Common and Dissociable Activation Patterns Associated with Controlled Semantic and Phonological Processing: Evidence from fMRI Adaptation

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Recent evidence suggests specialization of anterior left inferior prefrontal cortex (aLIPC; ~BA 45/47) for controlled semantics and of posterior LIPC (pLIPC; ~BA 44/6) for controlled phonology. However, the more automated phonological tasks commonly used raise the possibility that some of the typically extensive aLIPC activation during semantic tasks may relate to controlled language processing beyond the semantic domain. In the present study, an event-related fMRI adaptation paradigm was employed that used a standard controlled semantic task and a phonological task that also emphasized controlled processing. When compared with letter (baseline) processing, significant fMRI task and adaptation effects in the aLIPC and pLIPC regions (~BA 45/47, ~BA 44) were observed during both semantic and phonological processing, with aLIPC showing the strongest effects during semantic processing. A left frontal region (~BA 6) showed task and relative adaptation effects preferential for phonological processing, and a left temporal region (~BA 21) showed task and relative adaptation effects preferential for semantic processing. Our results demonstrate that aLIPC and pLIPC regions are involved in controlled processing across multiple language domains, arguing against a domain-specific LIPC model and for domain-preferentiality in left posterior frontal and temporal regions.

Keywords: brain activation, phonology, prefrontal cortex, priming, semantic

Introduction

The functional–anatomic organization of left inferior prefrontal cortex (LIPC) has been a topic of growing interest and debate over the past decade (Petersen *et al.* 1988; Zatorre *et al.*, 1992; Buckner *et al.*, 1995; Petrides *et al.*, 1995; Duncan and Owen, 2000). However, characterization of specific cognitive processes that map most reliably onto specific LIPC regions has remained elusive. In seminal studies, Petersen *et al.* (1988, 1989) reported prominent activation of an anterior–ventral portion of LIPC [aLIPC; approximate Brodmann area (BA) 45/47] during semantic (meaning-based) decision and semantic generation tasks, but not during single word reading. Importantly, whereas single word reading is thought to result in automatic activation of semantic representations (Neely, 1977; MacLeod, 1991), semantic decision tasks emphasize controlled semantic processes such as the strategic retrieval of meaning and/or working with and evaluating meaning. Several other early functional neuroimaging studies reported strong activation of aLIPC during controlled semantic tasks, with activation sometimes extending into posterior LIPC (pLIPC; ~BA 44) (Démonet *et al.*, 1992; Kapur *et al.*, 1994; Buckner *et al.*, 1995; Demb *et al.*, 1995; Martin *et al.*, 1995). Similarly, the continued trend of activation of both aLIPC and pLIPC during controlled semantic tasks compared with a range of comparison

tasks has confirmed an important role for these regions in controlled semantic processing (Gabrieli *et al.*, 1996; Price *et al.*, 1997; Chee *et al.*, 1999; Dapretto and Bookheimer, 1999; Poldrack *et al.*, 1999; Bokde *et al.*, 2001; Wagner *et al.*, 2001; Gold and Buckner, 2002).

Anatomically proximal LIPC regions have been implicated in phonological (speech-sound) processing (Démonet *et al.*, 1992; Zatorre *et al.*, 1992; Fiez *et al.*, 1996; Rumsey *et al.*, 1997; Burton *et al.*, 2000). These studies reported activation of pLIPC (~BA 44) and left precentral gyrus (~BA 6) during phonological tasks. A number of subsequent studies have observed a similar trend of LIPC recruitment patterns resulting from semantic–phonological comparisons, with greater activation in aLIPC for semantic tasks and greater activation in pLIPC/precentral gyrus for phonological tasks (Buckner *et al.*, 1995; Poldrack *et al.*, 1999; Bokde *et al.*, 2001; Otten and Rugg, 2001; Roskies *et al.*, 2001; McDermott *et al.*, 2003). Such findings have led to suggestions of functional heterogeneity of LIPC based upon semantic–phonological domain lines, with suggested functional segregation of aLIPC (~BA 45/47) from pLIPC/precentral gyrus (~BA 44/6) (Buckner *et al.*, 1995; Fiez, 1997; Poldrack *et al.*, 1999; Wagner *et al.*, 2000; Bokde *et al.*, 2001).

One potential difficulty in inferring a functional subdivision in LIPC along semantic and phonological domain lines is that semantic tasks have tended to place more emphasis on controlled processes. Controlled processes encompass a range of effortful cognitive operations that involve sequential steps, are capacity limited, and typically evolve more slowly than automatic processes (Neely, 1977; Schneider and Shiffrin, 1977). For example, in a commonly used semantic task, subjects decide if words represent concepts that are abstract or concrete. Because many words have representations that can be viewed in multiple ways depending on context, the task emphasizes controlled processes associated with attempting to map relatively underconstrained stimulus-to-representation relationships. By contrast, phonological tasks involving mapping *word* sounds tend to place less demands on controlled processing operations because the majority of words are constrained by the quasi-regular spelling-to-sound correspondences of English (Plaut *et al.*, 1996). For example, phonological rhyme generation is constrained by orthographic neighborhood (cake → fake, make, take), while semantic verb generation is underconstrained due to the arbitrary relationship between orthography and semantics (cake → eat, cut, celebrate). Thus, mapping underconstrained semantic relationships is likely to emphasize controlled processes associated with strategic retrieval and working with multiple potential stimulus-to-representation relationships.

The uneven controlled processing demands in many semantic–phonological comparisons raises the possibility that at least

some of the typically extensive LIPC activation during semantic tasks may be associated with controlled verbal processing generalizing beyond the semantic domain. A body of data has implicated lateral prefrontal cortex in controlled verbal processing. For example, neuropsychological studies suggest that patients with lesions of lateral prefrontal cortex show difficulty generating words beginning with a pre-specified letter (Milner, 1964), monitoring verbal material maintained over a brief interval (Petrides and Milner, 1982) and completing sentences in underconstrained contexts (Robinson *et al.*, 1998), among other impairments. Functional neuroimaging has also suggested a contribution of LIPC to controlled verbal processing operations that are used during semantic tasks but may be more general (e.g. Petrides *et al.* 1995; Thompson-Schill *et al.*, 1997).

Nevertheless, until recently, reports of aLIPC (~BA 45/47) activation have been restricted largely to tasks involving controlled semantic operations. In a noteworthy exception, Klein *et al.* (1995) reported aLIPC activation for lexical, phonological and semantic tasks in bilingual subjects. More recently, Gold and Buckner (2002) reported that aLIPC, although activated most strongly during a semantic task, also activated significantly more during a high control phonological condition (mapping pseudoword sounds) than a low control phonological condition (mapping word sounds). This finding was unlikely to be the result of semantic processing because pseudowords, which have no meaning, resulted in greater aLIPC activation than real words, which do have meaning. Moreover, MR signal in this region was negatively correlated with the consistency of the response across subjects. Conditions of high response variability showed the greatest aLIPC activation, suggesting a role for aLIPC in mapping relatively underconstrained stimulus-to-representation relationships across multiple language domains. Domain preferential activation was found in left posterior frontal cortex near the precentral gyrus (~BA 6) and left inferior parietal cortex near the supramarginal gyrus (~BA 40) for controlled phonological processing, and in left posterior temporal cortex near the middle temporal gyrus (~BA 21) for controlled semantic processing. The findings of Gold and Buckner (2002) suggested that aLIPC could participate in controlled processing across multiple language domains and that functional differentiation between semantic and phonological processing may be strongest in specific left posterior frontal, parietal and temporal regions.

At least two questions persist concerning the role of aLIPC in controlled phonological processing. The first question is whether prominent activation of aLIPC in phonological tasks is limited to contexts involving mapping pseudoword (pronounceable nonwords; e.g. banu) sounds. Several studies have reported aLIPC activation during tasks involving mapping pseudoword sounds (Pugh *et al.*, 1999; Hagoort *et al.*, 1999; Poldrack *et al.*, 2001; Clark and Wagner, 2003), and a number of studies have reported little or no activation of aLIPC during tasks involving mapping word sounds (Rumsey *et al.*, 1997; Poldrack *et al.*, 1999; Bokde *et al.*, 2001; Otten and Rugg, 2001; Roskies *et al.*, 2001; McDermott *et al.*, 2003; but see Klein *et al.*, 1995; Devlin *et al.*, 2003). A finding of prominent aLIPC activation during a phonological task performed with words, but emphasizing controlled processing, would indicate that aLIPC involvement in phonological processing is not stimulus (pseudoword) dependent, but rather relates to task requirements that emphasize controlled processing.

A second question is whether aLIPC shows reduced response under conditions in which controlled phonological mappings become automated through repetition [functional magnetic resonance imaging (fMRI) adaptation]. fMRI adaptation is the phenomenon that certain brain regions show decreased hemodynamic response as a correlate of behavioral repetition priming, a finding thought to reflect increased efficiency in a particular processing domain (reviewed in Henson, 2003). A number of studies have demonstrated significant aLIPC adaptation associated with semantic processing (e.g. Raichle *et al.*, 1994; Demb *et al.*, 1995; Wagner *et al.*, 1997, 2000; Buckner *et al.*, 2000; Maccotta and Buckner, 2004). fMRI adaptation in aLIPC during semantic processing has been interpreted as further evidence that the region plays an important role in controlled semantic processing (reviewed in Schacter and Buckner, 1998). In the present study, we explored whether aLIPC also reduces its response as phonological mappings become automated through repetition to test for converging evidence of a role for aLIPC in controlled phonological processing.

To address these questions, we conducted an event-related fMRI adaptation experiment comparing three tasks. In a semantic verb generation task, subjects generated verbs associated with nouns according to meaning (e.g. generate eat in response to cake). In a phonological regularization task, subjects generated regularized pronunciations of words with irregular spellings (e.g. generate the pronunciation of pint that rhymes with hint, mint) (Balota *et al.*, 2000). Given the present goal of exploring aLIPC response associated with controlled phonological processing, an important feature of the phonological regularization task is that it is guided by sublexical representations, minimizing semantic processes. Activation of aLIPC during phonological regularization is therefore unlikely to be associated with semantic processing. Like the semantic verb generation task, the phonological regularization task emphasizes controlled processing associated with mapping relatively underconstrained stimulus-to-representation relationships. For example, generation of the regularized pronunciation of the word pint involves controlled retrieval of multiple potential sublexical sound codes, and working with these codes in order to generate a pronunciation *de novo*. Evidence that the phonological regularization task emphasizes controlled processing comes from behavioral results indicating latency data comparable to that reported on the semantic verb generation task (Balota *et al.*, 2000). A letter processing (baseline) task was also included in the study to account for activation associated with lower-level orthographic processing. In the letter task, subjects decided if the first or last letter of each word came earlier in alphabetic order (e.g. in pint, p comes before t).

A schematic of the fMRI adaptation procedure used and sample stimuli are presented in Table 1. During a prescan phase, subjects performed each of the three tasks with a novel set of 10 items, repeated six times each. During subsequent scanned runs, subjects performed the same tasks, with runs divided equally between repeated items (processed during prescan phase), interspersed with novel items and fixation (+) baseline trials.

The event-related fMRI adaptation paradigm enabled examination of the pattern of semantic, phonological and letter (i) activations under novel processing conditions (task effects) and (ii) decreases under repeated processing conditions (adaptation effects). Given the distributed nature of the left-hemisphere language system and previous adaptation results, decreases were expected for all language tasks under repeated processing conditions. The key question of interest here was whether

Table 1
Schematic of fMRI adaptation design and sample stimuli

Experiment phase	Tasks			Repetitions/ (Category)
	Verb generate	Regularize	First/last letter	
Prescan phase	MATCH	GLOVE	TEACHER	6
Scanned runs	DOCTOR	EARTH	RAIN	(novel)
	+	+	+	(baseline)
	MATCH	GLOVE	TEACHER	(repeated)
	+	+	+	(baseline)
	LION	SWAB	SEAT	(novel)
	MATCH	GLOVE	TEACHER	(repeated)
	CAKE	PRIEST	SWORD	(novel)
	+	+	+	(baseline)
	MATCH	GLOVE	TEACHER	(repeated)

specific regions reduce their response significantly more as a function of repeated processing under semantic or phonological task conditions. To examine this question, results focus on relative adaptation effects (task by adaptation interactions).

Materials and Methods

Subjects
Thirty-two volunteers participated in the study and received \$25/h as payment. Subjects were native English speaking, right-handed, and had normal or corrected to normal vision and reported no significant neurological history. Four participants were either unable to complete tasks or produced data with sufficient artifacts to preclude further analyses. Thus, data from 28 participants (20 females), aged 18–27 years; mean ± SD = 22.3 ± 2.6 years) were included in analyses. Informed consent was obtained using procedures approved by the Washington University School of Medicine Human Studies Committee.

Imaging
Scanning was performed at 1.5 T on a Siemens Vision System (Erlangen, Germany). Structural images were acquired using a three-dimensional T_1-weighted (MP-RAGE) sequence (T_R = 9.7 ms, T_E = 4 ms, flip angle = 10°, T_I = 20 ms, voxel size = 1 × 1 × 1.25 mm). Functional images were acquired parallel to the anterior-posterior commissure plane of the structural image. Main field B_o homogeneity was optimized at the start of each fMRI session using an automated shimming routine. Functional runs consisted of 98 sequential whole brain acquisitions, each including 16 contiguous 8-mm-thick axial slices (T_R = 2.5 s, T_E = 37 ms, 3.75mm² in-plane resolution) using an asymmetric spin-echo, echo-planar sequence (Conturo et al., 1996). Foam padding and a thermoplastic face mask were used to limit head motion within the coil. Masks were fitted to subject head contours and extended from the top of the forehead to the tip of the nose.

Tasks and Stimuli
In a semantic verb generation task, participants generated aloud verbs corresponding to nouns (Petersen et al., 1988). In a phonological regularization task, subjects generated aloud the regularized pronunciation of words with irregular/inconsistent spellings by applying regular spelling-to-sound correspondence rules of English (pronounce pint to rhyme with mint, hint; Balota et al., 2000). In a first/last letter task, subjects pronounced aloud the letter corresponding to the earlier position in the alphabet (Demb et al., 1995). Subjects were given practice on all tasks prior to scanning.

A total of 80 nouns of medium frequency were used for each task. Task-specific word lists were used in order to maximize the appropriateness of stimuli for each task. Words used in the verb generation task were selected from a pool of items used in previous functional neuroimaging studies using the verb generation task (Petersen et al., 1988, 1989). Irregular/inconsistent words used in the regularization task were defined broadly as having an alternative and a common spelling-to-sound mapping at the level of graphemes or word bodies (Balota et al., 2000). Monosyllabic words came from Balota et al. (2004) and were inconsistent at the level of orthographic rimes (e.g. pint,

because 'int' is typically pronounced to rhyme with hint, mint). Disyllabic words were selected from a variety of sources and were either irregular by single graphemes (e.g. chaos; Venezky, 1970) or inconsistent at the level of word bodies (e.g. hospice; Glushko, 1979). For the first/last letter baseline task, to promote comparability with the verb generation and regularization tasks, half the words used (in each run) had regular spellings and half had irregular spellings.

Task-specific word lists did not differ in mean frequency ratings (verb generation, mean = 16 463; regularization, mean = 12 287; first/last letter, mean = 14 700; per hundred million observations; see Burgess and Livesay, 1998) [$F_{(2,237)}$ < 1; all posthoc Ps > 0.49], or in the percentage of words rated as concrete versus abstract (verb generation mean = 0.91; regularization mean = 0.88; first/last letter mean = 0.89) [$F_{(2,237)}$ < 1; all posthocs Ps > 0.47]. Task-specific word lists also did not differ in mean syllable number (verb generation mean = 1.33; regularization mean = 1.25; first/last letter mean = 1.20) [$F_{(2,237)}$ < 1; all posthocs Ps > 0.37]. However, word length differed across lists (verb generation mean = 4.93; regularization mean = 5.25; first/last letter mean = 5.11). Although differences in word length were not significant in the omnibus task comparison [$F_{(2,237)}$ = 1.9, P = 0.15], the difference between verb generation and regularization lists approached significance [$t_{(158)}$ = 1.9, P = 0.08]. Analysis of behavioral and fMRI data included word length as a nuisance covariate to deal with the differing word lengths across task lists.

The 80 words used per task were divided into eight task-specific lists of 10 nouns (matched for frequency and length) to allow for counterbalancing of novel and repeated items across subjects. Lists were rotated across subjects such that old items for one person were used as new items for another person. Order of tasks and stimuli within runs were counterbalanced across subjects.

Stimuli were projected centrally (24 pt Geneva font, white on black background) for a duration of 2000 ms, followed by presentation of a fixation cross-hair for the remainder of the trial (500 ms). Stimuli were projected onto a screen at the back of the magnet bore, viewed through a mirror. Stimulus presentation was implemented with Psyscope software (Cohen et al., 1993) run on a Power Macintosh computer (Apple, Cupertino, CA).

Prescan Phase
Tasks were performed in a prescan phase within the scanner immediately prior to each scanned run in order to engage subjects in the processing of a set of words that would later be re-processed during scanned runs (thus becoming repeated trials). During each prescan phase, subjects performed tasks with a novel set of items, consisting of 10 words, presented six times in random order. Six repetitions were chosen based upon prior research showing robust adaptation effects in LIPC regions using semantic tasks (Raichle et al., 1994; Buckner et al., 2000; Maccotta and Buckner, 2004).

Scanned Runs
During scanned runs subjects performed the same three tasks from the prescan phase in separate runs. Each task was scanned immediately following its prescan phase. An event-related design was employed, with runs divided equally between three trial types consisting of repeated (previously studied) words interspersed with novel words and fixation cross-hair (+) trials. Repeated trials were processed six times during the prescan phase and an additional three times during scanned runs. Novel trials were processed only once. Functional runs lasted ~4 min and consisted of 90 trials (30 of each trial type). Trial types within runs were pseudorandomly intermixed with first-order counterbalancing such that each trial type followed each other type equally often, creating temporal jitter between trials of the same type optimal for rapid event-related designs (Buckner et al., 1998; Dale, 1999; Miezin et al., 2000). In addition, functional runs began with 10 s of visual fixation to allow MR signal stabilization and ended with 10 s of visual fixation to capture the hemodynamic response.

Overt Speech in fMRI
Recording of subject verbal responses was important to the present study to ensure subjects engaged tasks appropriately. One concern with fMRI studies using overt speech involves potential for magnetic

susceptibility artifacts (Yetkin *et al.*, 1995). However, recent fMRI studies utilizing overt speech have shown that artifact-free images can be obtained when event-related designs are employed by implicitly taking advantage of the different timing characteristics associated with speech-related and hemodynamic-related signal changes (Birn *et al.*, 1999; Palmer *et al.*, 2001). For example, Palmer *et al.* (2001) demonstrated successful removal of artifact present in blocked designs when an event-related design was employed. Importantly, no special correction procedures were required to minimize artifact when event-related design and analysis procedures were employed (Palmer *et al.*, 2001). The present study employed an event-related design with overt speech to ensure appropriate task engagement.

Recording of Vocalizations

Subject vocalizations in the MRI scanner were recorded using the Resonance Technology Commander XG MRI audio system (Northridge, CA). The audio system's microphone was linked to a PC (Micron PC with a Pentium III @ 450 MHz) running CoolEdit 2000 (Syntrillium Software Corp., Phoenix, AZ) to create digital sound files (eight-bit recordings, sampled at 11 025 Hz in .wav format) for subsequent computer-based analysis. Vocal onset latencies were computed using the Adaptive Spectral Subtraction for Extracting Response Times (ASSERT) software program (Nelles *et al.*, 2003) implemented in MATLAB (The MathWorks, Natick, MA).

Computing Accuracy

Trials were scored from digital sound files played in Sound Edit. Trials were scored as either (i) correct (clear pronunciation appropriate to the task instructions); (ii) incorrect (clear pronunciation but not appropriate to task instructions, e.g. saying 'jump' in response to 'cake' during the verb generation task, pronouncing 'glove' normally instead of pronouncing it to rhyme with 'cove' in the regularization task, saying 'w' in response to 'wine' in the first/last letter task) or unclear pronunciation (e.g. a nonfluent pronunciation that was not recognizable); or (iii) no response.

MR Data Analysis

Images were preprocessed to minimize noise and artifacts. Slice-by-slice normalization (sinc interpolation) was used to correct for changes in signal intensity introduced by the acquisition of interleaved slices. Rigid-body translation and rotation was applied to each frame in order to realign images within and across runs (Snyder, 1996). The data were normalized to a whole-run mean magnitude of 1000 to allow for comparisons across subjects. Each subject's structural and functional data were then resampled into 2 mm isotropic voxels, warped to the standard stereotaxic atlas space of Talairach and Tournoux (1988), and smoothed with a Gaussian spatial filter (6 mm full-width half-maximum). Functional images were registered using the alignment parameters derived for the structural images. Preprocessed data were then analyzed using the general linear model (GLM) to estimate parameter values (Friston *et al.*, 1995), implemented in an in-house analysis program (Miezin *et al.*, 2000). Separate estimates were computed for trials occurring within the semantic, phonological and letter task runs. In addition, two behavioral regressors of no interest were included in the GLM to regress out differences in length between word lists used for different tasks (see Tasks and Stimuli), and latency differences between tasks (see Results section). Cross-correlation magnitude estimates were computed for each trial type of each task as the inner product of the estimated timecourse and a vector of contrast weights modeling the hemodynamic response function. Contrast weights were derived from a set of γ functions with a delay of 2 s and a time constant of 1 s, based upon peak magnitude (Boynton *et al.*, 1996). Single averaged magnitude estimates from each subject were used in a priori analyses using specific regions of interest (see A priori Region-wise Analysis). Estimates were also entered into whole-brain analyses on the basis of voxel-based paired *t*-tests that made no regional assumptions (see Whole-brain Voxel-wise Analyses).

A priori Region-wise Analysis

Specific regions of interest were hypothesized to be associated with 'controlled processing across multiple language domains', 'semantic-

preferential' or 'phonological-preferential' processing based on the literature and recent findings in our laboratory. Regions were selected and defined based upon locations of peak activations from a related study conducted in our laboratory (Logan *et al.*, 2002). This study involved a contrast between semantic and letter tasks using word stimuli. Five target regions were selected for a priori analyses from the semantic-letter whole-brain map [and were identical to the regions examined in Gold and Buckner (2002)]. For each location, a three-dimensional region was defined to include all activated voxels within 12 mm of the peak. These a priori regions were then applied to the present data. aLIPC (~BA 45/47) and pLIPC (~BA 44) regions were hypothesized to be involved in controlled processing across multiple language domains. Although these regions were originally defined based upon the semantic-letter comparison, our recent findings suggest that their involvement in controlled processing may generalize to multiple language domains. One region was hypothesized to be 'semantic-preferential' (~BA 21) and two were hypothesized to be 'phonological-preferential' (~BA 6, ~BA 40).

Estimates of signal change (magnitude referenced to fixation) were averaged across all voxels in a region and scaled to percent signal change for each subject. The average signal change within each region was then submitted as a single value to a series of statistical tests based on a mixed-effects model, treating subjects as a random effect.

Whole-brain Voxel-wise Analysis

To validate region of interest (ROI) results and explore other activations, a whole-brain analysis was also employed using a mixed-effect statistical model paired *t*-test at each voxel, treating subjects as a random effect. Contrasts of interest were regressed against a set of seven time-lagged γ functions, with a delay of 2 s and a time constant of 1 s, that approximate the range of hemodynamic responses typically encountered (Boynton *et al.*, 1996). Resulting *t*-statistics were converted to *z*-statistics and plotted over the whole brain. A threshold of $P < 0.001$ was employed. This threshold was conservative in the context of the conjunction contrasts used [e.g. adaptation effects were computed as novel item processing (– fixation) – repeated item processing (– fixation), within each task] and likely to minimize false positives. Whole-brain activation maps were projected onto an inflated cortical surface of the lateral left hemisphere using surface-based representations implemented using Caret software (Van Essen *et al.*, 2001) to visualize the spatial extent of common and dissociable activation patterns.

Results

Quality Control and Subject Exclusion

Examination of head translations and rotations in the *x*, *y* and *z* planes for each run indicated that 2 of 32 participants appeared to have shifted head position by >2 mm in at least one run, in at least one direction. Data from these subjects were not used in further analyses. As a second quality control step, signal-to-noise (SNR) mean maps were examined for each participant using raw data before movement correction. Visual inspection of the SNR maps did not reveal significant ghosting or blurring associated with overt verbal responses in blocked designs (Birn *et al.*, 1999). Finally, activation maps were produced for each individual contrasting all active conditions compared with visual fixation (+). Maps were inspected carefully for the presence of artifact in white matter regions, as has been reported in blocked design studies using overt speech (Birn *et al.*, 1999). Minimal artifactual activation was detected in any subject's data. The relative absence of artifactual activation, such as colored noise in white matter regions, suggests that the event-related fMRI data are relatively free from artifacts (replicating the event-related results of Birn *et al.*, 1999; Palmer *et al.*, 2001).

Finally, two subjects showed response patterns suggesting inappropriate task engagement during at least two of the three

tasks. The poor performance of these individuals (accuracies at least 3 SD from the group mean), suggested that they did not understand task instructions or were unable to perform the task. Data from these subjects were not analyzed further.

Behavioral Data

Accuracy data is reported for completeness, although only accurate trials were included in latency and fMRI data analyses (due to different accuracy rates between tasks). Table 2 presents mean accuracies and priming accuracy effect sizes for the semantic, phonological and letter tasks. ANOVA indicated a main effect of task [$F(2,54) = 158.0$, $P < 0.001$], with more accurate performance on the letter than the semantic [$t(27) = 9.0$, $P < 0.001$] or phonological [$t(27) = 16.8$, $P < 0.001$] tasks. Performance was also more accurate on the semantic than phonological task [$t(27) = 9.3$, $P < 0.001$]. However, performance on the phonological task was well above chance ($P < 0.001$). Errors in the phonological task consisted of omissions (12%), failures to regularize irregular words (using learned lexicosemantic pronunciation rules; 8%) and mispronunciations (3%). There was a main effect of repetition, with repeated processing resulting in significantly better performance than novel processing [$F(1,27) = 138.3$, $P < 0.001$]. Repeated processing resulted in significantly better performance than novel processing in each of the three tasks (all tasks, $P < 0.001$), indicating the presence of priming in each task. However, priming effects were significantly different between tasks [$F(2,54) = 15.9$, $P < 0.001$]. Priming effects were significantly greater in the phonological than semantic [$t(27) = 4.0$, $P < 0.001$] or letter [$t(27) = 4.3$, $P < 0.001$] tasks, and there was a trend toward greater priming in the semantic task than the letter task [$t(27) = 1.8$, $P = 0.08$].

Given the different accuracy rates between tasks, analyses of latency and fMRI data were restricted to correct trials. Table 3 presents mean median voice-onset latencies for correct trials, and corresponding priming latency effect sizes for the semantic, phonological and letter tasks. Latency data were first analyzed with a linear mixed-model of the covariance structure of the repeated measures design to determine whether differences in latency between tasks were affected by differing word length

across task lists. Results indicated that word length did not contribute significantly to latency differences between tasks [$F(1,27) = 0.37$, $P = 0.56$]. There was a main effect of task [$F(2,54) = 5.4$, $P < 0.01$], with the phonological task resulting in significantly longer latencies than the semantic task [$t(27) = 3.5$, $P < 0.01$], but not the letter task [$t(27) = 1.1$, $P = 0.30$]. There was a trend toward longer latencies in the letter task than the semantic task [$t(27) = 1.9$, $P = 0.07$]. Because task effects were moderated differentially by repetition, and task comparison between semantic and phonological tasks under novel processing conditions were important to interpretation of fMRI data, latency was also compared for the novel conditions only. Task latencies were not significantly different under novel processing conditions [$F(2,54) = 1.4$, $P = 0.24$]. Of particular importance, latency between semantic and phonological tasks was not different under novel processing conditions [$t(27) = 0.55$, $P = 0.56$]. Repeated processing resulted in significantly shorter latencies than novel processing ($P < 0.001$). The priming effect was present in each task ($P < 0.001$), indicating the presence of priming in each task. However, priming effects were significantly different between tasks [$F(2,54) = 15.6$, $P < 0.001$], with greater priming for the semantic than the phonological [$t(27) = 3.9$, $P < 0.001$] or letter [$t(27) = 5.0$, $P < 0.001$] tasks, and a trend for greater priming in the phonological task than the letter task [$t(27) = 1.9$, $P < 0.06$].

fMRI Regional Analyses

As with latency data, analysis of fMRI data was restricted to correct trials (due to different accuracy rates between tasks). Activation patterns in five a priori regions of interest were first examined. These included an aLIPC region (~BA 45/47), a pLIPC region (~BA 44), a region in left frontal cortex near the precentral gyrus (~BA 6) and two posterior regions previously implicated in semantic (~BA 21) and phonological (~BA 40) processing. Coordinate locations of peak activations defining the center of these five regions were taken from a related study (Logan et al., 2002), based on the prior literature discussed in the introduction. Coordinate locations of peak activations and reference papers that motivate interest in the regions are given in Table 4. For descriptive purposes, regions are labeled by their approximate Brodmann areas.

Table 2
Mean accuracies and repetition priming effects

Task	Condition	Accuracy, % (SD)	Accuracy priming effect
Semantic	Novel	82.2 (4.5)	
	Repeated	89.1 (3.7)	6.9
Phonological	Novel	74.4 (4.4)	
	Repeated	84.1 (5.0)	9.7
Letter	Novel	87.8 (3.8)	
	Repeated	92.8 (3.0)	5.0

Table 3
Mean median latencies and repetition priming effects for correct trials

Task	Condition	Latency, ms (SD)	Latency priming effect
Semantic	Novel	1131 (158)	
	Repeated	810 (124)	321
Phonological	Novel	1152 (152)	
	Repeated	979 (92)	173
Letter	Novel	1092 (151)	
	Repeated	985 (189)	107

Table 4
Regions of interest

Region[a]	Approximate gyral location	Atlas coordinates			Reference papers[b]
		x	y	z	
BA 45/47[c]	left (anterior) inferior frontal gyrus	−45	35	−4	1, 2, 3, 4, 5
BA 44[c]	left (posterior) inferior frontal gyrus	−47	17	24	4, 5
BA 21[d]	left middle temporal gyrus	−51	−55	2	2, 6, 7
BA 6[e]	left precentral gyrus	−55	−1	28	4, 6, 8, 9
BA 40[e]	left supramarginal gyrus	−41	−43	34	8, 6, 9, 10

[a]Regions are named based on their approximate Brodmann Area (BA) in the Talairach and Tournoux (1988) atlas. Region labels should be considered approximate.
[b]Selected reference papers that motivate interest in the regions: (1) Petersen et al. (1989); (2) Raichle et al. (1994); (3) Buckner et al. (1995); (4) Poldrack et al. (1999); (5) Wagner et al. (2000); (6) Gold and Buckner (2002); (7) Vandenberghe et al. (1996); (8) Jonides et al. (1998); (9) Paulesu et al. (1993); (10) Awh et al. (1996). See text for further discussion and additional references.
[c]Predicted to be involved in controlled processing in both semantic and phonological domains.
[d]Predicted to be involved in controlled semantic processing.
[e]Predicted to be involved in controlled phonological processing.

The two central issues explored in this study concerned (i) the degrees of response of specific brain regions during semantic and phonological processing associated with novel processing (task effects) and (ii) the degrees of response change in these regions associated with repeated processing across different tasks (relative adaptation effects: task × adaptation interactions). Semantic and phonological response patterns were contrasted with a letter processing task to control for orthographic processing and re-processing. Figure 1 plots representations of five a priori defined ROIs and corresponding fMRI response associated with semantic, phonological and letter tasks. The top panel (ROI Task Effects) displays task responses under novel processing conditions compared with a fixation (+) baseline. The bottom panel (ROI Adaptation Effects) displays task response changes associated with repeated processing compared with novel processing (novel – fixation) – (repeated – fixation). In order to correct for multiple comparisons across the five ROIs, a family-wise alpha threshold of $P < 0.01$ was adopted. Task effects are reported first below. As expected, all regions showed significant main effects of adaptation ($P < 0.001$). Most regions also showed significant within-task adaptation effects (as indicated in Fig. 1). Therefore, following description of task effects, we report relative adaptation effects (task × adaptation interactions).

aLIPC (~BA 45/47) showed an effect of task [$F(2,54) = 22.8$ $P < 0.0001$]. As can be seen in the top panel of Figure 1, BA 45/47 showed significantly greater activation during the semantic task than the phonological [$t(27) = 4.38$, $P < 0.001$] or letter [$t(27) = 5.6$, $P < 0.001$] tasks. Importantly, however, BA 45/47 also showed significantly greater activation during the phonological task than the letter task [$t(27) = 3.1$, $P < 0.01$], demonstrating significant response during controlled phonological processing. Relative adaptation effects in BA 45/47 were significantly different between tasks [$F(2,54) = 17.0$ $P < 0.0001$]. As can be seen in the bottom panel of Figure 1, BA 45/47 showed significantly greater adaptation in the semantic task than the phonological [$t(27) = 3.4$, $P < 0.01$] or letter [$t(27) = 4.8$, $P < 0.001$] tasks. In addition, however, BA 45/47 showed significantly greater adaptation in the phonological than the letter task [$t(27) = 3.2$, $P < 0.01$], demonstrating significant modulation as a function of repeated phonological processing.

Previous research suggested differential involvement of two regions in posterior frontal cortex in controlled semantic and phonological processing: a LIPC region near pars opercularis (~BA 44) and a posterior frontal region near the precentral gyrus (~BA 6). Examination of the present data confirmed dissociable response patterns between BA 44 and BA 6 regions, both for task and relative adaptation effects. BA 44 showed relatively graded task activation, and relatively graded adaptation, similar to BA 45/47, whereas BA 6 showed a response pattern preferential for controlled phonology. BA 44 showed an effect of task [$F(2,54) = 28.8$ $P < 0.0001$]. BA 44 showed significantly greater activation during the semantic task than phonological [$t(27) = 3.7$, $P < 0.01$] and letter [$t(27) = 7.3$, $P < 0.001$] tasks, and showed a significantly greater activation in the phonological task than the letter task [$t(27) = 4.1$, $P < 0.001$]. BA 6 also showed a main effect of task [$F(2,54) = 9.2$ $P < 0.001$], but demonstrated significantly greater activation during the phonological than the semantic [$t(27) = 4.1$ $P < 0.001$]) or letter [$t(27) = 4.3$, $P < 0.001$]) tasks, but not during the semantic compared with the letter task ($P = 0.82$). The different task

activation patterns between BA 44 and BA 6 were supported by a significant region × task interaction [$F(2,54) = 9.5$ $P < 0.001$].

In terms of relative adaptation, effects in BA 44 were significantly different between tasks [$F(2,54) = 9.8$ $P < 0.001$]. There was a trend toward a difference in relative adaptation in BA 44 between the semantic and phonological tasks ($P = 0.05$). The relative adaptation in BA 44 was significantly greater in the semantic task than the letter task [$t(27) = 4.0$, $P < 0.001$] and significantly greater during the phonological than the letter task [$t(27) = 2.8$, $P < 0.01$]. By contrast, unlike the graded adaptation effects in BA 44, relative adaptation effects in BA 6 [$F(2,54) = 6.8$ $P < 0.01$] were significantly greater in the phonological task than the semantic [$t(27) = 4.4$ $P < 0.001$] or letter [$t(27) = 4.1$, $P < 0.001$] tasks and did not differ between the semantic and letter tasks ($P = 0.71$). The different patterns of relative adaptation between BA 44 and BA 6 regions were supported by a significant region × relative adaptation interaction [$F(2,54) = 13.7$ $P < 0.0001$].

Previous research also raised the possibility that different posterior regions co-activate with aLIPC depending upon whether controlled processing is semantic (~BA 21) or phonological (~BA 40). Examination of current activation patterns provided evidence for preferential semantic task and relative adaptation effects in a region in left posterior temporal cortex near the middle temporal gyrus (~BA 21), but not for preferential phonological effects in the specific a priori region near the left supramarginal gyrus (~BA 40). Although there was a phonological task effect in the a priori parietal region, there was strong activation in this region for all tasks. Moreover, there was no preferential adaptation effect in the a priori parietal region (~BA 40).

BA 21 showed an effect of task [$F(2,54) = 32.1$ $P < 0.0001$]. BA 21 activation was significantly greater during the semantic task than the phonological [$t(27) = 8.6$, $P < 0.0001$] and letter [$t(27) = 6.1$, $P < 0.0001$] tasks, and did not differ between phonological and letter tasks ($P = 0.55$). Relative adaptation effects in BA 21 were significantly different between tasks [$F(2,54) = 11.1$ $P < 0.0001$]. Relative adaptation in BA 21 was significantly greater during the semantic than phonological [$t(27) = 4.8$, $P < 0.0001$] and letter [$t(27) = 3.7$, $P < 0.001$] tasks, and did not differ between the phonological and letter tasks ($P = 0.33$).

An effect of task was also found in a region in inferior parietal cortex near the left supramarginal gyrus (~BA 40) [$F(2,54) = 9.3$ $P < 0.01$]. BA 40 showed significantly greater activation during the phonological task than the semantic [$t(27) = 2.7$, $P < 0.01$] and letter [$t(27) = 4.2$, $P < 001$] tasks. However, as can be seen in Figure 1, significant activation was found in BA 40 in all three tasks compared with fixation. Similarly, adaptation effects in BA 40 were significant for all tasks. Although relative differences in degree of adaptation effects in BA 40 between tasks approached the corrected threshold cutoff [$F(2,54) = 4.4$ $P = 0.02$], the trend was presumably carried by the relatively smaller adaptation effects in the letter task, as opposed to differences between phonological and semantic tasks, which were not significant [$t(27) = 0.86$, $P = 0.40$]. Thus, BA 40 failed to show the predicted preferential response for controlled phonological processing. However, whole-brain analyses did reveal preferential adaptation for phonological processing in a slightly more dorsal portion of left parietal cortex near the left supramarginal gyrus (~BA 40) (see below). Given this post-hoc finding and previous results, we suspect that a region near the left supramarginal gyrus (~BA 40) is preferential for phonological processing.
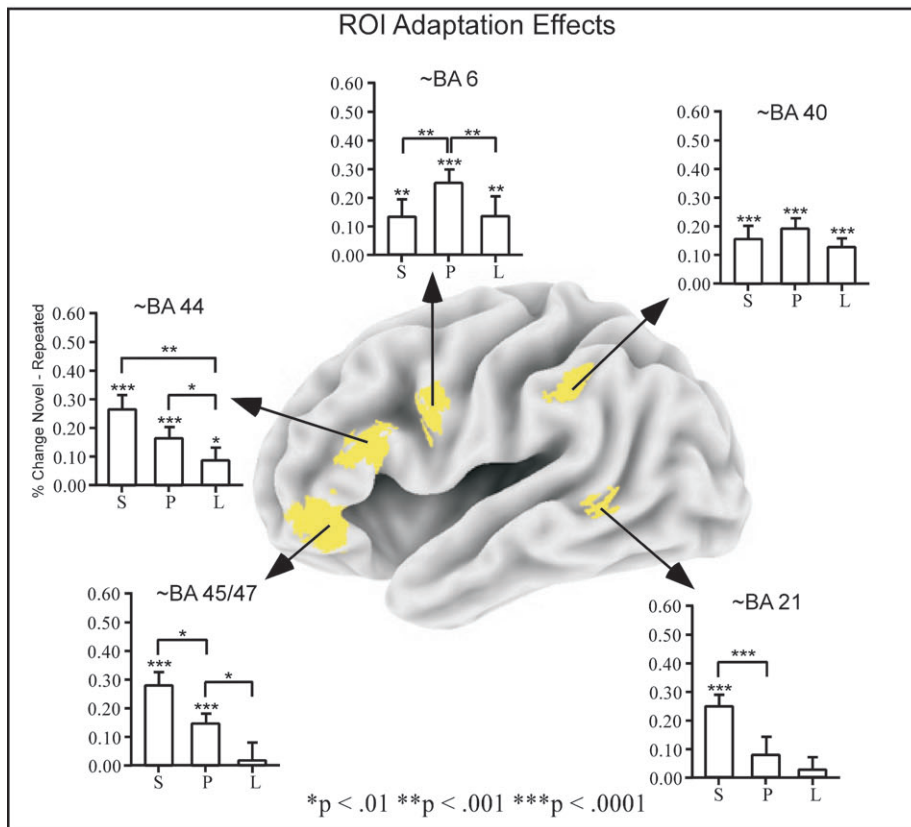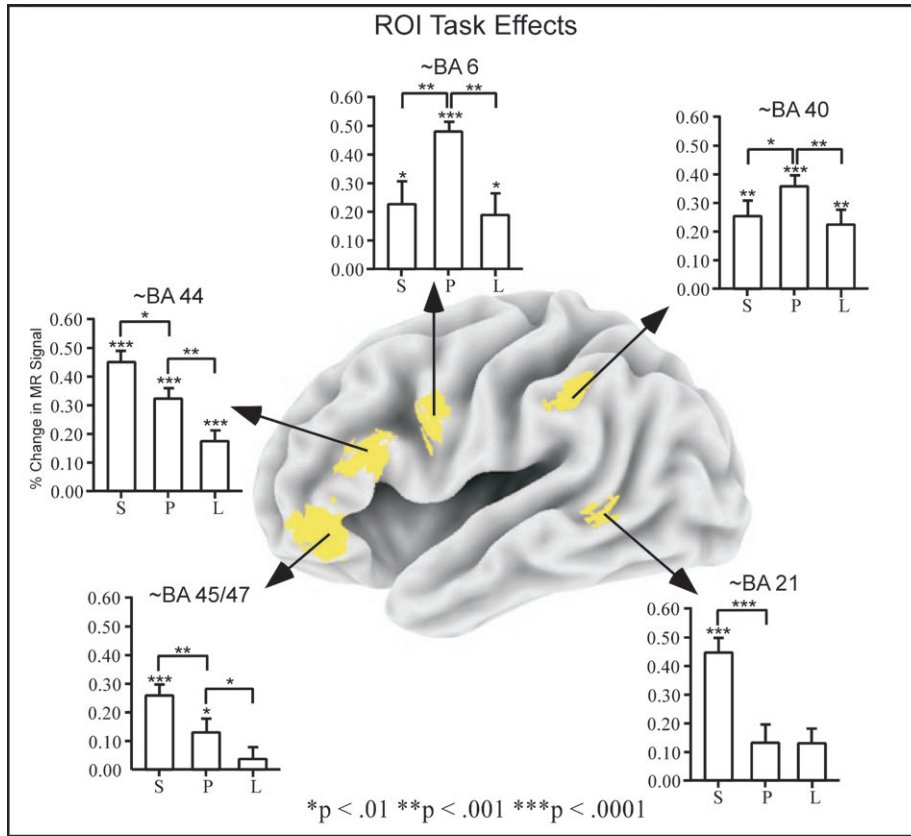
Figure 1. Task and adaptation effects in ROIs. Representations of a priori defined ROIs (in yellow) are overlaid on an averaged anatomic surface image of the lateral left hemisphere. Panels show task and adaptation effects as differences in MR signal amplitude (in percent) compared with fixation (+) baseline for semantic (S), phonological (P) and letter (L) tasks. Error bars show standard error of the mean. Asterisks denote significance levels for within-task effects relative to fixation baseline (above error bars) and between tasks (above horizontal bars). The top panel (ROI Task Effects) shows activations associated with each task, under novel processing conditions. The bottom panel (ROI Adaptation

However, because the post-hoc results may be in part due to thresholding effects, we restrict our interpretations about domain preferentiality to BA 6 and BA 21, which showed strong domain-preferential response patterns in a priori analyses, both for task and relative adaptation effects.

Whole-brain Exploratory Analyses

Results from a whole-brain analysis comparing both semantic and phonological task and adaptation effects are presented in Figure 2. Whole-brain analyses confirmed the pattern of tasks and relative adaptation effects found in ROI analyses. The top panel (Task Effects) displays the results of a comparison of semantic and phonological tasks with the baseline letter task, under novel item processing conditions, to identify common and dissociable response patterns after controlling for reductions associated with repeated letter processing. Portions of aLIPC (~BA 45/47) and pLIPC (~BA 44) showed significant activation in the controlled phonological task, in addition to the controlled semantic task. Thus, both BA 45/47 and BA 44 activated significantly under controlled phonological (novel) processing conditions. In addition, preferential activation for the controlled phonological task is seen in posterior left frontal cortex (~BA 6) and parietal cortex (~ BA 40), and preferential activation for the controlled semantic task is seen in left temporal cortex (~BA 21). Additional domain preferential effects not part of a priori hypotheses are seen for the phonological task in left inferior occipitotemporal cortex near the fusiform gyrus (BA 37/19). Additional domain preferential effects are seen for semantics in the left superior frontal gyrus (~BA 8) and in multiple foci in left middle and superior temporal cortex (~BA 21/22).

The middle panel of Figure 2 displays results from a direct comparison semantic and phonological tasks under novel processing conditions. A small portion of aLIPC (~BA 47) shows preferential activation for controlled semantic processing. In addition, preferential activation for the controlled semantic task is seen in left temporal cortex (~BA 21) and preferential activation for the controlled phonological task is seen in left posterior frontal cortex (~BA 6) and left parietal cortex (~BA 40). Additional domain preferential effects are seen for semantics in the left superior frontal gyrus (~BA 8) and in multiple foci in left middle and superior temporal cortex (~BA 21/22).

As noted, all regions showed significant effects of adaptation. The bottom panel of Figure 2 displays relative adaptation effects for semantic and phonological tasks compared with the letter processing task. A region in aLIPC (~BA 45/47) showed adaptation during both semantic and phonological processing. A similar pattern is evident in pLIPC (~BA 44), with a portion of activation overlapping semantic and phonological adaptation effects. We do not interpret the spatial extent of activations because thresholding can cause activations of greater magnitude to increase in extent. As predicted, preferential adaptation effects were observed outside prefrontal cortex: a region in left posterior temporal cortex (~BA 21) showed significant adapta-

tion effects during semantic processing, whereas regions in left posterior frontal cortex (~BA 6) and left parietal cortex (~ BA 40; slightly dorsal to the region examined in the ROI analysis; see above) showed significant adaptation effects during phonological processing. Additional domain preferential adaptation effects not part of a priori hypotheses are seen for phonological processing in left inferior occipitotemporal cortex near the fusiform gyrus (BA 37/19), while other additional domain preferential adaptation effects are seen for semantic processing in the left superior frontal gyrus (~BA 8) and in multiple foci in left middle and superior temporal cortex (~BA 21/22).

Discussion

Behavioral results demonstrated similar latencies for correct trials of the semantic and phonological tasks under novel processing conditions that were contrasted in fMRI task analyses. Robust behavioral priming was observed for both tasks, albeit of different magnitudes between tasks. Of importance to understanding the functional–anatomic organization of LIPC, aLIPC (~BA 45/47), a region linked consistently with controlled semantics, showed significant fMRI task and adaptation effects during phonological in addition to semantic processing. Similar results were found in pLIPC (~BA 44). Phonological-preferentiality was observed for task and adaptation effects in a left posterior frontal region (~BA 6), and semantic-preferentiality was observed for task and adaptation effects in a left temporal region (~BA 21). BA 40, a region implicated previously in phonological-preferential processing, showed an indication of phonological-preferentiality in several of the post-hoc analyses, but this were not supported by the a priori regional analyses and thus not discussed further. Taken together, these data demonstrate that aLIPC (~BA 45/47) and pLIPC (~BA 44) regions are involved in controlled processing across multiple language domains and that a functional subdivision between semantic and phonological processing exists outside left prefrontal cortex in specific left posterior frontal and temporal regions. In the discussion below, we elaborate on these findings.

fMRI Adaptation Effects in LIPC

An aLIPC region near pars triangularis/pars orbitalis (~BA 45/47) showed greatest task and adaptation effects during semantic processing, consistent with previous results (Raichle et al., 1994; Demb et al., 1995; Buckner et al., 2000; Wagner et al., 2000). Several early functional neuroimaging studies reported prominent activation of aLIPC during semantic tasks (Petersen et al., 1988, 1989; Démonet et al., 1992; Kapur et al., 1994; Buckner et al., 1995; Demb et al., 1995; Martin et al., 1995). A continued trend of activation of aLIPC during semantic tasks, compared with a range of comparison tasks, has served to confirm an important role for this region in some aspect of semantic processing (Gabrieli et al., 1996; Dapretto and Bookheimer, 1999; Poldrack et al., 1999; Bokde et al., 2001; Wagner et al., 2001; Gold and Buckner, 2002; McDermott et al, 2003).

Effects) shows degrees of change in activation associated with each task resulting from comparison of novel item processing (− fixation) − repeated item processing (− fixation). aLIPC (~BA 45/47; −45 35 −4) showed significant task and adaptation effects for both semantic and phonological tasks, with greatest effects for the semantic task. Dissociable effects were observed between a pLIPC region near the pars opercularis (~BA 44; −47 17 24), which showed significant task and adaptation effects for both semantic and phonological tasks (similar to ~BA 45/47), and a posterior left frontal region near the precentral gyrus (~BA 6; −55 −1 28), which showed significant task and adaptation effects for the phonological task compared with the letter task. Preferential effects were also observed in a left temporal region (~BA 21; −51 −55 2), which showed significant task and adaptation effects for the semantic task. Phonological adaptation effects in the a priori left parietal ROI (~BA 40; −41 −43 34) were not observed but preferential phonological effects were found in a slightly more dorsal portion of ~BA 40 in whole-brain analyses (see Fig. 2).
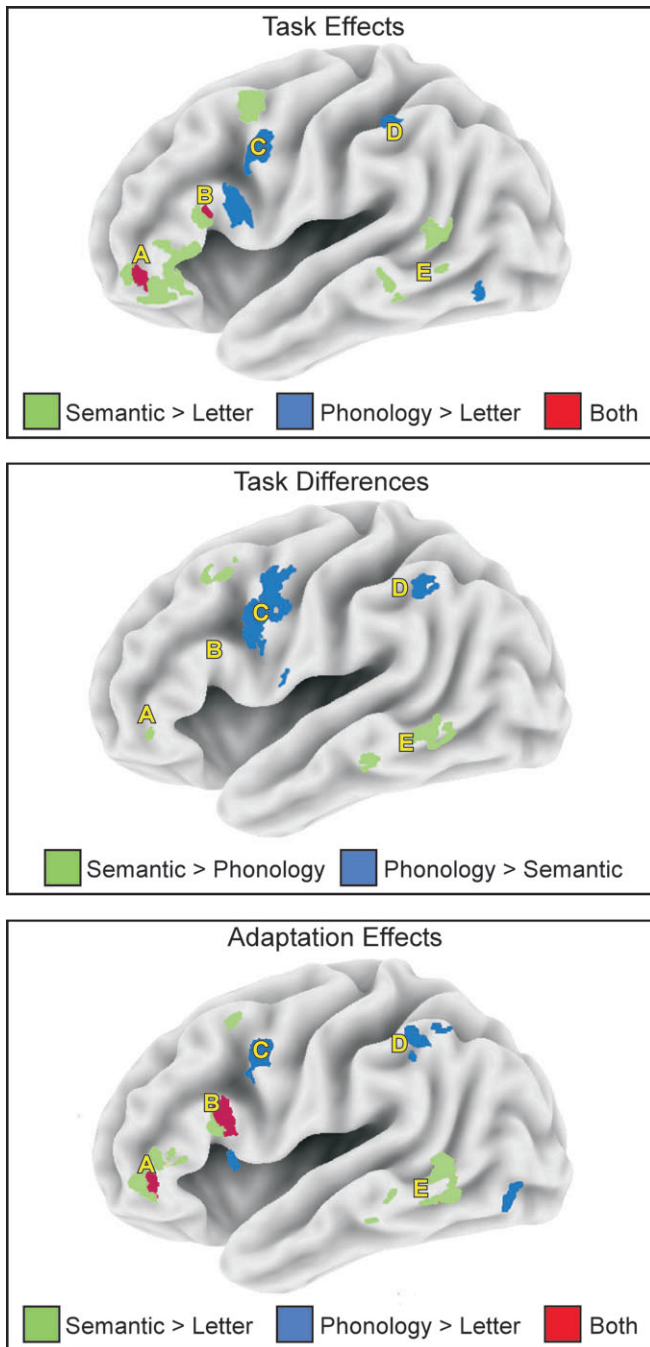
Figure 2. Task and adaptation effects at the whole-brain level. Maps plot *z*-values from a voxel-based, mixed effects analysis ($P < 0.001$), with subjects treated as a random effect. Maps are projected onto a semi-inflated surface of the lateral left hemisphere. Regions exhibiting activations preferential for controlled semantics (green), controlled phonology (blue) and common to both controlled semantic and phonological tasks (red) are displayed. The top panel (Task Effects) displays significant activations for controlled semantic and phonological tasks, compared with the letter task, under novel processing conditions. aLIPC (*A*; ~ BA 45/47) and pLIPC (*B*; ~ BA 44) regions showed overlapping activation patterns, with the most anatomically extensive activation for the semantic task. A region in left posterior frontal cortex (*C*; ~ BA 6) and a region in left parietal cortex (*D*; ~ BA 40) showed significant activation for phonological processing, whereas posterior temporal cortex (*E*; ~ BA 21) showed significant activation for semantic processing. The middle panel (Task Differences) displays results from a direct comparison of semantic and phonological tasks, under novel processing conditions. A small region in aLIPC (*A*; ~ BA 45/47) and a region in left posterior temporal cortex (*E*; ~ BA 21) showed significantly greater activation during controlled semantic processing than controlled phonological processing. A posterior left frontal region (*C*; ~ BA 6) and a region in left parietal cortex (*D*; ~ BA 40) showed

Although the precise contribution of aLIPC to semantic processing remains unknown, the region is thought to be important in controlled components of semantic processing associated with the strategic retrieval of meaning and/or working with and evaluating meaning (Petersen *et al.*, 1988, 1989; Kapur *et al.*, 1994; Buckner, 1996; Gabrieli *et al.*, 1996; Wagner *et al.*, 2001).

The consistency with which aLIPC has been reported to activate across a range of semantic tasks has raised the possibility that the region could be specialized for controlled semantic operations (Buckner, 1996; Gabrieli *et al.*, 1996; Fiez *et al.*, 1997; Poldrack *et al.*, 1999; Wagner *et al.*, 2000; Bokde *et al.*, 2001). However, Gold and Buckner (2002) demonstrated significantly greater activation in aLIPC during a controlled phonological task (mapping pseudoword sounds) than in a more automatic phonological condition (mapping word sounds). Moreover, the magnitude of the hemodynamic response in this region was negatively correlated with the consistency of the response across subjects (response consensus), suggesting a role with mapping relatively underconstrained stimulus-to-representation mappings across multiple language domains. Similarly, Clark and Wagner (2003) found significantly greater response in aLIPC during phonological processing of pseudowords compared with words, although aLIPC response demonstrated only partial correlation with subject response consensus in this study.

The present results expand upon such work by demonstrating that aLIPC is involved in controlled phonological processing of words in addition to pseudowords, and reduces its response significantly as phonological mappings become more automated through repetition. Such a view can accommodate the lack of prominent activation of aLIPC regions during tasks involving phonological processing of words (Rumsey *et al.*, 1997; Poldrack *et al.*, 1999; Bokde *et al.*, 2001; Otten and Rugg, 2001; Roskies *et al.*, 2001; McDermott *et al.*, 2003; but see Klein *et al.*, 1995; Devlin *et al.*, 2003). Many phonological tasks involving decisions about words place limited emphasis on controlled processing because the majority of word sounds are constrained by the quasi-regular spelling-to-sound correspondences of English (Plaut *et al.*, 1996). Thus, the reduced response observed in aLIPC following repeated regularization in the present study may represent an analog to the limited response of this region observed during the majority of phonological tasks employing words, which are based upon overlearned stimulus-to-representation mappings.

Given an established role of aLIPC in controlled semantic operations, its activation during the regularization task could be attributed to implicit semantic processing resulting from exposure to words, as opposed to controlled phonological processing. However, the available evidence argues strongly against this interpretation. First, previous behavioral research has found that the typical lexicality effect in naming (faster naming of words

significantly greater activation for controlled phonological processing than controlled semantic processing. The bottom panel (Adaptation Effects) displays significant adaptation effects associated with semantic and phonological tasks, compared with the letter task. aLIPC (*A*; ~ BA 45/47) and pLIPC (*B*; ~ BA 44) regions showed overlapping adaptation effects associated with semantic and phonological tasks, with the most anatomically extensive adaptation effects for the semantic task. A posterior left frontal region (*C*; ~ BA 6) and a left parietal region (*D*; ~ BA 40) showed significant adaptation associated with repeated phonological processing, whereas posterior left temporal cortex (*E*; ~ BA 21) showed adaptation for the semantic task. (See text for description of activations in other regions displayed in the figure.)

than pseudowords) was eliminated entirely under regularization conditions (Balota *et al.*, 2000). Specifically, facilitation in latency (76 ms) and accuracy (14%) were neutralized when subjects were asked to pronounce words using regular spelling-to-sound correspondences (1 ms and –2%, respectively). The neutralization of the typical lexicality effect suggests a minimizing of implicit lexicosemantic processing during word regularization. Second, our analyses were limited to correct trials. Implicit lexicosemantic processing should be minimal on these trials because such processing would lead to selection of the learned and, under regularization conditions, incorrect pronunciation. Third, the significant aLIPC response during regularization is not well explained by implicit lexicosemantic processing because aLIPC response was minimal in the baseline letter task, which also involved exposure to words. Finally, and more generally, the explanation that aLIPC activation associated with controlled phonological tasks is the result of implicit lexicosemantic processing, cannot account for previous results of significantly greater response in aLIPC during processing of pseudowords, which have no meaning, than words, which do have meaning (Gold and Buckner, 2002; Clark and Wagner, 2003).

How, then, is the observed pattern of response in aLIPC during the present regularization best explained? Leverage on this issue may be gained from the finding that the region showed significantly greater activation during regularization than letter processing under novel task conditions. In addition to orthographic processes, the first/last letter task likely involves relatively automated phonological processes associated with conversion of initial and final letters to phonemes and determination of responses on the basis of the overlearned alphabetic sound sequence. Such overlearned orthographic and phonological processing produced minimal activation of aLIPC compared with baseline fixation. The significantly greater activation of aLIPC during regularization compared with the letter task suggests that the region's contribution to phonological operations is associated with controlled processing encouraged by novel visual-to-sound mappings.

Our results also demonstrate that aLIPC responds most strongly during controlled processing within the semantic domain. Controlled processing encompasses a range of effortful cognitive operations including strategic retrieval of representations and/or working with and evaluating those representations. Controlled processing involves sequential steps, and has been shown to evolve more slowly than automatic processing (Neely, 1977; Schneider and Shiffrin, 1977). The regularization of words with irregular spelling-to-sound correspondences resulted in comparable average latency and lower accuracy than the semantic task under novel processing conditions. Yet, despite the fact that regularization emphasized controlled processing, activation in aLIPC was significantly greater in the semantic task. Similarly, fMRI adaptation effects in aLIPC paralleled the latency priming data, with greatest adaptation for repeated semantic processing, indicating a superior efficiency for aLIPC in establishing contingencies based upon semantic processing compared with other kinds of language processing. Thus, as a region capable of contributing resources to controlled processing operations in several language domains, aLIPC appears to contribute most strongly to controlled processing within the semantic domain. In a particularly elegant demonstration of this phenomenon, Wagner *et al.* (2001) showed that aLIPC activation increased as a function of the degree of controlled processing requirements associated with semantic decisions.

The Anterior–Posterior LIPC Semantic–Phonological Hypothesis

In one of the first functional neuroimaging studies employing both semantic and phonological tasks, Démonet *et al.* (1992) reported significant activation of aLIPC (~BA 45/47) only from a semantic-baseline comparison, and significantly greater activation of a more posterior region of LIPC (~BA 44), extending into the precentral gyrus (~BA 6), from a phonological-baseline comparison than a semantic-baseline comparison. A number of subsequent studies have observed a similar pattern of LIPC recruitment resulting from semantic–phonological comparisons (Buckner *et al.*, 1995; Poldrack *et al.*, 1999; Bokde *et al.*, 2001; Otten and Rugg, 2001; Roskies *et al.*, 2001; McDermott *et al.*, 2003). Such findings have led to suggestion of functional heterogeneity of LIPC based upon semantic–phonological domain lines, involving a specific functional segregation of aLIPC (~BA 45/47) from a posterior portion of LIPC/precentral gyrus (~BA 44/6) (Buckner *et al.*, 1995; Fiez, 1997; Poldrack *et al.*, 1999; Wagner *et al.*, 2000; Bokde *et al.*, 2001).

Our results from two studies comparing semantic and phonological tasks suggest revision of current semantic–phonological LIPC models. First, as discussed above, although aLIPC activates most strongly during controlled semantic tasks, it also activates significantly during controlled phonological tasks. Second, in terms of specific functional parcellation within LIPC, the large region often labeled posterior LIPC (~BA 44/6) appears to be functionally heterogeneous: the more anterior portion (~BA 44) shows a pattern of activation similar to aLIPC, contributing to controlled processing across multiple language domains, whereas the more posterior region outside prefrontal cortex, near the left precentral gyrus (~BA 6), shows strong preferentiality for controlled phonological processing. Finally, our results demonstrate a relative division of labor between semantic and phonological processes in regions posterior to LIPC (discussed below).

Task-preferential fMRI Adaptation Beyond LIPC

A left posterior temporal region near the middle temporal gyrus (~BA 21) showed robust task and adaptation effects during semantic processing. The semantic-preferential response pattern in left temporal cortex builds upon previous results reporting activation in this region across a number of tasks requiring meaning-based processing (Raichle *et al.*, 1994; Vandenberghe *et al.*, 1996; Binder *et al.*, 1997; Price *et al.*, 1997, 1999; Gold and Buckner, 2002). These functional neuroimaging data are broadly consistent with the neuropsychological record, which indicates that patients with temporal lobe lesions can exhibit deficits in the ability to appreciate the meanings of words and concepts (Kertesz, 1979; Naeser *et al.*, 1982; Goodglass and Kaplan, 1983). More specifically, extensive lesions of posterior portions of left temporal cortex can be associated with transcortical sensory aphasia (Damasio, 1981; Kertesz *et al.*, 1982), one of the classical aphasic syndromes involving impaired comprehension and fluent speech with semantic substitutions (Wernicke, 1874). In addition, damage of or near the left middle temporal gyrus is also associated with poor recovery of comprehension (Naeser *et al.*, 1987). Finally, semantic dementia involves a multi-modal, multi-domain breakdown of conceptual knowledge and begins with focal temporal lobe atrophy (e.g. Hodges *et al.*, 1992; Boxer *et al.*, 2003; Gold *et al.*, 2005).

Phonological-preferential task and adaptation effects were observed in a left posterior frontal region near the precentral gyrus (~BA 6). Activation of the precentral gyrus has been reported for tasks requiring verbal working memory, and the region is thought to participate in a phonological loop that supports rehearsal of phonological material within working memory (Paulesu *et al.*, 1993; Awh *et al.*, 1996; Jonides *et al.*, 1998). The present data provide further evidence that left posterior frontal cortex near the precentral gyrus is also involved in on-line computation of phonological codes (Zatorre *et al.*, 1992; Poldrack *et al.*, 1999; Gold and Buckner, 2002). In our previous work, we also reported additional preferential activation for controlled phonology in inferior parietal cortex near the supramarginal gyrus (~BA 40). In the present study, relative adaptation effects in this specific ROI were not significantly greater for the phonological than the semantic task. Whole-brain analyses did reveal significantly greater task and adaptation for phonological processing compared with semantic and letter tasks in a slightly more dorsal parietal region also near the supramarginal gyrus (~BA 40). However, further evaluation will be needed to establish whether this region shows a reliably preferential response for phonological processing compared with other language domains.

In summary, our results suggest a semantic–phonological gradient within left frontal cortex in which aLIPC (~BA 45/47) and pLIPC (~BA 44) contribute significantly to controlled processing within both semantic and phonological domains, and posterior left frontal cortex near the precentral gyrus (~BA 6) contributes preferentially to controlled phonological operations. Most importantly, results demonstrate that while aLIPC response is strongest during controlled semantic processing, the region contributes to controlled phonological processing of words and reduces its response as a correlate of behavioral facilitation in the phonological domain.

Notes

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