Potter (1984). The line drawings of real objects were selected from the Snodgrass and Vanderwart corpus (Snodgrass & Vanderwart, 1980).

There were five conditions used in this study, with two separate scans made for each of the conditions: fixation, and four different image presentation tasks. During the fixation condition, the subject was instructed to fixate on a crosshair target for the duration of the scan; this served as a baseline condition. The four cognitive tasks were to (1) view a line drawing of a real object, (2) name the viewed drawing of object, (3) view nonobject drawings (i.e., "figures"), and (4) view figure and speak ("Hiya"; see Figure 1). In each of the four task conditions, the stimuli were presented for 200 ms, with an 1800 ms intertrial interval to allow for a response (when appropriate). The task was started at the time

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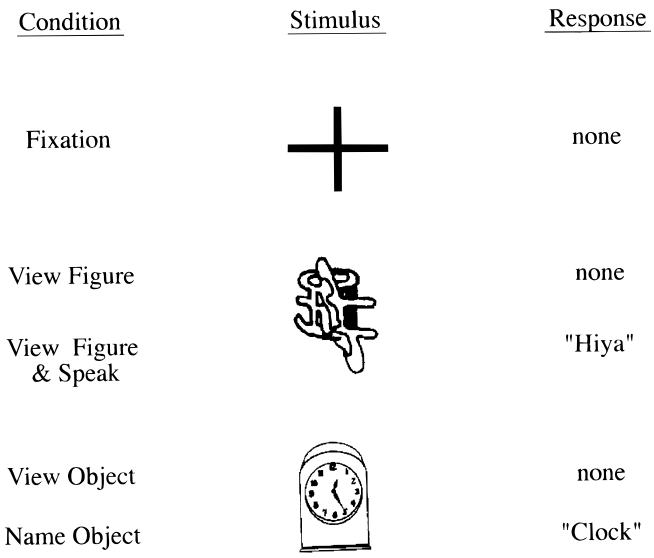

Fig. 1. PET study conditions. Each of the five trial types, an example of the type of stimulus presented, and an example of the response are shown.

of injection, and lasted for 48 trials, or 96 s. Figure 1 shows examples of the stimuli, each of which was used for one trial only, and was not repeated between trials or scans. Each session consisted of two blocks of five scans, with each condition occurring once within each block. The order of conditions within blocks was randomized both within and between participants.

RESULTS

The upper left-hand portion of Figure 2 shows the difference in relCBF when the fixation condition is compared with the view figure condition ($p < .001$). This contrast focuses on the activation of the visual system, but does not involve either speech (since no overt response was required) or semantics (since there is no referent for these stimuli). Focal activity was seen in BA18 (289 contiguous voxels), and the medial prefrontal cortex, BA8/BA9 (389 voxels; see Table 1). Also of interest was the increase in activity seen in the right hippocampus (68 voxels) when viewing these nonsense drawings. This was the only condition in which hippocampal activity was greater than that seen at fixation, although the mean relCBF was high under all conditions ($>$ 68 ml/100 ml/min).

We then examined the difference between the view object condition and fixation (Figure 2, upper right; Table 1). This contrast *does* involve automatic semantic retrieval, but still does not involve overt speech. As was seen in the previous contrast, there was a large, bilateral activation over visual cortex (BA18; see Table 1). There was a large region of activation over the fusiform gyrus (BA37) extending from the ventral occipital lobe. Also of significance, especially in light of the fact that no overt response was required, was an activation in the inferior frontal gyrus. This region was large (651 contiguous voxels) and included BA45 and BA47.

In order to examine the activation due to the task semantics and covert lexical production, we subtracted the view figure condition from the view object condition (Figure 2, bottom left). Under these circumstances there are two large regions of activation of particular interest ($p < .01$). The first (196 contiguous voxels) was centered on the inferior frontal cortex and insula, including BA45 (see Table 1). The second area (823 voxels), included the left ventral temporal lobe. This largest active region included the fusiform gyrus of ventral occipital–temporal region and extended at least 16 mm along its anterior–posterior extent.

Finally, we contrasted the name object condition with the view-figure-and-speak condition. In these tasks the subjects must view visual stimuli and speak. However, the conditions differ in that one involves naming real objects. Of particular importance is the fact that there was bilateral activation in the ventral occipital processing stream, and no significant activation in the left inferior frontal region. That is, relative to the nonobject viewing condition—with speech—the name object condition revealed no increase in the area normally activated by speech (or speech code generation).

DISCUSSION

Of the various studies that have examined the neuroanatomical basis of visual confrontation naming, perhaps that of Martin and colleagues (Martin et al., 1996) is closest in design to our protocol. The visual objects were both from the Snodgrass and Vanderwart corpus, and the nonsense objects were both from the Kroll and Potter set. The stimulus duration were similar (180 *vs*. 200 ms), and the rate of presentation was the same (1 every 2 s). The data gathered during the present protocol, therefore, provide strong evidence for the reliability and consistency of the principal findings: namely, that object naming requires components of the ventral visual processing stream including the inferior temporal cortex, as well as the left inferior frontal–insular cortex.

This pattern of regional activity associated with object naming is also consistent with the data of Bookheimer and colleagues (Bookheimer et al., 1995). All of these studies, including the present one, emphasize the importance of the fusiform cortex and the ventral temporal–occipital border in semantic processes related to object naming. We also saw consistent activation in the inferior frontal cortex with the objects relative to fixation. However, the activity seems more related to the generation of the phonological code than to semantics *per se*. When we compared the name object and view-figure-and-speak conditions, we saw the same pattern of activity as when we compared view object and view figure *except* that the contrast did not show significant frontal activation. This suggests that even repeatedly generating the code for "Hiya" may raise the level of inferior frontal activation due to speech generation. Further, in a related study on word reading (Herbster et al., 1997; see below), we also

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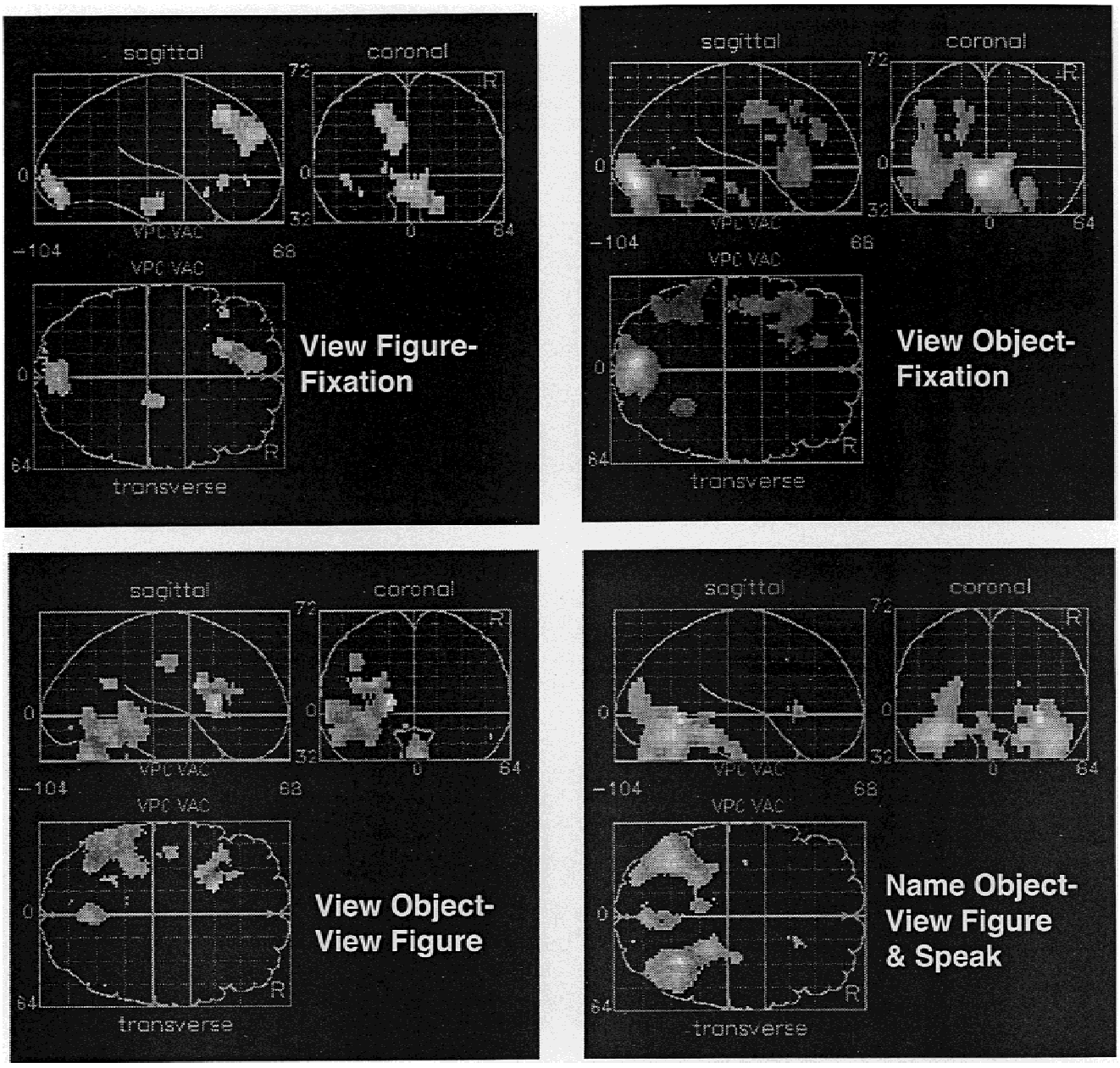

Fig. 2. Results of SPM analyses. Each set of images shows all significant voxels for the specific contrast in three planes (sagittal, coronal, transverse). In these "look-through" images all significant voxels are shown in all three views. See text for details.

found inferior frontal activation under certain conditions of word and nonword reading, which were thought related to the generation of speech code and not to word semantics.

Herbster and colleagues (Herbster et al., 1997) also reported activation of fusiform cortex when reading real words but not when reading pronounceable nonwords. By contrast, activation around BA45 (i.e., inferior frontal cortex) was seen only when reading aloud pronounceable nonwords or real words with nonstandard spelling (i.e., exception words). This finding was interpreted as being consistent with computational model of reading (Plaut et al., 1996), and as such the activation by the irregular words (e.g., "debt") was due to competition between the prepotent direct orthography–phonology translation and a bias from the semantic system. The activation during nonword reading was due to the unusual sequence of phonemes demanded by the orthography (e.g., "chourn"). Thus, we conclude based on these separate findings (see also Fiez et al., 1997) that this activity during object naming tasks is due to the (sometimes covert) generation of the phonology necessary to say the name of the object.

In an effort to examine the relationships between these regions of activity, we overlaid the *t*-maps from that study and the present study (view object–view figure; see Fig-

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Table 1. Regions of significant activation

Condition and region	*Z*	Coordinates		
		X	*Y*	*Z*
View figure–fixation				
BA18 (bilateral)	4.13	2	−88	−8
BA8 (left)	4.04	−20	26	44
Hippocampal formation (right)	3.74	20	−18	−16
BA45 (left)	3.37	−44	26	0
View object–fixation				
BA18 (bilateral)	5.57	−6	−88	−12
BA45 (left)	4.40	−46	22	4
Cerebellum (left)	4.16	26	−56	−16
BA37 (left)	4.13	−40	−50	−12
BA6 (left)	3.94	−42	−4	40
BA32 (left)	3.53	−18	36	24
	3.38	−14	24	36
BA20 (left)	3.49	−44	−12	−20
View object–view figure				
Inferior frontal (left)	3.46	−18	16	8
		−28	4	20
		−38	18	20
Cerebellum (bilateral)	3.19	0	−70	−28
BA37 (left)	3.17	−36	−42	−4
BA31 (left)	2.67	−22	−58	20
BA6 (left)	2.63	−42	−12	36
Name object–view figure and speak				
BA19 (right)	4.43	32	−60	−4
	4.24	40	−60	−20
	4.15	20	−40	−12
BA19 (left)	4.38	−34	−64	−12
	4.22	−28	−48	−12
	4.13	−44	−68	−12
Cerebellum	3.93	2	−82	−28
Insula	3.42	20	24	4

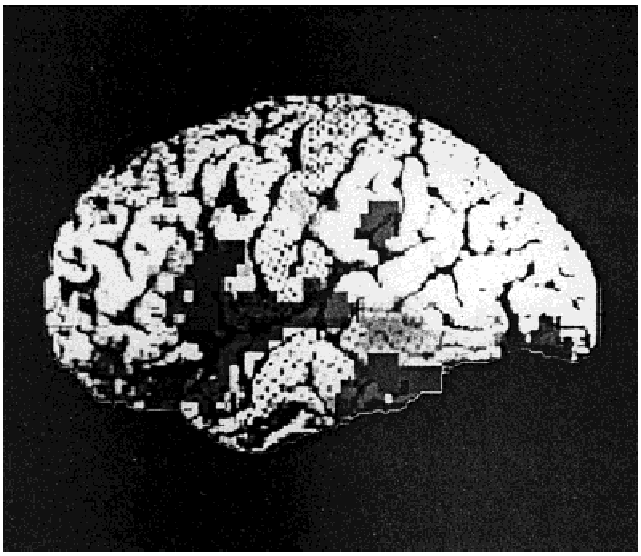

Fig. 3. Overlay of activation onto the left hemisphere of the MRC standard MR image. Yellow voxels are those activated by visual object naming (current study), blue voxels are those activated by irregular word reading (Herbster et al., 1997), and the green voxels are those activated by both types of stimuli.

ure 3). The regions of the left cerebral cortex marked in yellow are these activated while viewing real objects (present study); the blue areas are those activated while reading aloud irregularly spelled English words. The region of activity in the inferior frontal cortex is virtually identical in both studies, and appears as the color green. By contrast the region of activation in the inferior temporal lobe differs between studies. Object naming activates a more posterior and lateral region of the temporal lobe than did word reading. The small region of intersection may represent true overlap of activity (and thus, may represent modality-independent semantics) or simply measurement error. The fact that this is a between-study comparison, albeit with very similar stimulus and response demands, does not permit resolution of this issue. However, other similar studies would suggest a common system for words and drawings (e.g., Vandenberghe et al., 1996), and damage to this region has been implicated as critical for the development of a semantic dementia (e.g., Graham et al., 1997).

Table 2 summarizes the results of several studies (including the present one) in an attempt to compare word-generated and object-generated inferior temporal activation. The study that perhaps best compares word- and object-based activation is that by Bookheimer and colleagues (Bookheimer et al., 1995). That study found activation in the left fusiform cortex with word reading, and in the object naming conditions in areas very close to those seen here. There was similar activation seen in the inferior frontal–insular cortices as we reported, as well. Thus, the data from the present study appears to reliably replicate these earlier reports.

The impetus for our program of research is based on our studies of Alzheimer's disease (AD; Becker et al., 1996; Herbster et al., 1996). One of the principle symptoms of progressive degenerative disorders is difficulty with visual confrontation naming (Barker & Lawson, 1968; Bayles & Tomoeda, 1983; Hodges et al., 1990, 1992; Kirshner et al., 1984; Martin & Fedio, 1983; Nebes & Brady, 1989). While episodic memory loss may be the diagnostic hallmark of AD (American Psychiatric Association, 1994; McKhann et al., 1984), it is the decline in semantic memory performance that best tracks the clinical course of the disease (Locascio et al., 1995). In understanding the nature and extent of the CNS dysfunction in AD, therefore, the study of semantic memory using functional imaging is an extremely powerful tool.

However, prior to such studies, it is important to develop scanning protocols in young, healthy adults that can produce reliable and valid areas of regional activation; one purpose of this study is to develop such a protocol. Our research was guided by previous studies that compared and contrasted the regional cerebral blood flow during visual confrontational naming with that seen during viewing nonsense or impossible objects. Unlike many of these studies, how-

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Table 2. Results of studies comparing word-generated and object-generated inferior temporal activation

Study	Condition	Region	Coordinates		
			X	*Y*	*Z*
Menard	Words–crosshair	Frontal	−39	20	−4
Bookheimer et al. (1995)	Real-words–control	Frontal/insula	−32	18	8
		Fusiform	−42	−34	−16
Herbster et al. (1997)	Real-words–letter-string	Frontal	−46	0	−4
		Fusiform	−38	−40	−24
Menard	Object–crosshair	Frontal	−39	10	20
		Middle temporal	−41	−39	8
Bookheimer et al. (1995)	View-objects–control	Frontal/insula	−34	20	16
		Fusiform	−36	−54	−16
			−36	−32	−8
Martin et al. (1996)	View-objects–nonsense	Ant-insula	−28	16	8
		Fusiform	−28	−50	−16
Zelkowicz (this article)	View-object–fixation	Frontal	−46	22	4
		Fusiform	−40	−50	−12
	View-object–nonsense	Frontal	−18	16	8
			−28	4	20
		Inferior temporal	−36	−42	−4

ever, we required an overt naming response since among AD patients we would need to have evidence of orientation to task. Also, in AD we cannot assume the patients are correctly naming objects; rather, we need a measure of performance accuracy, and cannot rely solely on covert naming. Therefore, we needed to include control conditions which would account for the relCBF correlates of the auditory and verbal productive processes. Furthermore, because the protocol includes stimuli of both real and nonsense objects, and responses that were covert or overt, we will be able to track different aspects of information in the AD patients through the processing stream.

In summary, the results of these analyses demonstrate convergence at several points in terms of the brain region associated with word and object knowledge. Functional imaging studies can reliably demonstrate activation in the fusiform and frontal cortices; as such, we may now have a tool to investigate alterations in the functional neuroanatomy of semantic memory in clinical populations.

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