AGE-RELATED CHANGES IN OVERCOMING PROACTIVE INTERFERENCE IN ASSOCIATIVE MEMORY: THE ROLE OF VLPFC-MEDIATED POST-RETRIEVAL SELECTION

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Age-related changes in overcoming proactive interference in associative memory: the role of VLPFC-mediated post-retrieval selection

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LIST OF SYMBOLS AND ABBREVIATIONS

fMRI	Functional Magnetic Resonance Imaging
PFC	Prefrontal Cortex
VLPFC	Ventrolateral Prefrontal Cortex
DLPFC	Dorsolateral Prefrontal Cortex
MTL	Medial Temporal Lobe
PPA	Parahippocampal Place Area
FFA	Fusiform Face Area
ROI	Region of Interest
SPM	Statistical Parametric Mapping
RT	Response Time
ANOVA	Analysis of Variance
AC	Associative Correct
AI	Associative Incorrect
CR	Correct Rejection

SUMMARY

Behavioral evidence has shown that older adults are less able to overcome proactive interference in memory than young adults. However, it is unclear what underlies this deficit. Imaging studies in the young suggest overcoming interference may require post-retrieval selection, a process thought to be mediated by the left mid-ventrolateral prefrontal cortex (VLPFC). Further, selection may resolve interference by enhancing or suppressing perceptual processing. The present fMRI study investigated whether age-related changes in VLPFC-mediated post-retrieval selection underlie older adults' deficits in overcoming interference in associative memory. Participants were tasked with remembering which associate (face or scene) objects were paired with most recently during study, under conditions of high or low proactive interference. Behavioral results demonstrated that as interference increased, memory performance decreased similarly across groups. Across groups, activity in the left mid-VLPFC also increased with interference. However, right PFC post-retrieval monitoring effects, but not left mid-VLPFC, distinguished successful vs. unsuccessful resolution of interference for both young and older adults, suggesting selection alone may be insufficient for successful resolution of interference. Age-related memory deficits may be related to reduced recruitment of relational processing effects in the dorsolateral and anterior PFC, as well as reduced memory retrieval effects in the hippocampus. Lastly, results showed evidence that selection may modulate perceptual processing of retrieved memory representations. Namely, activity in the parahippocampal place area (PPA) was greater when participants selected scene, versus face, regardless of accuracy. Further, older adults showed reduced effects in the PPA, possibly reflecting reduced differentiation of perceptual processing. Taken together, these results suggest age-related deficits in overcoming proactive interference are not related to post-retrieval

selection, but reduced recruitment of PFC-mediated relational processes, coupled with reduced associative memory retrieval.

CHAPTER 1

INTRODUCTION

Behavioral evidence has suggested that older adults may be particularly impaired on memory tasks that require higher levels of recruitment of executive functions (Hasher & Zacks, 1979; Johnson, Hashtroudi, & Lindsay, 1993). Such tasks may include associative memory tasks in which participants must overcome proactive interference. Proactive interference is induced when previous, but no longer valid, information conflicts with current task goals. For example (Jacoby, Bishara, Hessels, & Toth, 2005), the word "knee" might be paired repeatedly with the word "bend." However, on the last pairing, it may be paired with "bone." Then, at test, the participant is shown the cue "knee-b_n_" and is asked to respond with the most recent pairing. The "knee-bend" pairing may be highly accessible due to its repeated exposure, but participants must inhibit this association and select "knee-bone." This experiment showed that older adults were less likely than young adults to respond with the correct associate and were more likely to be "captured" by the previous, but now invalid, associate.

Executive Processes

Recent evidence suggests that overcoming interference, like that present in the associative memory task described above, may require an executive process called post-retrieval selection (Badre and Wagner, 2007). Post-retrieval selection is a process that resolves competition between multiple active representations. That is, after information is retrieved, irrelevant/conflicting information must be suppressed and relevant information likely enhanced. For example, when a participant in the above experiment is shown "knee-b_n_", he/she may retrieve the words "bend" and "bone" from memory. To make a correct memory decision, the participant must engage in post-retrieval selection, wherein he/she selects the task-relevant word "bone" and inhibits the task-irrelevant "bend." An incorrect memory decision may reflect "capture" by the highly associated lure and a failure to engage in post-retrieval selection. Behavioral evidence also suggests that post-retrieval selection requires additional processing time, as correct responses to high interference trials are significantly slower than for low interference trials (Jonides & Nee, 2006). In the case of older adults, they may be more likely to fail to engage in this process, and thus are "captured" by the more accessible/familiar associate. This explanation could account the results identified by Jacoby and colleagues.

Imaging evidence has shown that this post-retrieval selection process may be mediated by the left mid-ventrolateral prefrontal cortex (VLPFC) (Badre & Wagner, 2007). For example, this region shows greater activity during source memory than item memory retrieval, for both conceptual and perceptual sources, suggesting a domain general role (Dobbins & Wagner, 2005). This selection process has also been observed across several other tasks (see Blumenfeld & Ranganath, 2007 for review), including working memory tasks involving proactive interference (Jonides & Nee, 2006), semantic interference (Atkins & Reuter-Lorenz, 2011), verb generation tasks that have high selection demands (Thompson-Schill, Bedny, & Goldberg, 2005), as well as semantic and non-semantic classification tasks (Wagner & Davachi, 2001). Taken together, this suggests that the mid-VLPFC selection process is likely not specific to episodic memory, and is engaged whenever resolution of interference is necessary (Badre and Wagner, 2007).

The frontal aging hypothesis suggests that aging leads to disproportionate alterations in PFC processes (West, 1996). There has been little research, however, as to the effects of age on VLPFC-mediated post-retrieval selection. As stated previously, behavioral evidence has consistently demonstrated that older adults show deficits on memory tasks involving proactive

(Jacoby et al., 2005) and semantic interference (Koutstaal & Schacter, 1997; Norman & Schacter, 1997). Given that older adults are more likely to be “captured” by highly familiar but invalid information, this may suggest that older adults either don’t, or can’t, engage this VLPFC-mediated post-retrieval process as well as young adults. However, to our knowledge, no one has directly assessed the effects of age on VLPFC-mediated post-retrieval selection.

A great deal of aging and neuroimaging research has focused on another post-retrieval process: post-retrieval monitoring. Post-retrieval monitoring is thought to reflect the evaluation and manipulation of the products of retrieval (Henson, Shallice, & Dolan, 1999b). This may involve judging one’s confidence in their memory decision, initiating additional searches of memory, etc. Critically, post-retrieval monitoring is thought to be engaged in situations where a participant is close to his/her decision criteria. Behavioral work has shown that older adults demonstrate disproportionate declines in tasks that place high demands on post-retrieval monitoring, such as source memory tasks (see Mitchell & Johnson, 2009 for review).

Neuroimaging research suggests that post-retrieval monitoring is supported, at least in part, by the right PFC including both dorsolateral and ventrolateral PFC (Donaldson, Wheeler, & Petersen, 2010; Dulas & Duarte, 2012, 2014; Henson et al., 1999b). Further, fMRI evidence has shown right DLPFC activity is greater for incorrect than correct source memory trials (Dulas & Duarte, 2012), as well as greater for low-confidence correct than high-confidence correct trials (Henson, Rugg, Shallice, & Dolan, 2000). These findings fit with the assertion that post-retrieval monitoring is engaged to a greater extent when a participant is close to their decision criteria. Further, imaging evidence suggests right PFC may also be involved in overcoming interference in memory (see Aron, Robbins, & Poldrack, 2004 for review).

Several studies investigating the effects of age on right PFC-mediated post-retrieval monitoring suggest that older adults under-recruit this process (Dulas & Duarte, 2012; Friedman, 2000). However, other studies, where performance was experimentally matched between groups, suggest that older adults can recruit this process to a similar extent as the young (Dulas & Duarte, 2013, 2014; Li, Morcom, & Rugg, 2004). This suggests that older adults may simply fail to engage in post-retrieval monitoring under certain conditions. Thus, it is possible that age-related alterations to VLPFC-mediated post-retrieval selection may be similar. That is, in older adults performing similarly to the young, VLPFC recruitment may also be similar. However, when older adults show impairments on such a task, they may show reduced VLPFC recruitment, corresponding to a failure to engage in post-retrieval selection to a similar degree as the young.

Perceptual Processing

Evidence from the attention literature suggests that attention can enhance activity related to perceptual processing of attended stimuli, while suppressing/inhibiting activity related to perceptual processing of to-be ignored stimuli (Gazzaley, Cooney, McEvoy, Knight, & D'Esposito, 2005). This previous working memory study asked participants to attend to faces, but ignore scenes (or vice versa). Compared to a passive viewing baseline task, results showed greater activity in the fusiform face area (FFA) and reduced activity in the parahippocampal place area (PPA) for the “attend faces, ignore scenes” condition (The inverse results were shown for the “attend scenes, ignore faces” condition). These results suggest the processing of attended information may be enhanced, while the processing of the ignored information is suppressed/inhibited. Further, using the same task, later work showed that older adults displayed a deficit in their ability to suppress the to-be-ignored information, though they showed no deficit in enhancement (Gazzaley, Cooney, Rissman, & D'Esposito, 2005).

One possibility is that post-retrieval selection may have similar effects as selective attention on perceptual processing. That is, if a participant is attempting to select retrieved face information, and must overcome interfering retrieved scene information, a similar pattern of FFA enhancement coupled with PPA suppression may be evident. However, to our knowledge, no study has assessed whether there are similar effects for post-retrieval enhancement/inhibition of perceptual processing. Further, it is unclear if the same age-related alterations seen in the attention literature (i.e. intact enhancement but impaired inhibition) would be seen during episodic memory retrieval.

The present study investigated the effects of age on post-retrieval selection using an associative memory task involving variable levels of proactive interference. During study, participants were shown objects paired with either a face or a scene. Similarly to Jacoby et al., 2005, each object was seen multiple times, and the paired associate changed across viewings. There were two encoding conditions: High Interference and Low Interference. Interference level depended on how often an object was seen with the critical (most recent) associate vs. the lure. In the High Interference condition, objects were seen three times with the lure and twice with the critical stimulus. For Low Interference, objects were seen four times with the critical stimulus and once with the lure. At test, participants were then shown each object again, as well as novel objects not seen previously. For each object, they were asked if it was old (seen previously) or new (not seen previously). They were then presented with a face and scene, and asked to determine which was most recently paired with the object (they were instructed to just press either button if the object was new). Thus, the critical stimulus was the most recently paired associate. Scanning only took place during test. The inclusion of new objects allowed us to use correct rejection trials as a baseline condition for comparison with the other trial types; and additionally distinguish age-related deficits in associative memory from recognition memory deficits, which should be smaller.

We predicted the following:

1. Behaviorally, associative memory accuracy would be poorer for high interference compared to low interference across age groups. Age-related performance deficits may be disproportionately evident for the high interference condition, as we predicted that this condition place higher demands on executive processes, such as post-retrieval selection, which may be impaired in older adults.
2. We predicted that we would observe greater activity in the left mid-VLPFC for correct memory responses to High Interference trials than Low Interference trials, reflecting greater recruitment of post-retrieval selection when demands are high.
3. When comparing memory judgments for the High Interference condition, we also predicted greater activity in left mid-VLPFC for correct trials than for incorrect trials. Incorrect trials may reflect "capture" by the interfering associate, and a failure to engage in post-retrieval selection (Jacoby et al., 2005). However, in line with previous evidence from the source memory literature (e.g. Dulas & Duarte, 2012), we predict that activity in right PFC may also dissociate correct from incorrect memory trials, reflecting post-retrieval monitoring.
4. We predicted age-related decreases in activity in both VLPFC and right PFC, particularly on high interference trials, representing a failure to engage in these processes. That said, we predicted that this decrease may be correlated with

performance, in that the lowest performing older adults may also show the lowest recruitment of these effects. A similar correlation may also be seen within the young adults.

5. Lastly, we also predicted evidence of inhibition (decreased activity compared to passive viewing correct rejection trials) and/or enhancement (increased activity compared to passive viewing) in face/scene processing regions. More specifically, on high interference correct trials, compared to incorrect trials, when participants successfully overcome proactive interference (e.g. correctly respond Old-Face when the object was most recently paired with a face but was paired three times with a scene before that), there will likely be increased activity in the corresponding perceptual processing region (in this example, FFA) and decreased activity in the perceptual processing region corresponding to the lure (in this example, PPA). However, older adults may show intact enhancement but impaired inhibition in perceptual processing activity.

As stated previously, older adults exhibit deficits in memory tasks placing heavy demands on executive processing. While fMRI evidence has shown older adults may show declines in PFC-mediated post-retrieval monitoring effects, such results have not been expanded to the rest of the prefrontal cortex. Thus, it is unclear if the frontal aging hypothesis (West, 1996) truly extends to the entire prefrontal cortex, or if some regions are more affected than others. Further, it is unclear whether alterations in PFC functioning are ubiquitous, or if there is some variation across tasks/people. The present study sought to expand our understanding of the effects of age on PFC-mediated processes supporting memory retrieval. To our knowledge, no one has investigated whether alterations in left mid-VLPFC mediated post-retrieval selection underlie the age-related deficits seen on memory tasks involving proactive interference.

CHAPTER 2

METHODS

Participants

22 young adults, ages 19-35, as well as 22 older adults, ages 60-80, were recruited from local universities, science and health fairs, and community solicitation. Groups did not significantly differ in gender [$\chi^2(1, N = 44) = 0.86, p = 0.35$] or education [$t(42) = 0.29, p = 0.77$]. Group characteristics may be seen in **Table 1**. An additional young adult was excluded due to terminating the experiment early. An additional four older adults were excluded as well: one due to terminating the experiment early, one due to metallic hair dye that caused drop out in the MRI signal, one due to claustrophobia, and one due to excessive motion artifacts during scanning. All included participants were right-handed, native English speakers, with normal or corrected-to-normal vision (using MRI-compatible glasses when necessary). No participants reported a history of psychiatric or neurological disorders, uncontrolled vascular disease, psychoactive drug use, or use of CNS-active. Georgia Tech students were compensated with 1 credit per hour for their time. All other participants were compensated with $10 per hour of their time, as well as an additional $5 to cover travel expenses. All participants signed consent forms approved by the Georgia Institute of Technology Institutional Review Board.

Table 1. Group characteristics.

Measure	Young (n = 22)	Old (n = 22)
Age	24.41 (4.65)	67.90 (4.61)
Gender	15/22 female	12/22 female
Education	16.34 (2.34)	16.55 (2.28)
Letter Fluency	49.64 (8.93)	57.00 (14.04)
List Recall (Immediate)	10.77 (1.45)	10.41 (1.53)
List Recall (Immediate, Cued)	10.95 (1.21)	10.59 (1.26)
List Recall (Delayed)	11.45 (0.67)	11.18 (1.40)
List Recall (Delayed, Cued)	11.23 (1.93)	11.50 (0.91)
List Recognition	12.00 (0.00)	11.95 (0.21)
MAS Digit Span Forward	6.82 (1.33)	6.55 (1.44)
MAS Digit Span Backward	4.73 (1.08)	4.73 (1.61)
Trails A (in seconds)	23.78 (5.46)	35.42 (10.62)*
Trails B (in seconds)	47.78 (15.22)	61.35 (21.93)*
Visual Recognition	19.05 (1.53)	16.86 (2.27)*
Delayed Visual Recognition	19.23 (1.02)	17.14 (2.66)*
Visual Reproduction	8.36 (1.97)	4.82 (2.06)*

Note: Standard deviations in parentheses. All neuropsychological test scores are reported as raw scores. * = significantly worse than Young ($p < 0.05$).

Neuropsychological Assessment

All participants were administered a battery of standardized neuropsychological tests upon completion of the experiment. Tests specifically assessed memory ability and executive functioning to ensure no gross differences in performance due to cognitive impairment such as dementia in the older group. The battery included subtests from the Memory Assessment Scale battery (Williams, 1991): digit span forward and backward, list learning, recognition, recall and delayed recall, object recognition, recall, reproduction, and delayed recognition. Additionally, the Trail making tests, A and B (Hedden & Gabrieli, 2005), as well as the Controlled Oral Word Association Test ("FAS") (Benton, Hamsher, & Sivan, 1983), were included. All participants were within the normal range for their age group.

Materials

Three hundred and sixty color photographs of nameable objects taken from Hemera Technologies Photo-Objects DVDs, or from the internet via Google search, were used. All objects appeared on a white background. There was no overlap of multiple images depicting the same object. In addition, eight pictures of young adult faces (4 male, 4 female) and 8 pictures of scenes (4 indoor, 4 outdoor) were used as associates for the experiment. The faces were taken from the Max Planck Institute's FACES database (Ebner, Riediger, & Lindenberger, 2010) and the scenes were taken from the SUN database (Xiao, Hays, Ehinger, Oliva, & Torralba, 2010).

Procedure

The study was divided into two phases: Encoding and Retrieval. A practice session for each phase was administered before the beginning of the experiment to familiarize the participants with the tasks and to ensure they could sufficiently perform the memory task before entering the scanner. Only the retrieval phase of the study was scanned. Stimuli were counterbalanced across participants, such that each object appeared different conditions across participants. There were 240 objects studied during Encoding, as well as an additional 120 new objects seen at Retrieval.

The Encoding phase was divided into 5 blocks, which were administered outside of the scanner. Each block consisted of 240 trials displaying all of the to-be-studied objects. For each trial, participants were shown an object and either a face or a scene for 3000 ms (see **Figure 1**). Participants were asked to imagine the images together and to rate how easy or hard it was to imagine the images together. This incidental orienting task was meant to facilitate encoding of both the images in the pair. There were three options: 1 = Easy, 2 = Medium, 3 = Hard. Each trial was followed by a fixation cross for 500 ms. Participants placed their right index finger on 1, their right middle finger on 2, and their right ring finger on 3. Objects were presented in a random order within each block. As each block was about 14 minutes, we also provided a 30 second break halfway through each block to prevent fatigue. The total time for the Encoding phase was about an hour and 15 minutes.

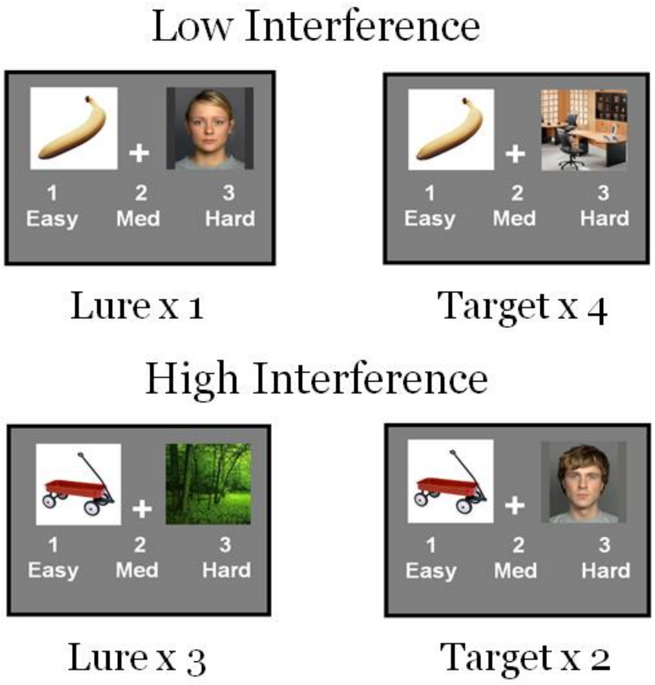

Figure 1. Encoding Design (not scanned). Examples of each condition are shown, the numbers indicating the number of times (across blocks) each object is shown with either the lure or the critical (most recent) associate. E.g. for High interference, the critical (last) pairing was only shown twice and the interfering pairing was shown the first 3 times.

Across the five Encoding blocks, objects were divided evenly across the High and Low interference conditions (120 objects per condition). For the Low Interference condition, each object was paired four times with one associate (e.g. a face) and once with an associate of the opposite type (e.g. a scene). Critically, the final time the object was viewed, it was shown with the most frequently paired associate (in this example, a face). For example, a picture of a banana may be paired first with a female face, then with a picture of an office, and then with the female face for the last 3 blocks. Thus, during retrieval, there may be some interference between the female face and the office, but the more highly associated image is also the critical (i.e. most recent) associate. For the High Interference condition, each object was paired three times with one associate (e.g. a scene) for the first three blocks, and then paired with the other associate (e.g. a face) in the final two blocks. For example, a wagon may be paired with a forest for the first three blocks, but paired with a male face for the final two blocks. Thus, at retrieval, there would be a strong association between the object and the irrelevant image (forest), creating a high level of interference.

After the Encoding phase, participants entered the scanner, and completed a short structural scan, and then started the Retrieval phase. The complete the structural scan, as well as the complete the localizer task (see **fMRI Analysis**) were conducted after the Retrieval phase to minimize delay between Encoding and Retrieval. Retrieval was divided into four blocks, consisting of 90 trials each (60 old items, 30 new items), for a total of 360 trials. The inclusion of new items allowed us to look for age-related old-new effects that may inform our data, as well as item recognition accuracy. Further, activity for correct rejections (“new” responses to unstudied items) may serve as a baseline condition relative to the other conditions of interest (as done in Duarte, Graham, & Henson, 2010; Duarte, Henson, & Graham, 2008). That is, there should be little to no evidence of processing such as post-retrieval selection during a correct rejection trial. On each trial, participants were shown an object in the center of the screen, which remained there across the entire trial, until the final fixation cross. Participants were first asked to determine if the object was Old (button 1) or New (button 2). This prompt was on the screen for 2000 ms. Then the question “Which image was paired with this object most recently” appeared for 1000 ms. Participants were instructed that they could still respond to the old-new question during this time. Then a face and a scene appeared below the object for 3000 ms. The image on the left corresponded to button 1 and the image on the left corresponded to button 2. For half the participants, the face was shown on the left and the scene on the right. For the other half this was reversed. The two images were always the critical stimulus and the lure for old objects. Participants were still shown this question even if they said the object was new. They were instructed to simply look at images and press either button. At the end of the trial, the object was removed and there was a 500 ms fixation cross, indicating the next trial was about to begin. Objects were presented in pseudorandom order within each block so that no more than 5 trials of the same condition (i.e. high interference, low interference, new item) were presented sequentially. Each block lasted about 10 minutes, for a total of 40 minutes.

For all behavioral analyses, significant interactions at an alpha (α) level of 0.05 were followed up with subsidiary ANOVAs and t-tests to determine the source of the effects. Where appropriate, reported p-values were corrected using Huynh-Feldt corrections.

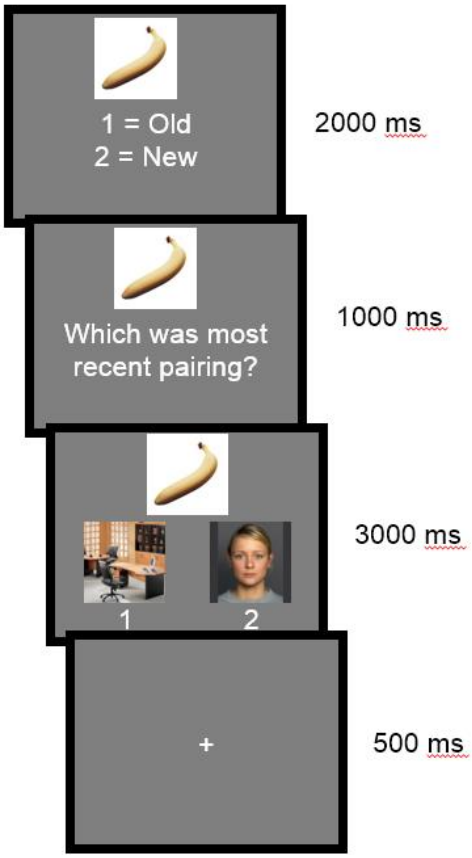

Figure 2. Retrieval Design (scanned). Examples corresponding to the previous Figure are shown.

fMRI Acquisition

Scanning was performed on a 3-T Siemens TIM Trio system. Functional data were acquired using a gradient echo pulse sequence (37 transverse slices oriented along the anterior--posterior commissural axis with a 30 degree upward tilt to avoid the eyes, repetition time of 2 s, echo time of 30 ms, 3 x 3 x 3.5 mm voxels, 0.8-mm interslice gap). Four Retrieval blocks of 303 volumes were acquired. The first 5 volumes of each block were discarded to allow for equilibration effects. A high-resolution T1-weighted magnetization-prepared rapid acquisition gradient echo (MPRAGE) image was collected for normalization (see below).

fMRI Analysis

Data were analyzed with SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/). Images were corrected for differences in slice timing acquisition using the middle slice of each volume as the reference, spatially realigned, and resliced with respect to the first volume of the first block. Each participant's MPRAGE scan was coregistered to the mean echo planar imaging (EPI), produced from spatial realignment. Each coregistered structural scan was then segmented using the diffeomorphic anatomical registration through exponentiated lie algebra (DARTEL) SPM 8 toolbox (Ashburner, 2007). DARTEL is a suite of tools fully integrated with SPM 8, which the SPM 8 manual recommends over optimized normalization, to achieve sharper nonlinear registration, for intersubject alignment. This method also achieves better localization of fMRI activations in Montreal Neurological Institute [MNI] space. This method has been used successfully in several previous studies with various healthy and neurological populations (Pereira et al.; Yassa & Stark, 2009). Briefly, the gray and white matter segmented images were used to create a study-specific template using the DARTEL toolbox and the flow fields containing the deformation parameters to this template for each subject were used to normalize each participant's realigned and resliced EPIs to MNI space. Normalized EPI images were written to 2 x 2 x 2 mm and smoothed with an 8 mm full-width at half-maximum isotropic Gaussian kernel. The EPI data were then high-pass filtered to a minimum of 1/128 Hz and grand mean scaled to 100.

Statistical analysis was performed in 2 stages. First, neural activity was modeled as a series of 4-s epochs of the various event types and convolved with a canonical hemodynamic response function. Though there were two response prompts, activity was only modeled to the onset of the first prompt, as participants were aware of the second prompt and may have been anticipating their responses (making it difficult to accurately model activity separately). The time courses were then down-sampled to the middle slice to form the covariates for the general linear model. For each participant and block, 6 covariates representing residual movement-related artifacts, determined by the spatial realignment step, were included in the first-level model to capture residual (linear) movement artifacts. Voxel-wise parameter estimates for these covariates were obtained by restricted maximum-likelihood estimation, using a temporal high-pass filter (cutoff 128 s) to remove low-frequency drifts and modeling temporal autocorrelation across scans with an AR(1) process.

Contrasts of the parameter estimates for each participant were submitted to the second stage of analysis (treating participants as a random effect). A mixed-ANOVA model was created for the test period that allowed us to examine both within-group effects and group interactions. The 7 x 2 model included factors of Condition (High Interference Face Correct, High Interference Face Incorrect, High Interference Scene Correct, High Interference Scene Incorrect, Low Interference Face Correct, Low Interference Scene Correct, and CR) and Group (young, old). There were insufficient numbers of “New” responses to studied (misses) and “Old” responses to unstudied (false alarms) objects for all participants to examine separately. Thus we did not include these in the ANOVA. Covariates modeling the mean across conditions for each participant were also added to each model, to remove between-subject variance of no interest. A weighted least squares estimation procedure was used to correct for inhomogeneity of covariance across within-group conditions and inhomogeneity of variance across groups.

The SPM for the main effect of Response (across groups) was masked exclusively with the SPMs for all relevant interactions, using a liberal uncorrected threshold of $P < 0.05$ for the masks in order to restrict memory effects to those ‘‘common’’ (i.e. similar size) across conditions, associates and groups (Note that a liberal threshold for an exclusive mask is more conservative in excluding regions from the masked SPM). The SPM for the main effects of Condition (across associates and groups) and Correct Associate (across conditions and groups) was similarly exclusively masked by their relevant interactions. Inclusive masks were applied to determine the overlap between these regions and associate-specific processing (regardless of memory judgment) and associate specific memory effects. Inclusive masking was applied using an uncorrected threshold of $P < 0.01$ for the mask. All masked, as well as unmasked, contrasts were evaluated using T-contrasts under an uncorrected alpha level of 0.001 and a minimum cluster size of 5 contiguous voxels.

Regions of Interest (ROIs), representing face- and scene-selective voxels were functionally defined using an ROI localizer task. After the Retrieval phase, participants performed a 1-back task in which they were presented with 24 16-sec blocks (~6.5 minutes) (see **Figure 3**). These blocks alternated between Face stimuli – Rest – Scene Stimuli – Rest – etc. During each block, 20 images were shown for 300 ms, with a 500 ms fixation cross between each image. The rest periods displayed a fixation cross for 8 seconds. Participants were instructed to attend to the stimuli and to indicate when each 1-back match occurred by pressing a button with their index finger. Similarly to the behavioral task, 8 faces and 8 scenes were used for each respective block. These faces and scenes were different from those used during the main experiment.

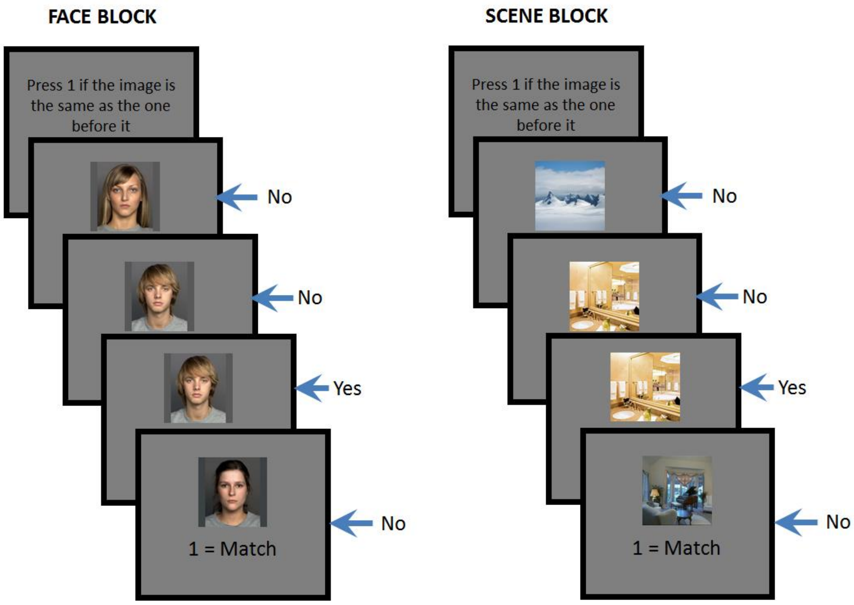

Figure 3. Face/Scene Localizer Tasks. Examples of face and scene trials for the localizer task.

MR data for the localizer task were processed as described above, and the face- and scene-stimuli regressors were contrasted to generate SPM[T] images. Face-selective (FFA) and scene-selective (PPA) ROIs were then identified both across and within groups. Each ROI was defined as the cluster of at least seven contiguous voxels (within the predetermined anatomical structures) with the highest *t*-values from the face–scene or scene–face contrast, respectively (Gazzaley, Cooney, McEvoy, et al., 2005).

For our whole-brain analyses, simple effect SPMs were performed to elucidate the source of interactions (e.g., Young > Old: High > Low) and to ensure that main effects were reliable for each group. Given that simple effect comparisons for a particular region were made independently from the initial contrast, they were not statistically biased.

Maxima of significant clusters were localized on individual normalized structural images. Neural activity from these maxima was plotted for Correct, Incorrect, and CR responses. Neural activity reflected the parameter estimates for the convolved regressors and had arbitrary units.

CHAPTER 3

RESULTS

Neuropsychological Assessment Results

Group characteristics and results for neuropsychological tests are shown in **Table 1**. All participants scored within 1 standard deviation of age-adjusted normative averages for all neuropsychological tests. Older adults exhibited significantly poorer performance than young adults on several tests including Trails A & B, Visual Recognition, Delayed Visual Recognition, and Visual Reproduction [t(42)’s > 2.38, p’s < 0.03]. There were no other significant group differences [t(42)’s < 1.00, *p*’s > 0.32].

Behavioral Results

Mean proportions for correct and incorrect associative memory judgments, incorrect “new” judgments to studied items (misses), and correct “new” judgments to novel items (correct rejections) are shown in **Table 2**. Item recognition accuracy was estimated by the Pr measure of discriminability (Snodgrass & Corwin, 1988), i.e. p(hits) – p(false alarms) for High and Low interference conditions. Associative memory accuracy was also estimated by Pr, i.e. Pr = p(correct) – p(incorrect), excluding misses.

We conducted a Memory (Item, Associative) x Interference (High, Low) x Age (young, old) ANOVA on the Pr measures of item and associative memory in order to evaluated the effects of interference and age on associative memory. The ANOVA revealed significant main effects of Memory [$F(1,42) = 446.30$, $p < 0.001$], Interference [$F(1,42) = 225.32$, $p < 0.001$], and Age [$F(1,42) = 4.52$, $p = 0.04$]. These were modified by a significant Interference x Memory interaction [$F(1,42) = 214.96$, $p < 0.001$]. No other effects were significant [F's < 2.23, p's > 0.14].

Table 2. Response proportions and performances indices times to studied and unstudied objects at test.

	Young Adults		Older Adults	
	High Interference	Low Interference	High Interference	Low Interference
Response proportions				
Studied Objects				
Correct Associate	0.63 (0.16)	0.84 (0.09)	0.55 (0.11)	0.77 (0.13)
Incorrect Associate	0.34 (0.14)	0.12 (0.05)	0.38 (0.07)	0.16 (0.08)
Miss	0.03 (0.03)	0.04 (0.04)	0.07 (0.07)	0.07 (0.07)
Unstudied Objects				
Correct Rejections (CR)	0.97 (0.03)		0.95 (0.06)	
Associative proportions of hits				
P(correct associate)	0.64 (0.15)	0.87 (0.06)	0.58 (0.09)	0.82 (0.09)
P(incorrect associate)	0.35 (0.15)	0.13 (0.06)	0.42 (0.09)	0.17 (0.09)
Performance Indices				
Item Memory Accuracy	0.95 (0.04)	0.94 (0.05)	0.90 (0.02)	0.91 (0.02)
Associative Memory Accuracy	0.29 (0.30)	0.74 (0.12)	0.16 (0.17)	0.65 (0.19)
Associative Memory – Faces	0.34 (0.31)	0.75 (0.13)	0.30 (0.31)	0.76 (0.18)
Associative Memory – Scenes	0.24 (0.39)	0.73 (0.20)	0.03 (0.28)	0.54 (0.33)
Response Times				
Studied Objects				
Correct Associate	1120 (326)	1095 (264)	1197 (203)	1198 (187)
Incorrect Associate	1088 (290)	1143 (341)	1225 (220)	1263 (227)
Unstudied Objects				
Correct Rejections (CR)	1153 (318)		1267 (189)	

Note: Standard deviations in parentheses. For Performance Indices, Chance = 0. * denotes performance indices for which there were age-related differences, $p < 0.10$. Item Memory Accuracy represents the Pr measure of item memory p(hits-false alarms). Associative Memory Accuracy represents the Pr measure of associative (or source) memory, p(associative correct – associative incorrect). Associative proportions represent the values used for the Pr calculation of associative memory, which consider only correct and incorrect associative judgments of all hits, excluding misses.

A follow-up ANOVA of just Item Memory, with factors of Interference (High, Low) and Age (young, old) revealed a marginal effect of Age [$F(1,42) = 3.63$, $p = 0.06$], but no other significant effects [F's < 2.24, p's > 0.14]. Thus, interference had no effect on Item Memory. Further older adults only showed modest declines in Item Memory accuracy.

A similar follow-up ANOVA for Associative Memory revealed a significant main effect of Interference [$F(1,42) = 225.72$, $p < 0.001$] and a marginally significant effect of Age [$F(1,42) = 3.90$, $p = 0.06$]. However, the interaction between Age and Interference was not reliable [$F(1,42) = 0.36$, $p = 0.55$]. Thus, while older adults did perform more poorly overall, and interference did greatly affect Associative Memory accuracy, older adults were not significantly more impaired for High, compared to Low, Interference trials.

We also conducted an Interference (High, Low) x Associate (face, scene) x Age ANOVA to determine if interference and/or aging impacted memory differentially for faces or scenes. Pr measures of associative memory for face and scene correct trials are shown in **Table 2**. Results showed a main effect of Associate type [$F(1,42) = 7.89$, $p = 0.01$], a significant interaction between Associate and Interference [$F(1,42) = 4.32$, $p = 0.04$] and a marginal interaction between Associate and Age [$F(1,42) = 2.97$, $p = 0.09$]. The three-way interaction was not reliable [$F < 1$]. Follow-up independent sample t-tests revealed that older adults, performed significantly worse than the young for scene trials for both High and Low interference [$t(42)$'s > 2.09, p's < 0.04], but showed no age-related differences for face trials across the two interference levels [$t(42)$'s < 1]. Paired-samples t-test revealed that young adults showed no difference between face and scene associative memory performance for either interference level [$t(21)$'s < 1.30, p's > 0.20]. However, older adults showed poorer performance for scenes than faces for both conditions [$t(21)$'s > 2.55, p's < 0.02].

Given this pattern of results, we wanted to determine whether response biases toward faces were more liberal in older than in young adults. That is, older adults may have been more likely to guess “face” when they were unsure, resulting in seemingly higher performance for face trials, and lower performance for scene trials. Thus, we calculated Br estimates of bias for faces separately for each interference level and group according to: Br = p(false alarms)/(1 – (p(hits) – p(false alarms))), after adjusting hit and false alarm rates according to the formula ((number of hits or false alarms, respectively, + 0.5)/(number of old or new items, respectively, + 1)) (Snodgrass & Corwin, 1988). In this analysis, hits = correctly saying face, and false alarms = incorrectly saying face. Young adults showed face Br measures of 0.53 and 0.50 for High and Low interference, respectively, reflecting little overall bias. Older adults showed face Br measures of 0.59 and 0.63 for High and Low interference, respectively, suggesting they showed a somewhat liberal bias to faces. An ANOVA of the Br measures with factors of Interference x Age revealed a main effect of Age [$F(1,42) = 4.05$, $p = 0.05$] but no other significant effects [$F(1,42)$’s < 1.87, p’s > 0.18]. Thus, older adults were significantly more biased to respond “face” than young adults.

Lastly, we also conducted analyses of response times (RTs). The response times for correct and incorrect responses to High and Low interference trials, as well as correct rejections, are shown in **Table 2**. An ANOVA of Correct Responses (High Correct, Low Correct, Correct Rejection) x Age revealed a main effect of Response [$F(2,84) = 10.83$, $p < 0.001$], but no other significant effects [F’s < 1.70, p’s > 0.20]. Follow-up ANOVAs revealed that Correct Rejections were faster than both High and Low Interference trials [$F(1,42)$’s > 10.21, p’s < 0.01], with no interaction with or main effect of Age [F’s < 2.22, p’s > 0.14]. Further, there were no significant differences between High and Low interference correct trials, nor an interaction with Age [$F(1,42)$'s < 1.45, p's > 0.23].

To compare RTs for correct and incorrect trials, we conducted an ANOVA with factors of Interference (High, Low), Accuracy (Correct, Incorrect), and Age (young, old). Results showed a main effect of Accuracy [$F(1,42) = 6.27$, $p = 0.02$], a significant interaction between Interference and Accuracy [$F(1,42) = 4.97$, $p = 0.03$], and a marginal interaction between Accuracy and Age [$F(1,42) = 3.13$, $p = 0.08$]. All other effects were not reliable [F's < 2.09, p's > 0.16]. Follow-up independent sample t-tests revealed that young adults had marginally faster responses for High Interference Incorrect Trials [$t(42) = 1.76$, $p = 0.09$], but no group differences for the other response types [$t(42)$'s < 1.50, p's > 0.14]. Paired-sample t-tests within groups revealed that Correct responses to Low Interference trials were faster than Incorrect responses, significantly in older adults [$t(21) = 2.70$, $p = 0.01$], albeit non-significantly [$t(21) = 1.50$, $p = 0.15$] in young adults. Correct responses to High Interference trials were marginally slower than incorrect responses [$t(21) = 1.95$, $p = 0.07$], for young adults. However this trend was reversed (Correct faster than Incorrect) and non-significant in older adults [$t(21) = 1.65$, $p = 0.11$]. Thus, in young adults, there was an interaction between Accuracy and Interference, where Correct trials were faster than Incorrect trials for Low Interference, but were slower for High Interference. In older adults, Correct trials were generally faster than Incorrect trials, regardless of interference level.

fMRI Results

In line with previous studies (Dulas & Duarte, 2012, 2014; Duverne, Habibi, & Rugg, 2008; Morcom, Li, & Rugg, 2007), we first conducted analyses of Associative Correct (ACs) responses and Correct Rejections (CRs) in order to identify regions involved in associative memory. However, while contrasts comparing AC and CR responses are robust, they may represent both associative and item memory effects, or brain regions supporting memory for old/new judgments). Thus, in addition, we examined associative memory specific effects (Associative Correct vs. Associative Incorrect responses) as we have done previously (Dulas & Duarte, 2012, 2014).

Old-New Effects Across Interference

The contrast of AC > CR across conditions and groups showed the typical pattern of activity: bilateral PFC and parietal activity. These data are not presented.

Young adults showed greater Old-New effects than older adults in the right middle frontal gyrus, right middle orbitofrontal gyrus, and right inferior parietal cortex. Meanwhile, older adults showed greater activity than the young in the bilateral aspects of the middle frontal gyrus (very posterior relative to the middle frontal region showing greater activation in the young), left angular gyrus and superior parietal cortex, as well as bilateral middle occipital cortex. These regions are shown in **Table 3**.

Table 3. Regions showing age-related differences in old-new effects across conditions.

Contrast		Region	L/R	MNI Coordinates (x, y, z)	BA	T score	Cluster Size
AC > CR							
	Young > Old						
		Middle Frontal Gyrus	R	48, 32, 36	45	3.92	130
		Inferior Parietal Cortex	R	54, -57, 45	39	3.59	30
		Middle Orbitofrontal Gyrus	R	41, 56, -5	46	3.55	45
	Old > Young						
		Angular Gyrus	L	-38, -70, 42	7	4.68	104
		Superior Parietal Lobe	L	-20, -69, 49	7	3.31	11
		Middle Frontal Gyrus	L	-27, 17, 52	8	4.66	262
			R	29, 11, 57	8	3.30	9
		Middle Cingulate	L	-3, -33, 40	23	4.53	169
		Middle Occipital Cortex	L	-38, -82, 28	19	4.15	235
			R	30, -76, 24	19	3.47	46

L = Left; R = Right; BA = Broadmann's area; AC = Associative Correct; CR = Correct Rejection.

Old-New Effects Differing by Interference

Several regions showed greater old-new effects for High Interference compared to Low Interference trials (**Table 4)**.

These regions included, most notably, the left parahippocampal cortex and the left inferior frontal gyrus (left mid-VLPFC) (**Figure 4**). No regions showed evidence of greater old-new effects for Low Interference compared to High Interference trials across groups.

No regions showed significant old-new effects that interacted between age and interference level.

Table 4. Regions showing alterations to old-new effects related to interference.

Contrast	Region	L/R	MNI Coordinates (x, y, z)	BA	T Score	Cluster Size
High AC > Low AC						
Across Groups						
	Middle Cingulate	R	10, 26, 34	32	4.31	78
	Middle Cingulate	L	-6, 21, 40	32	3.82	150
	Anterior Cingulate	*L*	*-9, 27, 30*	*32*	*3.70*	
	Precentral Gyrus	L	-36, -1, 40	6	3.92	70
	Parahippocampal Cortex	**L**	**-24, -36, -11**	**30**	**3.69**	**34**
	Supplemental Motor Area	L	-10, 9, 58	6	4.06	189
	Superior Frontal Gyrus	L	-21, -1, 60	6	3.65	35
	Ventrolateral Prefrontal Cortex	**L**	**-50, 24, 31**	**44/45**	**3.29**	**37**
	Middle Occipital Cortex	L	-21, -99, 1	18	3.61	40
	Cuneus	L	-14, -66, 27	23	3.39	9
	Inferior Parietal Cortex	L	-30, -48, 39	40	3.64	42
	Vermis	B	-2, -46, -18		4.92	97
	Caudate	R	16, 17, 3		4.34	300
	Cerebellum	R	15, -52, -47		3.93	14

L = Left; R = Right; B = Bilateral; BA = Broadmann’s area; AC = Associative Correct. Italicized regions represent sub-clusters. Regions in bold indicate regions show in **Figure 4**.

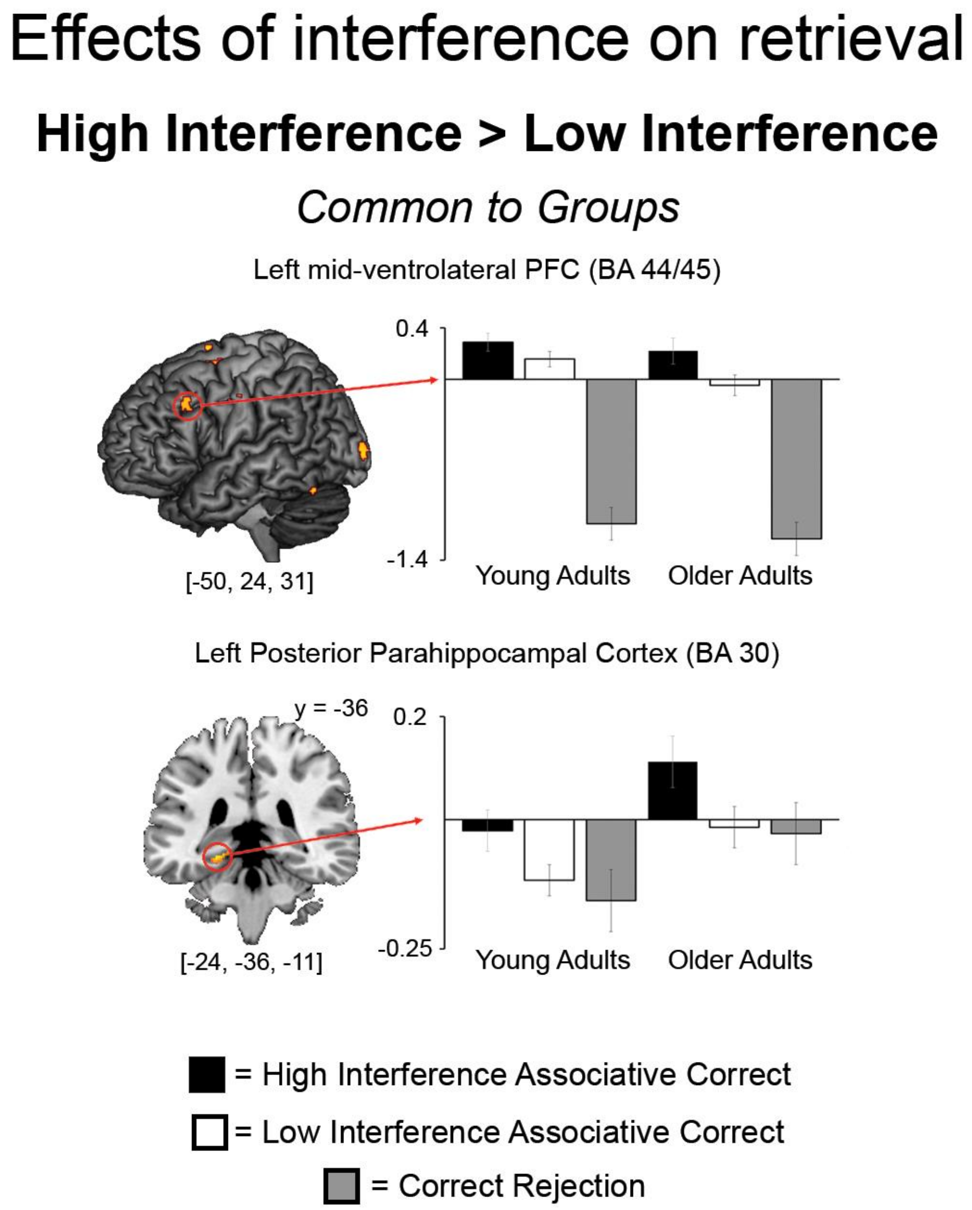

Figure 4. Effects of interference on retrieval. Old-new effects at test for selected regions are displayed on MNI reference brains. Plots show parameter estimates of Associative Correct trials for both High and Low Interference, as well as Correct Rejections for both groups. There was no true baseline for this study (i.e. fixation trials), thus the zero line of the x-axis cannot be interpreted as a baseline. Therefore, any “activations” or “deactivations” relative to the zero line are more apparent than real. Only the contrasts between conditions are interpretable. Error bars depict standard error of the mean across participants for each group [$p < 0.001$, uncorrected, with a 5 voxel extent; exclusive masking conducted as described in **fMRI Analysis**].

Effects of Interference on Associative Memory Accuracy

Associative accuracy effects (AC > AI) were only analyzed for High Interference trials, as most subjects did not have enough Low Interference Incorrect trials to analyze. These results are shown in **Table 5**.

Table 5. Regions showing associative memory accuracy effects for high interference trials.

Contrast	Region	L/R	MNI Coordinates (x, y, z)	BA	T Score	Cluster Size
AC > AI						
Across Groups						
	Hippocampus	**L**	**-20, -7, -12**	**35**	**4.16**	**56**
	Paracentral Lobule	L	-14, -24, 64	4	4.15	157
	Precentral Gyrus	L	-42, -7, 42	6	3.86	49
	Supplemental Motor Area	R	12, -12, 70	6	3.59	40
		L	-6, 12, 66	6	3.49	12
	Superior Frontal Gyrus	L	-20, -3, 69	6	3.54	30
		L	-12, 50, 22	32	3.32	7
	Ventrolateral Prefrontal Cortex	**R**	**34, 44, 5**	**47**	**3.33**	**6**
	Superior Medial Frontal Gyrus	L	-9, 38, 54	8	3.29	7
Young > Old						
	Anterior Prefrontal Cortex	**L**	**-9, 65, 19**	**10**	**3.65**	**38**
		R	12, 65, 13	10	3.61	41
	Dorsolateral Prefrontal Cortex	L	-16, 56, 37	9	3.49	12
		L	**-22, 39, 49**	**9**	**3.39**	**34**
	Anterior Cingulate	L	-15, 50, 1	10	3.41	9
	Middle Temporal Cortex	L	-55, -12, -15	20	3.78	64
	Hippocampus	**L**	**-24, -13, -21**	**36**	**3.29**	**5**
	Precentral Gyrus	R	16, -30, 66	4	3.57	127
	Middle Cingulate	R	6, -24, 49		4.27	137
	Supplemental Motor Area	R	8, 9, 63	6	3.96	73
		L	-12, -9, 70	6	3.72	274
	Cerebellum	L	-38, -78, -30		3.83	36
AI > AC						
Across Groups						
	Amygdala	R	33, -1, -23	36	3.63	22
	Superior Temporal Cortex	L	-46, -31, 7	48	3.44	15

L = Left; R = Right; BA = Broadmann’s area; AC = Associative Correct; AI = Associative Incorrect. Regions in bold indicate regions shown in **Figures 5** and **6**.

Across groups, High Interference Associative Correct trials showed greater activity than Associative Incorrect trials in several regions, most notably the left hippocampus and right middle frontal gyrus (anterior VLPFC) (**Figure 5**). Associative Incorrect trials showed greater activity than Correct trials in the right amygdala and left temporal cortex.

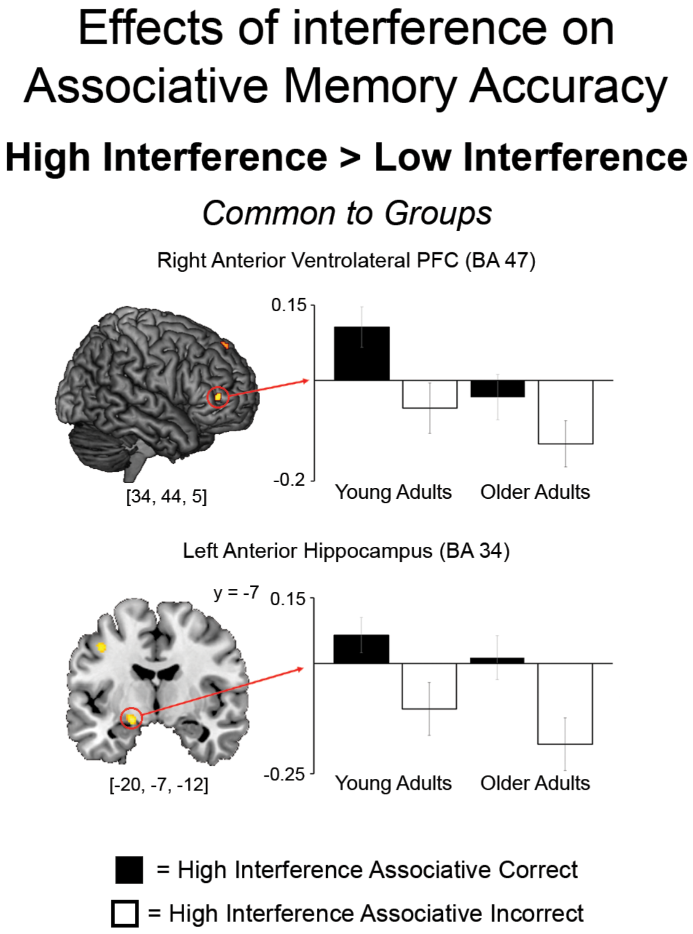

Figure 5. Effects of interference on associative memory accuracy. Associative memory accuracy effects at test for selected regions are displayed on MNI reference brains. Plots show parameter estimates of Associative Correct trials and Associative Incorrect trials for only High Interference. There was no true baseline for this study (i.e. fixation trials), thus the zero line of the x-axis cannot be interpreted as a baseline. Therefore, any “activations” or “deactivations” relative to the zero line are more apparent than real. Only the contrasts between conditions are interpretable. Error bars depict standard error of the mean across participants for each group [*p* < 0.001, uncorrected, with a 5 voxel extent; exclusive masking conducted as described in **fMRI Analysis**].

There were many regions showing Associative Correct > Associative Incorrect, Young > Old effects, most notably the left hippocampus (somewhat posterior to the region seen across groups), bilateral portions of the middle frontal gyrus (BA 9) (DLPFC), and the superior medial frontal gyrus (anterior PFC; BA 10) (**Figure 6**).

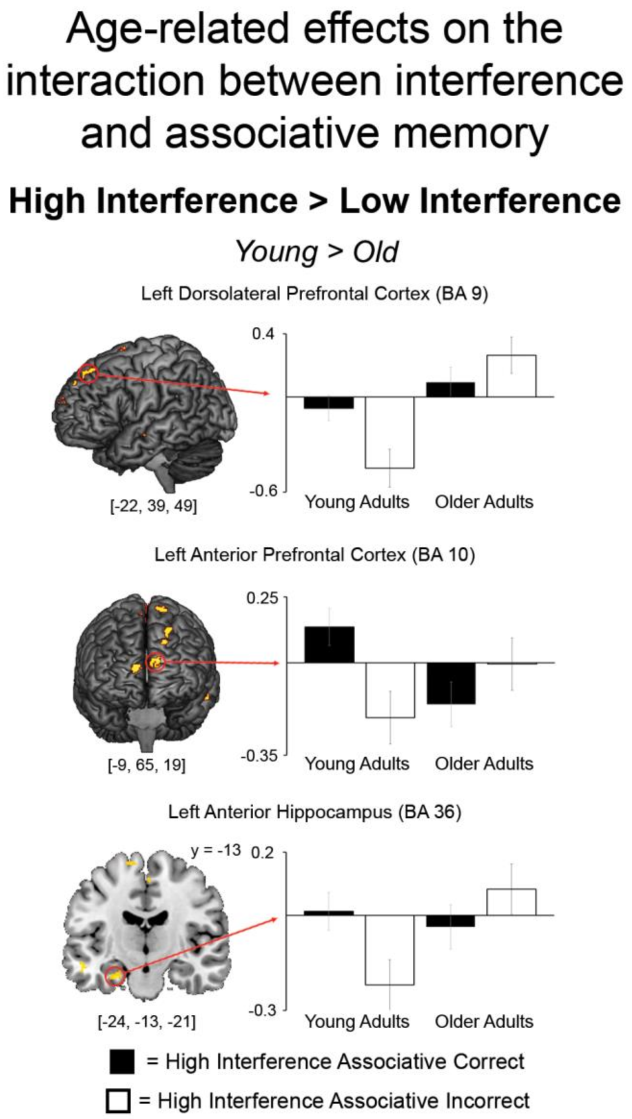

Figure 6. Age-related effects on the interaction between interference and associative memory. Associative memory accuracy effects at test for selected regions are displayed on MNI reference brains. Plots show parameter estimates of Associative Correct trials and Associative Incorrect trials for only High Interference. There was no true baseline for this study (i.e. fixation trials), thus the zero line of the x-axis cannot be interpreted as a baseline. Therefore, any “activations” or “deactivations” relative to the zero line are more apparent than real. Only the contrasts between conditions are interpretable. Error bars depict standard error of the mean across participants for each group [$p < 0.001$, uncorrected, with a 5 voxel extent; exclusive masking conducted as described in **fMRI Analysis**].

Perceptual Processing Effects

Lastly, we were interested in whether resolution of interference was related to modulations in perceptual processing at retrieval. Thus, for high interference trials, we were interested in whether selection of scene associates resulted in greater activity in scene processing regions (PPA) compared to when faces were selected and perhaps reduced activity in face processing regions (FFA) compared (and vice versa for successful selection of face associates). Initially, we had planned to use correct rejection trials as a passive viewing baseline to assess enhancement vs. inhibition. However, no regions showed effects for Face > CR > Scene (or vice versa) and thus we simply focused on Scene > Face and Face > Scene.

Further, while we also conducted ROI analyses using the ROIs from the localizer task, these regions either overlapped with regions already seen in the whole-brain analyses (e.g. PPA effects for scenes) or produced no additional significant results. Thus we will only discuss results from our whole-brain analysis. We first looked at effects that were present regardless of memory accuracy (e.g. regions that were active when the participant selected scene as the associate, regardless of whether it was correct) (**Table 6**).

Table 6. Regions showing effects based on selected associate, regardless of memory success.

Contrast	Region	L/R	MNI Coordinates (x, y, z)	BA	T score	Cluster Size
Face > Scene						
	Precentral Gyrus	L	-45, -4, 58	6	3.48	14
Young > Old						
	Precentral/Inferior Frontal Gyrus	L	-54, 0, 21	6/48	4.38	90
	Precentral Gyrus	R	57, 3, 19	48	4.05	45
	Postcentral Gyrus	L	-66, -19, 24	48	3.34	7
	Precuneus	L	-16, 60, 63	5	3.65	30
		R	9, -60, 55	5	3.50	6
Scene > Face						
	Calcarine	L	-14, -58, 19	23	5.25	403
	Middle Occipital Cortex	L	-32, -84, 36	19	4.84	401
		R	33, -81, 15	19	3.57	32
	Fusiform Gyrus	**L**	**-21, -36, -14**	**30**	**4.34**	**299**
	Parahippocampal Cortex	***L***	***-28, -33, -13***	***37***	***3.65***	
	Fusiform Gyrus	L	-24, -79, -6	18	4.13	63
	Lingual Gyrus	*L*	*-21, -81, -15*	*18*	*3.47*	
	Middle Frontal Gyrus	L	-30, 8, 45	6	4.36	188
	Middle Frontal Gyrus	L	-48, 51, -6	46	3.75	94
	Medial Superior Frontal Gyrus	L	-6, 29, 42	32	3.49	22
	Inferior Frontal Gyrus	R	27, 38, -6	47	3.34	13
	Angular Gyrus	R	42, -70, 49	39	3.33	7
	Superior Parietal Cortex	L	-24, -72, 54	7	3.28	7
Young > Old						
	Inferior Occipital Cortex	R	33, -85, -5	19	3.72	26
	Fusiform Gyrus	R	27, -84, -11		3.60	14
	Lingual Gyrus	**L**	**-26, -84, -12**	**18**	**3.38**	**17**

L = Left; R = Right; BA = Broadmann's area. Italicized regions represent sub-clusters. Regions in bold indicate regions shown in **Figure 7**.

For these analyses, across groups, selection of the face associate showed greater activity in the left precentral gyrus compared to scenes. However, several regions showed greater activity for scenes than faces, including the left fusiform gyrus/parahippocampal cortex (**Figure 7**).

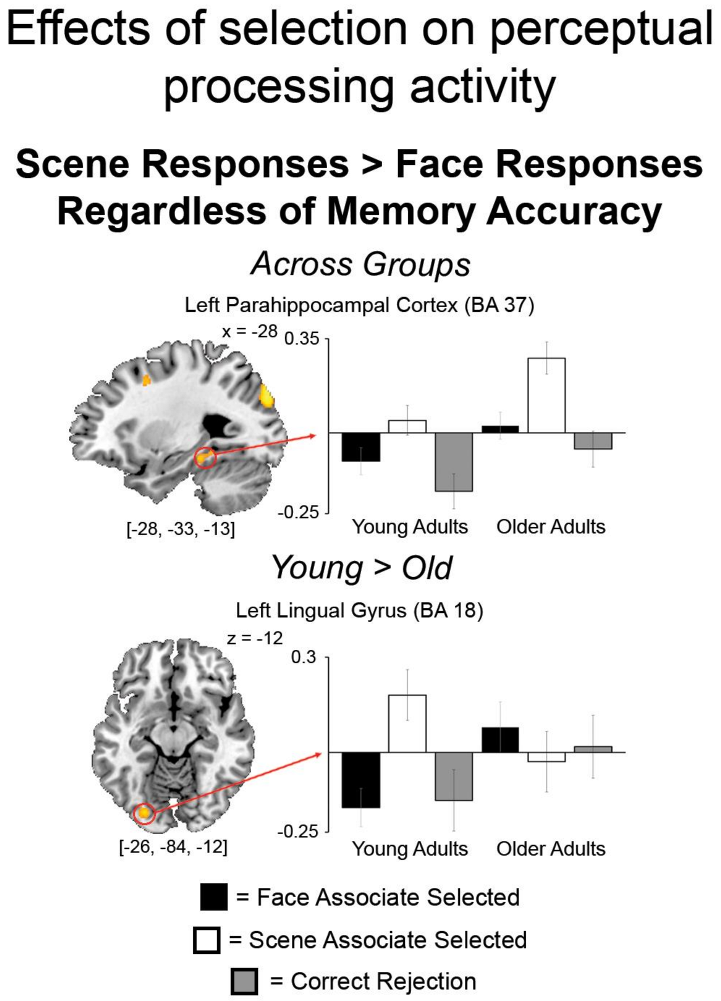

Figure 7. Effects of selection on perceptual processing activity. Effects at test for selected regions are displayed on MNI reference brains. Plots show parameter estimates of trials when the face associate was selected (Correct Face trials and Incorrect Scene Trials), when the scene associate was selected (Correct Scene trials and Incorrect Face trials), as well as correct rejection trials for High. Error bars depict standard error of the mean across participants for each group [*p* < 0.001, uncorrected, with a 5 voxel extent; exclusive masking conducted as described in **fMRI Analysis**].

When comparing these effects between age groups, several regions showed crossover interactions. Bilateral portions of the precentral gyrus and precuneus showed face > scene effects in young adults, but scene > face activity in older adults. The right inferior occipital cortex and fusiform gyrus showed scene > face activity in the young, but face > scene activity in the old. However, the left lingual gyrus showed scene > face activity for young adults, but no effects in the older adults (**Figure 7**).

We were also interested in whether there were perceptual processing effects specific to the successful resolution of interference. Thus we compared trials that showed scene correct > face correct responses, exclusively masked for incorrectly responding scene > incorrect responding face. The reverse of this was done for faces as well. Thus these effects should represent memory-specific effects, rather than selection (**Table 7**).

Table 7**.** Regions showing interactions between associate type and successful resolution of interference.

Contrast	Region	L/R	MNI Coordinates (x, y, z)	BA	T score	Cluster Size
High AC Only						
Face > Scene						
Across Groups						
	Middle Frontal Gyrus	R	47, -1, 57	6	3.36	12
Old > Young						
	Inferior Occipital/Fusiform	**R**	**34, -78, -6**	**19**	**3.51**	**26**
Scene > Face						
Across Groups						
	Lingual Gyrus	**L**	**26, -49, -6**	**37**	**3.43**	**14**

L = Left; R = Right; BA = Broadmann’s area; AC = Associative Correct. Regions in bold indicate regions shown in **Figure 8**.

Across groups, Associative Correct responses to faces showed greater activity than to scenes in the right middle frontal gyrus. Scenes showed greater activity than faces in the left lingual gyrus (**Figure 8**). Older adults showed greater effects for faces relative to the young in the right inferior occipital/fusiform gyrus (**Figure 8**). No other interactions between age, interference and/or associate type showed significant effects for successful associative memory.

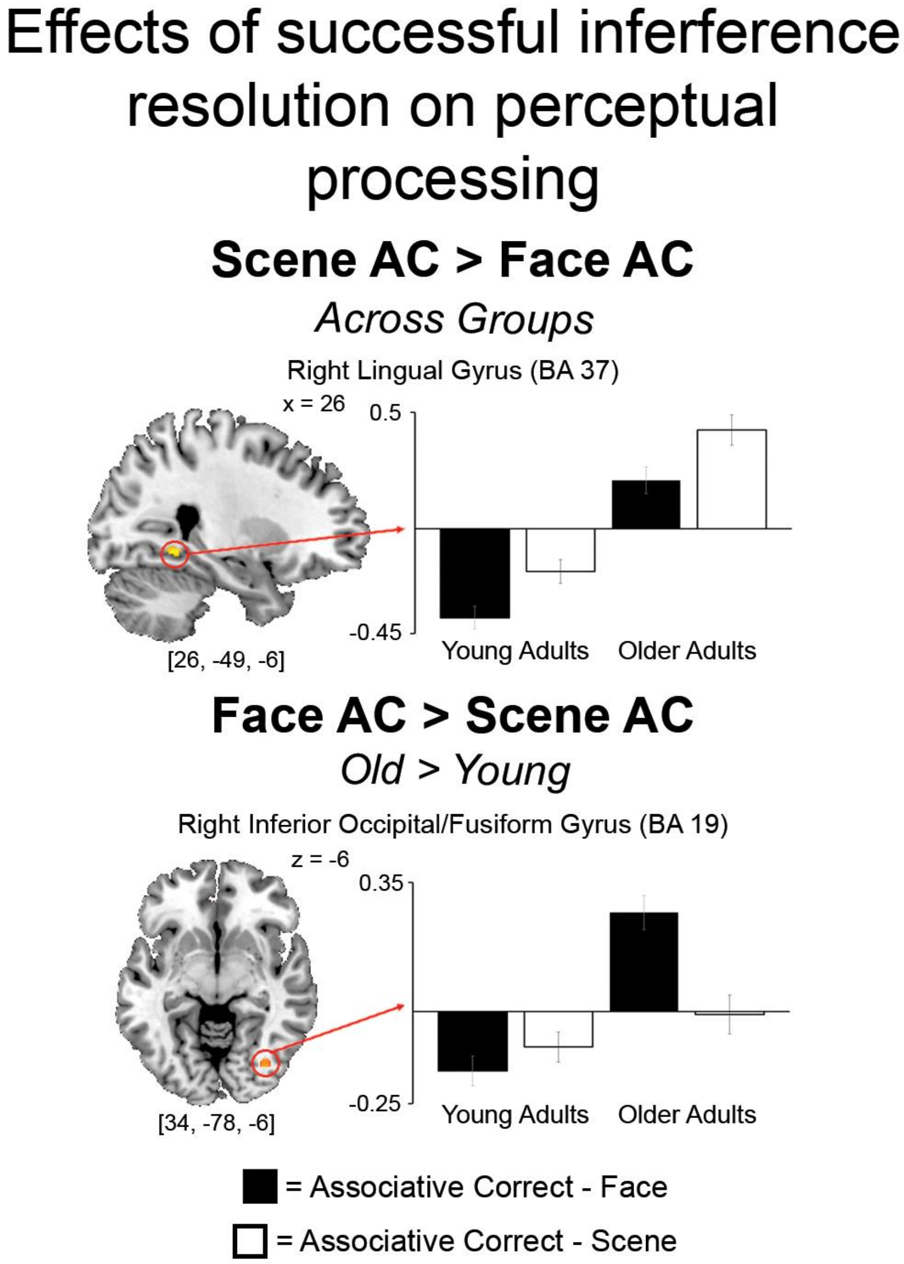

Figure 8. Effects of successful interference resolution on perceptual processing. Effects at test for selected regions are displayed on MNI reference brains. Plots show parameter estimates of trials when the face associate was correctly selected (Correct Face trials) and when the scene associate was correctly selected (Correct Scene trials). There was no true baseline for this study (i.e. fixation trials), thus the zero line of the x-axis cannot be interpreted as a baseline. Therefore, any "activations" or "deactivations" relative to the zero line are more apparent than real. Only the contrasts between conditions are interpretable. Error bars depict standard error of the mean across participants for each group [$p < 0.001$, uncorrected, with a 5 voxel extent; exclusive masking conducted as described in **fMRI Analysis**].

CHAPTER 4

DISCUSSION

The present study investigated the effects of aging on overcoming proactive interference in associative memory. We were particularly interested in the effects of aging on left mid-VLPFC-mediated post-retrieval selection, a process thought to be critical for overcoming interference. In line with previous results, associative memory accuracy was poorer for high compared to low interference across groups. However, age-related memory deficits were relatively small (only marginal), and there was no interaction between age and interference. Imaging result showed that, across groups, increasing levels of interference (High > Low > CR) resulted in increased recruitment of the left mid-VLPFC. However, while right anterior VLPFC and the hippocampus dissociated correct from incorrect associative memory responses, the left mid-VLPFC did not. Older adults showed reductions in associative retrieval effects in the hippocampus and strategic retrieval processes subserved by the DLPFC and anterior PFC, possibly underlying their age-related memory deficits. Lastly, we did find evidence of greater activity in PPA when participants responded scene (regardless of accuracy) compared to responding face, suggesting selection may modulate processing of retrieved perceptual representations. These results and their implications are discussed below.

Behavioral Results

As has been demonstrated previously (Jacoby et al., 2005; Jacoby, Wahlheim, Rhodes, Daniels, & Rogers, 2010; Nee, Wager, & Jonides, 2007; Yonelinas & Jacoby, 2012), associative memory accuracy was poorer for high levels proactive interference compared to low. This was true for both young and older adults. However, proactive interference had no effect on item memory across groups. Thus, when interference from a to-be-ignored association is high, the ability to correctly remember, or select, the weaker but goal-relevant association is reduced. Interestingly, there was only a marginal main effect of age across both item and associative memory, with no interaction between age, memory type (item or associative), and/or interference level. That said, numerically, there was a greater age-related deficit in associative memory (~9-13% poorer accuracy) compared to item memory (~3-5%).

The finding that age-related associative memory deficits in the present study were relatively small, and only marginally significant, stands in contrast to previous work from our lab (Duarte et al., 2008; Dulas & Duarte, 2011, 2012, 2013, 2014; Dulas, Newsome, & Duarte, 2011), as well as others (e.g. Chalfonte & Johnson, 1996; Glisky, Rubin, & Davidson, 2001; see Mitchell & Johnson, 2009 for review; Naveh-Benjamin, 2000; Naveh-Benjamin, Brav, & Levy, 2007), that suggests associative memory is disproportionately impaired with age. One possible reason for this finding could be that we provided participants with an integrative encoding task, wherein they had to imagine the images interacting, and rate how easy or hard it was to do so. Previous evidence has suggested that providing effective encoding strategies may reduce age-related associative memory deficits, given that older adults may simply fail to self-initiate such strategies (Glisky & Kong, 2008; Glisky et al., 2001; Naveh-Benjamin et al., 2007). That said, age-related differences did persist, falling in line with evidence that environmental support at encoding is insufficient to overcome age-related associative memory deficits (Dulas & Duarte, 2013, 2014; Naveh-Benjamin et al., 2007). These results may be in line with an overall associative binding deficit (Naveh-Benjamin, 2000; Old & Naveh-Benjamin, 2008), which suggests older adults exhibit an impairment in their overall ability to integrate information in memory. However, though not mutually exclusive, our results may provide further support to evidence that older adults exhibit deficits in strategic retrieval processes as well (Cohn, Emrich, & Moscovitch, 2008; Dulas & Duarte, 2012; Gallo, Bell, Beier, & Schacter, 2006; Hasher & Zacks, 1979). Previous behavioral evidence has shown that age-related associative memory deficits are only fully ameliorated when support is provided at both encoding and retrieval (Naveh-Benjamin et al., 2007). Future work in which both encoding and retrieval are supported may be able to determine whether age-related declines in overcoming proactive interference are due to binding deficits, or simply a failure to engage in effective retrieval strategies. Previous imaging evidence has suggested environmental support can ameliorate age-related under-recruitment of PFC strategic retrieval processes and reduce behavioral deficits (Logan et al., 2002; Dulas and Duarte 2013; 2014).

While we predicted that there would be an interaction between age and interference, in that older adults would be particularly impaired for high interference trials, we found no such interaction. It is possible that, even a single viewing of a lure is sufficient to cause interference deficits in older adults. Given that the present study did not employ a no-interference condition, it is unclear whether any amount of interference is sufficient to result in age-related deficits, or if this is truly just an overall associative memory deficit. Our response time results may speak to this possibility. Young adults showed an interaction between accuracy and interference, in that correct responses were faster than incorrect responses for Low Interference trials, but slower than incorrect responses for High Interference trials. These results may be in line with the “capture” model of proactive interference (Jacoby et al., 2005). That is, for both Low Interference Correct trials, and High Interference Incorrect trials, a response is being made to the stronger associate. Thus, it is possible that on such trials, young adults are less likely to engage in additional processes, such as post-retrieval selection or monitoring, in order to assess whether the more salient associate is in fact the most recent. Interestingly, for older adults, correct trials were always faster than incorrect trials, regardless of interference level. This may add to the suggestion that, even at low levels, older adults may still be adversely affected by interference. That is, even on low interference trials, older adults may need experience sufficient interference that would require additional monitoring processing. Failure to engage in these processes may result in poorer performance, and a lack of an interaction between interference and accuracy for response times. Future studies including a no interference condition might be better able to answer this question, as it is possible there would be an interaction between age and interference vs. no interference.

Lastly, our behavioral results showed an interaction between age and associate type, in that older adults were particularly impaired on memory for scenes compared to faces. To our knowledge, this pattern has not been seen in previous work using neutral faces and scenes. Results also showed that old, but not young adults, showed a bias to respond “face” as opposed to scene. Thus, one possibility is that, when older adults were unsure of the correct response, they were more likely to respond “face” than young adults. Such a behavioral pattern would result in better performance on trials where face was correct, and poorer performance on trials where scene was correct. It is unclear why older adults would adopt such a strategy. Given that half the participants were shown faces on the left (corresponding to button 1), while half were shown faces on the right (button 2), this result does not reflect a bias toward one button over another. It’s possible that the inclusion of a “don’t know” option would have ameliorated the bias toward guessing face in older adults. That said, these results may reflect a combination of bias and accuracy differences across groups and associate types. Future work investigating age-related changes in the ability to bind particular types of associates may be able to address this question.

Imaging Results

Left mid-VLPFC and post-retrieval selection

Our analyses of old-new effects revealed several regions where effects were greater for High Interference than Low Interference trials for both young and older adults. These regions included the parahippocampal cortex, inferior parietal cortex, and most notably, left mid-ventrolateral prefrontal cortex. Thus, as predicted, the left mid-VLPFC (BA 44/45) showed increased recruitment with increasing levels of interference. These results provide further evidence, in line with previous imaging results in young adults (Badre, Poldrack, Pare-Blagoev, Insler, & Wagner, 2005; Badre & Wagner, 2007; Dobbins, Rice, Wagner, & Schacter, 2003), that the left mid-VLPFC may be involved in post-retrieval selection. Notably, the peak voxel of this cluster in the present study [-50, 24, 31], was very close to the peak voxel reported in previous studies [-51, 15, 33] suggesting left mid-VLPFC mediates post-retrieval selection (Badre et al., 2005; Barredo, Oztekin, & Badre, 2013). Post-retrieval selection is thought to be engaged when multiple competing representations are simultaneously active in memory, and a goal-appropriate representation must be chosen, such as in the case of a proactive interference task (Badre & Wagner, 2007). It should be noted that this process is likely recruited across many tasks requiring resolution of interference (Atkins & Reuter-Lorenz, 2011; Blumenfeld & Ranganath, 2007; Jonides & Nee, 2006; Thompson-Schill et al., 2005), and is likely not memory-specific (Badre et al., 2005; Badre & Wagner, 2007).

While the finding in the young adds to the growing literature on the role of left mid-VLPFC in overcoming interference, to our knowledge, this is the first study to demonstrate that older adults show similar effects in the face of proactive interference. This is in contrast to the frontal aging hypothesis (Raz et al., 1997; West, 1996), as well as previous fMRI studies demonstrating age-related dysfunction in the PFC during similar source memory tasks (Dulas & Duarte, 2011, 2012; see Mitchell & Johnson, 2009; Rajah & D'Esposito, 2005 for reviews; Rajah, Languay, & Valiquette, 2009). However, recent work suggests that older adults may be able to recruit PFC processes (or at least some PFC processes) in a similar manner to the young (Dulas & Duarte, 2013, 2014; Li et al., 2004), namely when performance is matched between groups (Rugg & Morcom, 2005). Further, recent work from our lab has shown that older adults may recruit the VLPFC to a similar extent as the young, even while under-recruiting more anterior PFC regions (Dulas & Duarte, 2014). Similarly, previous imaging results have shown that young and older adults similarly recruit the VLPFC in response to increased task difficulty (Leshikar, Gutchess, Hebrank, Sutton, & Park, 2010). Taken together, these results suggest that aging may have less of an effect on the function of the ventrolateral prefrontal cortex compared to other PFC subregions.

While left mid-VLPFC-mediated post-retrieval selection has been repeatedly implicated in overcoming interference, few studies have investigated whether this process differentially supports successful versus unsuccessful resolution. In the present study, this region showed no difference between correct or incorrect associative memory responses on High Interference trials. This finding is in line with a previous semantic interference task (Atkins & Reuter-Lorenz, 2011), that also found increased left VLPFC activity with increasing interference, but no difference between correct and incorrect resolution of interference. Instead, right anterior VLPFC (BA 47) showed Associative Correct > Incorrect effects across groups. The right PFC, including both the dorsolateral and ventrolateral subregions, has consistently been implicated in a process called post-retrieval monitoring (Donaldson et al., 2010; Dulas & Duarte, 2012, 2014; Henson, Shallice, & Dolan, 1999a; Rugg, Henson, & Robb, 2003). Post-retrieval monitoring may involve the maintenance, manipulation, and evaluation of retrieved memory representations, particularly when a participant is at or near their decision criterion (Henson et al., 2000). In many of these previous studies, right PFC showed greater effects for incorrect than correct responses. However, in the present study, participants are likely closer to their decision criterion on correct trials for High Interference conditions. Behavioral evidence suggests that incorrect resolution of interference may reflect "capture," wherein the lure is simply so salient that it is immediately selected without additional processing (Jacoby et al., 2005). On correct trials, however, participants likely need to engage in the evaluation of both associates in order to successfully select the goal relevant stimulus. This finding also falls in line with the previously reference semantic interference task, that also found monitoring effects dissociating correct from incorrect resolution of interference (Atkins & Reuter-Lorenz, 2011).

Taken together, these results suggest that the left mid-VLPFC is engaged similarly for both correct and incorrect resolution of interference. One possibility is that, even when interference is incorrectly resolved, selection may still be engaged. That is, even for incorrect trials, one associate must still selected over its competitor. However, the successful resolution of interference likely requires additional evaluation of the products of retrieval, i.e. post-retrieval monitoring.

Alternatively, these results may instead suggest that the left mid-VLPFC does not in fact subserve the selection process posited by previous studies. Previous work has also suggested that this region simply acts to index interference, and passes on this information to other PFC regions for further processing (Atkins & Reuter-Lorenz, 2011). It should be noted that other regions thought to be involved in conflict monitoring, namely the anterior cingulate cortex, showed similar effects (High > Low interference). Previous work has shown that the anterior cingulate is involved in monitoring conflict across several domains (cognitive vs. affective) (Ochsner, Hughes, Robertson, Cooper, & Gabrieli, 2009) and tasks (response conflict and attention switching) (Kim, Johnson, & Gold, 2012), and that left mid-VLPFC may be additionally recruited to resolve semantic conflict (Kim et al., 2012; Ochsner et al., 2009), as opposed to response conflict (see discussion of premotor regions below). That said, it is still unclear whether left mid-VLPFC is simply indexing semantic interference, or if it truly is resolving it via selection. The present study is unable to dissociate these two possibilities, as interference and selection demands are directly related. It is possible that future studies employing effective connectivity analyses could determine the nature of the interaction between the mid-VLPFC and other PFC regions. That is, if mid-VLPFC is involved in selection, it may receive inputs from the anterior cingulate (indexing conflict) and possibly right PFC (post-retrieval monitoring) in service of making a selection. However, it is simply involved in indexing interference, it likely would show inputs to other PFC regions, which would then be involved in resolving the conflict.

Age-related under-recruitment of PFC-mediated relational processes

While older adults recruited both the left mid-VLPFC and right anterior VLPFC similarly to the young, results showed age-related under-recruitment of several other PFC subregions, namely the dorsolateral prefrontal cortex and anterior PFC. Recent evidence has suggested a possible hierarchical organization to the prefrontal cortex (Badre, 2008; Badre & D'Esposito, 2009), wherein more anterior subregions of the PFC are recruited with increased relational complexity. That is, the DLPFC, and in turn the anterior PFC, may be involved in processing more abstract relationships compared to the VLPFC. For example, it has been suggested that the

VLPFC may process within-item associations (such as object-color), while the DLPFC may process associations across items (Badre & D'Esposito, 2009). In line with this suggestion, a previous study directly manipulating relational complexity, albeit in a reasoning task, showed that activity in both DLPFC and anterior PFC increased with increasing complexity (Kroger et al., 2002). Further, the semantic interference task referenced previously (Atkins & Reuter-Lorenz, 2011) also showed evidence that left DLPFC was involved in successful resolution of interference. Taken together, this adds to the suggestion that, while left mid-VLPFC may be involved in either indexing interference, or selecting a memory representation in service of a response, additional relational and monitoring processes may be necessary to successfully resolve interference.

The finding that the DLPFC and anterior PFC showed age-related under-recruitment does fall in line with the frontal aging hypothesis (Raz et al., 1997; West, 1996). Further, previous results have suggested that, even with spared activity in VLPFC, older adults may showed deficits in DLPFC (Rypma & D'Esposito, 2000), and anterior PFC (Dulas & Duarte, 2014). What is unclear, however, is whether these age-related reductions represent an intractable deficit in DLPFC and aPFC functioning, or simply a failure to engage in these more complex processes. Behavioral evidence suggests that older adults may be less likely to self-initiate effective strategic processes (Luo & Craik, 2008; Naveh-Benjamin et al., 2007). Further, evidence has shown that providing environmental support, at both encoding and retrieval (Naveh-Benjamin et al., 2007), can improve performance in older adults and attenuate age-related under-recruitment (Logan, Sanders, Snyder, Morris, & Buckner, 2002). Given the suggestion that the DLPFC and aPFC subserve more complex relational processes (Badre & D'Esposito, 2009), it is possible that environmental support during the retrieval phase may encourage older adults to initiate these processes in a similar manner to the young. However, it is also possible the dorsolateral and anterior PFCs are simply more susceptible to age-related dysfunction than the VLPFC. Future work investigating the role of retrieval support in overcoming proactive interference may be better able to address whether these changes are truly intractable, or simply reflect a failure to initiate more complex retrieval strategies.

Future work using electroencephalography or magnetoencephalography may be better able to answer the question of whether the various PFC processes seen in the present study are engaged in a hierarchical temporal order. That is, if the role of the left lateralized PFC effect is simply to pass on interference information to other PFC regions, then we would predict that the corresponding event-related potential components would be engaged earlier than the monitoring and relational processing effects. However, if the products of retrieval are first evaluated, and then a selection is made, we would predict the reverse temporal order. Effective connectivity analyses could also potentially further address this issue, by assessing the directionality of the interaction between these effects, as well as other memory retrieval effects.

The medial temporal lobe and the resolution of interference

In addition to the effects seen in the PFC, several regions of the medial temporal lobe (MTL) were also shown to be involved in the resolution of interference. Across groups, the parahippocampal cortex showed greater old-new effects for High than Low Interference, and the anterior hippocampus showed associative memory accuracy effects for high interference trials. It has been well established that the MTL, including the parahippocampal cortex and hippocampus, is involved in associative/contextual binding and memory retrieval (Diana, Yonelinas, & Ranganath, 2007, 2009; Eichenbaum, Yonelinas, & Ranganath, 2007). The finding that High Interference trials showed greater MTL recruitment than Low Interference trials may suggest that successful resolution of interference requires a strong retrieved memory representation. That is, participants likely need to retrieve multiple pieces of contextual information to correctly respond to High Interference trials. Further substantiating this suggestion, the inferior parietal cortex also showed increased old-new effects with increasing interference. The ventral parietal cortex has been suggested to index the strength of retrieved memory representations, either via bottom-up attention to memory (Cabeza, 2008; Ciaramelli, Grady, & Moscovitch, 2008), or via maintenance of these retrieved representations (Vilberg & Rugg, 2007). Regardless of the interpretation, these results suggest that interference may only be successfully resolved when retrieved representations are sufficiently strong.

In line with previous evidence of age-related alterations in MTL function (Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006; Dulas & Duarte, 2014; Gutchess et al., 2005; Mitchell, Johnson, Raye, & D'Esposito, 2000; Raz, Rodrigue, Head, Kennedy, & Acker, 2004), older adults showed reduced associative memory accuracy effects in the hippocampus compared to young adults. Thus, another possible underlying cause of the age-related memory deficits in the present study is impaired associative memory retrieval. This decrease in MTL activity may be related to an age-related associative binding deficit (Naveh-Benjamin, 2000; Old & Naveh-Benjamin, 2008). That is, older adults may simply be impaired in their ability to bind and retrieve contextual associations. Given that our behavioral results showed a main effect of age, it is possible that this binding deficit underlies associative memory deficits regardless of interference.

A remaining question is whether these MTL-mediated associative retrieval effects interact with the executive control effects seen in the PFC. Older adults showed declines in both hippocampally-mediated associative retrieval, as well as DLPFC and aPFC mediated executive processing effects. One possibility is that older adults do not engage these relational processing effects to the same degree as the young simply because they do not retrieve as much associative information. As suggested previously, effective connectivity analyses may allow future studies to answer whether the strength of MTL-mediated retrieval mediates engagement of relational processing effects. Such a result would suggest that the PFC itself is not functionally impaired, but simply under-recruited as a result of impaired associative retrieval. This would go against the frontal aging hypothesis (West, 1996), which suggests the PFC is disproportionately impaired by aging.

Alterations in perceptual processing related to memory and selection

Lastly, we suggested that one mechanism by which post-retrieval selection may “select” the goal-appropriate associate in the face of competition is by modulating perceptual processing (Gazzaley, Cooney, McEvoy, et al., 2005). In the present study, several regions showed effects based on which associate was selected, regardless of whether it was correct or not. Namely, across groups, for High Interference trials, a cluster in the fusiform gyrus/parahippocampal cortex showed stronger effects both when a scene was correctly selected, as well as when a scene was incorrectly selected, compared to when a face was selected, as well as correct rejections of new items. This region falls in line with what is considered the parahippocampal place area (Epstein, Harris, Stanley, & Kanwisher, 1999) and was also observed in our localizer task for the scene > face contrast. Thus, similar to the selective attention literature (Gazzaley, Cooney, McEvoy, et al., 2005; Gazzaley & D'Esposito, 2007), perceptual processing effects tracked with selection effects. That is, when a participant attended to retrieved scene information (i.e. chose “scene”), we observed greater activity in PPA than when they ignored it (i.e. attended to retrieved face information). As stated previously, the left mid-VLPFC is thought to be the locus of this selection process. Further, the left mid-VLPFC was also not modulated by memory accuracy. Taken together with results in the PPA, this may suggest that the mechanism by which left mid-VLPFC mediates selection is by modulating perceptual processing downstream, in this case PPA activity related to scene processing. That being said, the present study is unable to rule out the possibility that participants simply select the scene associate whenever they have a strong retrieved perceptual scene representation. Future work using effective connectivity or time course analyses may be better able to answer whether the left mid-VLPFC is directly impacting perceptual processing, or vice versa.

Interestingly, young adults showed similar effects in the lingual gyrus, while older adults did not. Previous imaging evidence has suggested the posterior portion of the PPA may extend into the lingual gyrus (Epstein, 2008). It has been suggested that older adults may have deficits in their ability to modulate perceptual processing (Gazzaley et al., 2008; Gazzaley, Cooney, Rissman, et al., 2005; Gazzaley & D'Esposito, 2007). These studies generally showed that older adults could enhance attended-to perceptual processing, but showed deficits in their ability to suppress to-be-ignored perceptual information. The present analyses are unable to distinguish these two types of modulations. We originally predicted that correct rejection trials would act as a passive viewing baseline, allowing us to assess whether perceptual processing effects increased when the associate was attended to, or whether they decreased when the associate was ignored. However, perceptual processing regions did not show such an effect with relation to correct rejections. Still, it is possible that the age-related reduction in this scene > face effect reflects a suppression deficit. Interestingly, older adults were particularly impaired for trials where the scene was the correct associate. This may suggest that the age-related impairments in retrieving and selecting scene associates in the face of competition are related to a reduction in scene specific perceptual processing effects. That said, it is also possible that, given that older adults had far fewer trials where they “selected” scene, that this effect simply reflects a difference in power.

An alternative interpretation is that these effects are the result of an age-related decline in the specificity of processing in the ventral visual cortex (Park et al., 2004), both within and across stimulus types (Carp, Park, Polk, & Park, 2011). Previous evidence has suggested that neural effects related to faces and scenes are particularly susceptible to decreased specificity in older adults, at least compared to word and color processing (Voss et al., 2008). Thus, the age-related decrease in scene-selection effects in the present study may simply reflect increased dedifferentiation in the perceptual processing of scenes and faces, rather than differences in modulation of these processes in the face of interference.

It should be noted that there were very few regions showing face > scene selection effects, and none of these regions were in visual processing regions associated with faces (e.g. the fusiform face area). In the present task, while the scenes were all brightly colored and diverse, the faces were all relatively similar. All of the people in the images had neutral facial expressions, wore the same gray t-shirt, and were of a similar age and race. Thus, there may have been less variety in the stimuli, resulting in less perceptual processing at test. Another possibility is that participants encoded and retrieved faces in a non-perceptual manner, such as assigning a name or personality to each face. Such a strategy might have mitigated the perceptual processing effects related to faces, as participants may rely on semantic information to a greater extent.

While several regions showed selection effects for scenes, regardless of accuracy, the lingual gyrus also showed scene-specific effects related to successful resolution of interference. As stated previously, the parahippocampal place area is thought to extend into the lingual gyrus

(Epstein, 2008). Thus, while many of the perceptual processing effects reflected selection, regardless of memory accuracy, we do provide evidence that successful resolution of interference may be related to additional perceptual processing effects. Previous evidence using multi-voxel pattern analysis has suggested that stronger reactivation of goal-relevant perceptual information at test results in better memory in the face of competition (Kuhl, Bainbridge, & Chun, 2012). The present results may reflect a similar effect, in that stronger scene processing effects in PPA may result in better memory for scene associates.

Compared to young adults, older adults showed greater face-specific activity related to successful resolution of interference in the inferior occipital cortex/fusiform gyrus, i.e. the fusiform face area (Kanwisher, McDermott, & Chun, 1997). Given that older adults did not show declines in associative memory for faces, this may suggest older adults particularly attended to and retrieved face information. Interestingly, further investigation of this region revealed that, while there was a face > scene effect for correct trials, there was no difference in this effect between correct selection of faces, incorrect selection of faces, nor incorrect selection of scenes. This finding may fall in line with the result that older adults were biased towards responding "face." That is, older adult participants appeared to only correctly respond "scene" when processing in this region was reduced. On all other trials, older adults showed evidence of face processing, possibly resulting in an increased likelihood of responding face. Older adults also showed reduced scene-specific selection effects, further suggesting a possible bias toward faces. Given that older adults show increased effects related to face processing, and decreased effects related to scene processing, it may be that they simply are attending to faces more than scenes. However, it is still unclear why older adults would adopt such a strategy. As suggested previously, providing a "don't know" option may have reduced the bias to guess "face" when older adults were unsure. This could also reduce these age-related perceptual processing effects, if they are truly due to bias.

Dorsal premotor activity and response conflict

While not an initial focus of the present study, results showed increased activity in dorsal premotor areas, namely the precentral gyrus and supplemental motor area (BA 6/8) across multiple contrasts. Previous evidence has suggested these regions may be involved in preparation (Astafiev et al., 2003), maintenance (Curtis & D'Esposito, 2003), and selection (Goghari & MacDonald, 2009) of planned motor responses. Further, this region may correspond to the human equivalent of the Frontal Eye Fields (Paus, 1996), thought to be involved in oculomotor control and shifts in visual attention (Grosbras & Paus, 2002; Makino, Yokosawa, Takeda, & Kumada, 2004; Paus, 1996; Petit & Haxby, 1999; Srimal & Curtis, 2008). In the present task, the associative memory question predictably followed the old-new question. Thus, participants may have been able to prepare both their button press response, as well as saccades towards their selected associate, before the presentation of the face and scene stimuli.

Interestingly, the premotor effects were stronger for High compared to Low interference, and for correct compared to incorrect resolution of interference. Thus, in situations with greater conflict between retrieved representations, we show evidence of increased premotor activity. Previous evidence has shown increased activity in premotor areas, including the precentral gyrus, in response to increased response conflict (Hazeltine, Bunge, Scanlon, & Gabrieli, 2003; Ullsperger & von Cramon, 2001). Thus, in addition to competition in memory representations, successful resolution of interference in associative memory may also require mediating conflict in responses. It is unclear, however, if high interference trials simply necessitate additional motor planning, or if certain premotor areas are directly involved in resolving response conflict.

Further, it is unclear if these effects simply represent an index of response conflict, similarly to the possibility the left mid-VLPFC simply indexes interference in memory (rather than actively resolving interference) (Atkins & Reuter-Lorenz, 2011). Future work investigating the differential roles of premotor and lateral prefrontal regions in overcoming different types of interference is necessary to further address these questions. That is, is premotor cortex truly involved in overcoming response conflict, while mid-VLPFC is involved in overcoming semantic conflict? Or do these two regions work together to resolve conflict across these domains? Work manipulating response vs. semantic conflict may also be able to answer this question.

Resolution of interference during encoding?

A remaining question that the present study is unable to address is whether age-related declines in overcoming interference exist during encoding as well. Previous evidence using a similar encoding task showed increased activity in left inferior frontal gyrus across subsequent encoding attempts (roughly left mid-VLPFC), possibility reflecting interference resolution during study (Zeithamova & Preston, 2010). Studies looking at both encoding and retrieval have also shown that greater inferior frontal gyrus activity during encoding may result in less competition in the reactivation of perceptual processing at test (Kuhl et al., 2012). Further, using multi-voxel pattern analysis, previous studies have shown that the strength of this reactivation of perceptual processing during retrieval may mediate performance on associative memory tasks (Kuhl et al., 2012; Staresina, Henson, Kriegeskorte, & Alink, 2012). Thus, it is possible that differences in PFC-mediated processing at encoding, as well as reinstatement effects, may also underlie age-related memory deficits. Future studies investigating both encoding and retrieval in the face of interference may allow us to better understand age-related declines in overcoming interference.

Conclusions

In conclusion, the successful resolution of interference in memory requires multiple PFC-mediated processes, including the left mid-VLPFC, which may serve to index interference or to mediate post-retrieval selection,, but also right PFC-mediated post-retrieval monitoring, as well as DLPFC and aPFC-mediated relational processes. Further, one mechanism by which interference may be resolved is via top-down modulation of perceptual processing, though this modulation may occur similarly for correct and incorrect resolution of interference. The present study provides the first evidence that age-related impairments in overcoming interference are likely related to reduced engagement of the PFC-mediated relational processes (though VLPFC-mediated effects were spared), as well as reduced hippocampally-mediated contextual retrieval. Further, older adults showed reduced modulation of perceptual processing effects compared to the young, possibly reflecting reduced differentiation of perceptual processing. Future work employing effective connectivity analyses may further answer exactly how these regions interact to resolve interference. Additionally, future studies that attempt to support resolution of interference during retrieval may be able to determine if these age-related effects are intractable, or whether they simply represent a failure to self-initiate the most effective retrieval strategies.

REFERENCES

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends Cogn Sci, 8*(4), 170-177.

Ashburner, J. (2007). A fast diffeomorphic image registration algorithm. *Neuroimage, 38*(1), 95-113.

Astafiev, S. V., Shulman, G. L., Stanley, C. M., Snyder, A. Z., Van Essen, D. C., & Corbetta, M. (2003). Functional organization of human intraparietal and frontal cortex for attending, looking, and pointing. *J Neurosci, 23*(11), 4689-4699.

Atkins, A. S., & Reuter-Lorenz, P. A. (2011). Neural mechanisms of semantic interference and false recognition in short-term memory. *Neuroimage, 56*(3), 1726-1734.

Badre, D. (2008). Cognitive control, hierarchy, and the rostro-caudal organization of the frontal lobes. *Trends Cogn Sci, 12*(5), 193-200.

Badre, D., & D'Esposito, M. (2009). Is the rostro-caudal axis of the frontal lobe hierarchical? *Nat Rev Neurosci, 10*(9), 659-669.

Badre, D., Poldrack, R. A., Pare-Blagoev, E. J., Insler, R. Z., & Wagner, A. D. (2005). Dissociable controlled retrieval and generalized selection mechanisms in ventrolateral prefrontal cortex. *Neuron, 47*(6), 907-918.

Badre, D., & Wagner, A. D. (2007). Left ventrolateral prefrontal cortex and the cognitive control of memory. *Neuropsychologia, 45*(13), 2883-2901.

Barredo, J., Oztekin, I., & Badre, D. (2013). Ventral Fronto-Temporal Pathway Supporting Cognitive Control of Episodic Memory Retrieval. *Cereb Cortex*.

Benton, A. L., Hamsher, S. K. d., & Sivan, A. B. (1983). *Multilingual aplasia examination* (2nd ed.). Iowa City: AJA Associates.

Blumenfeld, R. S., & Ranganath, C. (2007). Prefrontal cortex and long-term memory encoding: an integrative review of findings from neuropsychology and neuroimaging. *Neuroscientist, 13*(3), 280-291.

Cabeza, R. (2008). Role of parietal regions in episodic memory retrieval: the dual attentional processes hypothesis. *Neuropsychologia, 46*(7), 1813-1827.

Carp, J., Park, J., Polk, T. A., & Park, D. C. (2011). Age differences in neural distinctiveness revealed by multi-voxel pattern analysis. *Neuroimage, 56*(2), 736-743.

Chalfonte, B. L., & Johnson, M. K. (1996). Feature memory and binding in young and older adults. *Mem Cognit, 24*(4), 403-416.

Ciaramelli, E., Grady, C. L., & Moscovitch, M. (2008). Top-down and bottom-up attention to memory: a hypothesis (AtoM) on the role of the posterior parietal cortex in memory retrieval. *Neuropsychologia, 46*(7), 1828-1851.

Cohn, M., Emrich, S. M., & Moscovitch, M. (2008). Age-related deficits in associative memory: the influence of impaired strategic retrieval. *Psychol Aging, 23*(1), 93-103.

Curtis, C. E., & D'Esposito, M. (2003). Persistent activity in the prefrontal cortex during working memory. *Trends Cogn Sci, 7*(9), 415-423.

Daselaar, S. M., Fleck, M. S., Dobbins, I. G., Madden, D. J., & Cabeza, R. (2006). Effects of healthy aging on hippocampal and rhinal memory functions: an event-related fMRI study. *Cereb Cortex, 16*(12), 1771-1782.

Diana, R. A., Yonelinas, A. P., & Ranganath, C. (2007). Imaging recollection and familiarity in the medial temporal lobe: a three-component model. *Trends Cogn Sci, 11*(9), 379-386.

Diana, R. A., Yonelinas, A. P., & Ranganath, C. (2009). Medial Temporal Lobe Activity during Source Retrieval Reflects Information Type, not Memory Strength. *J Cogn Neurosci*.

Dobbins, I. G., Rice, H. J., Wagner, A. D., & Schacter, D. L. (2003). Memory orientation and success: separable neurocognitive components underlying episodic recognition. *Neuropsychologia, 41*(3), 318-333.

Dobbins, I. G., & Wagner, A. D. (2005). Domain-general and domain-sensitive prefrontal mechanisms for recollecting events and detecting novelty. *Cereb Cortex, 15*(11), 1768-1778.

Donaldson, D. I., Wheeler, M. E., & Petersen, S. E. (2010). Remember the source: dissociating frontal and parietal contributions to episodic memory. *J Cogn Neurosci, 22*(2), 377-391.

Duarte, A., Graham, K. S., & Henson, R. N. (2010). Age-related changes in neural activity associated with familiarity, recollection and false recognition. *Neurobiol Aging, 31*(10), 1814-1830.

Duarte, A., Henson, R. N., & Graham, K. S. (2008). The effects of aging on the neural correlates of subjective and objective recollection. *Cereb Cortex, 18*(9), 2169-2180.

Dulas, M. R., & Duarte, A. (2011). The effects of aging on material-independent and material-dependent neural correlates of contextual binding. *Neuroimage, 57*(3), 1192-1204.

Dulas, M. R., & Duarte, A. (2012). The effects of aging on material-independent and material-dependent neural correlates of source memory retrieval. *Cereb Cortex, 22*(1), 37-50.

Dulas, M. R., & Duarte, A. (2013). The influence of directed attention at encoding on source memory retrieval in the young and old: an ERP study. *Brain Res*.

Dulas, M. R., & Duarte, A. (2014). Aging Affects the Interaction between Attentional Control and Source Memory: An fMRI Study. *J Cogn Neurosci*.

Dulas, M. R., Newsome, R. N., & Duarte, A. (2011). The effects of aging on ERP correlates of source memory retrieval for self-referential information. *Brain Res, 1377*, 84-100.

Duverne, S., Habibi, A., & Rugg, M. D. (2008). Regional specificity of age effects on the neural correlates of episodic retrieval. *Neurobiol Aging, 29*(12), 1902-1916.

Ebner, N. C., Riediger, M., & Lindenberger, U. (2010). FACES--a database of facial expressions in young, middle-aged, and older women and men: development and validation. *Behav Res Methods, 42*(1), 351-362.

Eichenbaum, H., Yonelinas, A. P., & Ranganath, C. (2007). The medial temporal lobe and recognition memory. *Annu Rev Neurosci, 30*, 123-152.

Epstein, R., Harris, A., Stanley, D., & Kanwisher, N. (1999). The parahippocampal place area: recognition, navigation, or encoding? *Neuron, 23*(1), 115-125.

Epstein, R. A. (2008). Parahippocampal and retrosplenial contributions to human spatial navigation. *Trends Cogn Sci, 12*(10), 388-396.

Friedman, D. (2000). Event-related brain potential investigations of memory and aging. *Biol Psychol, 54*(1-3), 175-206.

Gallo, D. A., Bell, D. M., Beier, J. S., & Schacter, D. L. (2006). Two types of recollection-based monitoring in younger and older adults: Recall-to-reject and the distinctiveness heuristic. *Memory, 14*(6), 730-741.

Gazzaley, A., Clapp, W., Kelley, J., McEvoy, K., Knight, R. T., & D'Esposito, M. (2008). Age-related top-down suppression deficit in the early stages of cortical visual memory processing. *Proc Natl Acad Sci U S A, 105*(35), 13122-13126.

Gazzaley, A., Cooney, J. W., McEvoy, K., Knight, R. T., & D'Esposito, M. (2005). Top-down enhancement and suppression of the magnitude and speed of neural activity. *J Cogn Neurosci, 17*(3), 507-517.

Gazzaley, A., Cooney, J. W., Rissman, J., & D'Esposito, M. (2005). Top-down suppression deficit underlies working memory impairment in normal aging. *Nat Neurosci, 8*(10), 1298-1300.

Gazzaley, A., & D'Esposito, M. (2007). Top-down modulation and normal aging. *Ann N Y Acad Sci, 1097*, 67-83.

Glisky, E. L., & Kong, L. L. (2008). Do young and older adults rely on different processes in source memory tasks? A neuropsychological study. *J Exp Psychol Learn Mem Cogn, 34*(4), 809-822.

Glisky, E. L., Rubin, S. R., & Davidson, P. S. (2001). Source memory in older adults: an encoding or retrieval problem? *J Exp Psychol Learn Mem Cogn, 27*(5), 1131-1146.

Goghari, V. M., & MacDonald, A. W., 3rd. (2009). The neural basis of cognitive control: response selection and inhibition. *Brain Cogn, 71*(2), 72-83.

Grosbras, M. H., & Paus, T. (2002). Transcranial magnetic stimulation of the human frontal eye field: effects on visual perception and attention. *J Cogn Neurosci, 14*(7), 1109-1120.

Gutchess, A. H., Welsh, R. C., Hedden, T., Bangert, A., Minear, M., Liu, L. L., & Park, D. C. (2005). Aging and the neural correlates of successful picture encoding: frontal activations compensate for decreased medial-temporal activity. *J Cogn Neurosci, 17*(1), 84-96.

Hasher, L., & Zacks, R. (1979). Automatic and effortful processes in memory. *Journal of Experimental Psychology: General, 108*, 356-388.

Hazeltine, E., Bunge, S. A., Scanlon, M. D., & Gabrieli, J. D. (2003). Material-dependent and material-independent selection processes in the frontal and parietal lobes: an event-related fMRI investigation of response competition. *Neuropsychologia, 41*(9), 1208-1217.

Hedden, T., & Gabrieli, J. D. (2005). Healthy and pathological processes in adult development: new evidence from neuroimaging of the aging brain. *Curr Opin Neurol, 18*(6), 740-747.

Henson, R., Shallice, T., & Dolan, R. J. (1999a). Right prefrontal cortex and episodic memory retrieval: a functional MRI test of the monitoring hypothesis. *Brain, 122 (Pt 7)*, 1367-1381.

Henson, R. N., Rugg, M. D., Shallice, T., & Dolan, R. J. (2000). Confidence in recognition memory for words: dissociating right prefrontal roles in episodic retrieval. *J Cogn Neurosci, 12*(6), 913-923.

Henson, R. N., Shallice, T., & Dolan, R. J. (1999b). Right prefrontal cortex and episodic memory retrieval: a functional MRI test of the monitoring hypothesis. *Brain, 122 (Pt 7)*, 1367-1381.

Jacoby, L. L., Bishara, A. J., Hessels, S., & Toth, J. P. (2005). Aging, subjective experience, and cognitive control: dramatic false remembering by older adults. *J Exp Psychol Gen, 134*(2), 131-148.

Jacoby, L. L., Wahlheim, C. N., Rhodes, M. G., Daniels, K. A., & Rogers, C. S. (2010). Learning to diminish the effects of proactive interference: reducing false memory for young and older adults. *Mem Cognit, 38*(6), 820-829.

Johnson, M. K., Hashtroudi, S., & Lindsay, D. S. (1993). Source monitoring. *Pschol. Rev., 114*, 3-28.

Jonides, J., & Nee, D. E. (2006). Brain mechanisms of proactive interference in working memory. *Neuroscience, 139*(1), 181-193.

Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. *J Neurosci, 17*(11), 4302-4311.

Kim, C., Johnson, N. F., & Gold, B. T. (2012). Common and distinct neural mechanisms of attentional switching and response conflict. *Brain Res, 1469*, 92-102.

Koutstaal, W., & Schacter, D. L. (1997). Gist-based false recognition of pictures in older and younger adults. *Journal of Memory and Language, 37*, 555-583.

Kroger, J. K., Sabb, F. W., Fales, C. L., Bookheimer, S. Y., Cohen, M. S., & Holyoak, K. J. (2002). Recruitment of anterior dorsolateral prefrontal cortex in human reasoning: a parametric study of relational complexity. *Cereb Cortex, 12*(5), 477-485.

Kuhl, B. A., Bainbridge, W. A., & Chun, M. M. (2012). Neural reactivation reveals mechanisms for updating memory. *J Neurosci, 32*(10), 3453-3461.

Leshikar, E. D., Gutchess, A. H., Hebrank, A. C., Sutton, B. P., & Park, D. C. (2010). The impact of increased relational encoding demands on frontal and hippocampal function in older adults. *Cortex, 46*(4), 507-521.

Li, J., Morcom, A. M., & Rugg, M. D. (2004). The effects of age on the neural correlates of successful episodic retrieval: an ERP study. *Cogn Affect Behav Neurosci, 4*(3), 279-293.

Logan, J. M., Sanders, A. L., Snyder, A. Z., Morris, J. C., & Buckner, R. L. (2002). Under-recruitment and nonselective recruitment: dissociable neural mechanisms associated with aging. *Neuron, 33*(5), 827-840.

Luo, L., & Craik, F. I. (2008). Aging and memory: a cognitive approach. *Can J Psychiatry, 53*(6), 346-353.

Makino, Y., Yokosawa, K., Takeda, Y., & Kumada, T. (2004). Visual search and memory search engage extensive overlapping cerebral cortices: an fMRI study. *Neuroimage, 23*(2), 525-533.

Mitchell, K. J., & Johnson, M. K. (2009). Source monitoring 15 years later: what have we learned from fMRI about the neural mechanisms of source memory? *Psychol Bull, 135*(4), 638-677.

Mitchell, K. J., Johnson, M. K., Raye, C. L., & D'Esposito, M. (2000). fMRI evidence of age-related hippocampal dysfunction in feature binding in working memory. *Brain Res Cogn Brain Res, 10*(1-2), 197-206.

Morcom, A. M., Li, J., & Rugg, M. D. (2007). Age effects on the neural correlates of episodic retrieval: increased cortical recruitment with matched performance. *Cereb Cortex, 17*(11), 2491-2506.

Naveh-Benjamin, M. (2000). Adult age differences in memory performance: tests of an associative deficit hypothesis. *J Exp Psychol Learn Mem Cogn, 26*(5), 1170-1187.

Naveh-Benjamin, M., Brav, T. K., & Levy, O. (2007). The associative memory deficit of older adults: the role of strategy utilization. *Psychol Aging, 22*(1), 202-208.

Nee, D. E., Wager, T. D., & Jonides, J. (2007). Interference resolution: insights from a meta-analysis of neuroimaging tasks. *Cogn Affect Behav Neurosci, 7*(1), 1-17.

Norman, K. A., & Schacter, D. L. (1997). False recognition in younger and older adults: exploring the characteristics of illusory memories. *Mem Cognit, 25*(6), 838-848.

Ochsner, K. N., Hughes, B., Robertson, E. R., Cooper, J. C., & Gabrieli, J. D. (2009). Neural systems supporting the control of affective and cognitive conflicts. *J Cogn Neurosci, 21*(9), 1842-1855.

Old, S. R., & Naveh-Benjamin, M. (2008). Differential effects of age on item and associative measures of memory: a meta-analysis. *Psychol Aging, 23*(1), 104-118.

Park, D. C., Polk, T. A., Park, R., Minear, M., Savage, A., & Smith, M. R. (2004). Aging reduces neural specialization in ventral visual cortex. *Proc Natl Acad Sci U S A, 101*(35), 13091-13095.

Paus, T. (1996). Location and function of the human frontal eye-field: a selective review. *Neuropsychologia, 34*(6), 475-483.

Pereira, J. M., Xiong, L., Acosta-Cabronero, J., Pengas, G., Williams, G. B., & Nestor, P. J. Registration accuracy for VBM studies varies according to region and degenerative disease grouping. *Neuroimage, 49*(3), 2205-2215.

Petit, L., & Haxby, J. V. (1999). Functional anatomy of pursuit eye movements in humans as revealed by fMRI. *J Neurophysiol, 82*(1), 463-471.

Rajah, M. N., & D'Esposito, M. (2005). Region-specific changes in prefrontal function with age: a review of PET and fMRI studies on working and episodic memory. *Brain, 128*(Pt 9), 1964-1983.

Rajah, M. N., Languay, R., & Valiquette, L. (2009). Age-related changes in prefrontal cortex activity are associated with behavioural deficits in both temporal and spatial context memory retrieval in older adults. *Cortex*.

Raz, N., Gunning, F. M., Head, D., Dupuis, J. H., McQuain, J., Briggs, S. D., . . . Acker, J. D. (1997). Selective aging of the human cerebral cortex observed in vivo: differential vulnerability of the prefrontal gray matter. *Cereb Cortex, 7*(3), 268-282.

Raz, N., Rodrigue, K. M., Head, D., Kennedy, K. M., & Acker, J. D. (2004). Differential aging of the medial temporal lobe: a study of a five-year change. *Neurology, 62*(3), 433-438.

Rugg, M. D., Henson, R. N., & Robb, W. G. (2003). Neural correlates of retrieval processing in the prefrontal cortex during recognition and exclusion tasks. *Neuropsychologia, 41*(1), 40-52.

Rugg, M. D., & Morcom, A. M. (2005). The relationship between brain activity, cognitive performance and aging: the case of memory. In R. Cabeza, L. Nyberg & D. C. Park (Eds.), *Cognitive Neuroscience of Aging* (pp. 132-154). Oxford: Oxford University Press.

Rypma, B., & D'Esposito, M. (2000). Isolating the neural mechanisms of age-related changes in human working memory. *Nat Neurosci, 3*(5), 509-515.

Snodgrass, J., & Corwin, J. (1988). Pragmatics of measuring recognition memory: applications to dementia and amnesia. *Journal of Experimental Psychology 116,* 34-50.

Srimal, R., & Curtis, C. E. (2008). Persistent neural activity during the maintenance of spatial position in working memory. *Neuroimage, 39*(1), 455-468.

Staresina, B. P., Henson, R. N., Kriegeskorte, N., & Alink, A. (2012). Episodic reinstatement in the medial temporal lobe. *J Neurosci, 32*(50), 18150-18156.

Thompson-Schill, S. L., Bedny, M., & Goldberg, R. F. (2005). The frontal lobes and the regulation of mental activity. *Curr Opin Neurobiol, 15*(2), 219-224.

Ullsperger, M., & von Cramon, D. Y. (2001). Subprocesses of performance monitoring: a dissociation of error processing and response competition revealed by event-related fMRI and ERPs. *Neuroimage, 14*(6), 1387-1401.

Vilberg, K. L., & Rugg, M. D. (2007). Dissociation of the neural correlates of recognition memory according to familiarity, recollection, and amount of recollected information. *Neuropsychologia, 45*(10), 2216-2225.

Voss, M. W., Erickson, K. I., Chaddock, L., Prakash, R. S., Colcombe, S. J., Morris, K. S., . . . Kramer, A. F. (2008). Dedifferentiation in the visual cortex: an fMRI investigation of individual differences in older adults. *Brain Res, 1244*, 121-131.

Wagner, A. D., & Davachi, L. (2001). Cognitive neuroscience: forgetting of things past. *Curr Biol, 11*(23), R964-967.

West, R. L. (1996). An application of prefrontal cortex function theory to cognitive aging. *Psychol Bull, 120*(2), 272-292.

Williams, J. (1991). *Memory assessment scales professional manual*. Odessa: Psychological Assessment Resources.

Xiao, J., Hays, J., Ehinger, K., Oliva, A., & Torralba, A. (2010). SUN Database: Large-scale Scene Recognition from Abbey to Zoo. *IEEE Conference on Computer Vision and Pattern Recognition*.

Yassa, M. A., & Stark, C. E. (2009). A quantitative evaluation of cross-participant registration techniques for MRI studies of the medial temporal lobe. *Neuroimage, 44*(2), 319-327.

Yonelinas, A. P., & Jacoby, L. L. (2012). The process-dissociation approach two decades later: convergence, boundary conditions, and new directions. *Mem Cognit, 40*(5), 663-680.

Zeithamova, D., & Preston, A. R. (2010). Flexible memories: differential roles for medial temporal lobe and prefrontal cortex in cross-episode binding. *J Neurosci*, *30*(44), 14676-14684.