

Language network specializations: An analysis with parallel task designs and functional magnetic resonance imaging

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Although the classical core regions of the language system (Broca's and Wernicke's areas) were defined over a century ago, it took the advent of functional imaging to sharpen our understanding of how these regions and adjacent parts of the brain are associated with particular aspects of language. One limitation of such studies has been the need to compare results across different subject groups, each performing a different type of language task. Thus, this study was designed to examine overlapping versus segregated brain activations associated with three fundamental language tasks, orthography, phonology and semantics performed by the same subjects during a single experimental session. The results demonstrate a set of primarily left-sided core language regions in ventrolateral frontal, supplementary motor, posterior mid-temporal, occipito-temporal and inferior parietal areas, which were activated for all language tasks. Segregated task-specific activations were demonstrated within the ventrolateral frontal, mid-temporal and inferior parietal areas. Within the inferior frontal cortex (Broca's regional complex), segregated activations were seen for the semantic and phonological tasks. These findings demonstrate both common and task specific activations within the language system.

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Introduction

In the latter half of the 19th century, careful case observations and remarkable insights by, Paul Broca, Carl Wernicke and others

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led to theories, which suggested that language functions in the human brain are controlled by two eponomously named regions (Broca's and Wernicke's areas), in the left inferior frontal and posterior superior temporal cortex respectively (Geschwind, 1965; Price, 2000). Over the ensuing decades, this anatomical organization was extended to include a number of additional areas such as the angular gyrus and heteromodal association cortex surrounding the two classical language areas.

In recent years, functional brain imaging studies have helped to reveal the internal organization of Broca's and Wernicke's regions and their interactions with additional cortical and subcortical components of the large-scale language network. Relevant developments include the identification of activations related to speech output and articulation in the anterior insula (Dronkers, 1996; Price et al., 1996; Wise et al., 1999), phonology in the posterior inferior frontal cortex (Dapretto and Bookheimer, 1999; Démonet et al., 1992, 1994; Fiez, 1997; Zatorre et al., 1996) and semantics or word selection in the anterior inferior frontal cortex (Chee et al., 1999; Dapretto and Bookheimer, 1999; Demb et al., 1995; Gabrieli et al., 1996, 1998; Kapur et al., 1994a,b; Petersen et al., 1988, 1989, 1990; Shaywitz et al., 1995a,b; Thompson-Schill et al., 1997).

Collectively, these results suggest that the classical language regions are not specifically devoted to single linguistic operations. Rather, it appears that they are comprised of several subregions each of which may show different specializations. Although functional imaging studies have extended our view of the language system, not all studies have shown consistent task-specific activations possibly because of the use of varying task designs and the reliance on single task subtraction methodology. In order to overcome these limitations, we have designed parallel language tasks that manipulate attention to orthographic, phonologic and semantic linguistic comparisons for single words relative to a common non-linguistic baseline task comparing letter strings. Comparisons are made within subjects using random-effects analyses with stringent statistical criteria. The results within our

single subject group confirm and extend findings previously achieved only through the meta-analysis of multiple studies or by using disparate task designs.

Methods

Subjects

Fifteen participants were included in the analysis. There were 8 males and 7 females with a mean (standard deviation) age of 29.9 (5.9) years. Subjects had no history of significant medical, neurologic or psychiatric illness. All subjects were right-handed by self-report and their mean handedness score was 85.3 (11.9) (Oldfield, 1971). All subjects gave their written informed consent and this study was approved by the Northwestern University Institutional Review Board.

Behavioral tasks

All 15 subjects performed the orthographic, phonologic and semantic tasks, described below. Twelve of the subjects also performed a syntactic task in the same session, which is not reported in this manuscript. Fourteen subjects performed the tasks within a single session, while one subject was studied over 2 sessions.

Each task was performed as a separate functional imaging run consisting of eight alternating 30.45-s blocks of the active and control conditions. During each active task, subjects were shown two words for 3400 ms and asked to respond if the words were identical along a specified linguistic parameter. Fig. 1 illustrates the comparisons. In the orthographic task (ANA), subjects responded if the words were anagrams; in the phonologic task (HOM), subjects responded if the words were homophones; in the semantic task (SYN), subjects responded if the words were synonyms. During the control task (CON), subjects were shown pairs of consonant letter strings and asked to respond if the strings matched.

The word lists were drawn from the MRC psycholinguistic database (Coltheart, 1981). Table 1 shows the ratings of the word and letter lists along various linguistic dimensions. Approximately 90% of the words on each list were open-class and 10% were closed-class. Seventy-five to 90% were nouns or verbs, 25 to 38% were adjectives, 10 to 20% were adverbs and 0.8 to 2% were prepositions, conjunctions or pronouns. Since each word could have more than one part of speech classification (based on the

MRC database), these percentages add up to more than 100%. Nouns could be concrete or abstract and were drawn from several categories. There were less than 20% irregularly spelled words as rated by two of the authors (ACN and DRG).

Because of differences in the linguistic ratings between the lists (or large standard deviations among the conditions), ratings for Kucera-Francis frequency, number of letters, familiarity, concreteness, and imageability were included as covariates of no interest in the functional imaging analysis (see below).

Subjects responded by pressing a button held in their right hand. Reaction times were recorded for all responses. Task accuracy was determined from the percentage of correct behaviors, that is, (number of hits + number of correct rejections)/total no. of stimuli. Stimuli were presented and responses were collected using Superlab software (Cedrus, San Pedro, CA) running on a Power Macintosh computer (Apple, Cupertino, CA). The stimuli were projected onto a custom-designed nonmagnetic rear projection screen using an active matrix liquid crystal display projector. Subjects viewed the screen, located approximately 170 cm from their eyes, through a non-magnetic mirror.

Ultimate inclusion of subjects in the group analysis was dependent on above-chance performance ($\geq 62.5\%$ accuracy, 24/40 correct), on each of the three tasks during the experimental session. The accuracy cut-off was based on the binomial test. This criterion was met by 14 of the 15 subjects.

MR imaging—anatomical scans

T1 weighted anatomic images were obtained on the 1.5 T Siemens Vision scanner, using a 3D FLASH sequence with the following parameters: TR/TE, 15 ms/6 ms; flip angle, 20°; FOV, 220 mm; matrix, 256 × 256; slice thickness, 1.0 mm. All anatomic and functional scans were obtained in transaxial planes parallel to the AC-PC line.

MR imaging—functional scans

Functional MRI volumes were acquired as thirty-two 4-mm slices using a single-shot EPI method (TR/TE, 4350/40 ms; flip angle, 90°; matrix, 64 × 64; FOV, 220 mm). For all functional runs, the signal was allowed to reach a steady state over four initial volumes that were excluded from the analysis.

Subjects had their head immobilized with a vacuum pillow (Vac-Fix, Bionix, Toledo, OH) and the restraint calipers built into the head coil. They were given a non-magnetic button, which

	<i>phonologic</i> (HOM)	<i>semantic</i> (SYN)	<i>orthographic</i> (ANA)	<i>control</i> (C)
<i>Match</i> (response)	rain reign	boat ship	aunt tuna	fplk fplk
<i>Non-Match</i> (no response)	axe ask	key lock	horse short	gkjs gskt

Fig. 1. Examples of stimuli in the three language tasks and the control condition.

Table 1
Linguistic parameters for word and letter lists

	Num. letters	Kucera-Francis	Familiarity	Concreteness	Imageability
ANA words	4.06 (0.85) ^{a,b}	184.1 (882.08)	543.2 (53.91)	471.7 (118.75) ^c	491.2 (98.38) ^d
ANA letters	4.67 (0.471) ^c	–	–	–	–
HOM words	4.4 (0.82)	132.9 (387.91)	522.7 (83.92)	456.3 (116.55) ^f	471.9 (100.09)
HOM letters	4.66 (0.655) ^g	–	–	–	–
SYN words	4.4 (0.74)	95.5 (123.20)	553.26 (64.39)	393.9 (85.77)	451.4 (67.72)
SYN letters	4.89 (0.439)	–	–	–	–

All values are reported as mean (standard deviation). Letter condition comparisons used a one-way ANOVA and post-hoc Tukey HSD; word condition comparisons used a multivariate ANOVA and post-hoc Tukey HSD.

^a $P < 0.001$ number of letters, ANA words vs. HOM words.

^b $P = 0.001$ number of letters, ANA words vs. SYN words.

^c $P < 0.001$ concreteness, ANA words vs. SYN words.

^d $P = 0.011$ imageability, ANA words vs. SYN words.

^e $P = 0.003$ number of letters, ANA letters vs. SYN letters.

^f $P < 0.001$ concreteness, HOM words vs. SYN words.

^g $P = 0.002$ number of letters, HOM letters vs. SYN letters.

enabled recording of their responses. A vitamin E capsule was taped to the left temporal region to mark laterality for image processing.

MR imaging—data analysis

The preprocessing and analysis of fMRI data were performed using the SPM-2 software (Wellcome Department of Imaging Neuroscience, London, UK, <http://www.fil.ion.ucl.ac.uk/spm>) running under the MATLAB environment (Mathworks Inc., Sherborn, MA) (Friston et al., 1995a,b; Worsley and Friston, 1995) on a PC workstation.

Preprocessing steps included slice-timing correction, motion correction within functional runs, coregistration between the functional and anatomic images within each subject and normalization to the Montreal Neurological Institute standard template brain (MNI-305) (Ashburner et al., 1997; Friston et al., 1995a,b). This template approximates the space described in the atlas of Talairach and Tournoux (1988). Functional data were then smoothed with a 10-mm FWHM isotropic Gaussian kernel, to enable intersubject comparisons.

Because the word and letter lists differed between tasks along various linguistic dimensions, these ratings were included as covariates of no interest in each subject's design matrix. This was done by calculating an average for each of the ratings in each of the condition blocks. These block-specific values for each rating were then included as parametric regressors for each condition. The letter blocks had only the number of letters as a regressor, while the word blocks included the number of letters, Kucera-Francis frequency, and ratings of familiarity, concreteness, and imageability.

SPM uses the technique of statistical parametric mapping and references the probabilistic behavior of a stationary Gaussian field for defining the probability density function of an image. It employs the general linear model for testing hypotheses at each voxel. Contrasts were set up to test for voxelwise effects of signal differences between the word and letter conditions, and statistical parametric maps were calculated in each subject (Friston et al., 1995b).

Random effects analyses were computed by generating for each subject parameter effects images for the three main contrasts (ANA-CON, HOM-CON and SYN-CON). The parameter effects

images were then entered into a second-level, one-way ANOVA with the language task as the grouping factor. A non-sphericity correction was included in the analysis to account for the use of the same subjects in all tasks (Friston et al., 2002).

Common areas of activation across all tasks were identified using a random effects conjunction analysis. Specialization within the word processing network was revealed by inclusive masking the main effect of one task (active task minus control) with its differential effects compared with the other tasks. For example, specialization within the network for orthography was identified by inclusively masking ANA-CON with ((ANA-CON)–(HOM-CON)) and with ((ANA-CON)–(SYN-CON)). This had the effect of showing activations in the (ANA-CON) contrast only where ANA-CON was more active than HOM-CON and SYN-CON. Similar analyses were performed for the other tasks. These contrasts will be referred to as masked analyses.

Voxels were considered significant at $P < 0.05$ after correction for multiple comparisons using the False Discovery Rate (FDR) (Genovese et al., 2002). The FDR is able to appropriately control the false positive rate while being less likely to result in Type II errors than the Family-wise Error. The conjunction analysis was considered significant at a corrected threshold of 0.05 based on corrected significance levels in the component contrasts. This ensured that voxels were significant in all contrasts comprising the conjunction (Nichols et al., 2005).

Results

Behavioral data

Fourteen of fifteen subjects met the inclusion criterion. One subject performed at chance on the ANA task (55% correct) so all their runs were excluded from analysis in order to maintain a balanced design. The mean response times and accuracies are shown in Table 2. Overall subjects were highly accurate on both the active and control tasks. There was a significant effect of condition on reaction time in the active condition, $F_{2,41} = 5.18$, $P < 0.01$. A post-hoc Tukey test showed that the difference was between the ANA and SYN conditions, $P < 0.01$. There was also an effect of condition on accuracy in the control task, $F_{2,41} = 6.65$, $P < 0.01$. Subjects were slightly more accurate during the control

Table 2

Response time (milliseconds) and accuracy (%) for the task and control conditions

	ANA (mean ± SD)	HOM (mean ± SD)	SYN (mean ± SD)
Active task	1728 ± 221* 92.7%	1558 ± 181 90.9%	1473 ± 235* 93.0%
Control task	1750 ± 259 97.0% ^a	1948 ± 299 97.7% ^b	1827 ± 241 92.9% ^{a,b}

^a $P < 0.05$ ANA vs. SYN post-hoc Tukey-HSD.

^b $P < 0.01$ HOM vs. SYN post-hoc Tukey-HSD.

* $P < 0.01$ ANA vs. SYN post-hoc Tukey-HSD.

periods for the ANA and HOM tasks than for the SYN task. This may be related to the slightly longer letter string length in the SYN task, Table 1.

fMRI results

The conjunction of all three conditions versus their respective controls showed that voxels that were significantly activated in all three tasks, Fig. 2 and Table 3. This analysis showed activations primarily within the left inferior and middle frontal gyri and lateral orbital gyrus overlying portions of Brodmann areas 6, 9, 10, 45, 46 and 47. Activations were also seen in the left anterior insula, supplementary motor area and right cerebellum, Fig. 2.

For the individual task activations, the masked ANA contrast, Fig. 3-top and Table 4, demonstrated frontal activations in the left anterior inferior frontal gyrus and bilateral frontal eye field regions. Bilateral activations were seen in the posterior parietal cortex,

Table 3

Random effects conjunction of ANA, HOM and SYN tasks

Location	x (mm)	y (mm)	z (mm)	Z score	P (voxel corrected)
Left PreCS (BA 6)	-36	3	39	3.89	0.0011
Left MFG (BA 9)	-51	24	30	6.54	2.43E-09
Left IFG (BA 45)	-48	33	18	5.19	4.31E-06
Left IFG (BA 47)	-51	27	-3	4.77	3.25E-05
Left LOG (BA 10/46)	-45	48	0	5.11	6.48E-06
Left anterior insula	-30	21	3	3.36	0.0066
SMA (BA 8/32)	-3	15	51	4.36	1.83E-04
	0	24	48	4.89	1.84E-05
Right cerebellum	15	-78	-33	3.42	0.0054
(crus I/lobule VI)	27	-69	-42	3.71	0.0021
	36	-69	-45	3.96	8.71E-04

which were more extensive on the left. The right cerebellum was also activated (not shown).

The masked HOM contrast showed activations at the junction of the left posterior inferior frontal gyrus and precentral sulcus corresponding to the pars opercularis region of Broca's complex, and the left superior precentral gyrus, Fig. 3-middle and Table 5. On the right, activations were seen in the orbital gyrus, ventral insula and parahippocampal gyrus (not shown).

Finally, the masked SYN contrast showed activations in the left lateral orbital and inferior frontal gyrus (pars orbitalis and pars triangularis regions of Broca's complex), a region in the left posterior superior temporal gyrus consistent with Wernicke's area, and several additional regions in the middle and anterior temporal cortex, Fig. 3-bottom and Table 6. Other areas of activation included the left supplementary motor cortex, right

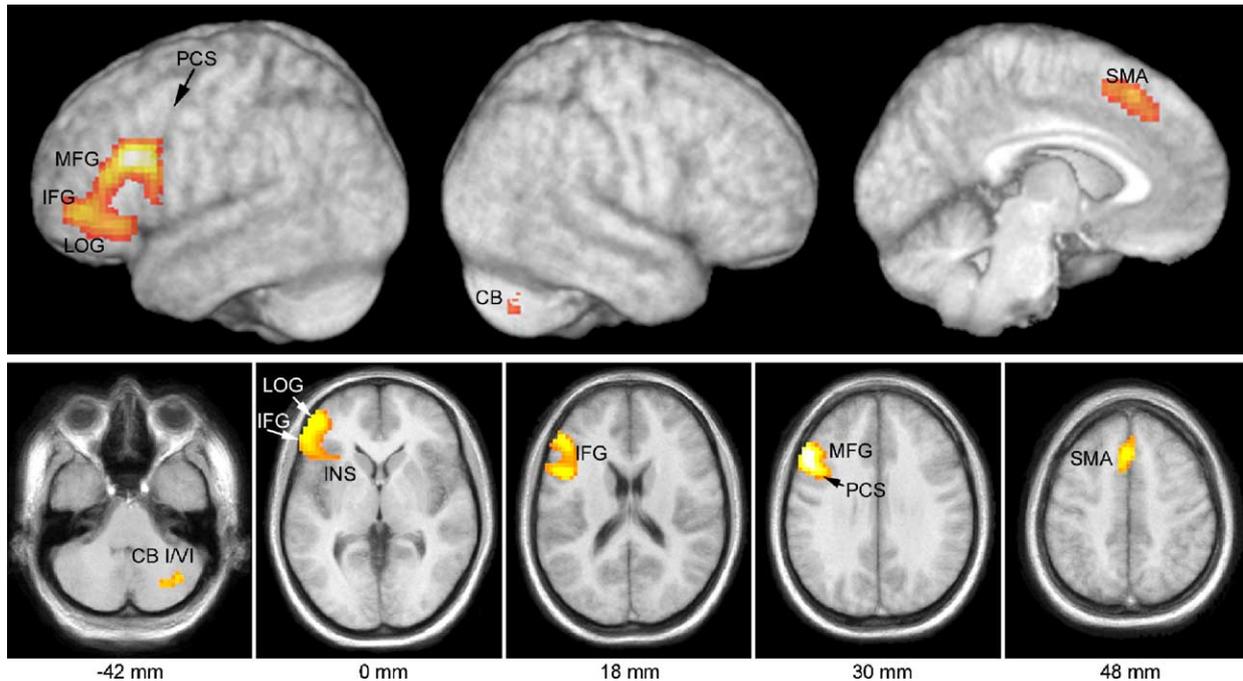


Fig. 2. Random effects conjunction of ANA, HOM and SYN tasks. All regions shown are significant at $P < 0.05$ corrected for each of the components in the conjunction. The activations are clearly left sided. The upper row shows a lateral rendered view of the activations on the mean brain of all subjects. The lower row shows the activations overlaid on axial slices. Key: CB (I/VI) = cerebellum (crus I/lobule VI); IFG = inferior frontal gyrus; INS = insula; LOG = lateral orbital gyrus; MFG = middle frontal gyrus; PCS = precentral sulcus; SMA = supplementary motor area.

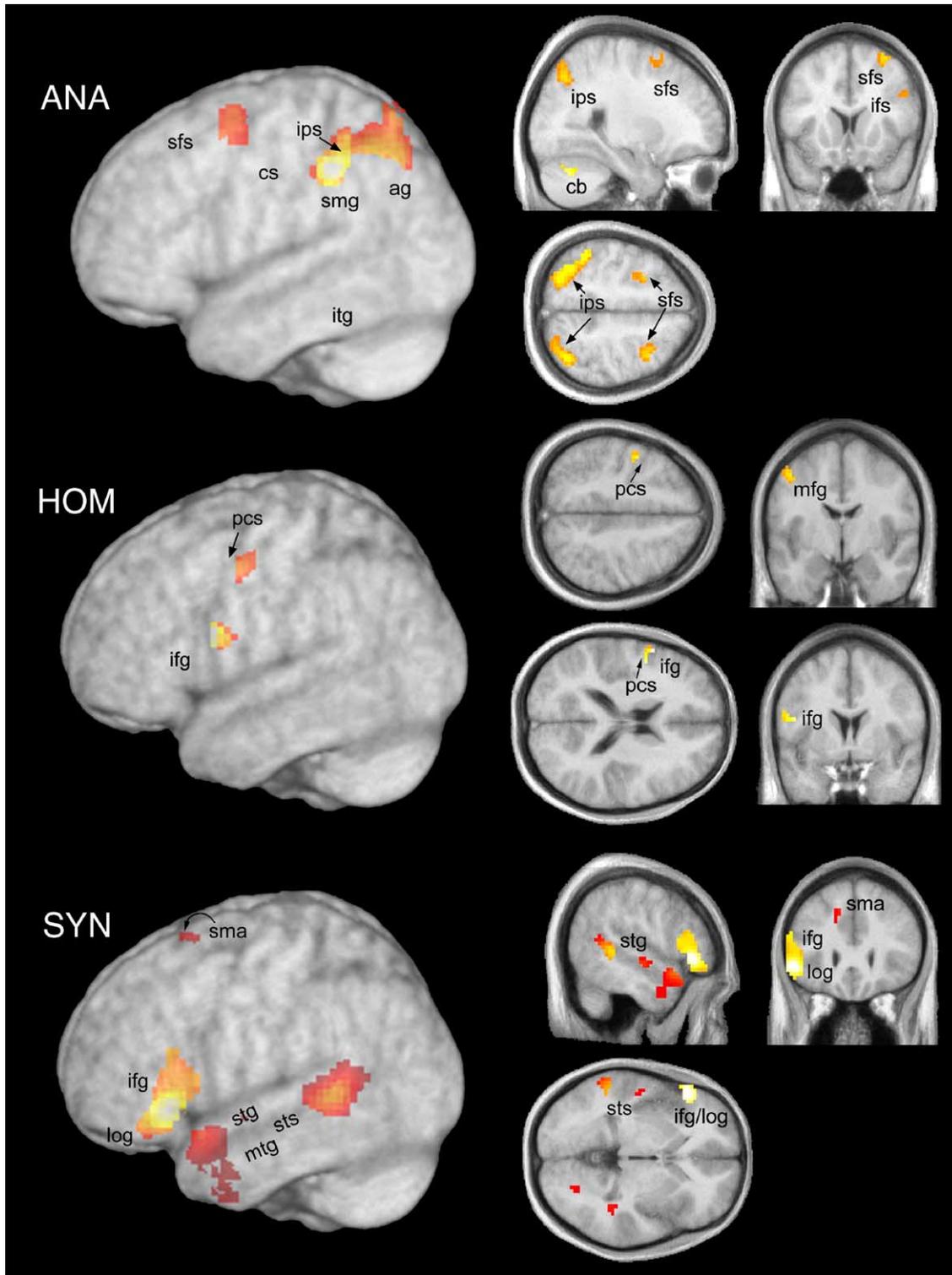


Fig. 3. Activations specific to each of the masked contrasts. ANA: ANA-CON inclusively masked by the conjunction of ((ANA-CON)–(HOM-CON)) and ((ANA-CON)–(SYN-CON)). HOM: HOM-CON inclusively masked by the conjunction of ((HOM-CON)–(ANA-CON)) and ((HOM-CON)–(SYN-CON)). SYN: SYN-CON inclusively masked by the conjunction of ((SYN-CON)–(ANA-CON)) and ((SYN-CON)–(HOM-CON)). See Fig. 2 for key. Additional areas: IFS = inferior frontal sulcus; IPS = intraparietal sulcus; SFS = superior frontal sulcus; STG = superior temporal gyrus; STS = superior temporal sulcus.

temporal cortex, fusiform gyrus, cuneus, and the right cerebellum, vermis and dentate (not shown). Fig. 4 illustrates the regional relationships among the masked contrasts and the conjunction of all three tasks.

Discussion

The current study has provided evidence of both general and task specific activations while subjects performed tasks of orthographic,

Table 4
Regional activations for ANA inclusively masked by HOM and SYN

Location	<i>x</i> (mm)	<i>y</i> (mm)	<i>z</i> (mm)	<i>Z</i> score	<i>P</i> (voxel corrected)	<i>k</i> (cluster size— voxels)
Left SFS (BA 6)	−27	6	54	3.43	0.010	52
Right SFS (BA 6)	36	9	57	4.11	0.0045	77
Right IFS (BA 46)	42	42	36	3.31	0.014	104
	51	30	30	5.04	8.60E−05	
Left SPL (BA 7)	−15	−69	63	3.83	0.0033	447
Left IPS (BA 7)	−33	−60	48	4.45	5.20E−04	
Left SMG (BA 7/40)	−48	−42	45	5.92	4.10E−06	
Left IPS (BA 7)	−30	−63	45	4.39	6.35E−04	
Right IPS (BA 7)	39	−57	51	5.03	6.38E−04	172
	33	−69	45	4.77	0.0011	
Right ITG (B 37)	51	−48	−18	3.63	0.0058	37
	51	−51	−27	3.24	0.0169	
Right Cerebellum (crus I/lobule VI)	30	−66	−33	5.09	7.13E−05	50
	36	−51	−33	3.44	0.010	

Reported activations are significant at $P < 0.05$ corrected at the voxel level and separated from other activations by a FWHM for the statistical map, in this case 12.4 mm.

phonologic and semantic analysis at the single word level. A number of previous functional imaging have examined similar aspects of language processing, but have generally not done so within the same individuals or have used less robust fMRI analytical techniques (Binder et al., 1997; Chee et al., 1999; Démonet et al., 1992, 1994; Devlin et al., 2003; Fiez, 1997; Petersen et al., 1988; Price et al., 1997; Rumsey et al., 1997; Sergent et al., 1992; Zatorre et al., 1996). Because this study used a random effects analysis with proper control of non-sphericity effects in the statistical design, the results are robust and generalizable to the overall population.

Although we tried to match the various tasks closely, differences were found for various linguistic parameters. Therefore, we included these parameters as covariates in all analyses, so that activation differences relate to the type of task and not aspects of the particular words used in each condition. Differences were also seen in reaction times and accuracy among the three tasks. While differences in difficulty may have contributed to the activation pattern differences among the three tasks, we think it is unlikely that difficulty was the sole determinant of the task-related activations, since each task was compared to both a control condition and to two other language tasks.

Common activations (conjunction analysis)

Common areas of cortical activation across all three tasks were seen in the left inferior frontal cortex, and supplementary motor area, Table 3 and Fig. 2. We suggest that these regions of activation are part of a common system providing post-lexical processing across all language tasks employed in this study (Hagoort et al., 2004). Similar frontal regions have also been activated in numerous previous studies of orthography (Booth et al., 2002a,b; Fiebach et al., 2002; Kuo et al., 2004; Tagamets et al., 2000), phonology (Binder et al., 1997; Démonet et al., 1992; Paulesu et al., 1993, 1997; Petersen et al., 1988, 1989; Sergent et al., 1992; Zatorre et al., 1992) and semantics (Binder et al., 1997; Chee et al., 1999; Démonet et al., 1992; Paulesu et al., 1997; Petersen et al., 1988; Vandenberghe et al., 1996).

Because these activations were seen in a conjunction analysis in which each of the component contrasts was significant, we can be

sure that the activated regions were common to all three tasks. Therefore, it is likely that we did not see activations within temporal or parietal lobes for this analysis because these regions may be involved with more specific aspects of language processing, and thus were not individually activated by all three tasks.

Because each task was compared with a condition in which subjects matched letter strings, the results suggest that these regions are activated when processing single words and not just for collections of letters in general (Sonty et al., 2003). These areas may thus collectively participate in those aspects of the tasks where post-lexical processing recruited greater neural activation than letter string processing. However, the degree to which any of these areas is critical for lexical or post-lexical processing can only be determined when analyzed in the light of focal lesion studies.

Inferior frontal cortex

This study was also able to demonstrate regional specializations within the language system. Specialization was found specifically within Broca's complex by showing the engagement of different subregions based on the linguistic goals of the task. More anterior aspects of Broca's region, within the anatomical regions of the pars triangularis and pars orbitalis (see Devlin et al., 2003, for definitions), were activated in the semantic task more than in either the phonological or the orthographic tasks. These results are consistent with several previous reports demonstrating activations particularly within the BA 47 region, and also BA 45, as being linked to semantics (Buckner et al., 1995a,b; Dapretto and Bookheimer, 1999; Demb et al., 1995; Démonet et al., 1992; Devlin et al., 2003; Fiez, 1997; Gold and Buckner, 2002; Kapur et al., 1994a,b; Martin et al., 1995; Petersen et al., 1989, 1990). Devlin and colleagues have further demonstrated the critical and specific involvement of BA 47 in semantics by showing that transcranial magnetic stimulation (TMS) over BA 47 selectively slows semantic but not phonological processing. In fact, the location of their mean stimulation site ($x = -52, y = +24, z = -2$) was less than 4 mm from the most significant site of activation for the semantic task in the current study, Table 6 ($x = -51, y = +27, z = -3$), providing a nice convergence of results (Devlin et al., 2003).

The BA 47 region activation was also within 1 cm of the activation reported by Hagoort et al., as an area integrating word meaning with world knowledge (Hagoort et al., 2004). The similar activation in this study may relate to subjects having to compare the meanings of different words.

Table 5
Regional activations for HOM inclusively masked by ANA and SYN

Location	<i>x</i> (mm)	<i>y</i> (mm)	<i>z</i> (mm)	<i>Z</i> score	<i>P</i> (voxel corrected)	<i>k</i> (cluster size— voxels)
Left precentral sulcus (BA 6/44)	−57	9	24	5.54	2.62E−06	21
	−48	3	18	4.62	1.15E−04	
Right lateral orbital gyrus (BA 11/47)	42	33	−12	3.81	0.0022	30
	51	39	0	2.98	0.025	
	51	45	−12	2.85	0.034	
Left precentral gyrus (BA 6)	−45	−3	48	3.43	0.0073	23
Right ventral insula	42	12	−18	3.19	0.014	23
	27	9	−21	2.91	0.030	
Right PHG (BA 28)	18	−15	−21	3.39	0.0082	16

Table 6
Regional activations for SYN inclusively masked by ANA and HOM

Location	x (mm)	y (mm)	z (mm)	Z score	P (voxel corrected)	k (cluster size—voxels)
Left superior postcentral sulcus (BA 3/4)	-15	-36	66	3.24	0.0089	24
Left superior frontal sulcus (BA 6)	-12	30	42	3.75	0.0022	42
	-24	12	39	3.43	0.0055	
	-24	21	36	2.54	0.043	
Left IFG (BA 45/47)	-51	27	-3	>8.0	<10E-020	278
Left IFG (BA 44)	-48	15	9	7.02	5.85E-10	
Left IFG (BA 45)	-54	27	24	7.01	7.18E-10	
Left SFG (BA 6)	-9	15	60	4.94	2.11E-05	12
Left angular/supramarginal gyrus (BA 39/40)	-39	-54	24	3.27	0.0082	26
Left temporal pole (BA 21/38)	-48	12	-15	5.61	9.24E-07	175
Left ITG (BA 20)	-42	0	-42	4.79	4.11E-05	
Left STS/STG (BA 21/22)	-57	-45	3	7.07	4.30E-10	220
Right STS (BA 20)	48	-15	-18	3.72	0.0023	82
	51	-9	-9	3.41	0.0058	
Left MTG/STS (BA 21/22)	-51	-15	-9	4.02	8.77E-004	18
Right fusiform gyrus (BA 19)	24	-72	-3	3.15	0.011	15
Right cuneus (BA 18/19)	15	-87	21	4.07	7.39E-04	98
Left dentate	-15	-45	-36	3.19	0.010	10
Right vermis (lobule IX)	6	-54	-33	4.19	4.61E-04	141
Right cerebellum (crus I/II)	27	-78	-42	5.71	5.62E-07	113
	15	-81	-36	5.70	5.76E-07	

Thompson-Schill and colleagues have suggested that the inferior frontal cortex may be linked to semantic choice rather than semantic retrieval, per se (Thompson-Schill et al., 1997). Although, our task design itself would not exclude this interpretation, the area of activation in the Thompson-Schill et al. study (mean $x = -44$, $y = +9$, $z = +30$, inferior frontal sulcus), while partly overlapping the frontal activation in the conjunction analysis, did not overlap the activations for either the masked semantic or phonological analyses. This also suggests that the region activated by the conjunction is engaged by all three language tasks, rather than specifically supporting just phonology

or semantics, again consistent with a potential general role in post-lexical processing.

The frontal activation associated with phonology in the current study was located at the junction of the precentral sulcus and posterior IFG within the pars opercularis region (see Devlin et al., 2003). Similar activations have been reported in other studies using tasks of phonological perception (Démonet et al., 1992, 1994; Devlin et al., 2003; Fiez, 1997; Fiez et al., 1995; Gold and Buckner, 2002; Paulesu et al., 1997; Rumsey et al., 1997; Zatorre et al., 1996). Part of this activation extended towards but did not overlap with the anterior insula, which has been suggested in both lesion

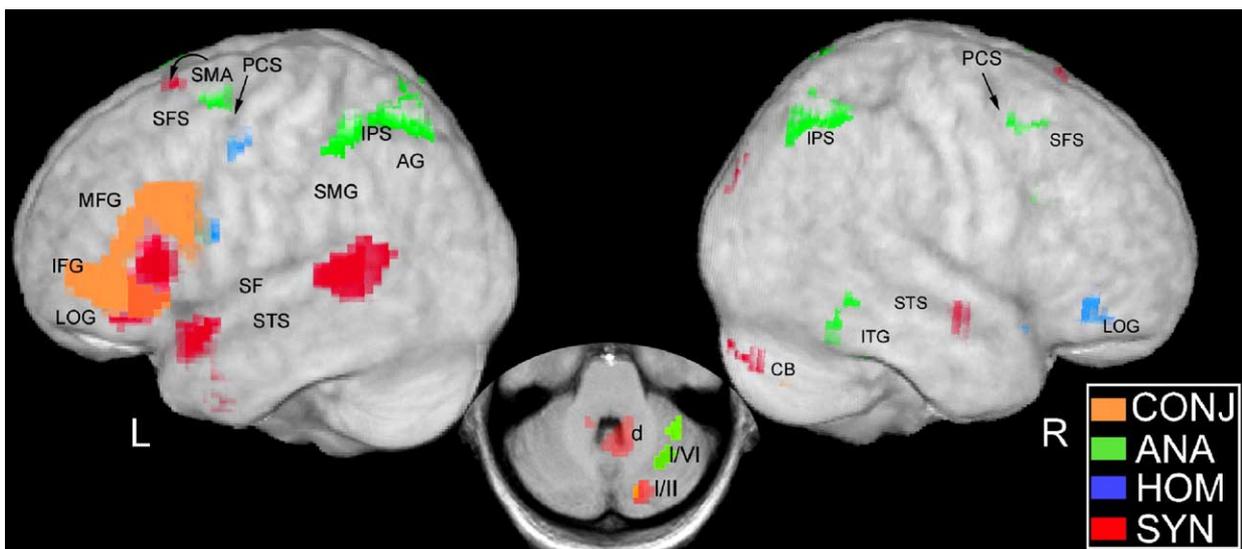


Fig. 4. Combined activations from each of the masked contrasts and the conjunction analysis illustrating their regional relationships. Inset—enlargement of cerebellar activations. See Figs. 2 and 3 for keys. Additional areas: AG = angular gyrus; d = dentate nucleus of cerebellum; SF = Sylvian fissure; SMG = supramarginal gyrus.

(Dronkers, 1996) and functional neuroimaging studies (Riecker et al., 2000a,b; Wise et al., 1999) to be closely linked with articulation. However, a recent study by Hillis et al., did not find an association between the anterior insula and articulation (Hillis et al., 2004). In the HOM task, subjects had to make phonological judgments without overt articulation, which may account for the absence of left insular activation. Another possibility, given the activation of the anterior insula in the conjunction analysis, is that the anterior insula may also be associated with general aspects of post-lexical processing or attention in all three tasks rather than articulation (Riecker et al., 2000a,b).

Other frontal activations

Supplementary motor cortex activation was seen in the conjunction and masked SYN analyses. Other studies have noted SMA activations for a variety of language tasks involving semantic, phonologic, and orthographic operations (Binder et al., 1997; Booth et al., 2002a,b; Buckner et al., 1995a; Chee et al., 1999; Kuo et al., 2004; Poldrack et al., 1999; Siok et al., 2003). Anterior SMA activations ($y = +10$ to $+40$) have been associated with semantic (Binder et al., 1997; Booth et al., 2002a; Buckner et al., 1995a; Poldrack et al., 1999) and syllabic processing tasks (Kuo et al., 2004; Siok et al., 2003). Posterior activations ($y = -22$ to 0) have been seen less consistently across studies, but have occurred in tasks involving word recall and repetition (Buckner et al., 1995a) or processing of letters/syllables compared with semantics (Booth et al., 2002a; Poldrack et al., 1999). Data from primates shows that anterior SMA has robust connections with anterior prefrontal and inferior frontal areas, while posterior SMA is connected to motor and posterior premotor regions (Rizzolatti et al., 1996). There are also connections with cerebellum. With respect to language, the SMA has been hypothesized to play a role in covert articulation and internally versus externally guided word generation (Fiez and Raichle, 1997). However, it has also been activated in motor planning and “complex” motor behaviors (Vorobiev et al., 1998).

Temporal cortex

In the masked semantic task, several regions of activation were seen in the lateral temporal lobe. The temporal cortex has been associated with semantics based on data from lesion (Damasio et al., 1996; Hart and Gordon, 1990), degenerative (Mummery et al., 1999) and multiple functional imaging studies (Démonet et al., 1992; Shaywitz et al., 1995a,b; Vandenberghe et al., 1996). A recent study by Hagoort et al. has further suggested that temporal cortex activity may be more specifically associated with the retrieval of word meaning (Hagoort et al., 2004). The current study is entirely consistent with these findings and provides a robust demonstration of the significant temporal activation found in semantic tasks.

Several functional imaging studies have also implicated middle and anterior portions of the temporal lobe in phonological processing (Démonet et al., 1992, 1994; Paulesu et al., 1993; Shaywitz et al., 1995a,b; Sergent et al., 1992). Anterior temporal activation was not seen in the masked phonology analysis. However, the phonology task used visual rather than auditory stimuli and did not involve word generation. Furthermore, the analysis technique stringently controlled for semantic processing. These factors suggest that the non-auditory regions of temporal lobe

may not be involved in phonologic processing, although it is possible that our criteria were so strict as to result in a Type 2 error.

Parietal cortex

Several studies have suggested that the supramarginal gyrus likely plays a role in the short-term storage of verbal information (Binder et al., 1997; Paulesu et al., 1993; Warrington et al., 1971). This role is consistent with the design of our tasks in which subjects would have maintained the phonological or semantic information of one word while looking at the other, or would have held online several letters while looking at the spelling of the second word. Activation in semantic tasks has not generally been seen unless the task includes a working memory component (Cabeza and Nyberg, 2000). In the current study, the activation of the inferior and medial parietal cortex in the semantic task therefore may have been related to greater working memory requirements during this condition.

In the case of the masked orthographic contrast, this condition activated the supramarginal gyrus on the left and the intraparietal sulcus bilaterally. Although the parietal and frontal eye field activations could just reflect recruitment of the spatial attention network, we hypothesize this may represent a form of material specific spatial attention processing. In both the orthographic and control tasks, subjects had to decide if the stimulus pairs contained the same letters. Subjects found the tasks equally difficult as reflected by the similar reaction time and accuracy measures; however, greater activations were seen in the ANA task (vs. the control), suggesting that the processing of word stimuli may have enhanced any activity related to spatial attention, consistent with a material specific stimulus effect.

Cerebellum

When functional imaging was first used to study language in the 1980s, one surprising finding was the activation of the cerebellum in apparently non-motor linguistic tasks. Many subsequent studies have demonstrated cerebellar activations in both motor and non-motor aspects of language including articulation, semantics, verbal fluency, response selection, sequence learning, and verbal working memory (see Fiez and Raichle, 1997, for a review). In the current study, cerebellar activations were seen on the right in crus I/lobule VI for the conjunction analysis, crus I/lobule VI for the masked orthographic analysis, and the right dentate nucleus and crus I/II for the masked semantic analysis. These locations are based on the nomenclature of Schmahmann et al. (1999).

Some of the activations in the current study overlap cerebellar regions that may be associated with articulatory processes while others occur in regions that seem related to non-motoric aspects of language. Although subjects did not overtly articulate words in the current study, cerebellar activation has also been seen in studies employing covert articulation, and the cerebellum is hypothesized to participate in a (possibly covert) articulatory loop that includes the inferior frontal cortex and the supplementary motor area (Fiez and Raichle, 1997).

In previous studies that have used tasks which emphasized orthographic processing, cerebellar activations have been seen in right crus I (Chen et al., 2002; Fullbright et al., 1999; Rumsey et al., 1997). Semantic tasks have also shown similar cerebellar activations as in the current study. Previous studies have further shown that cerebellar activations are sensitive to semantic task

demands (Fullbright et al., 1999; Roskies et al., 2001; Xiang et al., 2003), raising the possibility that the cerebellum may directly contribute to semantic computations or selection (Xiang et al., 2003).

We consider it unlikely that the cerebellum was activated in the current study merely as a consequence of subject responses because the motor requirements of the task were well matched between the active and control conditions, and across tasks. One concern regarding cerebellar involvement in language is that cerebellar lesions do not appear to result in linguistic deficits. Further studies will be necessary to elucidate the specific role of the cerebellum in language, beyond its motor associations.

Right hemisphere

In the right hemisphere, each of the tasks had specific areas of activation, parietal and superior frontal for masked ANA, inferior frontal for masked HOM and temporal for masked SYN. Multiple studies have noted right hemisphere activations for language tasks (Chee et al., 1999; Devlin et al., 2003; Fiez et al., 1995; Heim et al., 2003; Petersen et al., 1989; Mazoyer et al., 1993; McDermott et al., 2003; Rossell et al., 2003; Rumsey et al., 1997; Tagamets et al., 2000; Turkeltaub et al., 2002). The right hemisphere has been hypothesized to be particularly activated in response to interpreting sentence content, placing information in context, detecting semantic anomalies, interpreting prosody, and understanding metaphor, none of which should pertain to single word analysis (Bookheimer, 2002; Ross and Mesulam, 1979). The right hemisphere may also be involved when the task requires the integration of information over time (Bookheimer, 2002). However, as in the current study, right hemisphere activation has also been seen for language tasks requiring immediate responses to single words (Chee et al., 1999; Devlin et al., 2003; Heim et al., 2003; Petersen et al., 1989; Rossell et al., 2003; Rumsey et al., 1997; Tagamets et al., 2000; Turkeltaub et al., 2002). Although it is possible that right hemisphere regions were activated simply as a by-product of their connections with homologous regions on the left, it is also possible that these regions are playing a specific role in language, which has yet to be fully determined.

Conclusions

Through the use of subjects performing identical tasks probing different aspects of lexical processing, this study has examined brain activations related to three fundamental language processes (orthography, phonology and semantics). The results show that a common network of brain regions supports word processing, while each task is also associated with more specific activations. The results both confirm and extend findings from multiple studies in the literature by showing the extent of functional integration and segregation in the language network.

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