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Dissociable Controlled Retrieval and Generalized Selection Mechanisms in Ventrolateral Prefrontal Cortex

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Summary

How does ventrolateral prefrontal cortex (VLPFC) control mnemonic processing? Alternative models propose that VLPFC guides top-down (controlled) retrieval of knowledge from long-term stores or selects goal-relevant products of retrieval from among competitors. A paucity of evidence supports a retrieval/selection distinction, raising the possibility that these models reduce to a common mechanism. Here, four manipulations varied semantic control demands during fMRI: judgment specificity, cue-target-associative strength, competitor dominance, and number of competitors. Factor analysis revealed evidence for a meta-factor that accounted for common behavioral variance across manipulations and for functional variance in left mid-VLPFC. These data support a generalized control process that selects relevant knowledge from among competitors. By contrast, left anterior VLPFC and middle temporal cortex were sensitive to cue-target-associative strength, but not competition, consistent with a control process that retrieves knowledge stored in lateral temporal cortex. Distinct PFC mechanisms mediate top-down retrieval and postretrieval selection.

Introduction

Over a lifetime, humans accumulate knowledge about the world, including general facts, concepts, and word meanings. Making gainful use of this knowledge to comprehend stimuli and inform action in a variable environment requires a system for retrieving and selecting stored information as goals dictate (Miller and Cohen, 2001; Shimamura, 1995). Substantial evidence indicates that left ventrolateral prefrontal cortex (VLPFC) is critical for the performance of tasks that demand access to and evaluation of semantic knowledge (Demb et al., 1995; Devlin et al., 2003; Kapur et al., 1994; Köhler et al., 2004; Metzler, 2001; Noppeney and Price, 2004; Petersen et al., 1988; Poldrack et al., 1999; Sohn et al., 2003; Swick and Knight, 1996; Thompson-Schill et al., 1998; Wagner et al., 2001; Zhang et al., 2004), though the functional character and topographic organization of processing within left VLPFC remains highly controversial (Badre and Wagner, 2002; Dobbins and Wagner, 2005; Gold et al., 2005; Moss et al., 2005; Thompson-Schill, 2003). At the heart of the debate is whether left VLPFC mediates (1) the selection of goal-relevant knowledge over irrelevant competitors (Fletcher et al., 2000; Moss et al., 2005; Thompson-Schill et al., 1997, 1999), (2) the top-down activation (controlled retrieval) of semantic knowledge under situations in which bottom-up retrieval mechanisms fail to recover goal-relevant information (Bunge et al., 2005; Wagner et al., 2001), or (3) both selection and retrieval because these putatively distinct processes may reduce to a single, shared mechanism (Badre and Wagner, 2002). Here, we report behavioral and fMRI evidence supporting the existence of a generalized selection mechanism that accounts for behavioral variance under a variety of semantic processing contexts and that accounts for functional variance in left mid-VLPFC activation. We further report that this generalized selection mechanism is functionally and neuroanatomically distinct from a controlled retrieval process that depends on left anterior VLPFC and appears to activate stored semantic knowledge in left temporal cortex. As such, these data provide evidence for a mechanistic distinction between selection and retrieval with selection operating on active representations that emerge through bottom-up and top-down retrieval.

According to the selection hypothesis, left VLPFC control mechanisms are critical when a subset of knowledge that is task-relevant must be selected over a competing subset of irrelevant knowledge (Fletcher et al., 2000; Moss et al., 2005; Thompson-Schill et al., 1997, 1999). Hence, selection demands can be manipulated by requiring subjects to direct attention to a subset of cue-related knowledge. For example, when the similarity between stimuli must be judged along a specific semantic dimension (e.g., color or form), other semantic features of the stimuli are task-irrelevant and must be selected against in favor of the relevant feature. Left VLPFC activation is greater during performance of such feature-based judgments relative to global similarity judgments, for which selection demands are argued to be minimal because all features are relevant (Thompson-Schill et al., 1997). Selection demands also can be manipulated by varying the degree to which access to irrelevant and competitive information is facilitated. Thus, left VLPFC activation increases during picture naming when competing knowledge is primed—and thus competition is enhanced—and this is the case even when task demands

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putatively require minimal controlled retrieval (Moss et al., 2005). Likewise, activation increases in left VLPFC accompany other circumstances in which a primed feature of a stimulus becomes irrelevant upon repetition, thus increasing selection demands during repeated stimulus processing (Fletcher et al., 2000; Thompson-Schill et al., 1999). This pattern of PFC activation contrasts with across-feature priming reductions in left temporal cortices—structures thought to store long-term semantic knowledge and to mediate bottom-up retrieval (Thompson-Schill et al., 1999). These observations motivate the hypothesis that left VLPFC supports a postretrieval selection mechanism that operates on the products of bottom-up retrieval processes with selection demands increasing when multiple competing representations have been retrieved and when task-irrelevant representations are prepotent.

Alternatively, left VLPFC mechanisms have been hypothesized to directly support the top-down (controlled) retrieval of knowledge when bottom-up (automatic) processes are insufficient to retrieve task-relevant knowledge (Wagner et al., 2001). Controlled retrieval demands can be varied by manipulating the extent to which a cue is effective in eliciting retrieval of task-relevant information. For instance, greater left VLPFC activation is observed when the pre-experimental association between the retrieval cue and target knowledge is relatively weak compared to when a strong association exists (Bunge et al., 2005; Wagner et al., 2001). This is the case even within the context of a global-relatedness task in which selection demands may be minimal (Thompson-Schill et al., 1997). According to the retrieval perspective, top-down inputs from VLPFC trigger the recovery of long-term knowledge and, thus, should have a correlated activation increase in left temporal regions that store semantic knowledge. It is important to note, however, that a manipulation of associative strength may also result in increased selection demands because weak activation of relevant information may make this knowledge more susceptible to interference, a case similar to an underdetermined response (Thompson-Schill et al., 2005).

Given these competing models of VLPFC function, a critical challenge for theorists of cognitive control is to specify the relation between selection and controlled retrieval. One possibility is that a common process biases retrieval under any circumstance in which relevant knowledge does not come to mind automatically, either because of poor cue support (e.g., weak cue-target associative strength) or to competition from automatically retrieved, irrelevant competitors (Badre and Wagner, 2002). Alternatively, controlled retrieval and selection may be mechanistically and anatomically distinct processes mediated by left VLPFC (Dobbins and Wagner, 2005; Martin and Chao, 2001) with the former guiding retrieval of knowledge stored in temporal cortex and the latter operating on the products of retrieval to select relevant representations from among competitors. This latter possibility receives indirect support because studies putatively varying selection demands have typically identified activation in left mid-VLPFC (~Brodmann areas [BA] 45/44), whereas those putatively varying controlled retrieval have localized activation in a more anterior and ventral region of left VLPFC (~BA 47). However, at present, direct evidence for a functional anatomic dissociation between selection and retrieval is lacking. Moreover, a clear mechanistic distinction between these two processes has not been articulated nor empirically supported. These limits partly stem from the fact that, to date, no study has directly manipulated both selection and controlled retrieval demands and because of the exclusive reliance upon theoretical task analyses to support past inferences about the processes correlated with VLPFC activation.

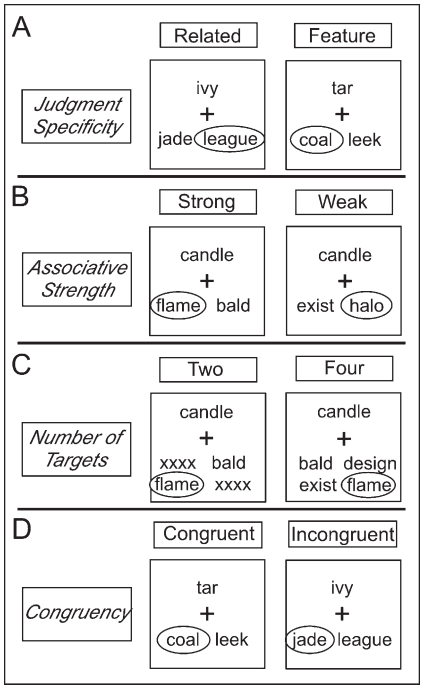

Figure 1. Task Schematic Depicting Four Manipulations of Control at Retrieval

In all trials, subjects selected a target (below fixation) based on its relation to the cue (above fixation). (A) Judgment specificity was manipulated by either requiring selection of the target most globally related to the cue (left) or most similar to the cue along a specific semantic feature (right), such as color in this example. (B) Within related blocks, associative strength manipulated whether the correct target was a strong (left) or weak (right) associate of the cue. (C) In experiment two, the number of targets during related blocks varied between two (left) or four (right). (D) Within the feature task, a trial was congruent (left) if the correct target was also a pre-experimental associate of the cue and incongruent (right) if the correct target was not the pre-experimental associate.

The present functional MRI (fMRI) study directly examined the functional and neuroanatomic relation between selection and controlled retrieval, combining four manipulations of control demands across two experiments (Figure 1). In both experiments, *judgment specificity* (Figure 1A) varied whether subjects selected a target based on its global relatedness to a cue (*related*; low selection) or its similarity to a cue along a specific dimension (*feature*; high selection). Within the related task, *associative strength* (Figure 1B) varied whether the correct target was a *strong* (low controlled retrieval; potentially low selection) or *weak* (high controlled re-

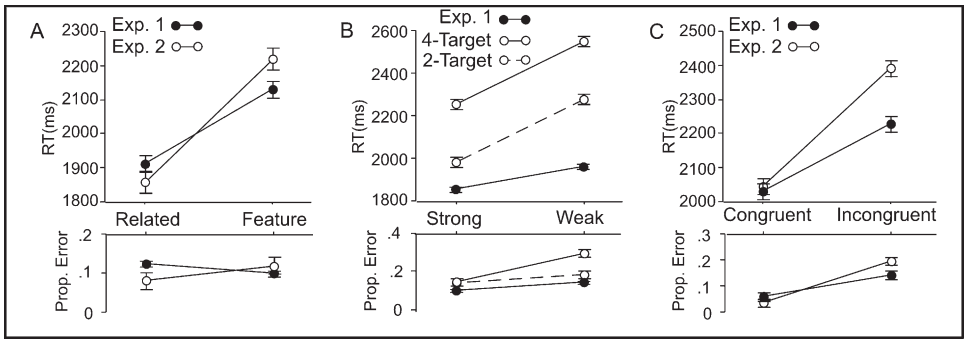

Figure 2. Behavioral Results from Experiments One and Two

Impact on RT and errors of (A) judgment specificity, (B) associative strength and number of targets (four targets, solid line; two targets, dashed line), and (C) congruency in experiment one (solid circles) and experiment two (open circles). In all figures, error bars reflect within-subject standard error.

trieval; potentially high selection) associate of the cue. During experiment two, *number of targets* varied whether the correct target was selected from amongst *two* or *four* alternatives, providing an additional manipulation of retrieval (be it automatic or controlled) and selection demands (Figure 1C). Finally, during the feature task, one of the targets was a normative associate of the cue (e.g., TAR → COAL), and *congruency* varied whether this associate was the target most similar to the cue along the relevant dimension (*congruent*) or was the competing distractor (*incongruent*) (Figure 1D). Selection demands were greater during incongruent trials as information retrieved automatically because of the associative linkage between the cue and distractor was irrelevant, yielding greater competition.

As suggested by the preceding task analyses, a common processing component—such as selection—may be engaged across the experimental manipulations. To the extent that this is the case, one might expect such a factor to account for a common portion of behavioral variance across the experimental manipulations. Accordingly, to quantify and assess the possible contribution of such a common control process across these semantic processing contexts, an exploratory factor analysis of behavior was performed to extract a metavariable that accounted for common behavioral variance across the manipulations. This metavariable, which emerged from the data rather than from theoretical task analyses, then served as a covariate during fMRI analysis to examine whether it accounted for functional variance within VLPFC.

Results

Simple Behavioral Effects

Behavioral effects were considered reliable at an α of .05 (see Supplemental Data available with this article online for details). Analyses of reaction time (RT) and errors confirmed the efficacy of the four control manipulations. Judgment specificity reliably impacted RT: feature judgments took longer than relatedness judgments (Figure 2A), indicating that RT slowed as putative selection demands increased. Weak cue-target associative strength resulted in longer RT and higher errors compared to strong associative strength, consistent with an increase in control demands (Figure 2B). Number of targets revealed that selecting from among four targets slowed RT and increased errors relative to selecting from two targets (Figure 2B). Importantly, there was no behavioral difference between weak-two versus strong-four trials, motivating an analysis to rule out time-on-task accounts of the fMRI data. Finally, the congruency manipulation impacted selection demands, evidenced by longer RT and higher errors on incongruent relative to congruent trials (Figure 2C).

Factor Analysis of Behavior

Factors extracted from a factor analysis can serve as metavariables that account for more total variance across behavioral measures than any of the measures contribute in isolation. In the current context, a component that accounts for variance across the experimental manipulations might reflect the influence of a common control process. Accordingly, factors were extracted from the standardized differences in errors and RT due to associative strength (weak–strong), judgment specificity (feature-related), and congruency (incongruent-congruent) for subjects in experiment one and experiment two (total n = 33). Number of targets was not included in this analysis as it only varied in experiment two.

Factor analysis revealed two factors that accounted for over half (54%) the variance in the six behavioral measures (Figure 3A). Loadings of the six individual measures on the first factor revealed a common component accounting for variance due to congruency, judgment specificity, and associative strength (Figures 3B and 3C and Table 1). Based on this metavariable's pattern of loadings—particularly noting the strong association with congruency—we suggestively refer to it as the "selection component." Congruency loaded heavily and almost exclusively on the selection component (Figures 3B and 3C) with this factor accounting for 51% and 71% of the variance in the congruency RT and error effects, respectively. Critically, manipulations of associative strength and judgment specificity also produced behavioral effects that loaded on the selection component (Figures 3B and 3C and Table 1).

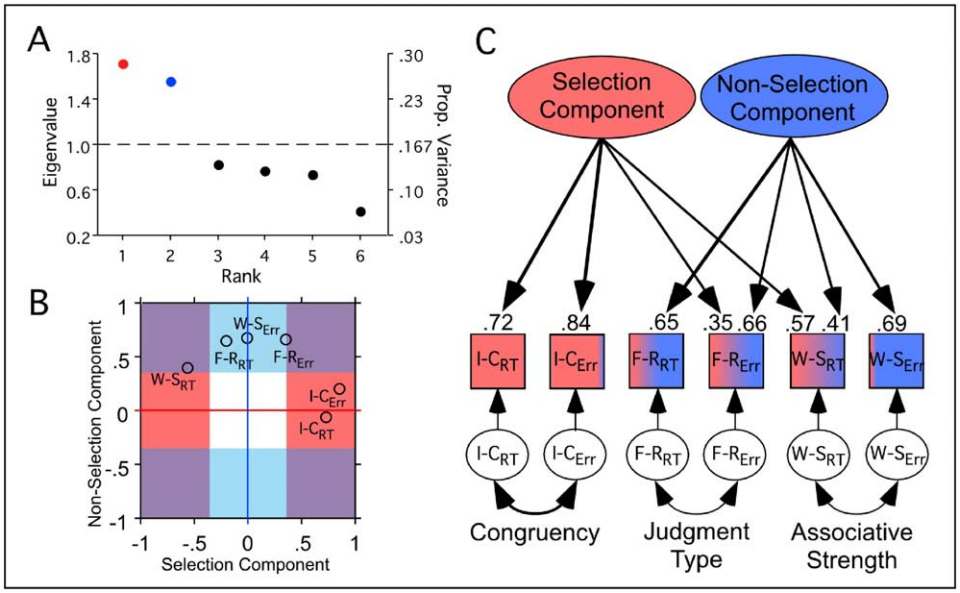

Figure 3. Results from the Factor Analysis

(A) The scree plot depicts the six initial unrotated factors ("selection component," red; "nonselection component," blue) including rank (x axis), eigenvalue (left y axis), and proportion of overall variance accounted for by each factor (right y axis).

(B) Spatial representation of the factor loadings of the six behavioral measures (points) plotted in a space defined on the selection component (x axis) and nonselection component (y axis). The further along a given axis a point is from the origin, the stronger its relationship with that component. Points in the red zone may be considered strongly related to the selection component and points in the blue zone are strongly related to the nonselection component.

(C) Diagram depicting the mapping of the two components (ovals) onto the variances (boxes) associated with each measure. Numbers represent factor loadings, curved arrows connect correlated factors, and colored shading represents the proportion of explained variance accounted for by the selection component (red) and nonselection component (blue). Together, (B) and (C) illustrate that the selection component is shared across all three manipulations of control. (Note: F-R, feature-related; I-C, incongruent-congruent; W-S, weak-strong; RT, reaction time; Err, errors.)

By contrast, the second factor ("nonselection component") accounted for variance in RT and error effects of associative strength and judgment specificity but accounted for practically no variance due to congruency (Figures 3B and 3C and Table 1). Hence, only the selection component indexed behavioral variance common to all three control manipulations, whereas the nonselection component, though accounting for variance common to associative strength and judgment specificity, was not associated with congruency and, thus, does not likely reflect a source of variance due to selection demands.

Correlates of Semantic Processing

Relative to fixation, semantic processing (collapsed across condition and restricted to accurate responses) elicited activation throughout left VLPFC, as well as in posterior cortices (Figure 4A). Within left VLPFC, activation extended from a posterior region (~BA 44/6) to a more anterior mid-VLPFC region (~BA 45), corresponding to inferior frontal gyrus pars opercularis and pars triangularis (Figure 4B), and also to an anterior and ventral VLPFC region (~BA 47), corresponding to inferior frontal gyrus pars orbitalis (Figure 4B).

It should be noted that the anterior and mid-VLPFC subregions defined here correspond to a division of what has been previously termed anterior left inferior prefrontal cortex (aLIPC). As noted above, these subregions correspond to existing anatomical and approximate cytoarchitechtonic subdivisions of the inferior frontal gyrus and may be largely distinguished in anterior slices based on their relationship to the horizontal ramus of the lateral fissure (Figure 4B). In part, this finer fractionation has been adopted in light of recent obser-

Table 1. Percentage of Variance in Each Behavioral Measure Accounted for by the Two Extracted Components

Measure	Selection Component	Nonselection Component	Total
Congruency RT	51.3	0.3	51.5
Congruency errors	70.7	4.6	75.3
Judgment type RT	4.3	42.5	46.8
Judgment type errors	12.3	43.8	56.1
Associative strength RT	32.6	16.7	49.3
Associative strength errors	0.0	47.2	47.2

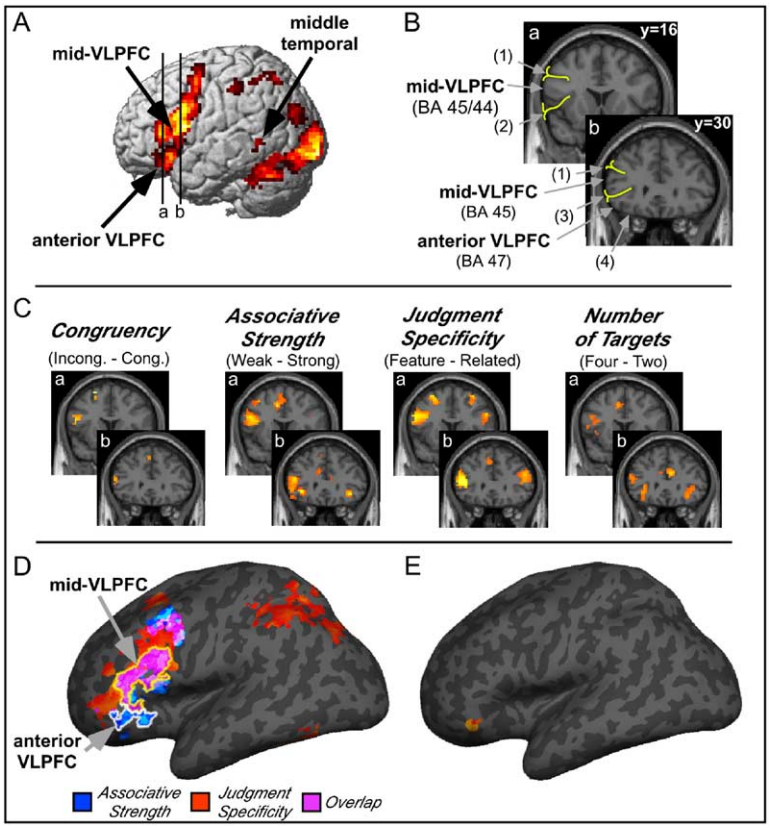

Figure 4. Left VLPFC Responses to Control Demands

(A) Surface rendered conjunction of all control conditions > fixation for the first and second epochs of experiment two with critical regions labeled.

(B) Coronal slices (y = 16 and y = 30) demarcating the anatomical boundaries by which activation foci were assigned to mid-VLPFC (inferior frontal gyrus pars triangularis and pars opercularis) or anterior VLPFC (inferior frontal gyrus pars orbitalis). Labeled anatomical landmarks are (1) inferior frontal sulcus, (2) insular sulcus, (3) horizontal ramus of the lateral fissure, and (4) orbital gyrus.

(C) Contrasts of congruency (conjunction of experiment one and experiment two, $p < 0.001$), associative strength (experiment two, $p < 0.001$), judgment specificity (conjunction of experiment one and experiment two, $p < 0.001$), and number of targets (experiment two, $p < 0.005$). The cross-experiment conjunction of associative strength was not calculated because differences in associative strength between experiments were not comparable (see Experimental Procedures).

(D) Contrasts of associative strength (blue) and judgment specificity (red) and their overlap (purple) are rendered on an inflated MNI canonical surface. Substantial anatomical and functional separability is observed between anterior VLPFC, which was selectively sensitive to associative strength, and mid-VLPFC, which was sensitive to associative strength and judgment specificity. Moreover, the effect of congruency (not plotted for ease of viewing) overlapped with those of associative strength and judgment specificity in mid-VLPFC (see C).

(E) Rendering of the weak-two > strong-four convergence map between experiment two from the present study and the corresponding contrast from a previous experiment (Wagner et al., 2001) revealed an effect restricted to the ventral anterior extent of left VLPFC.

vations (Badre and Wagner, 2005; Dobbins and Wagner, 2005) suggesting functional distinctions among these subregions. Posterior VLPFC corresponds to what has been previously referred to as posterior LIPC (pLIPC).

Beyond PFC, activation was evident in left middle temporal cortex (~BA 21/22), a region previously associated with semantic retrieval (Bokde et al., 2001; Dobbins and Wagner, 2005; Martin et al., 1994; Petersen et al., 1988; Wagner et al., 2001) and that functionally couples with left anterior VLPFC (Bokde et al., 2001; Dobbins and Wagner, 2005). Given the present focus on selection and controlled semantic retrieval, subsequent analyses focused on responses in left VLPFC and middle temporal cortex.

Neural Effects of Congruency

The congruency manipulation loaded most specifically on the selection component metavariable. Hence, this control manipulation putatively provides a relatively pure starting point for indexing the neural substrates of a generalized selection process. In experiment one, an incongruent > congruent effect was observed in left fronto-operculum ($p < 0.05$, corrected) with greater activation on incongruent trials also present in left mid-VLPFC (–54 15 18) at an uncorrected threshold ($p < 0.001$). Replicating this mid-VLPFC effect, comparison of incongruent > congruent feature trials in experiment two ($p < 0.05$, corrected) revealed reliable activation in left mid-VLPFC (–45 18 24) that extended posteriorly (–45 9 27). A formal test of the convergence of the congruency effects across experiments one and two revealed activation in left mid-VLPFC (–48 18 18), posterior (–42 9 21) and dorsal, anterior (–45 39 3) VLPFC subregions (Figure 4C), and bilateral fronto-operculum (Table S1).

Neural Effects of Judgment Specificity, Associative Strength, and Number of Targets

The selection component also accounted for a portion of the behavioral variance due to judgment specificity and associative strength, suggesting a common source of variance between these control manipulations and the congruency manipulation. This factor analysis outcome predicts a convergence in the patterns of left VLPFC activation engaged by these control manipulations. Consistent with this perspective, contrasts of associative strength (weak > strong) and judgment specificity (feature > related) revealed activation in left mid-VLPFC ($p < 0.05$, corrected) inclusive of the voxels showing a congruency effect (Figure 4C; Table S1). Direct overlap of the judgment specificity and associative strength contrast maps revealed extensive convergence in their engagement of left mid-VLPFC (~BA 45) extending into posterior VLPFC (Figure 4D, purple re-

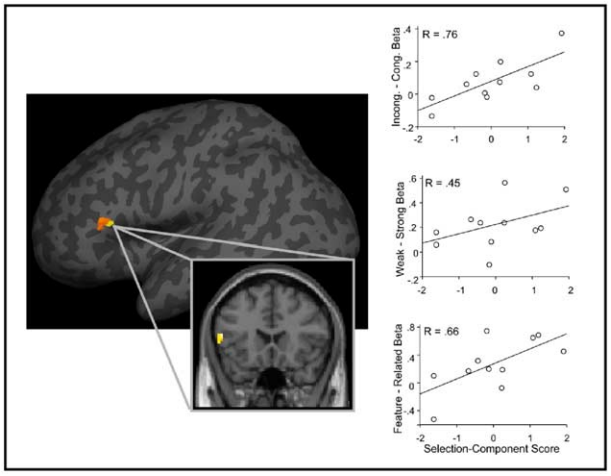

Figure 5. The Selection Component Accounted for Variance in Left Mid-VLPFC Functional Activation

The factor analysis metavariable served as a covariate during fMRI analyses of congruency, associative strength, and judgment specificity. Conjunction of these covariate effects (conjoint $p < 0.000125$) revealed that the selection component reliably accounted for function variance in left mid-VLPFC activation (–54 21 12), here rendered on an inflated canonical surface. Also, plotted are beta values extracted from left mid-VLPFC (y axis) against the selection component factor score (x axis) for congruency, associative strength, and judgment specificity manipulations.

gion). Given this high overlap, it is notable that the most anterior and ventral extent of left VLPFC (–51 27 –3 and –48 30 –12), corresponding to the inferior frontal gyrus pars orbitalis (~BA 47), appeared selectively sensitive to associative strength (Figure 4D, blue region), a finding to which we return below.

The number of targets manipulation (four > two) in experiment two revealed no reliable activation in left VLPFC at the corrected threshold. At a moderately reduced threshold ($p < 0.005$, uncorrected), activation was observed in left posterior (–45 12 27) and mid-VLPFC (–51 27 15) (Figure 4C), replicating number of targets effects identified in a prior experiment (Wagner et al., 2001) (–39 6 24 and –45 27 9). Importantly, localization of these effects converged with the mid-VLPFC activation common to the congruency, judgment specificity, and associative strength contrasts (Figure 4C).

Mid-VLPFC and the Selection Component

The three manipulations included behaviorally in the factor analysis resulted in functional effects within left VLPFC with overlapping activation in mid- to posterior VLPFC (Figure 4). This finding raises the possibility that this region supports a common control process that may be indexed by the selection component metavariable. To test this hypothesis, we correlated the fMRI indices of each control manipulation with the factor scores derived from the two extracted components. Specifically, a conjunction analysis was conducted to test for the convergence of regions showing a correlation between the selection component and the associated neural effects of congruency, associative strength, and judgment specificity. Significance was assessed at a conservative threshold (conjoint $\alpha = 0.000125$), providing confidence in rejection of the conjunction null (Nichols et al., 2005). Strikingly, this analysis implicated left mid-VLPFC (–54 21 12) as the only convergent site at which all control contrasts were correlated with the selection component (Figure 5). This novel analysis strongly implicates neural processes in left mid-VLPFC as coupled with the common variance in behavior indexed by the selection component. The nonselection component did not correlate with functional variance at standard thresholds (but see Supplemental Data).

Anterior VLPFC and Controlled Semantic Retrieval

In contrast to left mid-VLPFC, which was engaged across all control manipulations and was associated with the selection component, an anterior and ventral focus in left VLPFC was specifically sensitive to associative strength (Figures 4C and 4D). Moreover, the contrast of weak-two > strong-four trials, which is behaviorally matched for time on task, revealed differential activation restricted precisely to this anterior and ventral locus of left VLPFC (–45 27 –15) with this pattern converging with that seen in a prior study of controlled semantic retrieval (Figure 4E) (Wagner et al., 2001).

The selective nature of the response in the ventral anterior extent of left VLPFC was confirmed by ROI analyses (Figure 6). Specifically, the ventral anterior extent of left VLPFC (–45 27 –15) revealed a robust effect of associative strength ($F[1,10] = 20.1$, $p < 0.005$) but did not show reliable effects of judgment specificity ($F[1,10] = 2.5$, $p = 0.14$), congruency ($F[1,10] = 2.1$, $p = 0.18$), nor number of targets ($F[1,10] = 0.11$, $p = 0.75$). This pattern qualitatively differed from that in left mid-VLPFC (–51 15 33), which showed effects of all four manipulations, as evident in a Manipulation (associative strength, number of targets, judgment specificity, congruency) × region (anterior VLPFC, mid-VLPFC) interaction ($F[3,30] = 5.0$, $p < 0.01$). This outcome strongly supports an anatomical and functional delineation between controlled retrieval and selection.

Middle Temporal Cortex and Semantic Retrieval

Semantic processing elicited activation in a left middle temporal region (Figure 4A) previously implicated in studies of semantic retrieval. Given the distinct predictions made by the selection and controlled retrieval hypotheses regarding activation in regions thought to store long-term semantic knowledge, ROI analyses assessed the sensitivity of left middle temporal cortex (–48 –48 3) to the four control manipulations (Figure 6). There were two important findings. First, left middle

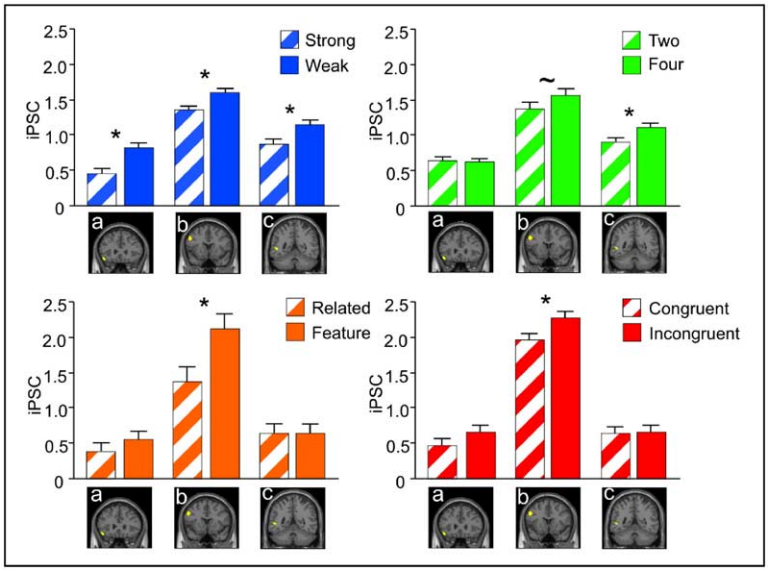

Figure 6. Integrated Percent Signal Change Data from ROI Analyses

Analysis of ROIs in (1) anterior VLPFC (–54 27 –9), (2) posterior/mid-VLPFC (–51 15 33), and (3) middle temporal cortex (–48 –48 3) reveal the sensitivity of each region to associative strength (top left), number of targets (top right), judgment specificity (bottom left), and congruency (bottom right) manipulations. Anterior VLPFC showed selective sensitivity to associative strength, middle temporal cortex showed sensitivity to associative strength and number of targets, whereas mid-VLPFC that was sensitive to all control manipulations. Note: asterisk represents $p < 0.05$; tilde, $p = 0.1$.

temporal cortex was sensitive to the two manipulations that putatively varied the amount of semantic knowledge retrieved (associative strength: $F[1,10] = 13.3$, $p < 0.005$; number of targets: $F[1,10] = 11.9$, $p < 0.01$). Semantic retrieval demands putatively increase across weak versus strong cue-target associative strength trials because during weak trials, additional knowledge, above and beyond that emerging through automatic retrieval processes, must be recovered in a top-down manner to guide the decision. Semantic retrieval is also greater when there are four versus two targets because semantic knowledge is recovered about more stimuli in the former case. In this instance, the differential semantic retrieval may emerge from bottom-up (automatic) processes, as argued by others (Thompson-Schill et al., 1997), thus resulting in an effect of number of targets in middle temporal cortex but not in left anterior VLPFC. Consistent with this perspective, left anterior VLPFC and middle temporal ROIs functionally dissociated across the two retrieval manipulations, as evidenced by a manipulation (associative strength, number of targets) × region interaction ($F[1,10] = 10.7$, $p < 0.001$).

Second, whereas left middle temporal cortex was sensitive to semantic retrieval, it was insensitive to judgment specificity and congruency (Fs < 1), providing evidence that the selection processes subserved by left mid-VLPFC operate postretrieval. Importantly, the pattern of left middle temporal activation, which may mark semantic retrieval, dissociated from that in left mid-VLPFC, which putatively marks selection, as evidenced by a manipulation (associative strength, number of targets, judgment specificity, congruency) × region interaction ($F[3,30] = 9.4$, $p < 0.0005$) and by a selection demands (judgment specificity, congruency) × region interaction ($F[1,10] = 7.8$, $p < 0.05$).

Discussion

The present data indicate that controlled retrieval and selection processes make distinct contributions to the regulation of memory and are mediated by anatomically separable subregions of left VLPFC. As such, these data offer resolution to the debate over left VLPFC function and advance mechanistic understanding of the relation between top-down retrieval and selection. Two central findings warrant attention.

First, our data provide evidence for a general selection process that operates across multiple semantic control conditions and is mediated by left mid-VLPFC. Process commonality was initially established through detection of functional overlap in left mid-VLPFC (~BA 45) across the four control manipulations, consistent with theoretical task analyses suggesting that each manipulation varied selection demands. Process commonality was further established through identification of a metavariable that accounted for behavioral variance common to three of the control manipulations. Strikingly, the variance in this metavariable correlated with variance in left mid-VLPFC activation.

Second, left anterior VLPFC (~BA 47) was exclusively engaged in response to increased demands on the top-down retrieval of semantic knowledge, rather than postretrieval selection. That is, left anterior VLPFC was selectively sensitive to cue-target associative strength, with this functional pattern dissociating from that in left mid-VLPFC, thus suggesting a role in activating long-term knowledge rather than resolving competition. This interpretation garners further support when considering the pattern of activation in left middle temporal cortex, a region that stores semantic knowledge and, thus, was expected to be sensitive to amount of semantic retrieval, be it knowledge accessed via controlled retrieval (indexed by associative strength) and via more automatic retrieval routes (indexed by number of targets). Importantly, left middle temporal activation varied with associative strength and number of targets but showed little sensitivity to selection demands (congruency and task specificity).

Collectively, these findings motivate a two-process model of fronto-temporal control of semantic memory.

Retrieval of semantic knowledge stored in lateral temporal cortex may emerge through bottom-up (automatic) and/or top-down (controlled) mechanisms, with the latter mediated by left anterior VLPFC. As knowledge is retrieved, selection of task-relevant representations from among retrieved competitors is required, with selection being mediated by left mid-VLPFC. Although the present data support this two-process model, it is important to note that the control of semantic memory is likely dynamic, such that selection operations may begin to be engaged even prior to completion of the retrieval stage (i.e., processing is likely to be parallel, rather than strongly serial).

Postretrieval Selection

The demand to select task-relevant representations from retrieved alternatives may be common to many contexts. Because stimuli are capable of automatically cueing more than one associate, any retrieval act holds the possibility of some competition from irrelevant, retrieved information (Anderson and Spellman, 1995; Badre and Wagner, 2002). Indeed, even the manipulation of associative strength, which we previously argued to impact controlled retrieval demands without consequences for selection (Wagner et al., 2001), can also result in variable competition because of the presence of irrelevant competitors or an "underdetermined response" on weak trials (Kan and Thompson-Schill, 2004; Thompson-Schill et al., 2005). Consistent with this perspective, increased semantic retrieval because of top-down (associative strength) or more automatic (number of targets) processes served to upregulate demands on left mid-VLPFC.

In contrast to left middle temporal cortex, however, upregulation of left mid-VLPFC activation did not simply track the amount of information retrieved. Rather, increased activation also accompanied manipulations that directly varied the degree of competition between retrieved alternatives while putatively holding semantic retrieval constant (judgment specificity and congruency). This pattern was further supported by the striking observation that across-manipulation behavioral variance in the "selection component" accounted for functional variance in left mid-VLPFC. Hence, going beyond a qualitative overlap in sites of activation across manipulations thought to vary selection demands, the factor analysis identified a metavariable corresponding to shared variance across the manipulations. That this quantitative index of a shared processing component accounted for functional variance in left mid-VLPFC, when considered in combination with the broader pattern of imaging data, provides particularly compelling evidence in favor of a selection interpretation of left mid-VLPFC function.

Critically, the dissociation between left mid-VLPFC and lateral temporal cortex suggests that the representations on which this general selection process operates are not necessarily long-term semantic representations of the sort thought to be stored in lateral temporal regions. In particular, it appears reasonable to designate this selection process as occurring postretrieval, operating on active representations that perhaps are being maintained in working memory. As noted above, this proposal does not require that retrieval itself is all or none. Indeed, active representations entering working memory may be partial, transient, and even weak. However, it does require a distinction between active representations (putatively maintained in working memory) and long-term memory representations. There is evidence for such a distinction in the nonhuman primate (Miller et al., 1996) in which disruption of active neural representations in temporal cortices through interference does not disrupt representations actively maintained in PFC, which are capable of subsequently guiding action. Furthermore, a distinction between stored long-term representations and working memory representations that guide action does have theoretical precedence (e.g., O'Reilly et al., 2002).

Although the present manipulations of selection demands were within the context of semantic processing, it is not necessarily the case that the operation of this mechanism must be restricted to task contexts of semantic control or even memory in general. Indeed, the common factor influencing whether tasks elicit activation in left mid-VLPFC appears to be whether they involve selection or interference resolution en route to generating a response. For example, left mid-VLPFC has been associated with increased interference within working memory (Badre and Wagner, 2005; Bunge et al., 2001; Jonides et al., 1998; Thompson-Schill et al., 2002), during task switching (Brass and von Cramon, 2004), and in response selection (Jiang and Kanwisher, 2003; Milham et al., 2001). Furthermore, during episodic remembering, left mid-VLPFC has been associated with selection of perceptual and conceptual episodic details (Dobbins and Wagner, 2005), suggesting that this region resolves conflict across memory and content domains. At a mechanistic level, this domain-general selection process may bias active representations maintained in working memory to overcome conflict, thereby permitting selection of relevant representations from "noise" because of other active competitors.

Controlled Semantic Retrieval

Though a generalized selection process may play a role in resolving interference, the present data provide evidence of a dissociation across left VLPFC subregions for which a single-process model does not provide an account. The anterior, ventral extent of left VLPFC dissociated from mid-VLPFC because left anterior VLPFC was exclusively sensitive to associative strength (Figure 4D). Importantly, this was the case even when pitting controlled retrieval demands (associative strength) against overall retrieval (number of targets) because left anterior VLPFC was the only region to show a weak-two > strong-four effect. This pattern suggests that left anterior VLPFC is uniquely sensitive to the need to control retrieval when available cues are insufficient to activate relevant knowledge through bottom-up processes.

In operation, a controlled retrieval mechanism may accumulate and maintain cues or retrieval goals to mediate retrieval of additional relevant information stored in left temporal cortices (e.g., Badre and Wagner, 2002). Consistent with this interpretation, left anterior VLPFC activation because of associative strength was accom-

panied by similar activation in left middle temporal cortex. Moreover, prior studies have demonstrated a functional coupling between left anterior VLPFC and left middle temporal cortex during semantic processing (Bokde et al., 2001) and episodic recollection of conceptual event details (Dobbins and Wagner, 2005). Collectively, these data suggest that left anterior VLPFC may operate on representations in middle temporal cortex, though a metric of causality or directionality of information flow awaits future research (Friston et al., 2003; Goebel et al., 2003; Sun et al., 2004).

In our account for the observed dissociation between anterior VLPFC and mid-VLPFC, the critical distinction between controlled retrieval and selection putatively derives from the nature of the representations on which each process operates. The controlled retrieval process subserved by left anterior VLPFC may directly influence long-term semantic representations stored in lateral temporal regions. By contrast, the generalized selection process supported by left mid-VLPFC may be critical in resolving interference among active representations maintained in working memory. One implication of the close association of controlled retrieval with the activation of stored representations is that this process should be tied more directly to tasks that demand access to long-term memory, whereas the selection process may be required to resolve interference among representations in working memory that came to be activated through means other than semantic retrieval.

The ability to flexibly and strategically access knowledge is a central feature of an adaptive control system (Anderson et al., 2004; Sohn et al., 2003). The present results argue that distinct control mechanisms in left VLPFC contribute to this process by guiding access to semantic knowledge not retrieved automatically and selecting from among retrieved representations. The network proposed here may be central to a number of task contexts in which representations must be retrieved or selected en route to generating a response. Future research promises to further specify the nature of these control mechanisms so as to better understand when they are necessary for successful adaptive behavior.

Experimental Procedures

Participants

Twenty-two right-handed, native English speakers (13 female; ages 18–25 years) were enrolled in experiment one, and an independent sample of 11 right-handed, native English speakers (four female; ages 18–30 years) were enrolled in experiment two. Data from two additional subjects recruited for experiment one were excluded because of significant artifacts. All participants received $50 remuneration for participation. Informed consent was obtained in a manner approved by the Human Subjects Committee of the Massachusetts General Hospital and the Committee on the Use of Humans as Experimental Subjects at MIT.

Design and Logic

Event-related trials were separated in time by jittered (0–8 s) null fixation periods and were grouped into task blocks. Blocks began with a baseline fixation period (12 s and 16 s for experiments one and two, respectively) followed by a 4-s instruction cue indicating the task (feature or related) to be performed for that block. On each trial, a cue word and a set of target words were presented for 3 s (Figure 1). Subjects chose one of the targets based on its semantic relationship with the cue and indicated their response on a keypad positioned under their left hand. Subjects were given 4 s to respond (inclusive of the 3-s cue-target set presentation). When the instruction cue was "RELATED," subjects were to select the target that was most globally related to the cue. Alternatively, if the instruction specified a semantic feature (e.g., "COLOR," "SHAPE," "SIZE," or "TEXTURE"), subjects were to select the target most similar to the cue along this dimension. This design permitted manipulation of judgment specificity (feature vs. related), cue-target associative strength (strong versus weak), number of targets (two versus four), and congruency (congruent versus incongruent) during semantic processing (Figure 1). The order of experimental and fixation events within a block was determined by optimizing the efficiency of the design matrix so as to permit event-related analyses (Dale, 1999); efficiency was equated across related and feature blocks.

Experiment one was designed to factorially combine control demands, crossing the associative strength, judgment specificity, and congruency manipulations within subject. Across four fMRI scan runs, subjects encountered 240 trials divided equally among the four associative strength × judgment specificity condition crossings. Furthermore, of the 120 feature trials, half were congruent and half were incongruent (Figure 1). Each scan contained four experimental blocks, two related and two feature, counterbalanced in an ABBA/BAAB fashion.

Experiment two was designed to maximize sensitivity and power of the control manipulations while still permitting within-subject analysis. This goal was achieved by isolating control manipulations into separate processing epochs within a single scan session. During an initial epoch, subjects performed the related task alone, with associative strength and the number of targets being manipulated (Figures 1A and 1B). In a second epoch, subjects alternated between feature and relatedness judgments, as in experiment one. However, unlike in experiment one, only judgment specificity and congruency manipulations were included. Otherwise, trial events in this epoch unfolded as with experiment one. Each of the epochs consisted of two fMRI scan runs. During epoch one, subjects encountered 288 related trials (Figure 1A). In the second epoch, subjects performed 80 related and 80 feature trials grouped into 8 related and 8 feature blocks counterbalanced in an ABBA/BAAB fashion. These blocks were divided equally and counterbalanced across the two scan runs. Furthermore, subjects encountered 40 congruent and 40 incongruent trials mixed across the feature blocks.

Stimuli

Stimuli for all experiments were chosen from single-response free-association norms (Moss and Older, 1996; Postman and Keppel, 1970) and were equated for word length and for normative frequency of use (Kucera and Francis, 1967) across experimental conditions. For each of 240 cues in experiment one, one strongly associated, one weakly associated, and one unassociated target were chosen. The mean normative probability that the item was generated as the associate of the cue differed across strong (0.11) and weak (0.02) targets, yielding a pre-experimental associative strength ratio of approximately 5:1 for strong:weak trials. This ratio was markedly lower than the 22:1 ratio adopted in epoch one of experiment two (see below) because of the additional counterbalancing constraints of the experiment one factorial design. Unassociated targets were determined based on their absence from a cue's normative list of associates.

Stimuli for epoch one of experiment two were taken directly from a prior study, and thus details of stimulus selection and counterbalancing have been described previously (Wagner et al., 2001). The mean normative probability that an item was generated as the associate of the cue differed substantially between strong (0.22) and weak (0.01) targets. For each of the 160 cues in epoch two of experiment two, one associated and one unassociated target were selected. The mean normative probability of item generation for the associated target (0.19) was comparable to strong trials of epoch one. Again, unassociated targets were determined based on their absence from a cue's normative list of associates.

fMRI Procedures

Whole-brain imaging for both experiments was performed on a 3T Siemens MRI system (experiment one, 3T Allegra MRI system; ex-

periment two, 3T Trio MRI system). Functional data were acquired with a gradient-echo echo-planar pulse sequence (experiment one, TR = 2 s, TE = 40 ms, 21 axial slices, 3.125 × 3.125 × 5 mm, 1 mm inter-slice gap, 208 volume acquisitions per run; experiment two, TR = 2 s, TE = 30 ms, 20 axial slices, 3.125 × 3.125 × 5 mm, 1 mm inter-slice gap, 408/284 volume acquisitions per epoch1/epoch2 run). High-resolution T1-weighted (MP-RAGE) anatomical images were collected for anatomical visualization. Head motion was restricted with firm padding that surrounded the head. Visual stimuli were projected onto a screen and were viewed through a mirror attached to the head coil.

Exploratory Factor Analysis

An exploratory factor analysis of the behavior was performed by standard procedures (Harris, 1967). To provide a sufficient number of observations, subjects from both experiments were included in the factor analysis. Absolute differences in RT and errors for associative strength, judgment specificity, and congruency were computed and standardized within experimental group for inclusion in the factor analysis. It should be noted that the inclusion of relative, rather than absolute, difference scores does not qualitatively change any of the obtained results. The six eigenvalues describing the variance-covariance matrix of these six scores were then extracted. Factors with eigenvalues greater than 1 were selected for additional analysis. Selected factors underwent oblique rotation with the Varimax algorithm. Regression estimate factor scores for inclusion in fMRI analysis were derived for each subject based on the oblique factor solution (Harris, 1967). Factor analysis was performed in StatView 5.0.1 (SAS Institute).

fMRI Data Analysis

Data were preprocessed with SPM99 (Wellcome Department of Cognitive Neurology, London). Functional images were corrected for differences in slice acquisition timing by resampling all slices in time to match the first slice followed by motion correction across all runs (by sinc interpolation). Structural and functional data were spatially normalized to an EPI template based on the MNI stereotactic space (Cocosco et al., 1997) with a 12-parameter affine transformation along with a nonlinear transformation with cosine basis functions. Images were resampled into 3-mm cubic voxels and then spatially smoothed with an 8-mm FWHM isotropic Gaussian kernel.

Statistical models were constructed with SPM99 under the assumptions of the general linear model. Experiment one and the second epoch of experiment two used a mixed fMRI design, such that judgment specificity was manipulated across blocks and associative strength and congruency were manipulated in an event-related manner within blocks (Donaldson et al., 2001). Because event and block regressors were correlated in these instances, all conditions were solely modeled as events by constructing regressors for each cell of the design (i.e., any effect of task "state" was not separately assessed). Similarly, the first epoch of experiment two was modeled in a standard event-related manner. Correct and incorrect trials were modeled separately; all statistical contrasts were restricted to correct trials.

Effects were estimated with a subject-specific fixed-effects model with session-specific effects and low-frequency signal components treated as confounds. Linear contrasts were used to obtain subject-specific estimates for each effect. These estimates were entered into a second-level analysis treating subjects as a random effect with a one-sample t test against a contrast value of zero at each voxel. Correlations of individual effects of control with factor scores were estimated with a multiple regression that included the factor scores as independent measures and the subject-specific estimate for each control contrast as the dependent measure at each voxel.

Voxel-based group effects were considered reliable to the extent that they consisted of at least five contiguous voxels that exceeded an uncorrected threshold of $p < 0.001$. Moreover, maxima reported in left VLPFC survived correction for multiple comparisons over the search volume by Gaussian random-field theory (Friston et al., 1995) (corrected $p < 0.05$); where effects in left VLPFC did not pass the corrected threshold, uncorrected results are reported to the extent that they constitute replications of findings from an independent data set. The volume used for correction included gray matter within left VLPFC and was generated in an unbiased manner based on the intersection of the automated anatomical labeling (AAL) regions (Tzourio-Mazoyer et al., 2002) that comprise the entire inferior frontal gyrus (AAL regions, 11—inferior frontal gyrus pars opercularis, 13—inferior frontal gyrus pars triangularis, and 15—inferior frontal gyrus pars orbitalis) and the SPM a priori gray image (50% prior probability of gray matter). Group statistical maps were rendered on a canonical brain with SPM99. For the purpose of additional anatomical precision, group contrasts were also rendered on an MNI canonical brain that underwent cortical "inflation" with FreeSurfer (CorTechs Labs, Inc.) (Dale et al., 1999; Fischl et al., 1999) and the SPM surfrend toolbox (written by I. Kahn; http://spmsurfrend.sourceforge.net/).

To reveal common effects at the voxel level across independent conditions and data sets, we performed conjunction analyses. Unless otherwise noted, conjunction analyses were assessed as significant at a conjoint α level of $p < 0.001$. That is, a significant conjunction does not indicate that both contrasts were individually significant at standard thresholds (Nichols et al., 2005) but rather means that both were significant at more lenient thresholds (with a joint probability of a Type I being less than 0.001).

The group-level voxel-based contrasts were supplemented with region-of-interest (ROI) analyses. All significant voxels within a 6-mm radius of a chosen maximum defined an ROI and unless otherwise noted, were defined from the conjunction of all control conditions > fixation for the first and second epochs of experiment two (Figure 4A). Selective averaging with respect to peristimulus time allowed assessment of the signal change associated with each condition. Integrated percent signal change (iPSC) was then computed based on the peak plus and minus one TR. The peak was defined neutrally for each ROI based on the average time course across all conditions. The resultant data were subjected to repeated-measures analyses of variance (ANOVA).

Supplemental Data

The Supplemental Data for this article can be found online at http://www.neuron.org/cgi/content/full/47/6/907/DC1/.

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Supplementary Note

Expanded Discussion of Behavioral Results

Initial analyses of reaction time (RT) and errors confirmed the efficacy of the four control manipulations. Judgment Specificity reliably impacted RT, such that Feature judgments took longer than Relatedness judgments (Exp. 1: $\underline{F}(1,21) = 70.6$, $p < .0001$; Exp. 2: $\underline{F}(1,10) = 114.1$, $p < .0001$; Fig. 2A), indicating that RT slowed as putative selection demands increased. Though errors were slightly higher during Related (12% errors) than Feature judgments (10% errors) in Exp. 1 ($\underline{F}(1,21) = 8.1$, $p < .01$), there was no such difference in Exp. 2 ($\underline{F}(1,10) = 2.7$, $p = .13$).

Cue–target Associative Strength impacted both RT and errors. RT was longer (Exp. 1: $\underline{F}(1,21) = 17.5$, $p < .0005$; Exp. 2: $\underline{F}(1,10) = 171.4$, $p < .0001$) and errors were higher (Exp. 1: $\underline{F}(1,21) = 7.5$, $p < .05$; Exp. 2: $\underline{F}(1,10) = 60.9$, $p < .0001$) when one of the targets was a Weak associate of the cue than when one of the targets was a Strong associate (Fig. 2B). The crossing of Associative Strength with Judgment Specificity in Exp. 1 revealed a reliable interaction (RT: $\underline{F}(1,21) = 11.4$, $p < .005$; errors: $\underline{F}(1,21) = 5.4$, $p < .05$), with the effects of Associative Strength being reliable during Relatedness judgments (RT: $\underline{F}(1,21) = 36.4$, $p < .0001$; errors: $\underline{F}(1,21) = 12.1$, $p < .002$) but not during Feature judgments (RT: $\underline{F} = 1.6$; Errors: $\underline{F} < 1$). This pattern is consistent with Associative Strength impacting controlled retrieval demands during the Relatedness task, but not during the Feature task (which requires selection of specific stimulus features).

Number of Targets impacted performance, such that selecting from amongst Four targets in Exp. 2 slowed RT ($\underline{F}(1,10) = 9.1$, $p < .05$) and increased errors ($\underline{F}(1,10) = 4.7$, $p = .055$; Fig. 2B) relative to when there were Two targets. Number of Targets and

Associative Strength did not interact ($F < 1$). Importantly, central to a subsequent analysis conducted to rule out time-on-task accounts of the fMRI data, there was no behavioral difference between Weak–Two vs. Strong–Four trials (RT: $F < 1$; Errors: $F(1,10) = 1.6$, $p = .23$). Finally, the Congruency manipulation of selection demands affected both RT and errors, such that RT slowed (Exp. 1: $F(1,21) = 66.2$, $p < .0001$; Exp. 2: $F(1,10) = 142.9$, $p < .0001$) and Errors increased (Exp. 1: $F(1,21) = 21.1$, $p < .0005$; Exp. 2: $F(1,10) = 24.9$, $p < .0005$) on Incongruent than Congruent trials (Fig. 2C).

The Non-Selection Component

The Non-Selection Component did not account for variance in the Congruency manipulation, but loaded strongly on the effects of Associative Strength and Judgment Specificity (Fig. 3). A conjunction analysis (conjoint alpha = .0025) between the correlation of the Non-Selection Component and the Associative Strength and the Judgment Specificity neural effects revealed convergent activation in left fronto-polar cortex (FPC; -42 45 –3), well rostral to the anterior VLPFC region selectively sensitive to Associative Strength (Fig. 4D).

Though the present focus was on left VLPFC, it may be of some interest that this analysis implicated FPC, a region that was also shown to be sensitive to Judgment Specificity (Fig. 4D). One possible account for this pattern is that FPC mediates episodic retrieval of the instructed task goal, a demand that is greater during Feature trials because the semantic dimension changed with each Feature block. Hence, subjects had to remember which feature was relevant for the current block of Feature trials based on the most recently encountered instruction. Another possibility, supported by recent studies

of FPC function (Bunge et al., 2005; Braver and Bongiolatti, 2002; Koechlin et al., 1999), is that FPC is engaged in an integration (and/or subgoaling) function whereby retrieved information about each cue-target pair is further processed with respect to maintained goal criteria. Such demands might be greater during Feature relative to Related trials, and also on Weak relative to Strong trials. Further research will be required to verify whether these or other conceptualizations of FPC function can account for why behavioral variance indexed by the Non-Selection meta-variable, on which both the Associative Strength and Judgment Specificity manipulations loaded heavily, was associated with functional variance in left FPC. Furthermore, such theories might also address how this FPC mechanism interacts with the controlled retrieval and selection mechanisms associated with VLPFC.

References

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Supplementary Table 1. PFC foci from the principal control contrasts.

Contrast	Stereotaxic Coordinates X	Y	Z	~Brodmann's Area	Peak Z
Incongruent - Congruent (Exp. 1 & Exp 2 Conj.)					
Left Posterior VLPFC/Premotor	-39	3	27	6/44	2.3
Left Posterior VLPFC	-42	9	21	44/6	2.5
Left Post./Mid-VLPFC	-54	12	18	45/44	2.8
Left Premotor	-21	15	60	8/6	3.4
Left Mid-VLPFC	-48	18	18	45	2.8
Left Operculum	-30	27	-18	47	3.8
Left Mid-VLPFC	-54	30	12	45	2.4
Left PreSMA	-3	33	48	8	2.0
Left (Dorsal) Anterior VLPFC	-45	39	3	45	2.5
Right Operculum	30	24	-15	47	3.2
Weak - Strong (Exp. 2)					
Left Premotor	-45	9	51	6/8	4.5
Left Posterior VLPFC	-51	9	33	44/6	5.2
Left Premotor	-39	12	48	6/8	4.7
Left Post./Mid-VLPFC	-42	12	18	45/44	4.3
Left Mid-VLPFC	-48	15	24	45/44	4.4
Left Mid-VLPFC	-51	21	21	45	4.0
Left ACC	-9	21	42	24/32	5.0
Left Mid-VLPFC	-45	27	15	45	4.4
Left Anterior VLPFC	-51	27	-3	47	4.3
Left Operculum	-33	27	-6	47	4.8
Left Mid-VLPFC	-48	30	12	45	4.3
Left Anterior VLPFC	-48	30	-12	47	3.4
Left Operculum	-36	30	-3	47	4.7
Left Anterior VLPFC/FPC	-45	42	-9	47/10	3.6
Right Motor/Premotor	33	0	57	4/6	3.5
Right Post./Mid-VLPFC	42	12	27	45/44	3.3
Right PreSMA	6	21	51	8	4.5
Right ACC	9	30	12	24/32	3.3
Right Operculum	36	30	-9	47	4.4
Feature - Related (Exp. 1 & Exp 2 Conj.)					
Left Posterior VLPFC	-45	6	15	44/6	3.2
Left Premotor	-48	9	45	6/8	2.4
Left Posterior VLPFC	-48	9	18	44/6	3.2
Left Post./Mid-VLPFC	-51	12	27	45/44	3.3
Left Premotor	-27	18	57	6/8	3.2
Left PreSMA	-6	21	51	8	2.6
Left Mid-VLPFC	-45	27	15	45	3.5
Left PreSMA	-6	30	42	8	2.3
Left Mid-VLPFC	-42	33	9	45	3.8
Left Orbital Frontal	-36	42	-15	11/47	2.5
Left FPC	-45	45	-3	10/46	2.9
Right Premotor	30	15	45	6/8	2.3
Right Premotor	33	18	57	6/8	3.0
Right Premotor	39	21	51	6/8	2.5
Right Mid-VLPFC	54	21	27	45	3.5
Right Mid-VLPFC/DLPFC	54	36	21	45/46	2.8
Right FPC	48	42	6	10/46	3.3

Note: Ventrolateral Prefrontal Cortex (VLPFC); Dorsolateral Prefrontal Cortex (DLPFC); Pre-Supplementary Motor Area (PreSMA); Anterior Cingulate Cortex (ACC); Fronto-Polar Cortex (FPC)