Functional MRI Studies of Auditory Comprehension

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Abstract: The location of brain regions essential for auditory language comprehension is an important consideration in the planning of neurosurgical procedures that involve resections within the dominant temporal lobe. Language testing during intraoperative and extraoperative cortical stimulation has been the primary method for localizing these regions; however, noninvasive alternatives using functional neuroimaging have been sought. Here we report on a study of 14 subjects who listened passively to alternating sentences spoken in their native English language and in unfamiliar Turkish while functional magnetic resonance images were acquired. The English sentences produced strong activation within the left superior temporal sulcus in all subjects. Lesser activation was seen in homotopic right hemisphere locations in several subjects. In addition to these posterior temporal activations, 8 subjects also showed activation to English sentences in the left inferior frontal gyrus. Turkish sentences evoked no coherent region of activation in any subject. As both the Turkish and English sentences were read by the same speaker, and were matched for length, volume, and intonation, we conclude that the activation pattern evoked by the English sentences reflects auditory comprehension. This conclusion is further supported by additional control studies that have shown a markedly different pattern of activation by pure tone frequency glides. *Hum. Brain Mapping 6:1–13, 1998.* © 1998 Wiley-Liss, Inc.

Key words: functional MRI; audition; speech; language comprehension

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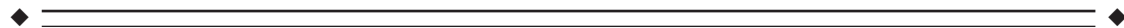
INTRODUCTION

The localization within the human brain of cortex specialized for language processing has important clinical value in planning surgery in the dominant hemisphere. Presurgical language assessment usually includes the sodium amobarbital test which can be used to determine language laterality [Wada, 1949; Wada and Rasmussen, 1960], but which provides no information about the location of "eloquent" cortex within the dominant hemisphere. When a planned procedure puts language cortex at risk, intraoperative language mapping using cortical stimulation is frequently performed [Lebrun and Leleux, 1993; Ojemann et al., 1989; Ojemann, 1993; Lesser et al., 1994; Buchtel et al., 1995]. Depending upon the planned resection, cortical stimulation mapping usually at-
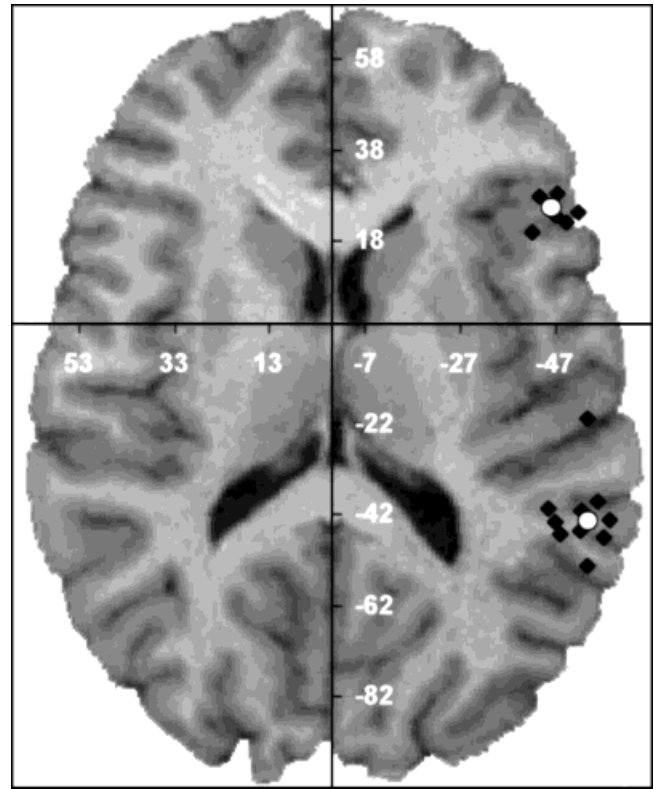
Figure 2.
Position of Talairach coordinates of the left posterior temporal lobe activation and left inferior frontal activation for the English-Turkish task for 11 subjects studied in axial slices. Individual subject data are represented as black diamonds, and group average data as white circles. The center of mass of each subject's activation is superimposed on a representative brain slice at z = +12.

tempts to identify the location and extent of inferior frontal (Broca's area) or posterior temporal (Wernicke's area) language regions. While the historical division of these respective regions into productive and receptive language regions has proved overly simplistic [Lebrun and Leleux, 1993; Ojemann et al., 1989; Ojemann, 1993; Schaffler et al., 1996], inferior frontal language regions

Figure 1.
Functional MRI activation to English sentences overlaid upon T1-weighted high-resolution axial oblique MR images. t-maps for all subjects were thresholded at a t-value of 1.96. Color scale represents increasing t-values from red to white. Four subjects (**A–D**) are shown at approximately the same slice location (slice 4). Activation is seen in the superior temporal sulcus and extends into the middle temporal gyrus or superior temporal gyrus in each subject. In this and all anatomical images, the left side of the brain is represented on the right side of the image.

TABLE I. Location in the coordinates of Talairach and Tournoux [1988] of centers of activation for this task and in previous studies of language comprehension*

Study	Auditory task	Location	X	Y	Z
Schlosser et al., 1997	English-Turkish	L post-STS	**−52**	**−44**	**12**
Petersen et al., 1988	Single words	L post-STS	−50	−45	15
Wise et al., 1991	Noun comparison	L post-STG	−43	−38	8
Fiez et al., 1996	Single words	L post-STS	−53	−55	18
Price et al., 1992	Single words	L post-STG	−58	−34	12
Howard et al., 1992	Single words	L post-STG	−48	−38	4
Average post-STG/STS			−50.4	−42.0	11.4
Schlosser et al., 1997	English-Turkish	L anterior STS	−53	−21	5
		L IFG	−47	24	12
		R STG	51	−27	8
	Frequency sweep	L anterior STG	−53	−21	14.5
		R Sylvian	53	3	−1.2
Demonet et al., 1992	Nonwords (phonemes)	L anterior STG	−56	−12	4
Petersen et al., 1989	Generate words	L IFG	−33	30	−6
Wise et al., 1991	Verb generation	L IFG	−40	14	16

*Top half: Across-subjects average Talairach coordinates for the left posterior superior temporal sulcus (L post-STS) in the English-Turkish comparison of the present study are shown in boldface. Coordinates for similar regions in related language activation studies are shown in normal typeface. Bottom half: Average Talairach coordinates for the left inferior frontal (IFG) and left anterior superior temporal sulcus (STS) for the English/Turkish task, and for the left anterior superior temporal gyrus (STG) and right Sylvian fissure for the frequency sweep task of the present study, are shown in boldface. Locations of related studies are shown in normal typeface.

are readily identified by stimulation-induced disruption or arrest of speech. In our experience, language deficits following stimulation of posterior temporal regions are often more subtle and usually involve deficits in naming and/or auditory comprehension. Intraoperative stimulation provides language localization with high anatomical resolution [Ojemann, 1993; Lesser et al., 1994], but its requirement of an awake and cooperative patient, and its attendant time demands during surgery, have led to the development of alternative noninvasive procedures which can be performed prior to surgery using neuroimaging [Leblanc et al., 1992; Martin et al., 1993; Latchaw et al., 1995; Maldjion et al., 1996] and/or neurophysiological [Eulitz et al., 1994] procedures.

Neuroimaging studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have demonstrated activation of the left inferior frontal cortex in a variety of language tasks involving noun reading, verb generation, silent speech, and naming [Buckner et al., 1995; Cuenod et al., 1995; Desmond et al., 1995; Eulitz et al., 1994; Hinke et al., 1993; Leblanc et al., 1992; Liotti et al., 1995; McCarthy et al., 1993; Petersen et al., 1990; Price et al., 1996; Yetkin et al., 1995]. Studies of single-word auditory comprehension using PET have shown reliable activation of the left posterior superior temporal lobe [Demonet et al., 1992, 1994; Fiez et al., 1996; Howard et al., 1992; Petersen et al., 1988, 1989, 1993; Price et al., 1992, 1996; Stromswold et al., 1996; Wise et al., 1991]. For example, Demonet et al. [1992] compared phonological and lexico-semantic processing in a [15]O PET study and found that phonological processing activated both the left superior temporal and inferior frontal gyri. Lexico-semantic processing activated the left middle and inferior temporal gyri, and left parietal and superior prefrontal regions. The same temporal lobe regions were also activated by passive word presentation and repetition tasks [Binder et al., 1995, 1997; Demonet et al., 1994; Fiez et al., 1996; Karbe et al., 1995; Petersen et al., 1988, 1989, 1993; Price et al., 1992, 1996; Wise et al., 1991]. Stromswold et al. [1996] compared semantic judgments about normal sentences and those containing nonsense words using [15]O PET and demonstrated that sentence processing was localized to the left perisylvian association cortex. Several studies have compared the pattern of activation in neuroimaging studies of language to the results of the sodium amobarbital or Wada test in the same subjects [Desmond et al., 1995; Brint et al., 1996; Pardo and Fox,
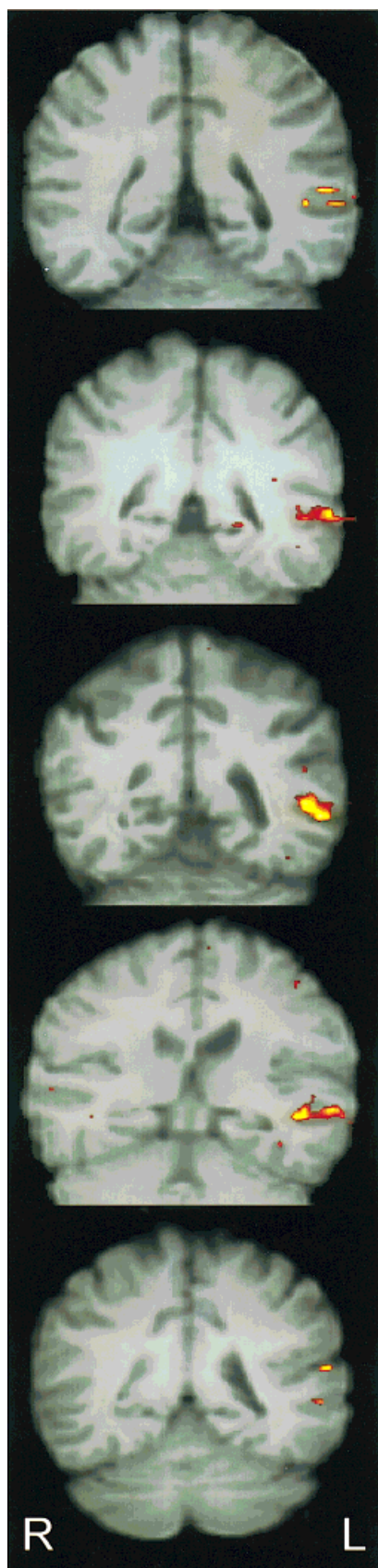
1993]. For example, Desmond et al. [1995] showed that semantic processing of visually presented words activated the inferior frontal cortex in the speech dominant hemisphere as determined by the Wada test.

With few exceptions [Desmond et al., 1995; Herholz et al., 1996; Pardo and Fox, 1993], PET studies of posterior temporal language processing have relied upon group averages, which has limited their clinical usefulness. Functional MRI has the potential to map posterior temporal regions in individual patients, but to date few studies have been completed [Alsop et al., 1996; Binder et al., 1995, 1997], and the results of these studies appear to indicate much larger areas of activation than the focal areas mapped with cortical stimulation. This may, in part, be related to task design. For example, Alsop et al. [1996] compared auditory language stimulation in a semantic judgment task to a baseline condition in which no auditory stimulus was present. The large activated regions they identified likely reflect primary auditory processing in addition to processing specific for auditory comprehension.

In our clinical intraoperative and extraoperative stimulation mapping studies, we have found auditory comprehension tasks to be sensitive indicators of posterior-temporal language areas, and preservation of auditory comprehension is an important consideration during dominant temporal lobe surgery [Lebrun and Leleux, 1993]. Here we demonstrate reliable focal activation of the posterior temporal cortex using a task designed to isolate auditory comprehension in individual subjects.

SUBJECTS AND METHODS

Subjects

A total of 14 neurologically normal volunteer subjects (7 male) participated in the auditory language comprehension studies. Subjects ranged in age from 22–42 (mean, 26.5 years), and all were right-handed. All subjects were native English speakers and none could comprehend the Turkish language. Yale University's Human Investigation Committee approved the experimental protocol, and all subjects provided in-

Figure 3.

Functional MRI activation to English sentences overlaid on T1-weighted high-resolution coronal oblique MR images. t-maps were thresholded at a t-value of 1.96. Five subjects are shown at an equivalent slice location (slice 2) in the posterior temporal lobe. Activation can be seen in the superior temporal sulcus in all 5 subjects.

formed consent. Eleven subjects were tested using axial slices, while 3 subjects were tested using coronal slices. Three subjects participated in both axial and coronal test sessions that were separated by several months. In addition to language testing, 5 subjects also participated in additional control activation studies using pure tone frequency glides.

Stimuli

Stimuli for the auditory comprehension task consisted of 112 digitized auditory segments. Each segment consisted of one or two sentences lasting for a total duration of 4.8–5.8 sec. Half of the segments were spoken in English, while in half the same sentences were spoken in Turkish. The same female speaker produced both language segments and she attempted to closely match intonation and prosody. Words that sounded similar in each language were avoided. The segments were processed by software to equalize their amplitude range and to ensure that each segment began precisely with the onset of the first word.

Subjects were presented with four runs, each consisting of an alternating series of English and Turkish auditory segments with 6 sec between the onsets of successive segments. Twenty-eight segments were presented in each run. Two runs started with English (E-T-E-T . . .) and the remaining two runs started with Turkish (T-E-T-E . . .). Successive English and Turkish segments were never the same sentences. Stimulation began 12 sec after the onset of image acquisition. Subjects were instructed to listen to all sentences for comprehension. Subjects were informed that half of the sentences would be in Turkish but were unaware that the same sentences were presented in each language over the course of the four runs. Experimental timing was controlled by computer, and the digitized sounds were reproduced using a computer soundboard. The sounds were conducted into the MRI system using plastic tubing that terminated in insert ear plugs. All stimuli were binaural.

In addition to the language stimuli, a 5.9-sec digitized segment was created consisting of two frequency glides from 200–5,000 Hz (voice range) embedded within a background of white noise with the same overall amplitude as the sentences. A second segment consisting only of the white noise was also created. These segments were alternated in the same manner as the Turkish and English segments in a subset of 5 subjects who also participated in the language comprehension study.

Imaging parameters

Images were acquired with a 1.5 T General Electric (Milwaukee, WI) Signa scanner equipped with a standard quadrature head coil and an ANMR (Wilmington, MA) echoplanar subsystem. The subject's head was positioned along the canthomeatal line and immobilized using a vacuum cushion and a forehead strap. T1-weighted sagittal scans were obtained, and the midsagittal image was used to identify the anterior (AC) and posterior (PC) commissures. For subjects participating in the axial study, a series of seven slices was selected parallel to the AC-PC plane, with the most inferior image taken at the level of the top of the pons on a midline sagittal image. For subjects participating in the coronal study, a series of seven slices was selected perpendicular to the angle of the Sylvian fissure, with the most anterior slice at the anterior tip of the temporal lobe. Functional images were acquired using a gradient-echo echoplanar sequence (TR = 1,500, TE = 45, α = 60°, NEX = 1, FOV = 40 × 20 cm, slice thickness = 9 mm, skip = 2 mm, imaging matrix = 128 × 64, voxel size = 3.2 × 3.2 × 9 mm). The images for each of the seven slices were acquired in equally spaced time intervals over the 1.5-sec TR in the slice order 1-3-5-7-2-4-6. Each of the four imaging runs consisted of 128 images per slice (196-sec scan time) preceded by four radio frequency (RF) excitations to achieve steady-state transverse magnetization. T1-weighted scans were acquired for anatomical coregistration at the same locations and in the same plane (axial or coronal) as the functional images.

Data analysis

Three consecutive images (per slice) were selected from each of the 56 (14 cycles × 4 runs) English segments and were compared to an equal number of images selected in the same manner from the Turkish segments, using an unpaired t-test on a voxel-by-voxel basis. The first image of each consecutive three images occurred at approximately 5 sec after the onset of either the English or Turkish segment to compensate for hemodynamic delay. The delay was corrected for the slice acquisition order. Voxels exceeding a t-value of ±1.96 were counted for each slice and hemisphere in the uninterpolated t-maps. These thresholded t-maps also were depicted as color overlays upon anatomical MR images. Because the functional images were lower

in resolution than the anatomical images, the t-maps were linearly interpolated prior to overlay. Since MR signal during English segments was compared to activation during Turkish segments, voxels with t-values corresponding to the positive tail of the t-distribution had greater signal during English than Turkish segments. Voxels with t-values corresponding to the negative tail of the distribution had greater signal during Turkish than English segments. All t-test analyses were performed on unsmoothed images.

In addition, a within-subjects analysis of variance (ANOVA) was performed in which the dependent variable was the number of activated voxels, and the independent variables were language, hemisphere, and slice. The significance of each independent variable was tested, using its interaction with subject as the error term. A similar ANOVA was performed using the t-statistic associated with each activated voxel as the dependent variable to get a sense of the strength of the activation. Finally, a between-subjects ANOVA was performed to test whether there were significant sex differences in the number of activated voxels.

RESULTS

Axial studies

A consistent pattern of activation was observed in the 11 subjects studied with axial slices. Images acquired following onset of the English sentences showed significant activation of the posterior temporal lobe, confined primarily to the left superior temporal sulcus (STS), including the superior bank of the middle temporal gyrus (MTG) and the inferior bank of the superior temporal gyrus (STG). This pattern is illustrated in Figure 1, which presents results at the same anatomical slice for 4 individuals (Fig. 1A–D). In addition to this large posterior activation, smaller areas of activation were observed in the left inferior frontal region (Fig. 1B) and in the right STS (Fig. 1D). In contrast to this consistent anatomical pattern of activation evoked by English segments, there were no areas of focal cortical activation to the Turkish sentences.

To summarize the mean activation pattern across subjects, the centroid of activation in each subject was measured in the coordinate system of the atlas of Talairach and Tournoux [1988] for all 11 subjects. Figure 2 illustrates the location for the left posterior STS activation and the left inferior frontal activation in 11 subjects (black squares) and the mean activation across subjects (white circles). A comparison of these average centroids to results of other studies of auditory word processing is shown in Table I.

Coronal studies

The pattern of activation seen in the axial slices was confirmed in the 6 subjects tested with coronal slices. Figure 3 presents activations for 5 of these subjects from a slice approximately perpendicular to the posterior temporal activations seen in Figure 1, affirming that the superior temporal sulcus was the principal site of activation. Figure 4 shows activation to both English and Turkish for all seven slices in one subject. The left STS activation is visible in slices 5–7, while activation of the left inferior frontal region can be seen in slices 1–2.

Combining axial and coronal studies, the most consistent finding was activation of the left posterior superior temporal sulcus, which was observed in all 14 subjects. This activation sometimes extended into the adjacent middle temporal gyrus and into the superior temporal gyrus (Brodmann's area 22). In 6 subjects, there was also a lesser activation in the right superior temporal gyrus. In addition to the posterior activation, 8 subjects showed activation in the anterior temporal lobe. In 6 of these subjects, the anterior temporal activation was bilateral. In all cases, the anterior temporal activation was discontinuous from the posterior activation. Finally, 8 subjects showed activation in the left inferior frontal region, and no subject showed activation of the homotopic region in the right hemisphere.

The results from the ANOVA confirmed that significantly more voxels were activated by the English segments in the left than right hemisphere ($F(1, 16) = 35.23$, $P = 0.0001$). In addition, the activated voxels from the left hemisphere had significantly greater t-values ($F(1, 16) = 7.64$, $P = 0.01$). The interaction of hemisphere by language was significant ($F(1, 16) = 8.51$, $P = 0.01$) and indicated that the relatively few voxels activated by Turkish had a symmetric pattern of activation, while those activated by English were strongly lateralized to the left hemisphere. These findings were confirmed by additional ANOVAs performed separately upon the axial and coronal studies. There were no significant differences in the number of

Figure 4.

Functional MRI activation for one subject is shown in seven coronal oblique slices. English activation is shown in the red color scale (thresholded at a value of 1.96) and Turkish in the blue color scale (thresholded at a value of −1.96). Activation to English is seen in the inferior frontal regions and middle temporal regions and in the superior temporal sulcus in the anterior and posterior temporal lobe. Activation to Turkish is nearly absent.
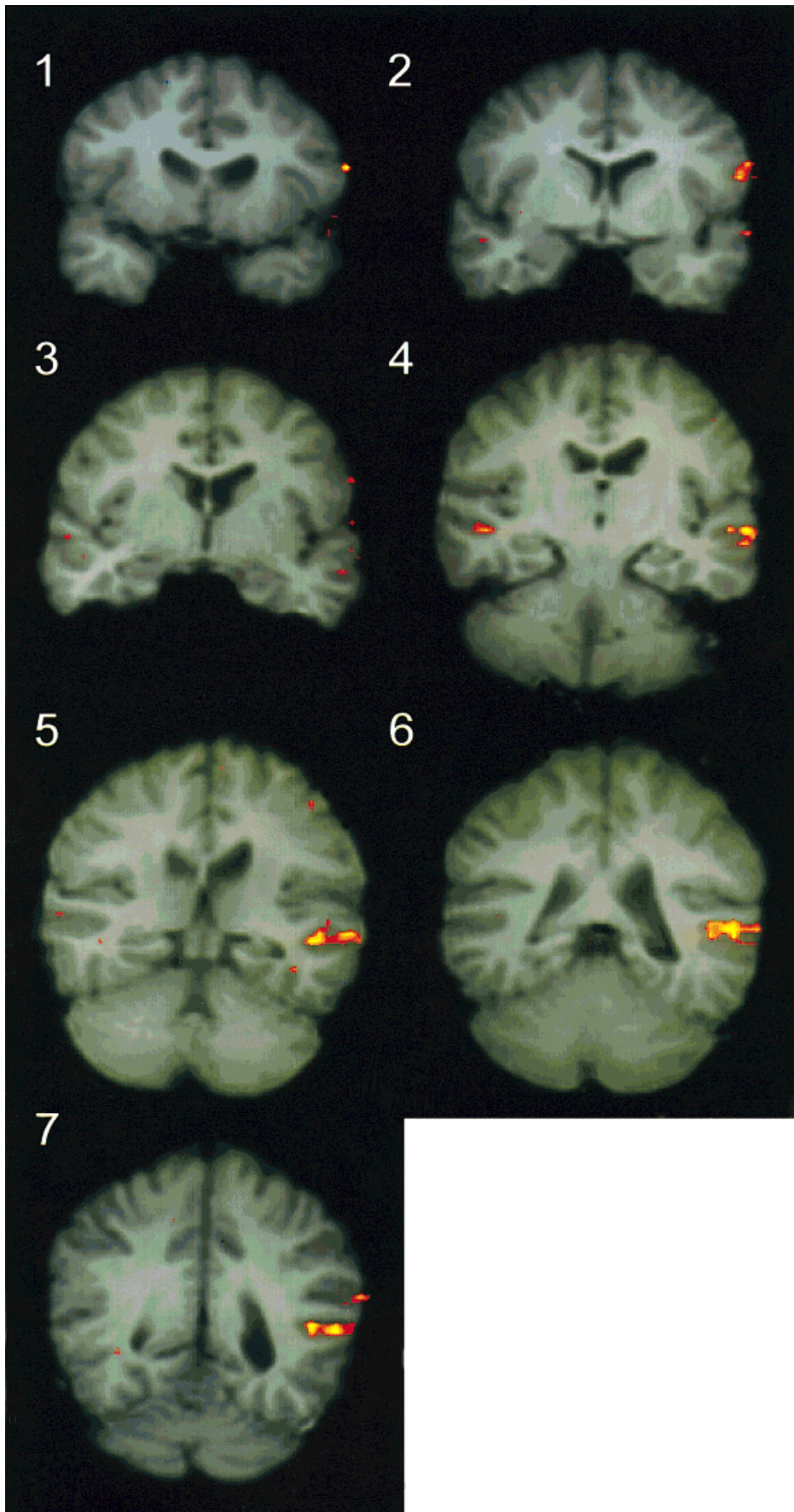
Figure 4.

activated voxels or their hemispheric pattern (F(1, 4) = 0.24, $P = 0.6326$ for axials; F(1, 4) = 0.04, $P = 0.85$ for coronals) as a function of the subject's sex.

The mean number of activated voxels per slice is shown in Figure 5 for the left and right hemispheres for the axial (Fig. 5A) and coronal (Fig. 5B) studies. The left hemisphere asymmetry is clearly apparent in both series. The difference between hemispheres significantly increased in slices 3–5 for the axial series (F(6, 60) = 4.57, $P = 0.001$) which included the middle and superior temporal gyri, and in slices 1–2 for the coronal series (F(6, 30) = 2.15, $P = 0.076$) which included the middle and superior temporal sulci of the posterior temporal lobe.

Frequency sweep control task

The auditory frequency sweeps produced a consistent pattern of activation that differed from that of the English sentences. Figure 6 presents an overlay of activated voxels evoked by English (Fig. 6A) and frequency sweeps (Fig. 6B) for five slices in the same subject (tested 3 months apart). The English sentences evoked strong activation in the posterior aspect of the left superior temporal sulcus (Fig. 6A, bottom slice) and in the left inferior frontal gyrus (Fig. 6A, top slice). In contrast, the frequency sweeps activated the right superior temporal gyrus and perisylvian region across several middle slices (Fig. 6B). Tested across subjects, there were more right than left hemisphere activations for the frequency sweeps (Fig. 7), but this difference was not statistically significant in this small sample. However, the t-values of activated voxels within the right hemisphere were significantly greater than those obtained in the left hemisphere (F(1, 4) = 8.4, $P = 0.04$), in contrast to the result obtained for English sentences. The anterior-posterior activation pattern also differentiated voxels activated by English compared to voxels activated by frequency sweeps. While English segments produced the greatest number of activations in posterior temporal slices (see Fig. 5B), the activation by frequency sweeps was greatest in the middle and anterior temporal lobe (Fig. 7).

DISCUSSION

Auditory sentences read in English produced focal activation in the posterior aspect of the left superior temporal sulcus and the immediately adjacent lateral cortex in all subjects. No anatomically coherent activations to sentences read in Turkish were obtained in any subject. Since the English and Turkish sentences were read by the same speaker and were controlled for

length, prosody, and overall volume, the differential activation pattern is presumed to be due to auditory comprehension and not to simple physical stimulus differences.

Prior PET studies have shown activation of posterior temporal language areas in both visual and auditory language tasks [Demonet et al., 1992; Karbe et al., 1995; Petersen et al., 1988, 1989, 1993; Wise et al., 1991]. Examination of Table I reveals similar loci of activation; indeed, the average location of the center of activation for the six studies referenced in Table I is within 2 mm in any dimension from the centroid of activation in this study. The PET findings represent the across-subjects average of spatially normalized data, a procedure that limits the clinical utility of PET in individual patients. In the present study, the activation pattern was clearly visible in individual subjects, and was reproducible in the 3 subjects tested twice in sessions separated by many months. In one subject, five different imaging sessions over a 1-year interval yielded virtually identical activation foci in the left posterior temporal lobe.
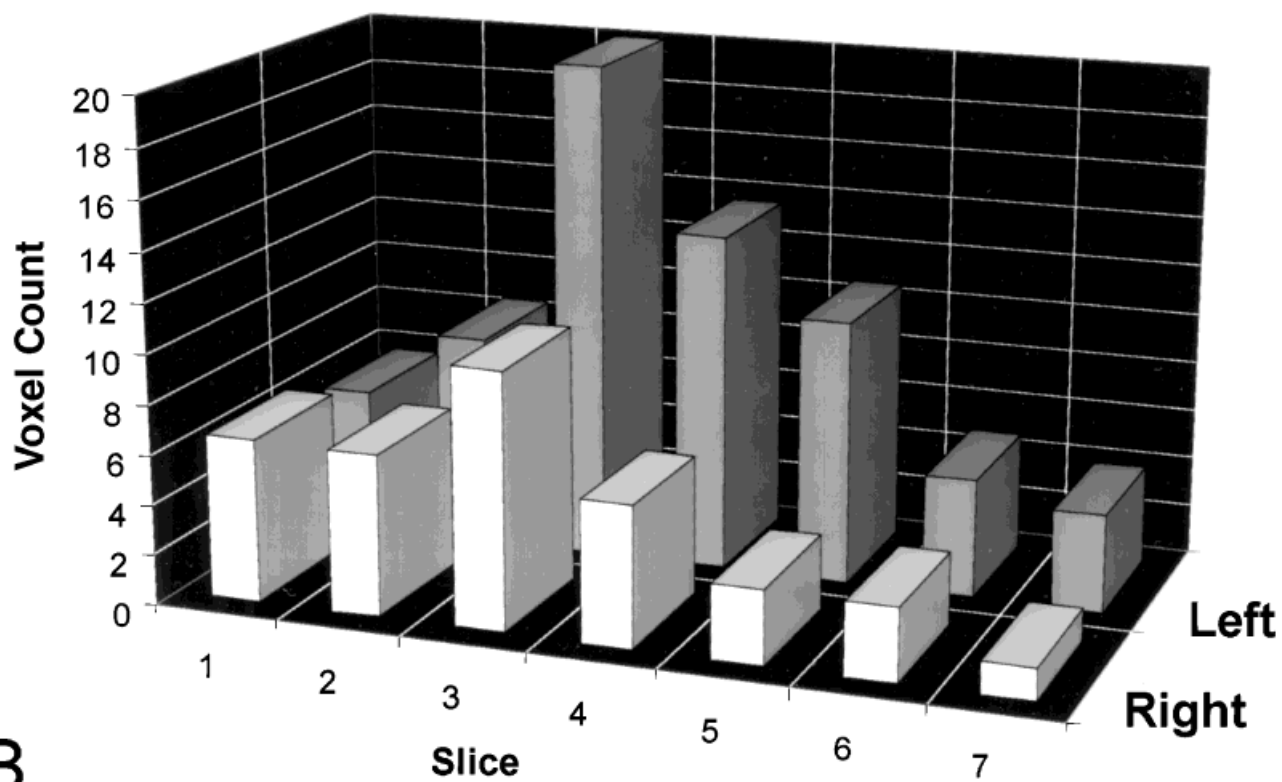
It is notable that the extent of the posterior activations obtained in the present study appears smaller than those reported in several recent fMRI studies [Alsop et al., 1996; Binder et al., 1995, 1997]. In each of these studies, auditory verbal stimuli (semantic judgment task) were compared to nonlinguistic sounds [Binder et al., 1995, 1997], or to nonstimulus baseline [Alsop et al., 1996]. We assert that the more focal activations in the present study likely reflect the isolation of language comprehension from lower-level auditory processing.

The activation of the left posterior region by English sentences was quantified by comparing the number of activated voxels for English and Turkish, and by comparing the strength of the activation as reflected by the magnitude of the t-value. English sentences produced significantly more activations of the left hemisphere, and these activated voxels had significantly greater t-values. A more conservative threshold than

Figure 5.
A: Average voxel counts in the left and right hemispheres for all 11 axial studies. Voxels with a t-value above 1.96 (activation to English) and located within the brain are included. Slice 1 is the most inferior and slice 7 the most superior. Left hemisphere showed significantly ($P = 0.0001$) more activation to English. **B:** Average voxel counts in left and right hemispheres for coronal studies. Slice 1 is most posterior and slice 7 is most anterior. Greater activation is seen in the left hemisphere, though more equally distributed by slice than in A.
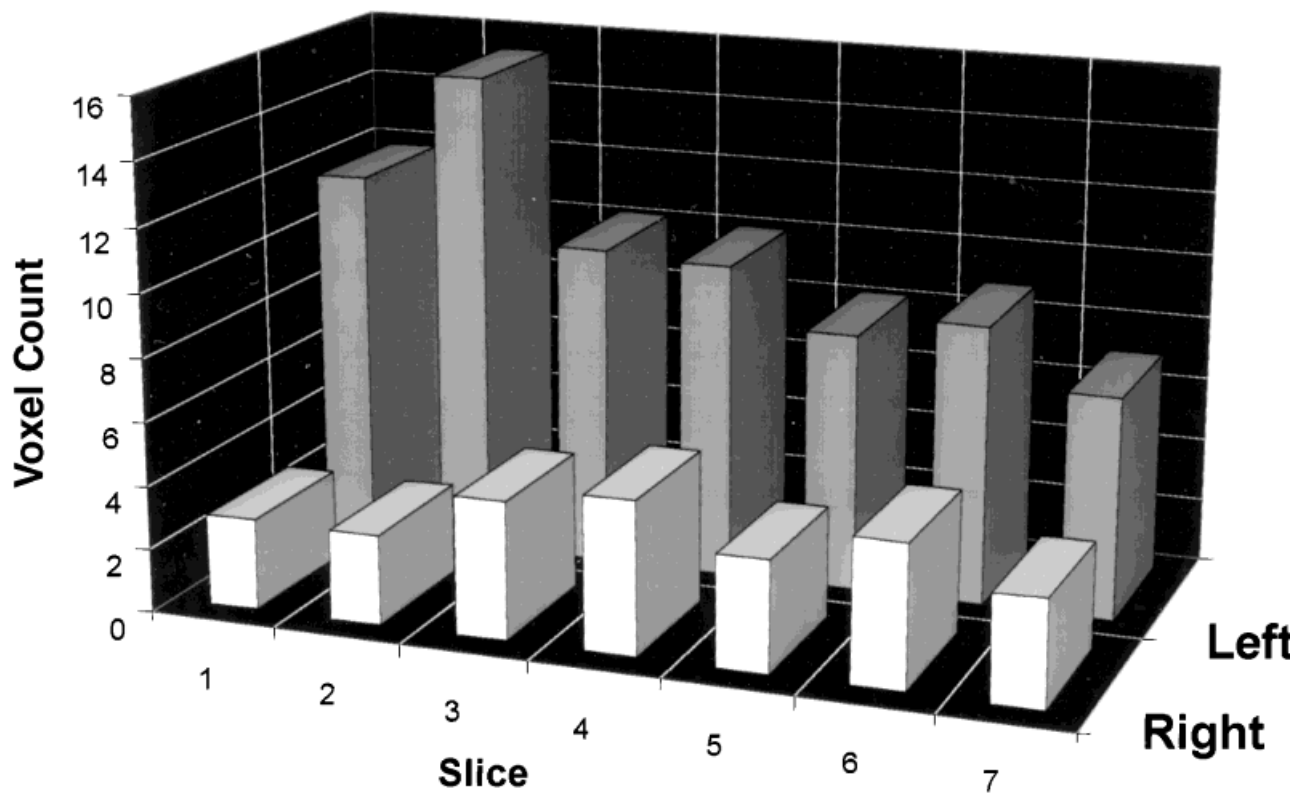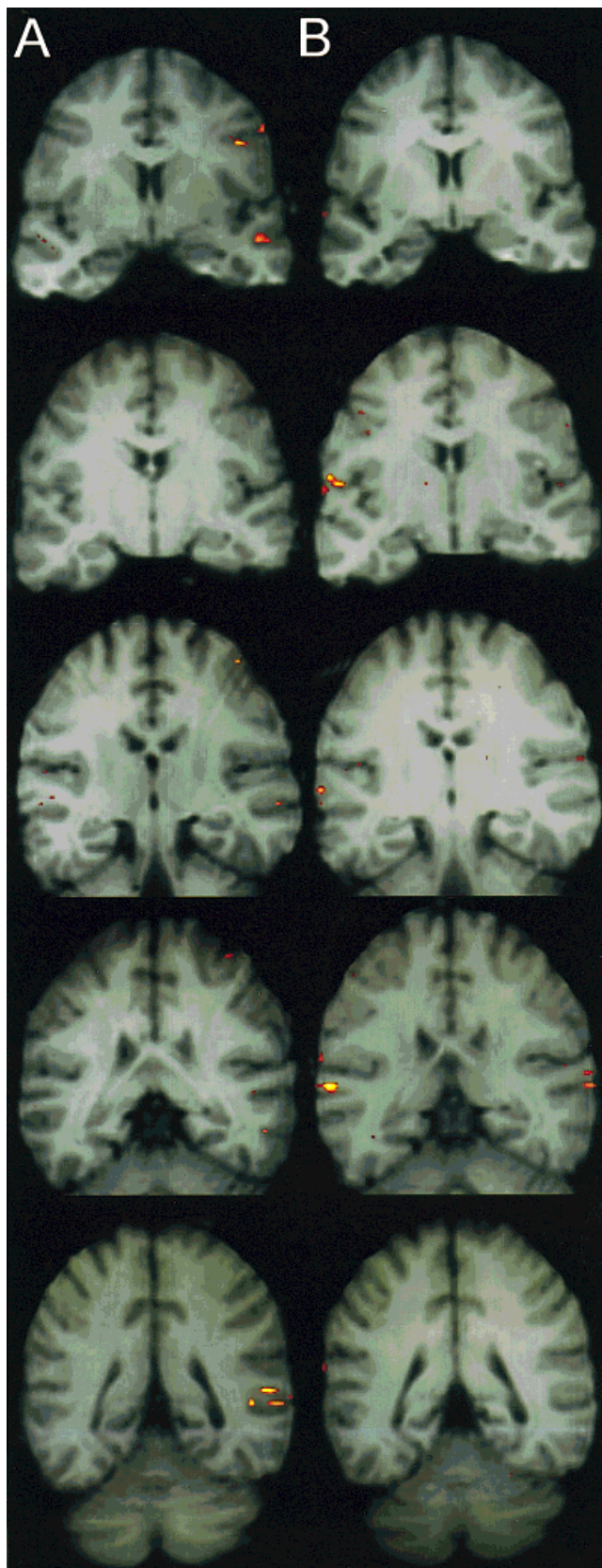
Figure 5.

Figure 6.

Functional MRI activation in a single subject, comparing auditory comprehension and frequency sweep tasks. Studies were completed 3 months apart but slices were taken at the same locations and with the same imaging parameters. T-maps shown for both tasks were thresholded to values above 1.96. **A:** Activation to English in over five continuous coronal-oblique slices overlaid upon T1-weighted images. **B:** Activation to frequency sweeps in the same subject at the same slice locations.
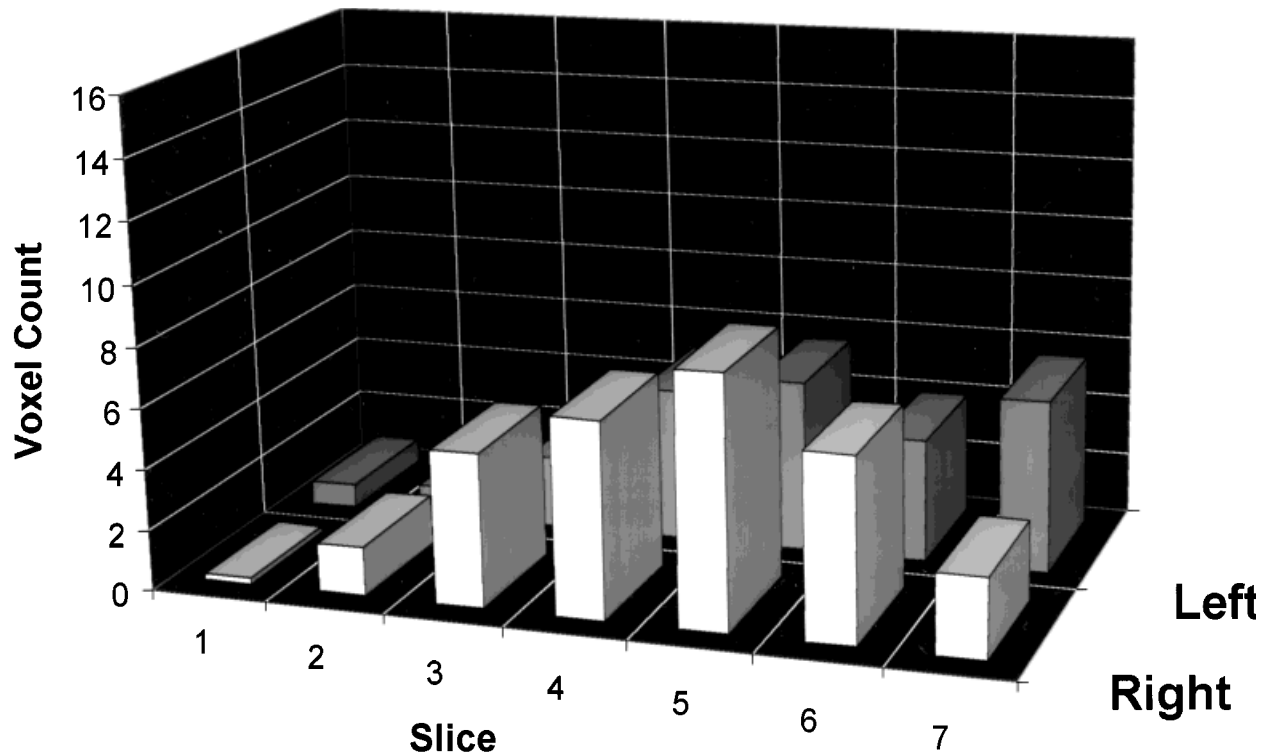
the value of 1.96 that was used would have largely eliminated the randomly distributed voxels "activated" by the Turkish sentences without diminishing the focal English sentence activations, suggesting that the Turkish sentence activations were primarily false positives [McCarthy et al., 1996].

Although our task showed a strong bias towards left posterior temporal activation, lesser activation was frequently observed in approximately homotopic regions of the right hemisphere. Laterality was therefore determined by the significantly greater (i.e., more voxels and higher t-values) activation in the left hemisphere. This is consistent with the group data from prior PET studies [Petersen et al., 1988, 1989, 1993] where bilateral, but clearly left dominant, posterior temporal activation was obtained.

While comprehensible speech differentially activated the left hemisphere, frequency sweeps activated the temporal lobe bilaterally, with more activation of the right hemisphere measured by the number of activated voxels and by strength of activation as measured by their associated t-values. Furthermore, frequency sweeps activated a region of the temporal lobe anterior and superior to those regions activated by comprehensible speech. As shown in Table I, the position in the left superior temporal gyrus activated by frequency sweeps closely matches the area found to be sensitive to phoneme monitoring in nonwords as shown by Demonet et al. [1992]. This supports our assertion that the activation by comprehensible speech was not due to the acoustic properties of the stimuli, or to phoneme monitoring.

The practical goal of this study was to reliably activate posterior temporal language regions in individual subjects using auditory comprehension tasks derived from our clinical experience with auditory comprehension tasks in cortical stimulation mapping. While this goal was attained, it is interesting that significant activation was found in the left inferior frontal region in 8 subjects. Prior neuroimaging studies have shown activation of left inferior frontal regions during overt and silent word production [Buckner et

Figure 7.
Average voxel counts for frequency sweep in a background of white noise. Voxels with a t-value above 1.96 and located within the brain were included. All frequency sweep studies were done on coronal-oblique slices, and the scale of the plot is identical to that in the coronal voxel counts for English activation shown in Figure 5B. More activation is seen in the right hemisphere than the left in this task.

al., 1995; Cuenod et al., 1995; Desmond et al., 1995; Eulitz et al., 1994; Hinke et al., 1993; Liotti et al., 1995; McCarthy et al., 1993; Price et al., 1996; Yetkin et al., 1995]. This suggests that our subjects may have been silently repeating or rehearsing the English sentences. However, Schaffler et al. [1996] also found that stimulation of both left inferior frontal and posterior temporal regions was associated with deficits in auditory comprehension, suggesting that frontal language areas may play a more direct role in comprehension.

While two languages were used as stimuli, none of the subjects were bilingual. Preliminary data have been obtained from 2 subjects whose native language was neither English nor Turkish. The pattern of activation seen to English in these subjects was more extensive and far less localized than in native English speakers. This result suggests that activation patterns may differ in bilingual subjects. From this anecdotal data one can conclude: 1) that clinical utility of this method may depend upon utilizing patients' native language and a suitable control language, and 2) that

the alternating procedure used here may prove useful for studying differential activation of language in bilingual subjects.

Though functional mapping of language has been compared to preoperative Wada testing [Brint et al., 1996; Desmond et al., 1995; Pardo and Fox, 1993], these studies considered productive language and frontal lobe language areas. The goal of this study was to develop a task suitable for preoperative language mapping in patients who will undergo dominant temporal lobe surgery. A preliminary study of 2 patients in which the activation produced by this task was compared to intraoperative stimulation mapping has shown good correspondence [Schlosser et al., 1997]. Further studies are underway.

ACKNOWLEDGMENTS

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