Neural mechanisms of semantic interference and false recognition in short-term memory

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ABSTRACT

Decades of research using the Deese–Roediger–McDermott (DRM) paradigm have demonstrated that episodic memory is vulnerable to semantic distortion, and neuroimaging investigations of this phenomenon have shown dissociations between the neural mechanisms subserving true and false retrieval from long-term memory. Recently, false short-term memories have also been demonstrated, with false recognition of items related in meaning to memoranda encoded less than 5 s earlier. Semantic interference is also evident in short-term memory, such that correct rejection of related lures is slowed relative to correct rejection of unrelated lures. The present research constitutes the first fMRI investigation of false recognition and semantic interference in short-term memory using a short-term DRM paradigm in which participants retained 4 semantic associates over a short 4-s filled retention interval. Results showed increased activation in the left mid-ventrolateral prefrontal cortex (BA45) associated with semantic interference, and significant correlations between these increases and behavioral measures of interference across subjects. Furthermore, increases in dorsolateral PFC occurred when related lures were correctly rejected versus falsely remembered. Compared with false recognition, true recognition was associated with increases in left fusiform gyrus, a finding consistent with the notion that increased perceptual processing may distinguish true from false recognition. Findings are discussed in relation to current models of interference resolution in short-term memory, and suggest that false short-term recognition occurs as a consequence of the failure of frontally mediated cognitive control processes which adjudicate semantic familiarity in support of accurate mnemonic retrieval.

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Introduction

Distortions of memory have been a subject of interest for cognitive psychology since its inception. One reason for this interest is that examination of the circumstances under which our memories fail us can illuminate our understanding of how memory is organized. In the last two decades, the term false memory has come to describe instances in which memories become distorted, leading to false recognition and false recall of previously unstudied items. In the Deese–Roediger–McDermott (DRM; Deese, 1959; Roediger and McDermott, 1995) paradigm, participants study lists of 12–15 words which are all related in meaning to a common unstudied theme word, or related lure. At test, participants are required to either recognize studied items from a list of probes that includes related lures, or to recall studied items in free report. Investigations using variants of this procedure have shown that participants consistently and confidently falsely recognize related lures, and even produce these items in free recall (see Gallo, 2006 for review).

Although initial investigations of this false memory phenomenon were limited to paradigms that included long study lists and retention intervals that varied from several seconds to many hours, there is recent evidence that false memories are produced rapidly, within the time and load constraints of traditionally defined short-term memory tasks (Atkins and Reuter-Lorenz, 2005, 2008; Coane et al., 2007; Flegal et al., 2010). For example, using a short-term variation of the DRM (ST-DRM) paradigm with 4-item lists, we recently demonstrated reliable false recognition and recall of unstudied lures only 4 seconds following encoding (Atkins and Reuter-Lorenz, 2008). Furthermore, in the recognition version of our task, we found strong evidence that the semantic relationship between related lures and memoranda induced interference even when related lures were not falsely recognized.
Specifically, participants took longer to correctly reject a related lure compared to one that was unrelated to the memoranda. We refer to this response time (RT) difference as semantic interference (SI).

The increased time required to reject related lures is consistent with the notion that correct rejection of these items requires a control process that resolves interference induced by the semantic familiarity of these items. When interference is resolved successfully, the related lure can be correctly rejected. False recognition of these items could indicate either a failure of this control process, or a failure to engage it at all.

Interestingly, false recognition has not been widely investigated as a failure of cognitive control. One reason for this is the paucity of crosstalk between research on false long-term memory, and investigations of cognitive control in short-term memory. The control of proactive interference in short-term memory is an executive process that has been studied extensively using the recent probes (RP) task (Jonides et al., 1998; Monsell, 1978) and may be relevant to controlling false recognition as well. In the RP task, participants study a set of 4 memoranda, typically letters or words. Following a brief retention interval, a probe item is presented that requires a yes/no recognition response. Generally, 4 probes types are employed. Probes that require a ‘No’ response include recent negative (RN) probes that are not present on the current trial, but were members of the memory set on the trial immediately preceding the current one, and non-recent negative (NRN) probes that are not members of the current set and have not appeared for the last several trials. A ‘Yes’ response is required to standard positive (POS) probes which are members of the current memory set, and recent positive (RPOS) probes that appeared as memoranda on both the current and immediately preceding trial.

Participants are markedly slower at rejecting RN relative to NRN probes, suggesting that temporal familiarity makes RN probes more difficult to reject. This slowing has been attributed to the engagement of an interference control process that adjudicates this familiarity in the service of accurate recognition memory. Numerous neuroimaging studies indicate an important role for left mid-ventrolateral prefrontal cortex (L VLPFC, in the region of Brodmann’s area 45) in the circuitry subserving this resolution process. Activation increases for RN relative to NRN probes have been shown and replicated across a variety of RP tasks (see Jonides and Nee, 2006 for review). Furthermore, behavioral indices of proactive interference (PI), calculated as the RT difference between correct responses to RN relative to NRN probes, show positive correlations with these increases L VLPFC activity (Badre and Wagner, 2005, 2007; Jonides and Nee, 2006).

The importance of L VLPFC is also demonstrated by patient studies demonstrating that focal lesions to this region are associated with behavioral increases in PI (Hamilton and Martin, 2005; Thompson-Schill et al., 1997). Furthermore, increased activity in L VLPFC regions has been linked to semantic elaboration during episodic retrieval (Raposo et al., 2009), and to selection between semantic competitors (Hirshorn et al., 2005; Thompson-Schill et al., 1997; see also Gold and Buckner, 2002; Oztekin et al., 2009; Poldrack et al., 1999). In the Verb Generate task, for instance, participants are asked to generate a verb corresponding to a noun, which is presented to them in the scanner. For example, given the noun SCISSORS, a participant may generate the response ‘CUT’. Both L VLPFC activity and RT have been found to increase when verbs must be generated in response to nouns that have many associated verbs (for example, ‘BALL’) than those that have few (for example ‘SCISSORS’; Nelson et al., 2009; Persson et al., 2004; Thompson-Schill et al., 1997). Under these conditions left VLPFC has been thought to contribute to a post-semantic retrieval process that selects between semantic competitors (Badre and Wagner, 2007; Kan and Thompson-Schill, 2004). Thus, converging evidence suggests that regions of L VLPFC may be involved in mediating interference from temporally familiar or semantically related competitors. Further, a recent investigation comparing the RP and Verb Generate tasks demonstrated overlap in the L VLPFC activations associated with interference in both tasks (Nelson et al., 2009). In the present study, we test the hypothesis that L VLPFC may also play a role in controlling SI and vulnerability to false memory in the ST-DRM task. In this task, correct rejection of related lures requires participants to overcome interference induced by semantic, rather than temporal familiarity, as in the RP task. Therefore a primary goal of the present study is to investigate the role of L VLPFC in SI. Whereas one prior study (Paz-Alonso et al., 2008) of false long-term memory has implicated more anterior regions of L VLPFC (Brodmann’s area 47) in semantic elaboration during retrieval, we were specifically interested in mechanisms associated with the cognitive control of semantic interference.

An additional goal of the present study is to more precisely examine the role of L VLPFC in cognitive control of interference. Although correlations between behavioral measures of interference and increases in L VLPFC activity are consistent with the interpretation that this region is primary involved in the resolution of interference (and therefore must work harder to resolve interference as it increases), such correlations are also consistent with the notion that L VLPFC does not play an active role in the resolution of interference per se, but rather provides an index of interference that is passed on to other regions within frontal cortex to support accurate task performance. Given high levels of task performance in the RP and Verb Generate tasks, research using these paradigms has focused almost exclusively on correct trials. Thus, little is currently known regarding the distinction between the neural mechanisms which respond to the presence of interference and those associated with successful versus unsuccessful resolution of this interference. By comparing the neural activity associated with correct rejection versus false recognition of lure items in the ST-DRM paradigm, the present study will directly assess this question. If L VLPFC plays a direct role in the resolution of semantic interference in our paradigm, we would expect L VLPFC to distinguish between these two trial types, demonstrating increased activity for correct rejections versus false recognitions. Alternatively, if L VLPFC provides an index of interference that is passed along to other regions which mediate the resolution process more directly, we would expect a positive relationship between increases in L VLPFC activity and behavioral measures of SI, but expect no difference in this region’s response to correctly rejected versus falsely recognized lure probes.

A final important goal of this work is to compare true and false recognition in the short-term memory domain. Several studies have examined neural regions that distinguish true from false retrieval in long-term memory (e.g. Abe et al., 2008; Cabeza et al., 2001; Garoff-Eaton et al., 2006; Johnson et al., 1997; Kim and Cabeza, 2007; Okado and Stark, 2003; Slotnick and Schacter, 2004). In one such investigation, Cabeza et al. (2001) demonstrated similar activation of the hippocampus during true and false recognition, but showed increased parahippocampal activation for true, and false recognition, thus demonstrating a dissociation between the neural mechanisms subserving true and false recognition. Additional work has highlighted remarkable overlap in the frontal, parietal and medial temporal regions subserving true and false recognition (e.g. Schacter and Slotnick, 2004 for review). More recently, interactions between memory veracity and confidence have also been demonstrated, with medial temporal lobe (MTL) regions showing increased activity during confident veridical recognition, and frontal–parietal regions showing increased activity during confident false recognition (Kim and Cabeza, 2007).

It is currently unknown whether distinctions such as these will carry over from the long-term to the short-term memory domain, or whether similar mnemonic signatures are available within seconds of stimulus encoding. The present study will address these questions, and will examine the relationship between neural regions supporting resolution of semantic interference and successful vs. distorted remembering over short delays.
Method

Participants

Twenty participants (12 females; mean age = 20) were recruited from the University of Michigan. All participants gave informed consent as reviewed by the university’s Institutional Review Board. Participants were paid $20 per hour for their participation.

Task and procedure

Participants completed the ST-DRM task (see Fig. 1; Atkins and Reuter-Lorenz, 2008) during 6 task runs. At the beginning of each trial, a blinking red fixation appeared for 500 ms to warn the participant the trial was beginning. This was followed by a memory set consisting of 4 semantically related items, all associated with a common theme word. The memory set appeared for 1200 ms. Five hundred milliseconds (ms) following the offset of the memory items, a dual-operation math equation appeared at the center of the screen for 3000 ms. This equation was solved either correctly for example, \((4\times3) - 2 = 10\), or incorrectly, and participants made a left-handed response to indicate whether the math was correct or incorrect.1 Five hundred milliseconds following the offset of the math problem, a memory probe appeared and participants made a right-handed yes or no response indicating whether or not the probe was a member of the memory set.

During this task, theme words served as the probes on all the trials. There were two variations of “No” trials. The first were unrelated lure (UL) trials, in which the probe consisted of the theme word associated with a nonpresented list. The second were related lure (RL) trials, in which the probe consisted of the (unstudied) theme associated with the present memory set. On positive (POS) trials, the associated theme was embedded in the memory set, and served as the positive probe.

With the exception of positive probes, which by definition occurred twice within the same trial, no participant was exposed to any theme or memoranda more than once during the experiment. Backward associative strength (BAS), a measure of the degree of association between theme words and memoranda (see Roediger et al., 2001; Hicks and Hancock, 2002), was equated across memory lists associated with each probe type, and probe type was counter-balanced with lists across participants. This procedure ensured that participants encountered the same probes, all theme words, but in different contexts, as related lures, unrelated lures, or positive probes.

Trials were presented in random order for each participant. Participants completed 102 ST-DRM trials that were distributed across 6 task runs. Trials were equally distributed across all three probe types in each run. We used a 16-s ITI to allow for the hemodynamic response to return to baseline between trials (Glover, 1999). Participants completed 2 practice runs prior to entering the scanner, in order to become familiar with task and response requirements.

fMRI data acquisition and preprocessing

Our data were collected using a 3-T GE whole-body scanner equipped with a standard quadrature headcoil. Head movement during scanning was minimized with the use of foam padding. Experimental stimuli were presented using E-Prime software.

Functional T2* blood oxygenation level-dependent (BOLD) images were collected using a spiral sequence with 40 contiguous slices of 3.44 × 3.44 × 3 mm voxels (repetition time (TR) = 2000 ms, echo time (TE) = 30, flip angle = 90, and field of view (FOV) = 22 cm). T1-weighted gradient echo (GRE) anatomical images were acquired in the same FOV and slices as were used in the functional data collection (TR = 250, TE = 5.7, and flip angle = 90). A high-resolution (106 slice) set of anatomical images was acquired via spoiled gradient-recalled acquisition in steady state (SPGR) imaging (TR = 10.5, TE = 3.4, flip angle = 25, FOV = 24, slice thickness = 1.5 mm). SPGR images were corrected for signal inhomogeneity (G. Glover and K. Kristoff, http://www.psych.stanford.edu/_kalina/SMP99/Tools/ vol_homocor.html) and skull-stripped using the Brain Extraction Tool provided by FSL (Smith et al., 2004). These images were then normalized to the Montreal Neurological Institute (MNI) template (avg152t1.img) using SPM5 (Wellcome Department of Cognitive Neurology, London, UK). Functional images were corrected for slice-time differences using 4-point sinc interpolations (Oppenheim et al., 1999), and were corrected for head movement using MCLHRT (Jenkinson et al., 2002). In order to reduce the effect of spike artifacts, functional images were winsorized on a voxel by voxel basis to ensure that no voxel had a signal more than 3.5 standard deviations greater than the mean of the current run (Lazar et al., 2001). Functional images were then normalized to MNI space using transformations from the normalization of structural images, and were smoothed using an 8-mm Gaussian kernel. All analyses included a 128-s high-pass filter and AR(1) modeling to correct for temporal autocorrelation. For all analyses, each image was scaled to a global mean intensity of 100.

fMRI data analysis

Neuroimaging analyses were conducted using the General Linear Model implemented in SPM5 (Wellcome Department of Cognitive Neurology, London, UK) with separate regressors for each trial type in each run. Event-related activity to probes was modeled by convolving probe onsets with the canonical HRF. Statistical models examined probe-related activations associated with correct recognition of positive probes (hits), correct rejection of unrelated lures, correct rejection of related lures, and false alarms to related lures (false recognitions). Statistical models were estimated for each participant. The number of observations per condition depended on participant performance and therefore varied by participant. All but one participant produced a sufficient number of observations to estimate probe-related activity in each condition, including an average of 29.6 hits, 31.2 correct rejections of unrelated lures, 26.9 correct rejections of related lures, and 7.5 false alarms to related lures. The single participant, who produced no false recognition responses, was excluded from analyses that included this condition. All other participants exceeded a minimum criterion of 4 observations per condition. For each comparison of interest described below, contrast maps for each participant were submitted to random effects comparisons.

Results

Behavior

Behavioral findings replicate the SI and false memory effects demonstrated previously (Atkins and Reuter-Lorenz, 2008). Mean accuracy and response time (RT; correct trials only) measures were submitted to a repeated measures analysis of variance (ANOVA). There were main effects of probe type (positive, unrelated, related) on both accuracy, \(F = 16.98, p < .001\), \(\eta^2 = .47\) and RT, \(F = 37.22, p < .001\), \(\eta^2 = .66\).

Post-hoc tests were conducted to examine false memory and semantic interference effects, and were submitted to a Bonferroni correction for multiple comparisons. Table 1 shows the proportion of POS, UL, and RL items that received a ‘yes’ response during item recognition. We found a reliable false memory effect, with participants falsely recognizing related lures at a rate over four times that for unrelated lures, \(t = 6.01, p < .001, d = 1.54\). Mean RTs for accurate responses were 900 ms (SE = 29) for POS, 905 ms (SE = 40) for UL,
and 1062 ms (SE = .41) for RL items. Mean RT for false alarms to RL items was 1132 ms (SE = .52). With respect to accurate trials, participants were reliably slower to correctly reject related lures compared to unrelated lures, t = 8.10, p < .001, d = .86. Our SI index, measured as the difference in RT for correct rejections of related lure vs. unrelated lures had a mean of 156.92 ms (SE = 19.36).

Paired t-tests comparing false recognition RTs (false alarms to related lures) to true recognition RTs (hits to positive probes) indicate that false recognition of related lures was reliably slower than true recognition (t = 4.40, p = .001, d = 1.02). Furthermore, RTs associated with false recognition vs. correct rejections of related lures did not differ reliably, indicating that false recognition did not result from fast responding.

Mean accuracy on the math verification task was .80 (SE = .02). Overall recognition performance did not vary as a function of incorrect or correct responding on the math task (p > .6). Furthermore, post-hoc tests examining each probe type separately revealed no significant differences in the accuracy of responses to positive, unrelated lure or related lure items following correct vs. incorrect math judgments (p > .3 for all).

Neuroimaging results
Whole brain analyses
Results from our whole-brain analyses are presented in Table 2, and summarized below. Unless otherwise stated all comparisons reported were significant at p < .005, uncorrected, with threshold requirement of 20 or more contiguous voxels (Forman et al., 1995; Lieberman and Cunningham, 2009).

In order to examine the neural mechanisms associated with SI, we identified regions that showed increased probe-related activity in response to correctly rejected related lures, relative to correctly rejected unrelated lures. In both cases, correct ‘No’ responses were made to unstudied items, but SI is present only for related lures. This comparison is thus directly analogous to the recent vs. non-recall negative probe comparisons used in investigations of PI in the RP task.

Fig. 2 displays regions with greater activity for correct rejections of related lures vs. unrelated lures. These included a large cluster of voxels in left mid-VLPFC, with a single peak in BA45. This suggests, consistent with predictions, that L VLPFC is recruited when there is interference from unstudied items that are semantically associated with items in memory. Smaller clusters of activation within the bilateral anterior cingulate (ACC, BA32) and bilateral inferior parietal cortex (BA 40/7) also distinguished related lures from unrelated lures.

We examined neural mechanisms of true and false memory by first identifying regions associated with true and false recognition separately. For true recognition, we compared correct recognition of positive probes to correct rejections of unrelated lures (Pos. Hit > Unrelated CR). For false recognition, we compared false alarms to related lures and correct rejections of unrelated lures (Related FA > Unrelated CR).

True recognition was associated with increased activity in a network of fronto-parietal regions consistently associated with verbal short-term memory (Bedwell et al., 2005; Cappell et al., 2010; Chein and Fiez, 2001; Cohen et al., 1997; D’Esposito et al., 1998; Rypma and D’Esposito, 1999). Most notably, these included large increases of activation in left anterior prefrontal/dorsolateral prefrontal cortex (BA 10/46) and bilateral inferior parietal cortices (BA 40). False recognition showed a similar pattern of fronto-parietal activation, as well as a large cluster of activation in left posterior cingulate/retrosplenial cortex, a region previously linked to phenomenal feelings of remembering that may be independent of retrieval accuracy (Wagner et al., 2005).

In order to examine regions common to both true and false memory, we conducted a conjunction analyses of our true and false memory contrasts. For each contrast, we utilized a threshold of p < .01 with a cluster extent of 10 or more contiguous voxels. The conjoint probability estimate for the conjunction thus approached p = .0001 (Lazar et al., 2002), but this value should be considered with caution given the non-independence of the two contrasts. Results (Fig. 3A) showed left frontal and bilateral parietal activations common to both true and false recognition. We next examined regions that distinguished true from false recognition by directly contrasting activation associated with correct recognition of positive probes and false recognition of related lures (Pos. Hit > Related FA). Results are displayed in Fig. 3B. Compared with false recognition, true recognition was associated with increased

**Table 1**

<table>
<thead>
<tr>
<th>Probe type</th>
<th>Proportion of positive, unrelated, and related lure probes to which participants responded ‘Yes’.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>.89 ± .02</td>
</tr>
<tr>
<td>Unrelated lure</td>
<td>.03 ± .01</td>
</tr>
<tr>
<td>Related lure</td>
<td>.13 ± .02</td>
</tr>
</tbody>
</table>

Note—A “Yes” response indicates that the probe was recognized as a member of the current memory set. The proportion recognized therefore represents the hit rate for positive probes, and the false recognition rate for unrelated and related lures. The mean false recognition rate, defined as the difference between false recognition for unrelated and related lures was .10 (SE = .01).
activity in the left putamen/parahippocampal gyrus (PHG), the left fusiform gyrus, and the right VLPFC.

In order to more directly examine regions mediating successful rejection of interference-inducing related lures, we identified regions that distinguished correct rejection vs. false recognition of these items. Unlike our SI contrast, which examined differences between correct rejection of related and unrelated lures, this contrast directly compared neural activity associated with correct rejection vs. false recognition of related lures (Related CR > Related FA). Results from this contrast revealed increased activation in left dorsolateral prefrontal cortex (L DLPFC, BA 46/9; see Supplementary Fig. 1), as well as the fusiform gyrus and putamen. This finding suggests that while L VLPFC becomes activated in the presence of SI, L DLPFC may play a larger role in supporting correct rejection of interfering items.

ROI analyses

VLPFC. Results from our whole brain analysis supported our hypothesis that L VLPFC would distinguish between unrelated lures and related lures that induce SI. In order to investigate the relationship between VLPFC activity in the present task and that observed in studies of proactive interference, we conducted an ROI analysis to determine whether activation in the L VLPFC region associated with PI is also relevant for the control of SI. An ROI was formed by creating a 10-mm sphere surrounding our whole brain peak for the Recent Negative—Non-Recent Negative contrast in the Repeated Probes task (MNI peak: −51 21 11; Jonides et al., 1998; Nelson et al., 2003).

Fig. 4A plots mean percent signal change in L VLPFC for hits to positive probes, correct rejections of unrelated lures, and both correct rejections and false alarms to related lures. Activity in this ROI was strongly and positively correlated with individual differences in SI, r = .45. Furthermore, change in L VLPFC activity was also slightly weaker, positive correlation between increased activity for lure vs. negative probes and increases in our behavioral SI measure, r = −.51, p < .05.

2 We also examined the correlation between individual variations in SI and changes in L VLPFC activity in a 10-mm sphere surrounding our whole brain peak for the semantic interference contrast (−48 21 21). For this ROI, we found a similar, though slightly weaker, positive correlation between increased activity for lure vs. negative probes and increases in our behavioral SI measure, r = −.67, p < .01 (Fig. 4B). A positive correlation between L VLPFC activity and PI has also been reported in the recent probes task (Jonides and Nee, 2006).
Compared to correct rejections of unrelated lures, L VLPFC activation showed similar numerical increases in activity during both correct rejection and false recognition of related lures (see Fig. 4A), although the VLPFC increase during false recognition did not reach statistical significance, a finding most likely due to increased variability in the VLPFC response during false recognition. Direct comparisons of ROI activity during both correct rejection and false recognition of related lures also showed no difference between the two ($t = .144, p > .8$). Although this is a null finding, this result coupled with results from our direct comparison of whole-brain activity during correct rejection versus false recognition of related lures suggests that L DLPFC, rather than L VLPFC, may play an important role in mediating whether or not semantic relatedness leads to false recognition.

Another possibility is that L VLPFC might simply respond to the presence of semantic familiarity rather than interference per say. We tested this possibility by examining activation associated with positive probes. Because positive probes were studied items, they should have been both semantically and temporally familiar. However, this familiarity should not have induced interference because it was consistent with veridical recognition. If L VLPFC responded to familiarity only, activation should increase to positive probes as well as related lures. This was not the case, however, as probe-related activity did not differ for positive and unrelated negative probes in this region ($t = .186, p > .8$).

MTL. Given previous findings indicating a role for MTL in distinguishing true and false long-term memories, we were particularly interested in examining differences between true and false short-term memory in this region. Although our whole brain analysis revealed a large cluster of activation extending from the left putamen into the L parahippocampal gyrus (PHG), no other MTL activations distinguished true from false memory. In order to increase our sensitivity to detect MTL differences, we conducted an exploratory analysis by examining true vs. false differences in bilateral MTL at reduced threshold of $p < .05$. Our MTL ROI was defined as the bilateral hippocampus, PHG and amygdala using the Pick Atlas (Wake Forest University; http://www.fmri.wfubmc.edu). Results showed a single cluster of 12 voxels in L PHG ($-28, -3, -12$), which distinguished between true and false. This cluster was contiguous with the putamen/PHG cluster observed in our whole brain analysis. No other portions of MTL distinguished between true and false recognition.
The present study investigated the neural mechanisms of semantic interference and false recognition in a short-term memory version of the DRM task (Atkins and Reuter-Lorenz, 2008; Deese, 1959; Roediger and McDermott, 1995). We examined the neural mechanisms of SI by identifying regions of increased activation during the correct rejection of probes related in meaning to current memoranda (i.e., related lures) as compared to unrelated probes (i.e., unrelated lures). Past research indicating a role for L VLPFC in resolving interference induced by temporal familiarity in the recent probes task (Jonides and Nee, 2006), led us to predict this region would also be involved in interference induced by the semantic familiarity or similarity of related lure items. Consistent with this prediction, we found increased L VLPFC (BA44S) activity associated with the correct rejection of related vs. unrelated lures (Fig. 2).

ROI analyses revealed that across individuals there was a strong positive correlation between the magnitude of SI and L VLPFC activity in response to related vs. unrelated lures (see Fig. 4). This finding demonstrates that the positive relationship between behavioral indices of interference and L VLPFC activity is not unique to temporal familiarity, and suggests that common neural substrates are engaged in response to interference induced by either temporal or semantic familiarity.

Positive correlations between behavioral measures of interference and increased activity in L VLPFC could be interpreted as evidence that this region is either (a) the site of interference resolution and therefore must work harder to resolve interference as it increases, or (b) a site that provides an index of interference for each trial that is used by other cortical regions to support accurate memory performance. We attempted to distinguish between these possibilities by comparing L VLPFC activity for related lures that were ultimately rejected to those that were falsely recognized. Results showed a similar increase in probe-related activity for both correct rejections of and false alarms to related lures, indicating that the L VLPFC activity alone does not distinguish between semantic interference that is resolved correctly or not. In contrast, whole brain comparisons showed L DLPFC activation does distinguish between correct rejections and false alarms to related lures (see Supplementary Fig. 1), indicating that this region may play an important role in determining the extent to which interference indexed by LVLPCF can be mitigated to reduce false memories. This interpretation is consistent with previous work linking L DLPFC to post-retrieval source monitoring (e.g. Achim and Lepage, 2005).

In addition to L VLPFC, our semantic interference comparison of correct rejections of related vs. unrelated lures also showed increased activation in the bilateral ACC. Given strong evidence associating similar increases in ACC (BA 32/24) activity with response-level conflict across a variety of tasks (e.g. Milham and Banich, 2005; Milham et al., 2001; Nelson et al., 2003), involvement of this region most likely reflects the need to forgo a ‘yes’ response to a probe that is familiar in favor of a correct ‘no’ response.

Our examination of neural activity common to true and false short-term recognition suggests some similarity between the neural mechanisms supporting short and long-term retrieval. True and false recognition were both associated with increased activity within the left anterior PFC and bilateral PPC, both regions which have been previously associated with retrieval effort and monitoring that may be independent of the success of retrieval from long-term memory (e.g. Cabeza, 2008; Cabeza et al., 2008; Kompus et al., 2011). These findings converge with previous reports of common prefrontal activations during short and long-term retrieval (Ranganath et al., 2003) and suggest a growing body of literature highlighting similarities between the neural mechanisms supporting retrieval from short-term and long-term memory (e.g. Cabeza et al., 2002; Ranganath et al., 2005; Ranganath et al., 2003). The common recruitment of bilateral prefrontal regions during both true and false recognition is also found in long-term memory tasks, and has been interpreted as reflecting perceived oldness that may occur independently of memory accuracy (Cabeza, 2008; Cabeza et al., 2008). Replication of this finding in the current task suggests common neural representations of perceived oldness may be active during true and false recognition that occurs over short and long retention intervals.

Our comparisons of neural activity associated with true and false short-term memory also suggest some overlap between the neural mechanisms that distinguish true and false recognition over the short- and long-term. Compared with false recognition, true recognition was associated with increased activation in the left fusiform gyrus, a finding consistent with the notion that increased perceptual processing may serve as a signature distinguishing true from false recognition (Slotnick and Schacter, 2004). Increased left fusiform activity is also consistent with previous work which has indicated a potential role for this region in semantic processing by showing repetition priming effects that are selective for semantically meaningful stimuli (see Vuilleumier et al., 2002; Simons et al., 2003).

Whole-brain and ROI analyses also showed increases left PHG activation associated with true versus false recognition, a result which is consistent with previous work in the long-term memory domain (Cabeza et al., 2001) and which indicates a role for left PHG in distinguishing veridical and false memories following short or long-term retention intervals. True recognition was also associated with increased activation in a region of right VLPFC (BA44) consistently implicated in inhibitory control across a variety of task contexts (Chikazoe et al., 2009; Chikazoe et al., 2007; Garavan et al., 1999). Taken together, these findings suggest increased perceptual processing, as well as the need to exert inhibitory control or increased task monitoring in order to support correct recognition of studied items within a task context which includes a high degree of interference.

**Fig. 4.** Mean percent signal change (PSC) in our L VLPFC ROI displayed as a function of trial type (A), Individual differences in L VLPFC activity for lure vs. unrelated negative probes was positively correlated with the RT index of semantic interference (B).
In summary, the present work extends our understanding of the neural mechanisms supporting the cognitive control of interference and veridical short-term memory. False alarm rates in RP tasks used to investigate the neural mechanisms of PI are normally quite low. As such, these investigations have focused almost exclusively on the successful resolution of interference, and have generally interpreted L.VLPFC increases in this context. Our findings are consistent with the interpretation that L.VLPFC responds to selection demands associated with multiple semantic competitors (Badre and Wagner, 2007; Thompson-Schill et al., 1997) but suggest that the region may not directly distinguish between interference that is successfully mitigated in service of accurate task performance, and that which is not. Furthermore, results suggest that when interference is sufficient to produce source confusion regarding the old or new status of a memory probe, monitoring operations mediated by the adjacent L.DLPPC may be critical for supporting accurate task performance. Finally, findings indicate that increased sensory and PHG activity may serve as neural signatures that distinguish true and false recognition even when memory is tested only seconds following initial learning. Supplementary materials related to this article can be found online at doi:10.1016/j.neuroimage.2011.02.048.

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References
