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Frontal Lobe Mechanisms that Resolve Proactive Interference

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Memory of a past experience can interfere with processing during a subsequent experience, a phenomenon termed proactive interference (PI). Neuroimaging and neuropsychological evidence implicate the left mid-ventrolateral prefrontal cortex (mid-VLPFC) in PI resolution during short-term item recognition, though the precise mechanisms await specification. The present functional magnetic resonance imaging (fMRI) experiment sought to further constrain theorizing regarding PI resolution. On each trial, subjects maintained a target set of words, and then decided if a subsequent probe was contained in the target set (positive) or not (negative). Importantly, for half of the negative and half of the positive trials, the probe had been contained in the previous target set (recent). Relative to non-recent trials, negative–recent trials produced an increase in response times and error rates, behavioral markers of PI. In fMRI measures, negative recency was associated with increased activation in the left mid-VLPFC, as well as in the bilateral fronto-polar cortex, providing evidence for multiple components in PI resolution. Furthermore, recency effects were evident during both negative and positive trials, with the magnitude of the recency effect in the mid-VLPFC being greater on negative trials. Collectively, these results serve to specify and constrain proposed models of PI resolution.

Keywords: cognitive control, episodic memory, executive function, prefrontal cortex, working memory

Introduction

Memory for the past shapes processing in the present, though such influences sometimes prove detrimental, a phenomenon termed proactive interference (PI). For example, the frustrating experience of forgetting where your car is parked in a regularly used lot is attributable, at least in part, to interference from memories established during prior occasions of parking your car in the lot. The importance of PI as a fundamental processing constraint in memory and cognition is well recognized, being highlighted in classic work implicating interference as a cause of forgetting from long-term memory (McGeoch, 1942), as well as a source for age-related declines in cognitive function (Hasher and Zacks, 1988). Importantly, PI can constrain active memory processing, potentially contributing to short-term forgetting (Brown, 1958; Peterson and Peterson, 1959; Keppel and Underwood, 1962). It follows, then, that processes that resolve or resist PI may be critical for the flexible updating and maintenance of task-relevant goals, stimuli and responses. Given the processing costs of interference, specifying the neural mechanisms that overcome or resolve PI is a fundamental objective (Shimamura, 1995).

An illustrative paradigm in which mechanisms that resolve PI have been examined is short-term item recognition (Fig. 1), wherein subjects judge whether a probe stimulus matches (positive) or mismatches (negative) one of a set of maintained target stimuli (Monsell, 1978; Jonides *et al.*, 1998). During the critical condition, trials are arranged such that the current probe overlaps the target set on the previous trial (recent). By this arrangement, negative–recent probes, though not members of the currently maintained target set, nevertheless give rise to a sense of familiarity due to their presence in the previous target set, an attribute they share with positive probes (which are items in the currently maintained target set). Hence, the familiarity of negative–recent probes is thought to elicit conflict at the response and/or stimulus representation levels (Jonides *et al.*, 1998; D'Esposito *et al.*, 1999; Mecklinger *et al.*, 2003; Nelson *et al.*, 2003). Behaviorally, this PI-derived conflict is reflected in elevated response times (RT) and errors to negative–recent probes relative to negative–non-recent probes. At the neural level, functional imaging studies have revealed increased activation in the left mid-ventrolateral prefrontal cortex [VLPFC; roughly corresponding to Brodmann's area (BA) 45] during negative–recent relative to negative–non-recent trials (Jonides *et al.*, 1998, 2000; D'Esposito *et al.*, 1999; Bunge *et al.*, 2001; Mecklinger *et al.*, 2003; Nelson *et al.*, 2003; Postle and Brush, 2004), and neuropsychological data indicate that lesions of this PFC region result in greatly enhanced PI-related errors and response slowing (Thompson-Schill *et al.*, 2002). Thus, a left mid-VLPFC mechanism appears to contribute to resolving PI during short-term item recognition, though the nature of this mechanism remains underspecified.

Extant accounts of left mid-VLPFC involvement in PI resolution have focused on the potential role of this region in inhibiting or selecting against the irrelevant attribution of familiarity to the negative–recent probe (Jonides *et al.*, 1998; Nelson *et al.*, 2003) or familiarity-triggered inappropriate response tendencies (Jonides *et al.*, 1998; D'Esposito *et al.*, 1999). From these perspectives, interference on negative–recent trials arises directly or indirectly from conflict between the familiar nature of the probe (due to its presence in the previous target set) and the status of the probe as a non-member of the current target set. The resolution of this conflict may proceed through inhibition of the familiar representation, the inappropriate response or the attribution of familiarity (Jonides *et al.*, 1998; D'Esposito *et al.*, 1999; Nelson *et al.*, 2003). Hence, it is posited that conflict resolution in this task has the effect of bringing responses arising from mnemonic signals, including familiarity, in line with response decision criteria that depend on the temporal context of a given probe. To date, theorizing has largely considered this mechanism to be restricted in scope and interaction, being active principally on negative–recent trials

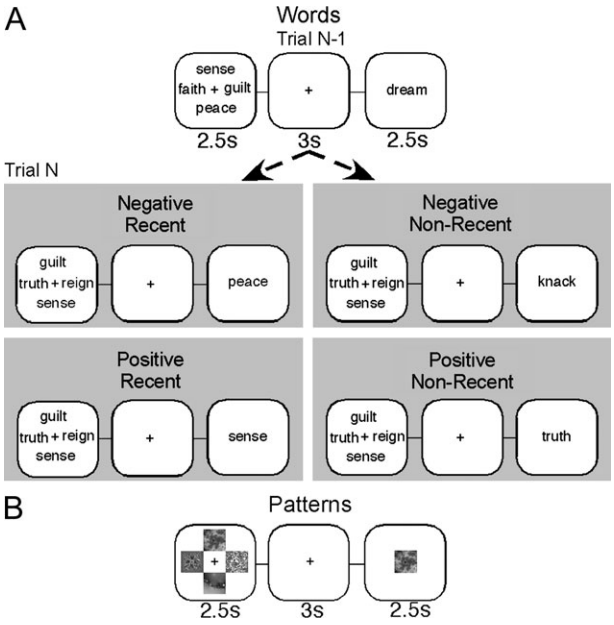

Figure 1. Schematics depicting the trial elements (upper) and the four critical conditions (gray) for the words task (*A*) and a sample trial from the patterns task (*B*). Probe type reflects the presence (positive) or absence (negative) of the probe in the current trial's memory set (trial *n*). Recency reflects the presence (recent) or absence (non-recent) of the probe in the previous trial's memory set (trial *n* – 1).

and not necessarily requiring the simultaneous operation of additional cognitive control processes.

Further insight into the nature of the mechanism(s) supporting PI resolution may be gleaned from consideration of the neural correlates associated with performance of other memory paradigms that require determining the context in which a familiar item was previously encountered in order to guide a response. For example, in episodic retrieval tasks that require context or source recollection, subjects must determine the context in which a familiar memory probe was encountered (Johnson and Raye, 1981; Johnson *et al.*, 1993). Similarly, in the *N*-back working memory task, performance partially rests on determining whether a familiar probe occurred within a specific temporal context (*N* trials back) or a different temporal context (*N* + 1 or *N* – 1 trials back) (Braver *et al.*, 2001; Nyberg *et al.*, 2003). Intriguingly, in contrast to studies of PI resolution during short-term item recognition, these other mnemonic tasks have strongly favored a multi-component cognitive control system that both guides ongoing processes as well as evaluates/monitors the results of those processes and integrates them with currently maintained goals or decision criteria (Wagner, 1999; Cabeza *et al.*, 2002; Dobbins *et al.*, 2002; Buckner, 2003; Johnson *et al.*, 2003).

The fronto-polar cortex (FPC), in particular, has been implicated in evaluation, monitoring or integration processes (Koechlin *et al.*, 1999; Braver and Bongiolatti, 2002; Dobbins *et al.*, 2002; Christoff *et al.*, 2003; Badre and Wagner, 2004; Bunge *et al.*, 2005). In the domain of working memory, activation in FPC has been reported during *N*-back tasks relative to control conditions (Braver *et al.*, 2001; Nyberg *et al.*, 2003). Similarly, tasks that involve selecting responses or response rules from working memory based on maintained contextual rules also implicate the FPC in integrating across time and goals (Koechlin *et al.*, 1999, 2003; Braver *et al.*, 2003; Bunge *et al.*, 2003; Christoff *et al.*, 2003; Sakai and Passingham, 2003; Badre and Wagner, 2004). Finally, FPC activation has been consistently observed during studies of episodic retrieval (Squire, 1992; Tulving *et al.*, 1994; Buckner *et al.*, 1995; Nyberg *et al.*, 1996; Rugg *et al.*, 1996; Wagner *et al.*, 1998; Fletcher and Henson, 2001), with the left FPC being particularly engaged during retrieval tasks that require assignment of a familiar item to the source in which it was previously encountered (Nolde *et al.*, 1998; Ranganath *et al.*, 2000; Cansino *et al.*, 2002; Dobbins *et al.*, 2003). Such effects have been interpreted as reflecting sub-processes during retrieval, wherein the mnemonic products elicited by current retrieval cues are evaluated/monitored and integrated with decision criteria (Rugg and Wilding, 2000; Dobbins *et al.*, 2002).

Given these observations, one might anticipate that PI resolution will also depend on FPC processes, given the importance of monitoring the relationship between target familiarity and the criterial context (in this case, membership in the current target set). Intriguingly, though no study to date has reported reliable activation in the FPC during negative–recent versus non-recent trials, the inaugural PET study of PI during short-term item recognition appears to have observed sub-threshold activation in FPC (see fig. 1 in Jonides *et al.*, 1998), raising the possibility that a multi-component cognitive control network operates in the service of resolving PI. One objective of the present study was to directly consider the sensitivity of the FPC to interference during short-term item recognition.

Beyond determining whether PI resolution depends on a single mechanism or multiple control mechanisms, the nature of the inhibitory/selection mechanism putatively supported by the left mid-VLPFC awaits further specification. Leverage on the nature of left mid-VLPFC contributions to PI resolution may come from considering how this region is engaged by positive–recent trials, on which the test probe is a member of the current and the preceding target set, such that familiarity is in concert with current set membership and a positive response. Critically, all positive test probes are familiar, as they were recently encountered in the current target set. However, relative to positive–non-recent probes, positive–recent probes may possess enhanced familiarity, having been present in the previous target set as well the current target set. The impact of this enhanced familiarity on positive–recent relative to positive–non-recent trials has yet to be formally investigated.

Both congruency-based decreases and congruency-based increases in neural activation have precedent elsewhere in the cognitive control literature, and have provided important constraints on mechanistic models of cognitive control. For example, functional imaging studies of the Stroop task (Stroop, 1935) have revealed facilitative decreases in the dorsolateral PFC (DLPFC) and anterior cingulate cortex activation on congruent trials (e.g. when the word names the color of ink in which it is printed) compared with neutral trials, suggesting that these activation reductions reflect decreased demands on response selection processes due to multiple converging sources of evidence in support of a response (Carter *et al.*, 1995; Milham *et al.*, 2001, 2002). By contrast, facilitative increases in the left VLPFC on congruent compared with neutral Stroop trials have also been reported, with these effects being similar to those observed for incongruent trials (Milham *et al.*, 2001, 2002). In this case, congruent trial increases were interpreted as reflecting general sensitivity to multiple sources of response relevant information (e.g. a nameable color and word), even if these sources were not

in conflict. As with Stroop, inspection of the neural responses during positive–recent trials during short-term item recognition may provide additional leverage on the interference-resolution mechanism putatively mediated by left mid-VLPFC.

The present functional magnetic resonance imaging (fMRI) experiment was designed to further specify the PFC mechanisms that resolve short-term PI. In particular, the design and analyses emphasized two novel aspects of the functional imaging data, with the goal of providing constraints on theorizing regarding PI resolution. First, voxel-based, region-of-interest and cross-experiment convergence analyses assessed the multi-component nature of PI resolution, focusing on the impact of recency on activation in FPC as well as in VLPFC. Second, the impact of the enhanced familiarity during positive–recent trials was assessed in these regions. Finally, an attempt was made to assess the domain generality of the neural responses to PI by including verbal (words) and non-verbal (visual patterns) stimuli in separate blocks, though, as will be described, issues with behavioral performance complicate interpretation of the data from the non-verbal condition.

Materials and Methods

Subjects

Seventeen right-handed, native English speakers (seven female; aged 18–31 years) gave informed consent in a manner approved by the institutional review boards at Massachusetts General Hospital and MIT. Data from three additional subjects were excluded due to fMRI spike artifacts. Subjects received $50 remuneration.

Design

Subjects performed alternate blocks of a short-term item recognition task using words and patterns. The word stimuli consisted of 20 five-letter, one-syllable abstract nouns; word frequency (mean = 114) was matched across experimental conditions. Pattern stimuli consisted of 20 abstract visual patterns. On each trial in the words blocks (Fig. 1*A*), subjects were presented with a memory set of four target words about a central fixation cross. Subjects had 2.5 s to encode the set and 3 s to maintain the set over a delay, and then were centrally presented a word probe. Upon probe presentation, subjects were to endorse the probe as matching one of the items in the currently maintained memory set or to reject it as a non-match. Subjects had 2.5 s in which to respond, pressing one of two buttons under their left hand; failures to respond were scored as incorrect. Across all words trials, 50% of the probes matched one of the items in the current memory set (positive probes) and 50% were non-matches (negative probes).

Trial events in the patterns blocks paralleled those in the words blocks, except that stimuli were abstract visual patterns (Fig. 1*B*). Abstract visual patterns (fractals) were selected with the goal of minimizing participants' ability to adopt a verbal naming strategy. Based on a pre-experimental questionnaire (n = 10), 20 difficult-to-name abstract visual patterns were selected from a set of 91, selecting those for which the fewest number of participants were able to generate a single name for the items (median and mode = 2/10 participants; max = 3/10 participants). On a post-scanning questionnaire, fMRI participants reported naming an average of 7 of the 20 images (SD = 4).

The relation between the probe on a given trial (trial n) and the items presented in the previous trial (trial $n-1$) was arranged to elicit proactive interference (PI) on a subset of events. Specifically, memory sets were constructed such that two items from the previous trial's memory set were repeated in the current trial's memory set, with the additional constraint that no single item was repeated more than three times in a row. This arrangement permitted 50% of all probes to match (recent) one of the items in the previously encoded, but now irrelevant, memory set (i.e. trial $n-1$) and 50% to mismatch (non-recent) any of the previously (trial $n-1$) encoded items. Hence, on recent trials, the recent exposure to a given stimulus on trial $n-1$ should elicit a sense of familiarity when encountering the probe on trial n, and thus could potentially give rise to PI. Of the recent trials, half entailed a positive probe (i.e. the stimulus was in the trials n and $n-1$ memory sets) and half a negative probe (i.e. the stimulus was not in trial n but was in $n-1$). It is of further note that, because all memory sets had an equal number of items repeating from the previous trial's memory set (n = 2) and of items that were not in the prior set (n = 2), any effects of recency or probe type were restricted to the probe phase of a trial. In addition to isolating the effects of familiarity to those deriving from the probe, this design also permitted event-related analysis to focus specifically on the probe phase (see below).

Subjects encountered 240 words trials and 240 patterns trials, which were divided into 16 fifteen-trial blocks of each stimulus type. Within each of four scan runs, subjects alternated between four words blocks and four patterns blocks in an ABBA fashion. Blocks were separated by 12 s periods, during which a cue was presented that named the upcoming task (WORD or PATTERN). Although stimulus type was blocked, within each block, trial types (positive–recent, negative–recent, positive–non-recent, and negative–non-recent) were intermixed in an event-related manner, with variable duration fixation events (0–4 s) permitting signal deconvolution (Dale, 1999). The order of blocks and stimuli were counterbalanced across subjects.

fMRI Procedures

Whole-brain imaging was performed on a 3 T Siemens Allegra system. Functional data were acquired using a gradient-echo echo-planar sequence (TR = 2 s, TE = 30 ms, 21 axial slices, 3.125 × 3.125 × 5 mm, 1 mm skip, 692 vols/run). High-resolution T1-weighted (MP-RAGE) anatomical images were collected for visualization. Head motion was restricted using firm padding that surrounded the head. Visual stimuli were projected onto a screen, and viewed through a mirror attached to a standard head coil.

Data were preprocessed using SPM99 (http://www.fil.ion.ucl.ac.uk/spm/). Functional images were corrected for differences in slice acquisition timing, followed by motion correction (using sinc interpolation). Structural and functional data were spatially normalized to the MNI template (Cocosco *et al.*, 1997) — an approximation of canonical space (Talairach and Tournoux, 1988) — using a 12-parameter affine transformation along with a nonlinear transformation using cosine basis functions. Images were resampled into 3 mm cubic voxels and spatially smoothed with an 8 mm full-width half-maximum isotropic Gaussian kernel.

fMRI Analyses

Statistical models were constructed using SPM99 under the assumptions of the general linear model. Trial events were modeled as two components—encoding/delay and probe. As described above, for each content type (words or patterns), events from the initial portion of each trial — encoding of the memory set and maintenance of the set across the delay — were identical across all four probe conditions (i.e. recent/non-recent × negative/positive). Accordingly, the encoding/delay period was modeled as a 5.5 s epoch according to content, irrespective of probe condition. Hence, though the presentation of the memory set and the delay period always preceded presentation of the probe, the regressors for each phase (e.g. encoding/delay versus probe) were sufficiently uncorrelated to permit assessment of the unique contribution of each to the overall variance in MRI signal. The probe portion of the trial, which corresponds to the data of interest, was modeled as an event according to content (words/patterns), probe (positive/negative) and recency (recent/non-recent). Correct trials were modeled separately from incorrect trials.

Effects were estimated using a subject-specific fixed-effects model, with session effects treated as confounds. Estimates were entered into a second-level group analysis treating subjects as a random effect, using a one-sample t-test against a contrast value of zero at each voxel. Unless otherwise noted, regions were considered reliable to the extent that they consisted of at least five contiguous voxels that exceeded an uncorrected threshold of $P < 0.001$.

To reveal common effects of recency (i.e. familiarity) across positive and negative trials in *a priori* predicted regions (i.e. left mid-VLPFC and FPC), a conjunction analysis was performed at a conjoint alpha level of $P < 0.001$ at each voxel, using the independent contrasts

negative–recent > non-recent and positive–recent > non-recent (each thresholded at $P < 0.032$). This method may be interpreted as setting the probability of a Type I error occurring in both contrasts to be less than 0.001. That is, a significant conjunction does not indicate that both contrasts were individually significant at standard thresholds (Nichols et al., in press), but rather means that both were significant at more lenient thresholds (with a joint probability of a Type I being less than .001).

Voxel-based contrasts were supplemented with region-of-interest (ROI) analyses that provided quantitative characterization of the effects. ROIs included all significant voxels within a 6 mm radius of each *a priori* targeted maximum. Selective averaging permitted extraction of the peak percent signal change associated with each condition; ROI data were submitted to repeated-measures analyses of variance.

Results

Behavioral Markers of PI

Accuracy and reaction time (RT; restricted to correct trials) data revealed three central results that ground understanding of the imaging data (Fig. 2). (i) Though subjects performed well, patterns trials were more difficult than words trials. (ii) PI was observed, wherein encountering a negative–recent probe resulted in interference (increased errors and longer RTs) relative to encountering a negative–non-recent probe. (iii) Though within-content recency effects in RT and accuracy were restricted to negative–recent trials, recency main effects were evident in accuracy for both negative and positive probes collapsed across content type.

The patterns condition was more difficult. Subjects responded more slowly [$F(1,16) = 17.0$, $P < 0.001$] and considerably less accurately [$F(1,16) = 70.4$, $P < 0.0001$] on patterns than on words trials (RT: 1138 versus 1016 ms; proportion errors: 0.23 versus 0.06, respectively). The increased error rate was partially attributable to a bias to respond 'non-match' on patterns trials, evident in a reliable interaction of content (words/patterns) × probe (positive/negative) on accuracy [$F(1,16) = 31.3$, $P < 0.0001$].

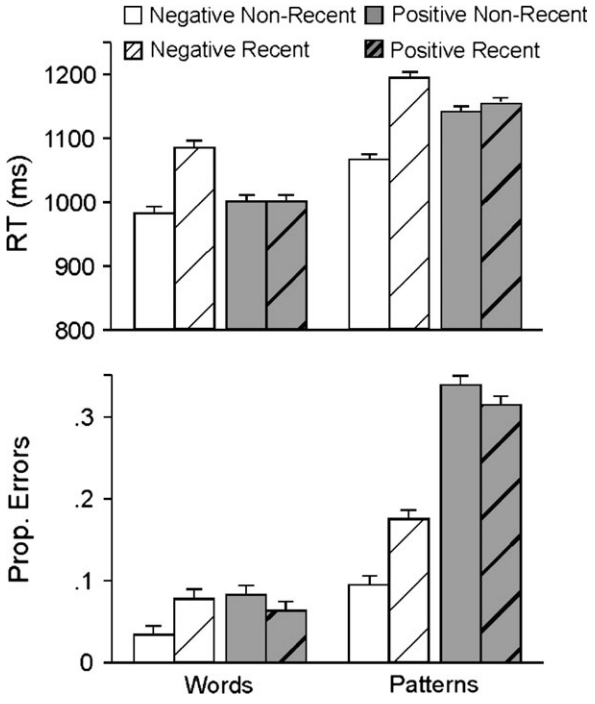

Figure 2. Behavioral reaction times (RT) and proportion of errors.

Recency affected RT, such that overlap of the current probe with one of the memoranda in the preceding trial slowed RTs [$F(1,16) = 81.4$, $P < 0.0001$]. Although subjects were slower on recent (1108 ms) relative to non-recent trials (1046 ms), a probe × recency interaction [$F(1,16) = 38.3$, $P < 0.0001$] indicated that this recency-induced RT slowing was reliable for negative probes [1139 versus 1023 ms; $F(1,16) = 86.0$, $P < 0.0001$] but not for positive probes (1076 versus 1070 ms; $F < 1$). Recency-induced slowing was present for both words [$F(1,16) = 37.3$, $P < 0.0001$] and patterns [$F(1,16) = 47.7$, $P < 0.0001$].

Though recency did not reliably affect RT to endorse positive probes, it did impact on the accuracy on positive and negative trials, albeit in different directions (Fig. 2). Specifically, although overall accuracy was lower on recent relative to non-recent trials [proportion errors: 0.16 versus 0.14; $F(1,16) = 17.3$, $P < 0.001$], a probe × recency interaction [$F(1,16) = 45.1$, $P < 0.0001$] indicated that, consistent with PI, accuracy declined on negative–recent relative to negative–non-recent trials [proportion errors: 0.13 versus 0.07; $F(1,16) = 49.2$, $P < 0.0001$], whereas accuracy modestly increased on positive–recent relative to positive–non-recent trials [proportion errors: 0.19 versus 0.21; $F(1,16) = 6.2$, $P < 0.05$]. The recency-induced decline in accuracy on negative trials was present when collapsing across both words and patterns (Fs > 9.3, Ps < 0.01). By contrast, the modest increase in accuracy on positive trials was not reliable when considering words or patterns alone (Fs < 3.1, Ps > 0.09).

Neural Responses to the Probe

Initial fMRI analyses identified structures that were active when generating a response during the probe stage collapsed across all conditions. Comparison of all probes versus the fixation baseline revealed broad activation inclusive of regions commonly associated with cognitive control and working memory, including the bilateral VLPFC (~BA 44/45), bilateral anterior DLPFC (~BA 9/46/10), left mid-DLPFC (~BA 9/46), and superior (~BA 7) and inferior parietal cortices (~BA 40). In addition, bilateral activation was observed in the posterior hippocampus/parahippocampal gyrus, and in fusiform and lateral temporal cortices (a complete list of coordinates is available upon request).

We primarily consider the effects of recency and probe type on activation during words trials, as these conditions are most analogous to previous reports that investigated PI using verbal stimuli (in particular, published reports have used letters as stimuli; Jonides *et al.*, 1998, 2000; D'Esposito *et al.*, 1999; Bunge *et al.*, 2001; Thompson-Schill *et al.*, 2002; Mecklinger *et al.*, 2003; Nelson *et al.*, 2003). Moreover, and of greater importance, the data from the words trials provide a sufficient basis on which to further specify the PFC mechanisms that resolve short-term PI. We conclude by briefly examining recency and probe effects during patterns trials, which warrant interpretative caution given the low accuracy levels during the patterns task.

Neural Response to PI during Words Trials

Activation associated with performance in the face of PI was assessed through the contrast of negative–recent to negative–non-recent words trials (Fig. 3*A*). Consistent with prior reports, negative-recency produced activation in the left mid-VLPFC (~BA 45; MNI coordinates of –51, 21, 6). However, in contrast

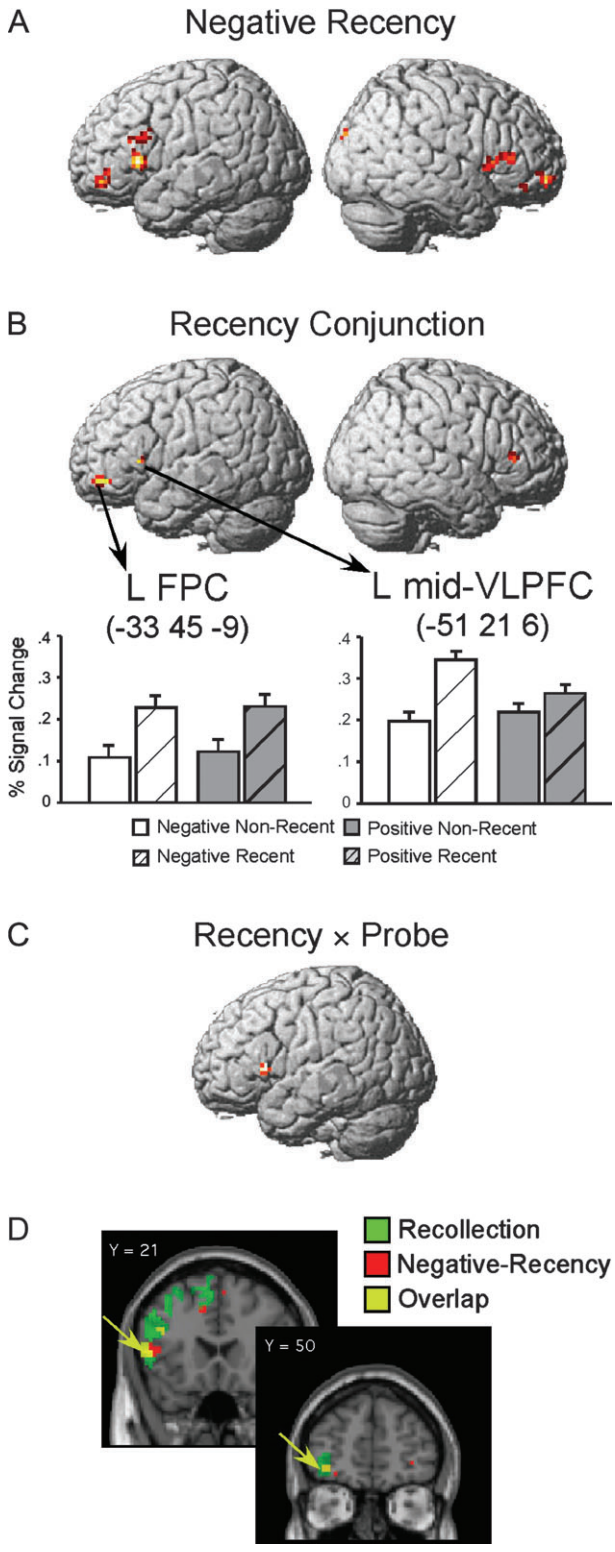

Figure 3. The effects of recency on activation during words trials, as depicted in surface renderings and graphs of peak percent signal change. (*A*) The contrast of negative–recent to negative–non-recent trials ($P < 0.005$). (*B*) Common effects of positive and negative recency (cojoint probability, $P < 0.001$). (*C*) Voxel-based recency × probe interaction ($P < 0.005$). (D) Overlap of regions showing greater activation during negative–recent versus negative–non-recent trials with regions associated with episodic contextual recollection. Episodic recollection effects were defined as demonstrating greater activation during both perceptual recollection and conceptual recollection compared with a novelty detection task (Dobbins and Wagner, 2005).

to earlier reports, reliable activation was also observed in the right FPC (~BA 10; 36, 57, –6) and right VLPFC/fronto-operculum (~BA 47/45; 42, 15, 6), a finding that bears on the potential multi-component nature of PI resolution. Given the *a priori* prediction that the left PFC regions associated with mnemonic monitoring/integration processes—notably the left FPC—may also be engaged by PI, the effect of negative recency was further assessed at a slightly more lenient statistical threshold ($P < 0.005$). Consistent with this *a priori* expectation, at this threshold negative recency also elicited activation in the left FPC/anterior VLPFC (~BA 10; –33, 45, –9 and ~BA 47/10; –45, 42, –3) and in a more superior extent of the left VLPFC (~BA 44/45; –42, 21, 24). In addition, the response in the right fronto-operculum spread at its most anterior extent into the right mid-VLPFC (~BA 45). Collectively, these data suggest that PI and its resolution engage multiple prefrontal cognitive control mechanisms, including bilateral FPC mechanisms that are often engaged during mnemonic monitoring/evaluation and integration processes.

Neural Overlap between PI during Words Trials and Episodic Recollection

As introduced above, one mnemonic context in which the FPC is thought to play a central role is in post-retrieval monitoring/decision processes during episodic retrieval. In particular, the FPC is thought to contribute to evaluating the products of retrieval attempts, integrating emerging mnemonic information with decision criteria so as to guide action (Rugg and Wilding, 2000; Dobbins *et al.*, 2002). As has been argued elsewhere, FPC activation during episodic recollection is not thought to reflect memory-specialized mechanisms, but rather the recruitment of basic cognitive control processes—monitoring/evaluation, integration and/or subgoaling—in the service of guiding memory decisions (Wagner, 1999; Buckner and Wheeler, 2001; Christoff *et al.*, 2001; Dobbins *et al.*, 2002). Here, we sought to determine whether PI resolution elicits activation in PFC regions also engaged during episodic recollection. To do so, we explored the anatomic overlap between the presently observed regions showing a negative–recent > negative–non-recent pattern and regions engaged during source recollection versus novelty detection in a recent episodic retrieval study (Dobbins and Wagner, 2005).

In particular, the episodic recollection data derive from a study that identified regions of the left PFC—specifically, the FPC, mid-VLPFC and posterior DLPFC—that were more active during recollection of perceptual episodic details (namely, details about the perceptual size of an object's prior presentation) and during recollection of conceptual episodic details (specifically, details about the semantic task performed during prior object presentation) compared with during assessment of relative stimulus novelty/familiarity (Dobbins and Wagner, 2005). This pattern of activation suggests that specific left PFC subregions are generally engaged during episodic recollection regardless of the domain of the to-be-recollected details (i.e. perceptual or conceptual), and thus may subserve basic cognitive control processes recruited during attempts to remember details about the past (see also Buckner, 2003). Furthermore, Dobbins and Wagner (2005) report strong within-experiment evidence of a domain-general selection process in the left mid-VLPFC that may be distinguished from an FPC monitoring mechanism operating in the service of episodic recollection. As such, this study provides a highly appropriate basis of comparison with the current results.

Comparison of the present left FPC and mid-VLPFC regions elicited by PI resolution during short-term item recognition to the left PFC regions engaged during recollection was performed through superposition of the domain-general recollection effect of Dobbins and Wagner with our contrast of negative–recent > negative–non-recent. This analysis revealed high overlap within the left mid-VLPFC and FPC, though the posterior DLPFC region observed during recollection was not observed to be sensitive to PI in the present experiment (Fig. 3*D*). Importantly, this high degree of convergence was not simply a by-product of the data chosen for comparison. Indeed, the focus in the left FPC arising from the contrast of negative–recent > negative–non-recent in the present study fell in close proximity to findings of left FPC activation reported in a number of previously published studies of episodic retrieval [e.g. Rugg *et al.*, 1996 (−30, 48, −2); Wagner *et al.*, 1998 (−43, 50, 4); Ranganath *et al.*, 2000 (−53, 41, 0); Dobbins *et al.*, 2003 (−45, 45, −6); Kahn *et al.*, 2004 (−48, 42, −6)].

In contrast to this correspondence between the left mid-VLPFC and FPC regions engaged during PI resolution and those associated with recollection of episodic detail, there was remarkably little overlap between the presently observed PI effects and a left anterior VLPFC region (~BA 47) that Dobbins and Wagner (2005) observed to be selectively engaged during controlled retrieval of semantic information. This outcome provides an important control, demonstrating that PI resolution does not overlap with PFC regions engaged simply during any retrieval condition requiring cognitive control, but rather seems relatively specific to left FPC control processes associated with monitoring and integration, and left mid-VLPFC processes associated with selecting target representations in the face of interference/competition (or, alternatively, actively inhibiting competing item or response representations).

Neural Response to Recency during Words Trials

Assessment of recency effects on positive trials may provide important constraints on theoretical accounts of the mechanisms of PI resolution. In particular, it is critical to assess whether regions that show an increase in response to negative–recency are also sensitive to the enhanced familiarity of positive–recent probes, and whether this sensitivity is reflected in a signal increase or decrease relative to positive–non-recent probes.

Accordingly, we performed a conjunction analysis to determine whether a convergent effect of recency was present during negative and positive trials, and subsequently performed an interaction analysis to determine whether the magnitude of the recency effect differed across probe type. The conjunction analysis, targeting the independent effects of recent > non-recent on negative and on positive trials (conjoint alpha-level = 0.001), revealed recency-induced activation increases in the left mid-VLPFC (~BA 45), left FPC (~BA 10) and right VLPFC (~BA 45) (Fig. 3*B*). The recency × probe analysis ($P < 0.005$) revealed a reliable interaction only in left mid-VLPFC—the recency-induced activation increase in this region was greater on negative than on positive trials (Fig. 3*C*; see also Fig. 3*B*), whereas the magnitude of the recency effects in the left FPC and right VLPFC were comparable on the negative and positive trials (Fig. 3*B*). These results were confirmed using independent *t*-tests contrasting the average beta values within each region of interest against zero. Specifically, the extracted beta values from the contrast of negative–recent > negative–non-recent in the left mid-VLPFC [$t(16) = 4.5$, $P < 0.0005$] and left FPC [$t(16) = 3.6$, $P < 0.005$] were reliable, as were those from the contrast of positive–recency > positive–non-recent in the left mid-VLPFC [$t(16) = 2.4$, $P < 0.05$] and left FPC [$t(16) = 3.6$, $P < 0.005$].

Two central findings emerged from these analyses. First, despite the limited impact of recency on behavior during positive trials and PI during negative trials, the effect of recency on left mid-VLPFC, left FPC, and right VLPFC activation was similar on positive and negative trials; all regions showed a recent > non-recent effect. Additional analyses revealed that no region showed a non-recent > recent pattern. Second, the effect of recency in the left mid-VLPFC was modulated by probe type, being greater during negative than during positive probes. This interaction is important, and may distinguish the left mid-VLPFC from the other PFC regions that were affected by recency but were otherwise insensitive to probe type. Indeed, the recency × probe × region interaction was reliable when comparing the left mid-VLPFC with the right VLPFC [$F(1,16) = 6.0$, $P < 0.05$], though this interaction did not reach significance when comparing the left mid-VLPFC with the left FPC [$F(1,16) = 2.7$, $P = 0.12$].

Patterns Task: Domain Generality of PI Resolution

Evidence for the domain generality of PI resolution mechanisms would provide an important additional theoretical constraint. To the extent that the mechanisms recruited to resolve PI are domain general, the regions showing a negative–recency effect for words should also show such an effect for the non-verbal patterns task. However, voxel-based comparison of Negative–recent to negative–non-recent trials revealed no reliable activation in the PFC at a standard threshold ($P < 0.001$) or at a more lenient one ($P < 0.005$) during the patterns task. Furthermore, though peak signal differences in the left mid-VLPFC region that showed a negative–recency effect for words also showed a qualitative pattern of recent > non-recent for patterns, this difference was not reliable ($F = 2.5$, $P = 0.13$). Hence, similar to previous reports (Mecklinger *et al.*, 2003), the present experiment failed to provide evidence in favor of domain general PI resolution in the mid-VLPFC. However, strong inferences cannot be drawn from this null finding because accuracy was markedly lower in the patterns tasks.

Discussion

The present experiment sought to advance understanding of the nature of PFC mechanisms that resolve PI during short-term item recognition. Four central findings emerged from consideration of PI during the words task. First, an extended set of PFC regions were sensitive to negative–recency, including a left mid-VLPFC region previously associated with PI resolution in addition to bilateral FPC. Second, convergence analyses revealed that these regions anatomically overlapped with left PFC regions engaged during domain-general episodic recollection. Third, probe recency also elicited greater PFC activation during positive trials. Finally, probe type modulated the magnitude of the recency effect in the left mid-VLPFC, but not in the FPC or right VLPFC, suggesting that multiple cognitive control processes may be recruited to resolve PI. We consider each of these findings in turn, and then discuss how these observations provide important constraints on mechanistic accounts of PI resolution.

The Frontopolar Cortex and Proactive Interference

The observed sensitivity of the FPC to recency is broadly consistent with studies that have assessed the contributions of

cognitive control to working memory and episodic memory. Such studies have reported increased FPC activation during the performance of tasks that involve minimal response conflict or selection but require the generation of subgoals and the integration of representations deriving from different subgoal stages (Koechlin *et al.*, 1999; Braver and Bongiolatti, 2002; Bunge *et al.*, 2003; Badre and Wagner, 2004). In the context of episodic retrieval, the FPC may support post-retrieval monitoring, which also putatively requires integration of retrieved mnemonic information with decision criteria *en route* to a response (e.g. Rugg *et al.*, 1999; Wagner, 1999; Rugg and Wilding, 2000; Buckner and Wheeler, 2001; Fletcher and Henson, 2001; Dobbins *et al.*, 2002, 2003; Kahn *et al.*, 2004).

During short-term item recognition, a similar integration process might be differentially required to guide a decision on how to respond when the probe was a member of the previous target set (i.e. a recent probe). Specifically, multiple mnemonic signals, including familiarity and information about membership in the current and/or previous target set, must be evaluated with respect to decision criteria, such as with respect to the appropriate temporal context. Consistent with this perspective, the present study provides the first compelling evidence that the FPC is engaged in the face of PI during short-term item recognition, extending a previously suggested subthreshold effect by Jonides *et al.* (1998). Reliable detection of this effect may derive from increased power due to the inclusion of more experimental trials (~50% more on average) than in previous reports (Jonides *et al.*, 1998, 2000; D'Esposito *et al.*, 1999; Bunge *et al.*, 2001; Thompson-Schill *et al.*, 2002; Mecklinger *et al.*, 2003; Nelson *et al.*, 2003), thus increasing sensitivity to detect effects in the FPC, a region that suffers modest susceptibility-induced signal loss.

To the extent that a similar FPC process supporting monitoring and/or integration is engaged during both episodic retrieval and PI resolution, one might expect that the regions showing sensitivity to PI during short-term item recognition would overlap with those engaged during episodic recollection. Consistent with this prediction, the left FPC and mid-VLPFC regions observed to be sensitive to recency converged with those implicated in domain-general retrieval of episodic details in an independent sample of subjects (Fig. 3*D*). This convergence analysis provides evidence for the hypothesized commonality in process, moving beyond a qualitative or general 'regional' similarity to that of voxel-level overlap.

Of course, this convergence cannot provide irrefutable evidence of reliance on a common process, because, even at the resolution of fMRI, two distinct and independent neural processes may occupy co-local PFC voxels. Such additivity of processes within a single region of FPC is not without precedent in the cognitive control literature (e.g. Badre and Wagner, 2004). Moreover, it is also clear that the PFC regions observed during episodic recollection and PI resolution do not overlap perfectly, particularly with respect to the posterior DLPFC. Hence, the convergence analysis suggests that some of the cognitive control processes engaged during episodic recollection—in particular, those subserved by the left FPC and mid-VLPFC—may also be engaged in the face of PI.

Positive Recency Effects

Analysis of the effects of recency revealed increased activation in the left mid-VLPFC and FPC on both negative– and positive–recent trials. Interestingly, in the present experiment mild recency-induced facilitation was evident behaviorally on positive trials, consistent with quantitative patterns reported in at least two previous studies using this paradigm (D'Esposito *et al.*, 1999; Thompson-Schill *et al.*, 2002). Though the positive trial effects on activation levels diverge somewhat from these corresponding behavioral effects, such divergence is consistent with prior reports of left VLPFC increases during congruent trials in the Stroop paradigm (Milham *et al.*, 2001), a task in which behavioral facilitation effects are more substantial than those reported here. Similarly, within the context of a conceptual repetition priming experiment, within-feature behavioral priming (RT speeding) has been associated with reduced left VLPFC activation relative to an unprimed baseline (e.g. Demb *et al.*, 1995; Wagner *et al.*, 2000), whereas across-feature behavioral priming can be accompanied by increased left VLPFC activation relative to baseline (Thompson-Schill *et al.*, 1999). Thompson-Schill *et al.* (1999) hypothesized that this latter activation increase reflects greater demands on selection processes that resolve interference due to the priming of a task-irrelevant feature. Within the present context, the observed activation increases in the FPC and mid-VLPFC during positive–recent trials are particularly important as they argue strongly against a mechanistic framework that predicts a uniform reduction in control demands due to the convergence of multiple sources of evidence favoring a particular response.

Of further theoretical significance, the pattern of activity in the FPC and left mid-VLPFC across positive and negative trials is inconsistent with a hypothesis that these regions are globally sensitive to the presence or absence of familiarity. In particular, the magnitude of activation in these regions did not differ between positive–non-recent trials and negative–non-recent trials (see Fig. 3*B*), even though a positive probe's membership in the current target set ensures that it will be relatively more familiar than a negative probe.

Analysis of positive trials also suggested functional differences between the FPC and left mid-VLPFC. Activity in the FPC increased comparably in response to recency, irrespective of whether the probe was positive or negative. That is, the FPC was not sensitive to the congruency between familiarity and a response, as this would have produced a probe × recency interaction. By contrast, a probe × recency interaction was observed in the left mid-VLPFC. This interaction may suggest that the left mid-VLPFC is not exclusively sensitive to the history of a given probe (i.e. its presence or absence in the previous trial target set), but is also modulated by the response attribution of the probe. This characteristic may differentiate processing in this region from the FPC, and further points to multi-component cognitive control contributions to PI resolution.

Supplemental exploratory correlation analyses further associate the control processes mediated by the FPC and left mid-VLPFC with different components of behavior. Specifically, we assessed the relation between behavioral indices of PI—expressed as recency-induced increases in RT and decreases in corrected recognition (computed on hits – false alarms) during negative trials—and recency-induced changes in left mid-VLPFC and FPC activation (Fig. 4). Interestingly, across-subject differences in PI-related activation increases in the mid-VLPFC tended to be positively related to differences in RT slowing ($R = 0.44$, $P < 0.07$), whereas PI-related activation

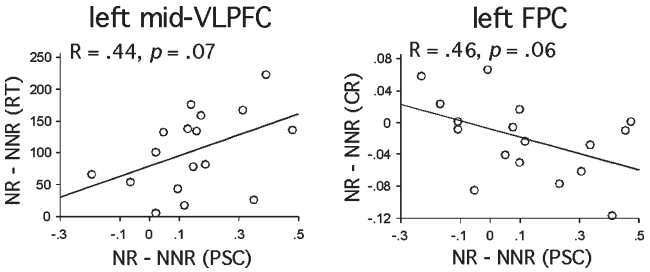

Figure 4. Correlations between behavioral indices of PI and PFC activation in response to PI. Individual differences in percent signal change (PSC) during negative–recent (NR) relative to negative–non-recent (NNR) words trials positively correlated with differences in RT slowing due to recency. Individual differences in left FPC activation in the face of PI were negatively correlated with differences in recency-induced declines in corrected recognition (CR).

increases in the left FPC tended to negatively correlate with interference-related declines in response accuracy ($R = 0.46$, $P = 0.06$). Though strong conclusions are not warranted based on these outcomes alone, these trends are intriguing as they suggest that the mid-VLPFC and FPC were associated with different aspects of behavioral performance. This qualitative difference is consistent with distinct control processes that operate on separable components of PI resolution.

One such distinction, suggested by the extant functional literature on these regions, might lie between selection/retrieval mechanisms that overcome interference and so impact RT (correlated with the left mid-VLPFC) and post-retrieval monitoring/integration processes related to arriving at a decision for action that might impact recognition outcome (correlated with the FPC). It is notable that the direction of correlation also differed between the left mid-VLPFC (positive with RT) and FPC (negative with corrected recognition). However, without an estimate of baseline impact of interference on behavior in each subject, it is difficult to interpret the direction of correlation. For example, the positive correlation between interference RT and left VLPFC might reflect increased processing to overcome greater interference, interference that would be even greater were that processing to have not been engaged. Indeed, damage inclusive of the left mid-VLPFC produces greatly enhanced behavioral interference (Thompson-Schill *et al.*, 2002), potentially consistent with such a complex relationship. Nevertheless, the qualitative difference in the direction of correlation further points to a process distinction between the mid-VLPFC and FPC. In the final section, we consider such mechanistic perspectives in greater detail.

Frontal Lobe Mechanisms that Resolve Proactive Interference

The full complement of observed results provides insight into the processes that resolve PI. Specifically, it is evident that multiple cognitive control processes contribute to performance under conditions of PI, including those mediated by the left mid-VLPFC and FPC. Moreover, because recency has the effect of up-regulating engagement of these processes, even when the recent probe is a member of the current target set, control demands are not uniformly reduced when multiple sources of evidence converge to guide a response. However, responses to recency cannot be simply interpreted as a general sensitivity to item familiarity. Finally, functional differences appear to distinguish the control processes mediated by the FPC and left mid-VLPFC. Positive–recency and negative–recency effects were comparable in the FPC whereas the consequence of positive–recency was more modest than that of negative–recency in the left mid-VLPFC, and activity in the FPC and mid-VLPFC tended to differentially correlate with separate components of behavior. Constrained by these findings, we will attempt to specify two classes of mechanistic perspectives on PI resolution.

Prior mechanistic accounts of PI resolution assign a response- or attribute-selection function to the left mid-VLPFC that is differentially necessary when recency induces conflict (Jonides *et al.*, 1998, 2002; D'Esposito *et al.*, 1999; Mecklinger *et al.*, 2003). Such models, which we generally term familiarity-inhibition models, at least implicitly suggest that because all positive probes have just been encountered, and so are familiar, familiarity itself may come to be associated with a positive response. During short-term item recognition, a process of matching a presented probe to the currently maintained target set is required on every trial. Interference during the processing of negative–recent probes may therefore arise from conflict between the result from this matching process ('negative') and the learned tendency to respond 'positive' to probes that are familiar. When activation of the competing 'positive' response makes selection of the 'negative' response more difficult, a response selection process is putatively required to select the 'negative' response. Alternatively, the attribution of familiarity itself might interfere with selecting the appropriate response, and PI resolution proceeds, in this case, through inhibition of the influence of familiarity on assigning a probe to a target context (as opposed to directly selecting the target response).

Past formulations of this familiarity-inhibition mechanism have focused on delineating this single form of control, which depends specifically on the left mid-VLPFC mechanisms. However, in isolation, such a selection mechanism would need to operate without prior knowledge of which response to select, or which attribute (familiarity or set membership) to favor. For example, there might be task contexts in which familiarity should govern a response and so selection should proceed in favor of the attribution of familiarity. By way of extending these models, a plausible variant might include an additional process—partially dependent on FPC—that monitors the results of the biasing process in the context of task-specific decision criteria, such as prioritizing set membership or temporal context. Under such a circumstance, facilitation on positive trials is not necessarily predicted and FPC activation is anticipated. However, it is not entirely clear how such a model would account for the increased activation on positive–recent trials, while also distinguishing between interference from familiarity due to membership in the previous set but not from familiarity due to membership in the current set. Hence, though still plausible, the modified familiarity-inhibition model appears challenged by key aspects of the present findings.

An alternative class of models, which we term context-retrieval models, considers PI resolution with respect to those control processes also engaged during retrieval from episodic memory. Context-retrieval proposes that PI resolution proceeds by selecting relevant episodic details in order to assign a probe to a task-relevant temporal context. Hence, the familiarity-inhibition and context-retrieval models both propose similar cognitive control processes to overcome PI, namely representational selection and monitoring, and also both recognize that the critical PI manipulation may arise from a long-term memory signal (e.g. familiarity) cued by a recently encountered item that has dropped from active memory.

However, context-retrieval and familiarity-inhibition differ fundamentally with respect to the nature of the representations that give rise to PI, and thus those representations that are selected and monitored to ultimately guide action. Specifically, whereas familiarity-inhibition assigns PI to conflict between stimulus attributes or between mappings that give rise to responses, context-retrieval posits interference as competition amongst specific episodic details that can assign an item to a particular temporal context.

From one such perspective, PI resolution depends on the retrieval and evaluation of context information. Context information refers to any retrieved detail that can be used to assign a probe to the context in which it was encoded. Examples of such information may include the associated targets in a probe's memory set, its spatial location, or a temporal tag. From this perspective, multiple PFC subregions contribute to context retrieval and the integration of retrieved information with the decision criteria, including mechanisms that retrieve target contextual information (e.g. the left mid-VLPFC) and mechanisms that monitor recovered information in the service of arriving at a decision for action (e.g. the FPC). Because not all familiar probes are members of the current target set, when presented with a familiar probe, context retrieval processes are engaged to assign a probe to the context in which it was recently encountered. Importantly, when a probe can be associated with more than one source, interference may arise, consistent with classical accounts of PI in episodic memory. Thus, retrieval demands vary depending on the extent that one retrieved piece of contextual information needs to be favored over another interfering contextual representation.

Critically, this mechanistic hypothesis may provide a parsimonious account of the present results. On negative–recent trials, interference emerges because the familiar probe induces activation of associated details from the previous (trial $n - 1$) context in which the probe had appeared. This competes with retrieval or selection of details from the current (trial n) context. Consequently, demands on selection and monitoring processes increase, as reflected in the left mid-VLPFC and FPC, respectively. On positive–recent trials, the association of the probe with the previous trial context also results in competition during context retrieval, reflected in a recency effect in the left mid-VLPFC, and an increase in monitoring demands, reflected in a recency effect in the FPC. However, positive trials were also members of the currently maintained target set. This may make the relevant context information prepotent and thus easier to retrieve. Hence, relative to negative–recent trials, selection demands on positive–recent trials are more modest. Accordingly, this model accounts for the probe × recency interaction observed in the left mid-VLPFC. Though further empirical work is needed to distinguish definitively between this model and the familiarity-inhibition account, the present results lend some support to the context-retrieval hypothesis.

Conclusions

PI places considerable constraints on cognition, and thus its resolution is critical for execution of goal-relevant behavior. The evidence reported here indicates that, during short-term item recognition, PI is resolved by multiple cognitive control mechanisms, including those mediated by the left mid-VLPFC and FPC. Additional work may further distinguish and constrain the mechanistic perspectives on PI resolution described here. This work has important and broad implications for the study of memory and cognitive control, as it suggests that the PFC mechanisms responsible for PI resolution during short-term item recognition may be common with those required to resist the more classic effects of PI associated with forgetting from episodic memory. Indeed, a neurally specified mechanism of PI resolution may contribute fundamentally to our knowledge of the manner and processes through which mnemonic obstacles to successful memory performance and action are overcome.

Notes

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References

Badre D, Wagner AD (2004) Selection, integration, and conflict monitoring: assessing the nature and generality of prefrontal cognitive control mechanisms. Neuron 41:473–487.

Braver TS, Barch DM, Kelley WM, Buckner RL, Cohen NJ, Miezin FM, Snyder AZ, Ollinger JM, Akbudak E, Conturo TE, Petersen SE (2001) Direct comparison of prefrontal cortex regions engaged by working and long-term memory tasks. Neuroimage 14:48–59.

Braver TS, Bongiolatti SR (2002) The role of frontopolar cortex in subgoal processing during working memory. Neuroimage 15:523–536.

Braver TS, Reynolds JR, Donaldson DI (2003) Neural mechanisms of transient and sustained cognitive control during task switching. Neuron 39:713–726.

Brown J (1958) Some tests of the decay theory of immediate memory. Quart J Exp Psychol 10:12–21.

Buckner RL, Petersen SE, Ojemann JG, Miezin FM, Squire LR, Raichle ME (1995) Functional anatomy studies of explicit and implicit memory retrieval tasks. J Neurosci 15:12–29.

Buckner RL, Wheeler ME (2001) The cognitive neuroscience of remembering. Nat Rev Neurosci 2:624–634.

Buckner RL (2003) Functional–anatomic correlates of control processes in memory. J Neurosci 23:3999–4004.

Bunge SA, Ochsner KN, Desmond JE, Glover GH, Gabrieli JD (2001) Prefrontal regions involved in keeping information in and out of mind. Brain 124:2074–2086.

Bunge SA, Kahn I, Wallis JD, Miller EK, Wagner AD (2003) Neural circuits subserving the retrieval and maintenance of abstract rules. J Neurophys 90:3419–3428.

Bunge SA, Badre D, Wendelken C, Wagner AD (2005) Analogical reasoning and prefrontal cortex: evidence for separable retrieval and integration mechanisms. Cereb Cortex 15:239–249.

Cabeza R, Dolcos F, Graham R, Nyberg L (2002) Similarities and differences in the neural correlates of episodic memory retrieval and working memory. Neuroimage 16:317–330.

Cansino S, Maquet P, Dolan RJ, Rugg MD (2002) Brain activity underlying encoding and retrieval of source memory. Cereb Cortex 12:1048–1056.

Carter CS, Mintun M, Cohen JD (1995) Interference and facilitation effects during selective attention: an $H_2{}^{15}O$ PET study of Stroop task performance. Neuroimage 2:264–272.

Christoff K, Prabhakaran V, Dorfman J, Zhao Z, Kroger JK, Holyoak KJ, Gabrieli JD (2001) Rostrolateral prefrontal cortex involvement in relational integration during reasoning. Neuroimage 14: 1136–1149.

Christoff K, Ream JM, Geddes LP, Gabrieli JD (2003) Evaluating self-generated information: anterior prefrontal contributions to human cognition. Behav Neurosci 117:1161–1168.
Cocosco CA, Kollokian V, Kwan RKS, Evans AC (1997) Brainweb: online interface to a 3D MRI simulated brain database. Neuroimage 5:425.
Dale AM (1999) Optimal experimental design for event-related fMRI. Hum Brain Mapp 8:109–114.
Demb JB, Desmond JE, Wagner AD, Vaidya CJ, Glover GH, Gabrieli JDE (1995) Semantic encoding and retrieval in the left inferior prefrontal cortex: a functional MRI study of task difficulty and process specificity. J Neurosci 15:5870–5878.
D'Esposito M, Postle BR, Jonides J, Smith EE (1999) The neural substrate and temporal dynamics of interference effects in working memory as revealed by event-related functional MRI. Proc Natl Acad Sci USA 96:7514–7519.
Dobbins IG, Foley H, Schacter DL, Wagner AD (2002) Executive control during episodic retrieval: multiple prefrontal processes subserve source memory. Neuron 35:989–996.
Dobbins IG, Rice HJ, Wagner AD, Schacter DL (2003) Memory orientation and success: separable neurocognitive components underlying episodic recognition. Neuropsychologia 41:318–333.
Dobbins IG, Wagner AD (2005) Domain-general and domain-sensitive prefrontal mechanisms for recollecting evens and detecting novelty. Cereb Cortex (in press).
Fletcher PC, Henson RN (2001) Frontal lobes and human memory: insights from functional neuroimaging. Brain 124:849–881.
Hasher L, Zacks RT (1988) Working memory, comprehension, and aging: a review and a new view. In: The psychology of learning and motivation (Bower GH, ed.), pp. 193–225. Orlando, FL: Academic Press.
Johnson MK, Raye CL (1981) Reality monitoring. Psychol Rev 88:67–85.
Johnson MK, Hashtroudi S, Lindsay DS (1993) Source monitoring. Psychol Bull 114:3–28.
Johnson MK, Raye CL, Mitchell KJ, Greene EJ, Anderson AW (2003) FMRI evidence for an organization of prefrontal cortex by both type of process and type of information. Cereb Cortex 13:265–273.
Jonides J, Smith EE, Marshuetz C, Koeppe RA, Reuter-Lorenz PA (1998) Inhibition in verbal working memory revealed by brain activation. Proc Natl Acad Sci USA 95:8410–8413.
Jonides J, Marshuetz C, Smith EE, Reuter-Lorenz PA, Koeppe RA, Hartley A (2000) Age differences in behavior and PET activation reveal differences in interference resolution in verbal working memory. J Cogn Neurosci 12:188–196.
Jonides J, Badre D, Curtis C, Thompson-Schill SL, Smith EE (2002) Mechanisms of conflict resolution in prefrontal cortex. In: Principles of frontal lobe function (Stuss DT, Knight RT, eds), pp. 233–245. Oxford: Oxford University Press.
Kahn I, Davachi L, Wagner AD (2004) Functional–neuroanatomic correlates of recollection: implications for models of recognition memory. J Neurosci 24:4172–4180.
Keppel G, Underwood BJ (1962) Proactive inhibition in short-term retention of single items. J Verb Learn Verb Behav 1:153–161.
Koechlin E, Basso G, Pietrini P, Panzer S, Grafman J (1999) The role of anterior prefrontal cortex in human cognition. Nature 399:148–151.
Koechlin E, Ody C, Kouneiher F (2003) The architecture of cognitive control in the human prefrontal cortex. Science 302.
McGeoch JA (1942) The psychology of human learning. New York: Longmans, Green.
Mecklinger A, Weber K, Gunter TC, Engle RW (2003) Dissociable brain mechanisms for inhibitory control: effects of interference content and working memory capacity. Brain Res Cogn Brain Res 18:26–38.
Milham MP, Banich MT, Webb A, Barad V, Cohen NJ, Wszalek T, Kramer AF (2001) The relative involvement of anterior cingulate and prefrontal cortex in attentional control depends on the nature of conflict. Cogn Brain Res 12:467–473.
Milham MP, Erickson KI, Banich MT, Kramer AF, Webb A, Wszalek T, Cohen NJ (2002) Attentional control in the aging brain:Insights from an fMRI study of the Stroop task. Brain Cogn 49:167–202.
Monsell S (1978) Recency, immediate recognition memory, and reaction time. Cogn Psychol 10:465–501.
Nelson JK, Reuter-Lorenz PA, Sylvester C-YC, Jonides J, Smith EE (2003) Dissociable neural mechanisms underlying response-based and familiarity-based conflict in working memory. Proc Natl Acad Sci USA 100:11171–11175.
Nichols T, Brett M, Andersson J, Wager T, Poline J-B (2005) Valid conjunction inference with the minimum statistic. NeuroImage (in press).
Nolde SF, Johnson MK, D'Esposito M (1998) Left prefrontal activation during episodic remembering: an event-related fMRI study. Neuroreport 9:3509–3514.
Nyberg L, McIntosh AR, Cabeza R, Habib R, Houle S, Tulving E (1996) General and specific brain regions involved in encoding and retrieval of events:what, where, and when. Proc Natl Acad Sci USA 93: 11280–11285.
Nyberg L, Marklund P, Persson J, Cabeza R, Forkstam C, Petersson KM, Ingvar M (2003) Common prefrontal activations during working memory, episodic memory, and semantic memory. Neuropsychologia 41:371–377.
Peterson LR, Peterson MJ (1959) Short-term retention of individual items. J Exp Psychol 58:193–198.
Postle, B. R., Brush, L. N. (2004). The neural bases of the effects of item-nonspecific proactive interference in working memory. Cogn Affect Behav Neurosci 4:379–392.
Ranganath C, Johnson MK, D'Esposito M (2000) Left anterior prefrontal activation increases with demands to recall specific perceptual information. J Neurosci 20:RC108.
Rugg MD, Fletcher PC, Frith CD, Frackowiak RSJ, Dolan RJ (1996) Differential activation of the prefrontal cortex in successful and unsuccessful memory retrieval. Brain:2073–2083.
Rugg MD, Fletcher PC, Chua PM, Dolan RJ (1999) The role of the prefrontal cortex in recognition memory and memory for source: an fMRI study. Neuroimage 10:520–529.
Rugg MD, Wilding EL (2000) Retrieval processing and episodic memory. Trends Cogn Sci 4:108–115.
Sakai K, Passingham RE (2003) Prefrontal interactions reflect future task operations. Nat Neurosci 6:75–81.
Shimamura AP (1995) Memory and frontal lobe function. In: The cognitive neurosciences (Gazzaniga MS, ed.), pp. 803–813. Cambridge, MA: MIT Press.
Squire LR (1992) Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. Psychol Rev 99: 195–231.
Stroop JR (1935) Studies of interference in serial verbal reactions. J Exp Psychol 18:643–662.
Talairach J, Tournoux P (1988) A co-planar stereotactic atlas of the human brain. Stuttgart: Thieme.
Thompson-Schill SL, D'Esposito M, Kan IP (1999) Effects of repetition and competition on activity in left prefrontal cortex during word generation. Neuron 23:513–522.
Thompson-Schill SL, Jonides J, Marshuetz C, Smith EE, D'Esposito M, Kan IP, Knight RT, Swick D (2002) Effects of frontal lobe damage on interference effects in working memory. Cogn Affect Behav Neurosci 2:109–120.
Tulving E, Kapur S, Craik FIM, Moscovitch M, Houle S (1994) Hemispheric encoding-retrieval asymmetry in episodic memory: positron emission tomography findings. Proc Natl Acad Sci USA 91:2016–2020.
Wagner AD, Desmond JE, Glover GH, Gabrieli JDE (1998) Prefrontal cortex and recognition memory: fMRI evidence for context-dependent retrieval processes. Brain 121:1985–2002.
Wagner AD (1999) Working memory contributions to human learning and remembering. Neuron 22:19–22.
Wagner AD, Koutstaal W, Maril A, Schacter DL, Buckner RL (2000) Task-specific repetition priming in left inferior prefrontal cortex. Cereb Cortex 10:1176–1184.