Neural correlates of post-retrieval monitoring in older adults are preserved under divided attention, but are decoupled from memory performance

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Title: Neural correlates of post-retrieval monitoring in older adults are preserved under divided attention, but are decoupled from memory performance

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Abstract

Post-retrieval monitoring is associated with engagement of anterior cingulate and dorsolateral prefrontal cortex. Recent fMRI studies reported age-invariant monitoring effects in these regions and an age-invariant correlation between these effects and memory performance. The present study examined monitoring effects during associative recognition (difference in activity elicited by 'rearranged' and 'intact' test pairs) under single and dual (tone detection) task conditions in young and older adults (Ns = 28 per group). It was predicted that, for the older adults only, dual tasking would attenuate memory performance and monitoring effects and weaken their correlation. Consistent with this prediction, in the older group imposition of the secondary task led to lower memory performance and elimination of the relationship between monitoring effects and performance. However, the size of the effects did not differ between single and dual task conditions. The findings suggest that the decline in older adults' memory performance in the dual task condition resulted not from impaired monitoring, but from a different cause that also weakened the dependence of performance on monitoring.

Keywords: episodic memory; aging; fMRI; prefrontal cortex; cognitive control; dual task

Journal

1 Introduction

Episodic memory – memory for unique events – declines with advancing age (for reviews see Grady, 2012; Nyberg, Lovden, Riklund, Lindenberger, & Backman, 2012). Episodic memory is assumed to be supported by a combination of domain-specific and domain-general cognitive processes, and age-related episodic memory decline likely reflects the vulnerability of both classes of process to increasing age (for reviews see Buckner, 2004; Grady, 2012; Rugg, 2004). In the case of episodic memory retrieval – the focus of the present study – domain-general processes include those that fall under the general rubric of executive function (Diamond, 2013), such as the selection and maintenance of task goals, and the monitoring and evaluation of the outcome of retrieval attempts in light of these goals (Rugg, 2004). Here, we investigate how manipulating demands on these domain-general processes during an associative recognition task impacted the behavioral and neural (fMRI) correlates of retrieval monitoring in young and older adults.

fMRI correlates of retrieval monitoring have consistently been identified in right dorsolateral prefrontal (rDLPFC)¹ and anterior cingulate cortex (ACC; e.g., Achim & Lepage, 2005; de Chastelaine et al., 2016; Henson et al., 2000; Henson, Rugg, Shallice, Josephs, & Dolan, 1999; Wang, Johnson, de Chastelaine, Donley, & Rugg, 2015; see Fletcher and Henson, 2001, for an early review; for discussion of the role of these regions in executive control networks more generally see Cocchi et al, 2013 and Duncan, 2010). Only a handful of fMRI studies have contrasted monitoring effects between samples of young and older adults, and these have reported mixed findings: whereas some studies did not identify reliable age-related differences (de Chastelaine et al., 2016; Dulas & Duarte, 2014; Giovanello et al., 2010; Wang et al., 2015), age differences were reported in three others (Duarte et al., 2010; McDonough, Wong, & Gallo, 2013; Mitchell, Ankudowich, Durbin, Greene, & Johnson, 2013).

As was just noted, four recent studies reported null effects of age on monitoring-related neural activity in rDLPFC and ACC. In two of these studies, the null effects were accompanied by robust, age-invariant, positive correlations between episodic memory performance and the fMRI effects (de Chastelaine et al., 2016; Wang et al., 2015). In both studies, the neural correlates of monitoring were operationalized as a relative enhancement in fMRI BOLD signal for unsuccessfully vs. successfully recollected items ('Know' vs. 'Remember' recognition memory judgments in Wang et al., 2015, incorrect 'rearranged' vs. correct 'intact' associative recognition judgments in de Chasletaine et al, 2016; see those citations for the rationale underlying these contrasts). In each case memory performance was lower in the older adults, but neither the magnitude of the fMRI monitoring effects nor their relationship with performance differed with age. In light of the well-attested vulnerability of both executive control processes and the structural integrity of the PFC to increasing age (e.g., Buckner, 2004; Grady, 2012) these null findings might be regarded as surprising. We return to this issue below.

¹ We note that while DLPFC monitoring effects typically predominate in the right hemisphere, they can be accompanied by robust effects in the left hemisphere also (e.g., de Chastelaine et al., 2016 and the present findings).

The findings of preserved fMRI monitoring effects in older adults stand in contrast to the findings of other studies in which monitoring effects were reported to differ with age. In two of these studies (McDonough et al., 2013; Mitchell et al., 2013), monitoring effects were manipulated by varying the difficulty of the retrieval task, and monitoring was operationalized as the contrast between activity elicited during the 'hard' vs. the 'easy' task. In each study, activity in DLPFC and ACC was enhanced in the hard task in young, but not older adults, prompting both sets of authors to conclude that older adults fail to appropriately modulate neural resources supporting monitoring. As was noted by de Chastelaine et al. (2016), however, there is evidence that older adults are less adept than young individuals in adopting test-appropriate 'retrieval orientations' (Morcom and Rugg, 2004; Jacoby et al., 2005; Duverne et al., 2009). Thus, it is possible that the failure of the older participants in McDonough et al. (2013) and Mitchell et al. (2013) to demonstrate task-dependent monitoring effects in the PFC reflected a more general difficulty in adopting differential task sets. Moreover, the prefrontal regions where monitoring effects were evident in these two studies differed markedly in location from those identified by Wang et al. (2015) and de Chastelaine et al. (2016); for example, the effects predominated in the left rather than the right hemisphere and barely encroached on the DLPFC (i.e., Brodmann Areas 9/46). Thus, it is possible that the monitoring-related contrasts employed in those studies engaged cognitive processes distinct from those engaged in de Chastelaine et al. (2016) and Wang et al. (2015). In the third study to report age differences in putative monitoring effects (Duarte et al. 2010), monitoring was operationalized in the same manner as in Wang et al. (2015; see above), that is, in a contrast between test items afforded 'Know' vs. 'Remember' judgments. Unlike in Wang et al. (2015), Duarte et al. (2010) reported that the monitoring effects that were evident in the rDLPFC of their young participants were attenuated in older adults. We have no ready explanation for these conflicting findings.

We propose that a crucial factor influencing whether age differences are observed in the neural correlates of retrieval monitoring is the availability of the cognitive and neural resources required to support monitoring operations. According to the CRUNCH model (Reuter-Lorenz & Cappell, 2008; for review see Cabeza et al., 2018), for example, task-related neural activity tracks task demands until a resource limit is reached, at which point (the 'crunch point') the activity will plateau or drop off, and task performance will suffer. The CRUNCH model predicts that older adults will reach this resource limit at lower levels of task demand than will young adults. Thus, it is possible that in prior studies where age-invariant prefrontal monitoring effects were reported (e.g., de Chastelaine et al, 2016; Wang et al, 2015), task demands were so low that monitoring was not resource-limited.

In the present study, we examined this proposal by combining a retrieval task that varied demands on retrieval monitoring with a secondary task manipulation, under the assumption that a relatively high secondary task demand would deplete resources otherwise available to support monitoring operations (cf. Craik, Govoni, Naveh-Benjamin, & Anderson, 1996; Craik, Naveh-Benjamin, Ishaik, & Anderson, 2000; Naveh-Benjamin, Craik, Guez, & Kreuger, 2005). We employed tone detection as the secondary task because the task is attentionally demanding but does not impose a memory load, thereby allowing us to increase demands on

processing resources without generating interference with domain-specific mnemonic operations. For the purposes of the present study we selected associative recognition as the retrieval test. The rationale for the selection of this test – the essence of which is the requirement to discriminate between pairs of studied words that were either studied on the same (intact pairs) or on separate (rearranged pairs) study trials - was two-fold. First, we have previously reported that both the prefrontal monitoring effects elicited in this task, and their relationship with memory performance, are age-invariant (de Chastelaine et al. 2016). Second, the nature of the task affords a specific prediction about the class of memory judgment that should be most vulnerable to the disruption of post-retrieval monitoring. Specifically, we predicted that, relative to a single task condition (during which responding to tones was not required), engagement in the secondary tone detection task would result in a disproportionate increase in 'associative false alarms' (incorrect endorsements of rearranged test pairs as intact) in older relative to young adults, with minimal impact on correct detection rates for intact test pairs. This prediction arises from the assumption that an 'intact' associative judgment requires only that a recollection 'signal' is detected. Thus, only modest evaluation of recollected content is required prior to response selection and demands on post-retrieval monitoring are relatively low. By contrast, when the items are familiar but a recollection signal cannot be detected - the situation for most test pairs that end up attracting a 'rearranged' judgment - monitoring must be engaged more heavily, and for a more prolonged period, as memory search is extended in an effort to detect a recollection signal.

In the case of monitoring-related neural activity, we expected to replicate prior findings by identifying age-invariant monitoring effects in rDLPFC and ACC, and an age-invariant relationship between these effects and memory performance, in the absence of a secondary task load (cf. de Chastelaine et al., 2016; Wang et al., 2015). Crucially, we further predicted that when participants were required to perform the retrieval test under dual task conditions, older adults would demonstrate a greater reduction in the magnitude of their monitoring effects than young individuals, reflecting their more limited attentional and control resources (Craik, 1983). We predicted that the relationship between monitoring effects and memory performance would remain robust in young adults, on the assumption that the secondary task would deplete, but not exhaust, the resources available to support monitoring. In older adults, on the other hand, we predicted that the demands of the secondary task would deplete control resources to the extent that the relationship between monitoring-related activity in frontal cortex and associative memory performance would break down. To explore these issues, we obtained single-trial parameter estimates of fMRI BOLD responses from regions of interest in frontal cortex, allowing us to analyze both mean across-trial activity and across-trial variability in item-related BOLD responses (see Methods). We adopted this approach to examine the possibility that the imposition of a secondary task might impact not only the magnitude but also the trial-wise variability of monitoring-related neural activity (cf. Abdulrahman & Henson, 2016).

2 Methods

The experimental procedures described below were approved by the Institutional Review Boards of UT Dallas and The University of Texas Southwestern Medical School (UTSW). All participants provided written informed consent prior to participation in the experiment.

2.1 Participants

Twenty-eight young adults (aged between 18-30 years) and 28 older adults (aged between 65-76 years) were recruited from the UT Dallas and surrounding metropolitan Dallas communities. Participants were compensated at the rate of \$30 per hour for the experimental fMRI session and reimbursed for travel. Participants were right-handed, had normal or corrected-to-normal vision, scored a minimum of 27 on the Mini-Mental State Examination (MMSE) and were eligible for MRI. Exclusion criteria included a history of cardiovascular disorder (with the exception of treated hypertension), diabetes, psychiatric disorders, disorders of the central nervous system, substance abuse, current or recent use of sleeping aids, and inadequate standardized test performance.

An additional eight participants were tested but excluded for the following reasons: three older adults were excluded due to insufficient trial numbers in one or more critical conditions, three older and one younger adult were excluded for behavioral performance below the predetermined cut-off on the associative recognition task under single task conditions (pR < .05), and one younger adult was excluded for excessive motion in the scanner. An additional eight participants were scheduled but unable to complete the experiment for the following reasons: three older adults withdrew from the experiment due to claustrophobia, one older adult was deemed potentially unsafe for the MR environment during screening, and two older and two younger adults were unable to complete the experiment due to technical issues after they had completed the study phase.

2.2 Neuropsychological Testing

A standard battery of neuropsychological tests was administered to participants on a separate day prior to the experimental session. We used the same test battery as in previous work by our group (e.g., de Chastelaine et al., 2016), which included the following tests: CVLT composite recall (average number of words recalled on the short- and long-delay free- and cued-recall tests), number of CVLT recognition hits, number of CVLT recognition false alarms, logical memory composite recall (average of immediate and delayed recall), completion time for Trails A and B, number of valid responses on the SDMT, FAS, and Raven's, and estimated full-scale intelligence quotient derived from the WTAR. A potential participant did not proceed to the experiment if: 1) they scored greater than 1.5 standard deviations below age- and education-adjusted norms for any long-term memory measure, 2) their estimated full-scale IQ on the Wechsler Test of Adult Reading was less than 100, or 3) they scored greater than 1.5 standard deviations below age- and education-adjusted norms on two or more non-memory tests.

2.3 Materials

2.3.1 Critical stimuli

Critical stimulus lists were yoked across young and older participants. Experimental stimuli consisted of 320 semantically unrelated word pairs taken from the word association norms of Nelson, McEvoy, and Schreiber (2004). All words were concrete nouns between three and nine letters in length. The stimulus pool was divided randomly into five lists containing 64 word pairs each; lists were counterbalanced across participants so that each pair was used in all conditions. For the study phase, critical stimuli consisted of two pseudo-randomly ordered lists of word pairs (with no more than three successive trials of the same expected encoding judgment, as determined by majority agreement of three experimenters' independent ratings). For the test phase, critical stimuli consisted of 192 intact pairs (words presented together at study), 64 rearranged pairs (words paired with different words at study), and 64 new pairs (words from the final list not seen at study). Critical items were pseudo-randomly ordered and intermixed with 104 null trials such that there were no more than three successive trials of the same type. Two buffer pairs were inserted at the beginning and middle of all experimental task blocks. Practice lists for study and test phases were drawn from a separate pool of word pairs.

All test lists also included auditory tone presentations. Tones consisted of pure sine waves. Low frequency (400 Hz) and high frequency (900 Hz) tones were randomly assigned a stimulus onset asynchrony (SOA) that varied continuously between 1000-3000 ms and were interspersed throughout each test block, such that one to three tones occurred during each trial (including null trials). Tone onsets were restricted such that they could not occur concurrently with the red fixation cross immediately prior to each word pair, nor during the first 500 ms of each word pair presentation. This was done to avoid the possibility of cross-modal perceptual interference (although participants were informed that tones could occur at any time during the test trials). Each stimulus list was associated with a 'target' tone, and the proportion of target tones in each list was 0.33. Both single and dual task test blocks contained tones, with the same ratio of low to high tones in each type of block.

2.3.2 Practice lists

Practice lists were created using 96 additional word pairs with similar characteristics to the critical stimuli. For study, one practice list comprising 50 intact and 23 rearranged pairs was created. For test, the intact and rearranged pairs were split across two practice lists (single and dual task). Practice test 1 (single task) comprised 30 intact pairs, 15 rearranged pairs, 15 new pairs, and 12 null trials. Practice test 2 (dual task) comprised 20 intact pairs, 8 rearranged pairs, 8 new pairs, and 12 null trials. For practice test 2, tones were added following the procedure described above for the critical lists. A tone detection practice list was also created, consisting only of tones (as above) that were presented while a white fixation cross was continuously present. The tone-only practice list was three minutes in duration and was used to establish a baseline reaction time for the secondary tone task. Separate dual task practice lists were created for low and high target tones by adding tones with the appropriate ratio of low to high tones for each target to the same list of associative recognition test items.

2.4 Experimental Procedure

2.4.1 Study phase

Presentation and timing of experimental stimuli were controlled using the Cogent software package (http://<u>www.vislab.ucl.ac.uk/cogent.php</u>). All experimental study items were presented in uppercase 30-point Helvetica font, in white text on a black background. Word pairs were presented for a duration of 2000 ms and were preceded by a red fixation cross for 500 ms. A white fixation cross followed for 1000 ms, giving a response window of 3000 ms per trial. The study phase, which was administered outside the scanner on a laptop computer, lasted approximately 18 minutes (see Figure 1 for task schematic). Encoding was intentional, as participants were aware of the subsequent associative recognition test and trained on both study and test phases before beginning the experiment. The study session consisted of two task blocks with a brief rest in between. Study words were presented simultaneously, one above and one below fixation. The task was to judge which of the two objects denoted by the words would more likely 'fit' into the other and to respond via a button press. To encourage relational encoding of the word pairs, participants were instructed to focus on imagining a scenario (constructing a vivid visual image or verbal story) to determine which item would fit into the other. Participants were instructed to respond as quickly as possible without sacrificing accuracy. Following the study session, participants were escorted to the scanner and prepared for the test phase.



Figure 1. Experimental task schematic for the study phase.



Figure 2. Experimental task schematic for the test phase. Response options depicted apply to the dual task condition; the single task procedure was identical except participants were instructed to ignore the tones.

2.4.2 Test phase

All experimental test items were presented in uppercase 30-point Helvetica font, in white text on a black background. The members of each test pair were presented simultaneously, one above and one below fixation. Items subtended a vertical visual angle of 2.7° and a maximum horizontal visual angle of 6.2° and were viewed via a mirror attached to the head coil. Word pairs were presented for a duration of 2000 ms and were preceded by a red fixation cross for 500 ms. A white fixation cross followed for 2000 ms, giving a response window of 4000 ms per trial. Null trials consisted of a white fixation cross displayed for the same duration as a critical trial (4.5 seconds). Rest periods interposed halfway through each task block were 30 seconds in duration. Test hand, response-finger mapping, single/dual task block order, and frequency of the target tone (low vs. high) were counterbalanced across participants. The test session took place inside the scanner and began approximately 25 minutes after completion of the study session (see Figure 2 for task schematic). The session comprised four blocks, separated from one another by short rest periods. Test blocks alternated between single task (associative memory task only) and dual task (associative memory plus tone detection) blocks. Participants heard tones during all test blocks but were instructed to ignore them during the single task blocks. During the dual task blocks, participants were instructed to give equal emphasis to both tasks. For the associative memory task, participants viewed word pairs with the requirement to judge whether each pair was 'intact', 'rearranged', or 'new'. Participants were instructed to respond 'intact' when they could recall with high confidence and specificity that the two items had been studied together, and to respond 'rearranged' when the words were recognized as having been studied but there was either no memory of their having been studied together, or the memory was uncertain. Participants were informed that the test list did not include mixed pairs of new and

studied words. They were however instructed to respond 'new' whenever they could recognize only one of the words as studied, or when both words were judged to be unstudied. Participants again indicated their responses via a button press; they were instructed to respond as quickly as possible without sacrificing accuracy.

2.4.3 Training and practice

Prior to the experiment proper, but on the same day as the fMRI session, participants were fully instructed on all tasks and given a chance to practice them until they felt comfortable with the requirements. Participants completed practice phases in the following order:

- Study practice (first 9 trials self-paced)
- Test practice single task (first 20 trials self-paced)
- Tone practice single task (establish RT baseline)
- Test practice dual task (all trials timed)

Participants were allowed to repeat practice phases until they felt comfortable with the task demands, pacing, and response options, and the experimenter was satisfied that they were performing the task adequately. A legend of response options remained on-screen for the duration of all task blocks during the practice and experimental phases. Immediately prior to the test phase, participants underwent functional scans (approx. 30 second duration), during which they practiced responding to target tones in the presence of background scanner noise. The experimenter adjusted the volume of the tones according to the participants' feedback and the procedure was repeated until the experimenter was confident that the participant could comfortably detect and discriminate between the high and low tones while the scanner was running, as determined both by verbal confirmation and by the accuracy of responses to the practice tones.

2.5 fMRI Acquisition

Participants were scanned using a 3 Tesla Philips Achieva MRI scanner (Philips Medical Systems) equipped with a 32-channel parallel imaging receiver head coil. Anatomical data were obtained using a T1weighted 3D magnetization-prepared rapid gradient echo (MP-RAGE) pulse sequence (FOV 256 x 256, 1x1x1 mm voxel size, 176 slices, sagittal acquisition). Functional data were obtained using a T2*-weighted echo-planar imaging (EPI) sequence (270 volumes, 33 axial images per volume, TR = 2 s, TE = 30 ms, flip angle 70°) with 3 mm thick slices (1 mm interslice gap, 3x3 mm in-plane resolution). Slices were acquired in ascending order with a sensitivity encoding (SENSE) reduction factor of 2 for the functional data. The first 5 volumes of each block were discarded to allow tissue magnetization to reach equilibrium.

2.6 fMRI Preprocessing

The data were preprocessed and analyzed using SPM12 (<u>http://www.fil.ion.ucl.ac.uk</u>). Imaging timeseries from the different scanner runs were concatenated using the *spm_concatenate* function. Functional images

were realigned to the mean EPI template, motion and slice-time corrected, spatially normalized, and smoothed using an 8 mm full-width half-maximum (FWHM) Gaussian kernel. Data were normalized to a sample-specific template created from 26 younger and 22 older adults included in the present sample. The sample-specific template used in the normalization step was created by first normalizing each participant's mean functional volume to the MNI template, averaging the normalized volumes within each group, and averaging the group mean images to form a sample-specific template that takes into equal account the contribution of each age group. Two young and six older adults were excluded from template creation due to poor initial normalization to the MNI template, but normalization to the sample-specific template was of sufficient accuracy to include them in the final analysis sample (per consensus of the first and second authors' visual inspection).

2.7 Statistical analyses

Critical trial types utilized in analysis of the fMRI data were *associative hits* (intact pairs correctly endorsed as intact), *associative misses* (intact pairs incorrectly endorsed as rearranged) and *associative correct rejections* (rearranged pairs correctly endorsed as rearranged). Due to insufficient trial numbers for some participants, associative misses and associative correct rejections were collapsed at the first level into a single bin for fMRI analyses. We refer to associative hits as 'intact' and the combination of associative misses and associative correct rejections as 'rearranged' responses throughout for simplicity. Rearranged test pairs incorrectly endorsed as intact are referred to hereafter as *associative false alarms*.

2.7.1 Behavioral analysis

Measures of task performance and response time (RT) were calculated separately for the associative memory and tone detection tasks. Associative memory performance was indexed as pR (proportion of associative hits – proportion of associative false alarms) and was calculated separately for single and dual task blocks. Tone detection performance was similarly indexed as proportion of hits – proportion of FAs (i.e., button presses to target and non-target tones, respectively). These metrics were calculated separately for the tone task practice phase (serving as a baseline for tone RT) and dual task test blocks. Associative memory and secondary tone task performance measures were entered into separate 2 (task: single vs. dual) x 2 (age group: younger vs. older) ANOVAs. Response times for the associative memory task were entered into a 2 (task) x 2 (age group) x 2 (memory judgment: 'intact' vs. 'rearranged') ANOVA, and RTs to hits in the secondary tone task were entered into a 2 (task: baseline vs. dual) x 2 (age group) ANOVA. As appropriate, significant effects were followed up by within-group ANOVAs or t-tests. The Greenhouse-Geisser correction was applied to ANOVA contrasts where appropriate.

2.7.2 fMRI analysis

2.7.2.1 Whole-brain univariate analysis

The fMRI data were subjected to whole brain, mass univariate analysis using a two-step procedure implemented in SPM12. The first stage was conducted with separate general linear models (GLMs) for each participant. The neural activity elicited by test pairs was modeled as a delta function and convolved with two canonical hemodynamic response functions (HRFs): a canonical and an orthogonalized, delayed HRF, generated by shifting the canonical HRF one TR (2 seconds) later and applying the Gram-Schmidt procedure to ensure that variance shared between the regressors was attributed uniquely to the canonical HRF (Andrade, Paradis, Rouquette, & Poline, 1999). The results from the late covariate model did not reveal any effects of theoretical significance additional to those obtained from the early covariate model, and therefore are not discussed further. Events of interest (see above) were modeled separately for single and dual task blocks, along with events of no interest and the 30-second rest period midway through each block. Six motion regressors and three constants for means across test blocks were also included in the design matrix. During parameter estimation, an autoregressive AR(1) model was used to correct for time-series correlations.

In the second stage, participant-specific parameter estimates for events of interest were brought forward into an ANOVA model with the between-participants factor of age group and the within-participants factors of task condition and memory judgment. Levels of the memory judgment factor included 'intact' responses to intact pairs, 'rearranged' responses to intact or rearranged pairs, and correctly rejected new pairs. As described below, the 'rearranged > intact' contrast derived from this model was employed to select participant-specific seed regions for the functional connectivity analyses. The model was also employed to examine the data for possible influences of age group and task condition on monitoring effects outside of the ROIs described below. These whole brain analyses and their findings (which were null) are described in the Supplemental Materials.

2.7.2.2 Region of Interest Selection

To obviate the possibility of bias in favor of one or the other age group, regions of interest (ROIs) corresponding to the three frontal regions where monitoring effects have been consistently identified in prior studies – ACC and right and left DLPFC – were defined by reference to the monitoring effects identified in an independent study of associative recognition (de Chastelaine et al., 2016). The MNI co-ordinates of the peaks of these effects were: ACC (9, 23, 43; Brodmann Area (BA) 8/32), left DLPFC (-48, 29, 25; BA 9/46), and right DLPFC (51, 32, 22; BA 9/46). The ROIs comprised all voxels contained within 5mm radius spheres centered on each peak. As is evident from Table S1 (Supplemental Materials), the loci of the ROIs are within a few mm of the peaks of the frontal monitoring effects identified from the whole brain analyses described above.

2.7.2.3 Single-trial GLMs

Given that our experiment was motivated by the question of how task demands modulate monitoringrelated activity during retrieval, we considered it important to investigate across-trial variance in BOLD

responses as well as their magnitude (see Section 1). To this end, we constructed participant-specific first level GLMs using the least squares all (LSA) approach (Abdulrahman & Henson, 2016; Mumford et al., 2012), such that each trial was modeled as a separate event of interest. Analyses were conducted on mean across-trial parameter estimates for 'intact' and 'rearranged' judgments, segregated by task condition, extracted from the three *a priori* ROIs corresponding to the frontal monitoring effects reported by de Chastelaine et al. (2016) and described in the preceding section. Mean monitoring effects (i.e., the difference in BOLD signal between 'rearranged' and 'intact' responses) were estimated and employed in the analyses described here. We first conducted a 2 (age group) x 3 (ROI: ACC, LDLPFC, RDLPFC) x 2 (task) ANOVA on these effects. Significant ANOVA findings were followed up with ANCOVA models controlling for the potentially confounding influence of associative memory performance (cf. de Chastelaine et al., 2016). An analogous approach was employed to examine across-trial variability of the single-trial parameter estimates as a function of age group, ROI, task condition, and response type ('rearranged' vs. 'intact').

2.7.2.4 Relationship between fMRI activity and associative recognition performance

To investigate the relationship between fMRI monitoring effects and memory performance in each age group, we constructed linear regression models with mean across-trial parameter estimates of monitoring-related differences in activity ('rearranged' – 'intact' monitoring effects, derived from the same ROIs as in the preceding analyses) as a predictor of interest. Predictor variables were age group, the monitoring effect x age group interaction, RT differences between 'rearranged' and 'intact' memory judgments, and the RT difference x age group interaction. The dependent variable was associative recognition performance (pR). Regression models were constructed separately for the single and dual task conditions, collapsing across the three frontal ROIs (preliminary analyses revealed no significant inter-regional differences in the strength of the relationship between monitoring effects and performance in either task condition). For models where a significant interaction with age group was identified, we computed separate models for each age group and contrasted the resulting partial correlations between monitoring effects and performance. The outcomes of all regression analyses are reported after the removal of non-significant interaction terms from the model.

2.7.2.5 Functional connectivity analysis

In addition to investigating the responses of individual brain regions during associative memory retrieval, we conducted exploratory psychophysiological interactions (PPI) analyses (Friston et al., 1997; O'Reilly et al., 2012) to examine monitoring-related modulation of functional connectivity. For the purposes of these analyses, 'seed regions' were derived separately for each participant (cf. King et al., 2015, 2018). Using the outcome of the mass univariate analysis described above and reported in Supplemental Materials (section S1), peak monitoring effects (collapsed across task) falling with a 10mm radius of each of the three frontal ROIs were identified for each participant. The seeds were then defined as all voxels falling within a 3mm radius sphere centered on each peak. Separate first level PPI analyses were conducted for the single and dual task blocks for

each participant and seed region. The outcomes of these first-level contrasts were carried forward into second level models, with age group modeled as a between-participants factor and task condition a within-participants factor (following the methods described by King et al., 2015, 2018). No significant clusters could be identified for the age group, task condition, or the age group x task condition interaction terms for any of the three seed regions, even at the relatively liberal voxel-wise threshold of p < .001. Therefore, we went on to construct single PPI models for each seed region, collapsing across task condition and age group. The functional connectivity data reported in Section 3.3.4 were extracted from these models.

3 Results

3.1 Neuropsychological Tests

A summary of the neuropsychological test scores is provided in Table 1. The pattern of the scores is typical of that reported for cross-sectional studies of cognitively healthy young and older adults (e.g., de Chastelaine et al., 2016; Wang et al., 2015), with higher scores for the younger adults on tests involving episodic memory, processing speed, and fluid intelligence.

Table 1. Neuropsychological test scores (SD) for young and older adults. CVLT: California Verbal Learning Test, WTAR: Wechsler Test of Adult Reading, WMS: Wechsler Memory Scale (WMS-IV). Significant age group differences are marked with an asterisk.

	Younger	Older	Age Group Differences (p-values)
Ν	28	28	
Sex(M/F)	13/15	11/17	
Age	22.46 (3.57)	69.61 (3.14)	
Years of education	15.43 (2.47)	16.79 (2.22)	0.679
MMSE	29.39 (0.83)	29.18 (0.98)	0.627
CVLT Recall (composite)	13.94 (1.69)	12.37 (2.43)	0.007*
CVLT Recognition - Hits	15.71 (0.53)	15.32 (0.77)	0.006*
CVLT Recognition - FAs	0.54 (0.92)	1.79 (1.97)	<.001*
SDMT	63.32 (10.85)	49.75 (7.31)	0.030*
Digit Span (Total)	19.79 (4.39)	18.96 (3.63)	0.333
Trails A	19.61 (5.32)	27.62 (9.62)	0.041*
Trails B	47.92 (15.97)	67.48 (26.95)	0.024*
FAS (Total)	48.21 (12.78)	49.68 (12.15)	0.639
Category Fluency (Animals)	24.54 (5.40)	22.54 (5.25)	0.652
WTAR (Raw)	42.21 (4.17)	44.11 (4.33)	0.877
WMS (composite)	30.66 (5.19)	27.57 (5.28)	0.032*
Raven's (List 1)	10.96 (1.14)	9.54 (2.10)	0.001*

3.2 Behavioral Results

3.2.1 Associative Memory Performance

The proportions of accurate responses to intact, rearranged, and new pairs are listed in Table 2 for each task condition. Associative memory performance (pR) for young and older adults is illustrated in Figure 3. Mean pR estimates for young adults were 0.53 (SD = 0.19) and 0.49 (SD = 0.18), in the single and dual tasks, respectively. Mean pR estimates for older adults were 0.31 (SD = 0.14) in the single task and 0.22 (SD = 0.15) in the dual task. Estimates of pR were entered into a 2 (age group) x 2 (task) ANOVA. The analysis identified main effects of task (F1,54 = 11.88, p < .001, partial $\eta^2 = 0.18$) and age group (F1,54 = 35.32, p < .0001, partial $\eta^2 =$ 0.40). Despite the absence of a task condition x age group interaction (F1,54 = 2.13, p = .150, partial $\eta^2 = 0.04$), we went on to test the effects of task in each age group separately, given our *a priori* prediction that these effects should differ in the two groups (see Section 1). Consistent with the prediction, paired sample t-tests indicated that younger adults' associative memory performance did not significantly differ by task condition (t27 = 1.59, p = .123, Cohen's d = 0.31), whereas older adults' associative memory performance was significantly lower in the dual relative to the single task condition (t27 = 3.14, p = .005, Cohen's d = 0.58). Also in line with our predictions, older adults' associative false alarm rates (incorrect endorsements of rearranged pairs as intact) were elevated in the dual relative to the single task condition (t27 = 2.54, p = .017, Cohen's d = 0.48), while there was no significant difference between conditions in younger adults' associative false alarm rates ($t_{27} = 1.07$, p = .292, Cohen's d = 0.20).

Table 2. Mean proportions (SD) of intact, rearranged, and new responses given to intact, rearranged, and new test pairs for each age group and task condition. Correct responses in **bold** font. Associative false alarms in italics.

	Young		Old	der
	Single task	Dual task	Single task	Dual task
Intact responses				
Intact pairs	0.71 (0.15)	0.70 (0.16)	0.58 (0.16)	0.56 (0.21)
Rearranged pairs	0.18 (0.12)	0.20 (0.11)	0.27 (0.18)	0.33 (0.19)
New pairs	0.04 (0.05)	0.04 (0.05)	0.10 (0.09)	0.12 (0.11)
Rearranged responses				
Intact pairs	0.17 (0.09)	0.18 (0.12)	0.28 (0.13)	0.27 (0.15)
Rearranged pairs	0.56 (0.14)	0.57 (0.13)	0.45 (0.16)	0.37 (0.15)
New pairs	0.22 (0.14)	0.22 (0.13)	0.28 (0.12)	0.27 (0.16)
New responses				
Intact pairs	0.12 (0.09)	0.12 (0.07)	0.14 (0.06)	0.17 (0.10)
Rearranged pairs	0.26 (0.12)	0.23 (0.09)	0.29 (0.14)	0.30 (0.15)
New pairs	0.74 (0.15)	0.73 (0.16)	0.62 (0.16)	0.61 (0.19)



Figure 3. Associative memory performance (pR) by age group and task condition (S: single task, D: dual task). Horizontal bars depict the mean for each age group and condition, and the corresponding mean pR estimates are noted along the bottom of the plot.

3.2.2 RTs to test items

Mean RTs for the critical trial types are shown in Table 3. ANOVA identified main effects of task (F1,54 = 15.99, p < .001, partial $\eta^2 = 0.23$), memory judgment (F1,54 = 200.10, p < .001, partial $\eta^2 = 0.79$), and an age group x memory judgment interaction (F1,54 = 7.97, p = .007, partial $\eta^2 = 0.13$). For both age groups, mean RTs to 'intact' responses were faster than those to 'rearranged' responses, and mean RTs in both age groups for both response types were faster during dual task blocks. Independent sample t-tests (equal variance not assumed) confirmed that the age group x memory judgment interaction reflected slower RTs for 'intact' responses in older relative to young adults in both task conditions (single task: t53.76 = 2.11, p < .05, Cohen's d = 0.56; dual task: t53.88 = 2.19, p < .05, Cohen's d = 0.57) in the absence of an age difference in RTs for 'rearranged' responses (single task: t51.96 = 0.03, p = .97, Cohen's d = 0.01; dual task: t51.44 = 0.21, p = .83, Cohen's d = 0.06).

Table 3. Mean RT (SD) for the associative memory task by age group and critical trial types for fMRI analyses. Intact: 'intact' responses to intact pairs (associative hits), Rearranged: 'rearranged' responses to intact or rearranged pairs (associative misses and associative correct rejections).

	Younger		Older	
	Single task	Dual task	Single task	Dual task
'Intact'	1608 (311)	1546 (294)	1790 (333)	1716 (308)
'Rearranged'	2131 (424)	2028 (407)	2128 (347)	2049 (325)

3.2.3 Secondary task performance

	Hit - FA (tones)		Mean RT to target tones	
	Baseline Dual task		Baseline	Dual task
Younger	0.99 (0.02)	0.90 (0.13)	451 (97)	709 (157)
Older	0.99 (0.01)	0.85 (0.17)	486 (77)	816 (118)

Table 4. Performance on the tone detection task (SD) by age group and task condition.

Secondary task performance is summarized in Table 4. Below, we present a comparison of tone detection performance at baseline vs. dual task, but with a caveat: while tones were presented but ignored during the single task blocks of the associative recognition task, word pairs were not presented to participants during the baseline tone practice phase (see Section 2.3.2). Therefore, we do not suggest that the attentional demands of the tone baseline and single task conditions were equivalent, and we present the following results as only a rough estimate of the effect of divided attention on secondary task performance. Baseline performance on the tone detection task was at ceiling for both groups. ANOVA identified a main effect of baseline vs. dual task (F1,54 = 35.13, p < .0001, partial $\eta^2 = 0.39$), but no effects of age group (F1,54 = 1.36, p = .248, partial $\eta^2 = 0.03$) nor an age group x task interaction (F1,54 = 1.48, p = .229, partial η^2 = 0.03). These results indicate that, consistent with our expectations, tone detection performance during dual task blocks relative to baseline was significantly lower for both groups. The ANOVA of mean RTs to target tones identified main effects of baseline vs. dual task $(F1,54 = 386.01, p < .001, partial \eta^2 = 0.88)$ and age group $(F1,54 = 6.80, p = .012, partial \eta^2 = 0.11)$, as well as an interaction between these factors (F1,54 = 5.74, p = .020, partial η^2 = 0.10). As expected, both groups were slower to respond to target tones under dual task conditions, relative to baseline RT. Independent sample t-tests on mean RTs to target tones for baseline and dual task revealed that older adults were significantly slower to respond to target tones than younger adults under dual task conditions (t50.08 = 2.88, p = .006, Cohen's d = 0.77) but not at baseline when tone detection was the only task (t51.23 = 1.50, p = .141, Cohen's d = 0.40).

3.3 fMRI Results

3.3.1 Monitoring Effects

Mean across-trial parameter estimates (derived from the LSA model; see Section 2.7.2.3) extracted from each of the three frontal ROIs are depicted in Figure 4B (as the difference between the estimates for 'rearranged' and 'intact' responses; the separate parameter estimates for these two classes of responses can be found in Supplementary Materials, Figure S5). Results from the 2 (age group) x 3 (ROI) x 2 (task) ANOVA of the monitoring effects illustrated in Figure 4B are given in Table 5. As is evident from the table, the ANOVA revealed a significant main effect of age group and an age group x task interaction. Since no interaction terms including the factor of ROI approached significance, subsequent analyses were performed after collapsing across ROIs. To follow up on the significant age x task interaction, we conducted paired t-tests for each age group; single and dual task monitoring effects did not significantly differ in magnitude for either the young (t28 = 1.65, p = .110, Cohen's d = 0.31) or the older adults (t28 = 1.32, p = .199, Cohen's d = 0.25). Independent sample ttests revealed a significant age difference in single task monitoring effects (t54 = 3.05, p = .004, Cohen's d = 0.82). This difference was not evident, however, for the dual task (t54 = 0.76, p = .451, Cohen's d = 0.20). When the ANOVA was repeated as an ANCOVA with associative memory performance in the single and dual task conditions included as covariates, neither the main effect of age group (F1,52 = 0.22, p = .644, partial $\eta^2 = 0.00$ nor the age group x task interaction (F1,52 = 0.55, p = .463, partial $\eta^2 = 0.01$) now attained significance; adjusted parameter estimates are depicted in Figure 5. ANCOVA of the single task monitoring effects (with memory performance as a covariate) also failed to identify a significant age effect: F1,54 = 9.29, p < .004, partial η^2 = .147 and F1,53 = 1.109, p = .297, partial η^2 = .021 without and with the covariate respectively.



Figure 4. A) Main effects of monitoring (collapsing across task and age group) from the whole-brain univariate GLM reported in Supplementary Materials (section S1). Effects are displayed on an inflated brain at p < .05, FWE-corrected. B) Mean across-trial monitoring effects ('rearranged' – 'intact' parameter estimates) for each of the a priori-determined frontal ROIs (parameter estimates extracted from the single-trial GLM). Error bars represent SEM. C) Mean across-trial monitoring effects averaged across the three frontal ROIs. BOLD signal change is depicted in arbitrary units, and all bar graphs are on a common scale.

Table 5 ANOVA results for parameter estimates ('Rearranged' – 'Intact' difference) extracted from frontal ROIs reported in de Chastelaine et al. (2016). Significant effects in bold font. Group (younger, older), Region (ACC, Left DLPFC, Right DLPFC), Task (single, dual).

Effect	df	F	p value	partial η^2
Group	1, 54	5.05	.029	0.09
ROI	1.96, 105.92	1.59	.210	0.03
Task	1, 54	0.00	.998	0.00
ROI x Group	1.96, 105.92	0.53	.586	0.01
Task x Group	1, 54	4.25	.044	0.07
ROI x Task	1.56, 84.35	0.41	.613	0.01
ROI x Task x Group	1.56, 84.35	0.38	.633	0.01



Figure 5. Monitoring-related activity adjusted for associative memory performance (estimated marginal means). Monitoring effects are displayed as the difference in BOLD signal between 'rearranged' – 'intact' responses. BOLD signal change is depicted in arbitrary units.

3.3.2 Across-trial variability of fMRI monitoring effects

To investigate across-trial variability in monitoring effects, we entered the standard deviations of the single-trial parameter estimates into a 2 (task) x 2 (memory judgment: 'intact' vs. 'rearranged') x 2 (age group) ANOVA. Results revealed a main effect of memory judgment (F1,54 = 7.83, p = .007, partial $\eta^2 = 0.13$), reflecting greater variability for 'intact' than for 'rearranged' judgments, and an age group x task interaction (F1,54 = 4.21, p = .045, partial $\eta^2 = 0.07$); no other effects approached significance (min. p = .137). Post hoc analyses revealed that while variability was greater in the single than in the dual task for young participants (t27 = 2.83, p = .009, Cohen's d = 0.54), no such effect was evident for the older adults (t27 = 0.35, p = .731, Cohen's d = 0.07). Additional pairwise contrasts failed to identify age differences in either task condition, however. Similar to the analysis of the magnitude of the monitoring effects described above, the inclusion in the ANOVA of memory performance as a covariate eliminated the age group x task interaction effect (F1,52 = 2.14, p = .150, partial $\eta^2 = 0.04$).

3.3.3 Relationship between fMRI monitoring effects and associative recognition performance

We constructed separate multiple regression models for the single and dual task conditions to examine the relationships between associative recognition performance and frontal monitoring-related activity (averaged across ACC and bilateral DLPFC ROIs), with age group, RT differences between 'intact' and 'rearranged' responses, the interaction between age group and monitoring-related activity, and the interaction between age group and RT differences as initial additional predictor variables. Consistent with prior findings (de Chastelaine et al., 2016; Wang et al., 2015), an age-invariant relationship between the magnitude of monitoring effects in frontal cortex and associative recognition performance was identified for the single task condition (partial r = 0.31, p = .021; Figure 6A and Table 6). By contrast, the regression model for the dual task condition included a significant age group x monitoring effect interaction. Accordingly, separate regression models were run for each age group in this condition, employing monitoring-related activity and RT differences as the predictor variables. As is evident from Figure 6B and Table 6, there was a significant relationship between monitoring effects and associative memory performance for the young adults. By contrast, there was no evidence of such a relationship in the older group. As would be expected given the significant interaction term in the initial regression model, the partial correlations between dual task monitoring effects and memory performance differed significantly between the age groups (young: partial r = 0.47; older: partial r = -0.18; p = .016). Together, the findings are suggestive of a breakdown in older adults in the relationship between monitoring-related activity and performance in the dual task condition.



Figure 6. Relationship between monitoring effects and associative memory performance for each task condition. Fit lines: blue = young adults, red = older adults, black = all participants. A) In the single task condition there was an age-invariant relationship between monitoring activity and performance, controlling for age group and RT differences. Removing the potential young and older adult outliers (circled) from the model did not affect the statistical outcome. B) In the dual task condition there was a positive relationship between monitoring-related activity and performance for young adults, controlling for RT differences. Removing the potential young adult outlier (circled) from the model did not affect the statistical outcome. No significant relationship between

monitoring effects and associative memory performance was identified for older adults in the dual task condition.

Table 6. Results of the across-group regression models predicting associative memory performance for the single and dual task conditions. b: unstandardized coefficient; SEb: standard error of the unstandardized coefficient; β : standardized coefficient. Nonsignificant interaction terms were dropped from the models.

Model	b	SEb	β	partial r	p value	
		<u>Singl</u>	<u>e task</u>			
Intercept	0.3873	0.06			< .001	
Age group	-0.1458	0.05	-0.38	-0.41	0.002	
Monitoring effect	0.0446	0.02	0.28	0.31	0.021	
RT differences	0.0002	0.00	0.20	0.24	0.088	
		Dual	<u>task</u>			
Intercept	0.2967	0.05			< .001	
Age group	-0.1567	0.05	-0.37	-0.41	0.002	
Monitoring effect	0.0590	0.02	0.32	0.37	0.006	
RT differences	0.0003	0.00	0.36	0.46	< .001	
Group x monitoring	-0.0826	0.04	-0.30	-0.31	0.023	
Dual task - young adults						
Intercept	0.3014	0.07			< .001	
Monitoring effect	0.0590	0.02	0.43	0.47	0.013	
RT differences	0.0003	0.00	0.40	0.44	0.022	
Dual task - older adults						
Intercept	0.1370	0.04			0.004	
Monitoring effect	-0.0245	0.03	-0.16	-0.18	0.382	
RT differences	0.0003	0.00	0.52	0.50	0.009	

3.3.4 Functional Connectivity

Separate PPI models were constructed using as seeds participant-specific peaks adjacent to each of the three frontal regions demonstrating a main effect of monitoring in the univariate analysis (see Section 2.7.2.5). We first investigated whether the separate single and dual task PPI models differed significantly from one another by combining SPMs for single and dual task PPI models to examine interaction effects; we did not identify any significant clusters demonstrating effects of age group, task condition, or an age group x task interaction. We therefore collapsed the PPI analyses for each of the three seed regions across age group and task condition (see Section 2.7.2.5). As is summarized in Table 7 and illustrated in Figure 7, for all three seeds, robust (height threshold p < .05, FWE-corrected) monitoring-related connectivity increases with bilateral occipital cortex were observed. For the left and right DLPFC seeds, increased connectivity with left intraparietal sulcus (IPS) was also observed when an uncorrected statistical threshold of p < .001 was employed. Because the same IPS region cluster was identified for both DLPFC seeds we consider this finding to be highly robust (conjoint

statistical significance of p < .00002 according to Fisher's method, although it should be noted that because the respective PPI analyses are not fully independent, the true significance level is likely somewhat higher than this method would suggest).



Figure 7. At top, seed regions demonstrating a main effect of monitoring ('rearranged' > 'intact' responses). At bottom, regions where functional connectivity with frontal seed regions increased as a function of monitoring. Bottom left: bilateral occipital cortex (results inclusively masked across ACC, left DLPFC, and right DLPFC seeds). Bottom right: left IPS (results inclusively masked across left and right DLPFC seeds). Results are shown on the sample-specific T1 template at p < .001, uncorrected, with a 50-voxel cluster extent threshold for display purposes.

Table 7. Regions demonstrating a monitoring-related increase in functional conne	ctivity with three frontal seed
regions, collapsed across task condition and age group. ^a threshold of p < .001 unco	prrected rather than $p < .05$
FWE-corrected.	

Seed Region		Coordinates	7	Peak Z	Region
	Х	У	Z		
ACC					
	-21	-100	-1	4.49	Left occipital cortex
	15	-100	-7	5.23	Right occipital cortex
LDLPFC					
	-39	-88	-16	5.09	Left occipital cortex
	33	-88	-13	5.47	Right occipital cortex
	-30	-70	41	3.76	Left IPS ^a
RDLPFC					
	-21	-100	-4	5.23	Left occipital cortex
	21	-97	-1	6.03	Right occipital cortex
	-30	-70	44	3.95	Left IPS ^a

4 Discussion

In samples of cognitively normal young and older adults, we utilized fMRI to investigate the relationship between neural activity in the frontal cortex supporting post-retrieval monitoring (operationalized as increased activity for 'rearranged' relative to 'intact' judgments in an associative recognition task) and secondary task demand (operationalized as ignoring (single task) or discriminating between (dual task) concurrently presented tones). Consistent with our predictions, older adults' associative memory performance decreased under dual task conditions as a result of an increase in associative false alarms, while young adults' memory performance was not significantly affected by the task manipulation. Contrary to our predictions, however, monitoring-related activity in three frontal ROIs (ACC, left DLPFC, and right DLPFC) was not modulated significantly by the addition of the secondary task in either age group. In the single task condition, older adults' monitoring effects were smaller than those of the young sample. This age difference was accompanied by an age-invariant positive relationship between monitoring-related activity in this task condition and associative memory performance. Intriguingly, there was a breakdown in the relationship between performance and monitoring-related activity in older adults in the dual task condition, while in the young adults a positive relationship was still apparent. Increased monitoring-related functional connectivity between each of the frontal ROIs and bilateral occipital cortex, and between the two lateral ROIs and the left IPS, was observed regardless of age group or task condition. Below, we expand on these and other findings.

4.1 Behavioral results

As noted above, behavioral performance was consistent with our pre-experimental predictions. Overall associative memory performance was lower for the older than the young adults, in line with numerous prior findings of decreased recollection performance with increasing age (e.g., de Chastelaine et al., 2016; Wang et al, 2015; see Koen & Yonelinas, 2014 for review). Additionally, while associative recognition performance was unaffected by the imposition of the secondary task in the young sample, performance was lower in this task condition than in the single task condition in the older adults. Of importance, this decrement was entirely due to an increased associative false alarm rate, with no evidence of a corresponding decrease in associative hits. This pattern of findings arguably rules out the possibility that older adults' lower recollection accuracy in the dual task condition was caused by disrupted retrieval cue processing. Rather, the null finding for associative hits is consistent with the view that memory retrieval *per se* is little affected by divided attention because the processing of retrieval cues is in some sense 'protected', allowing it to 'capture' attentional resources at the cost of secondary task performance (Craik et al., 1996). And once a retrieval cue has been appropriately processed, any pattern completion processes that it might elicit are thought to occur largely automatically (for review see Rugg, 2004; see also Tulving, 1983). From this perspective, therefore, the functional locus of the detrimental effect of the secondary task on older participants' memory performance is likely to be downstream of cue processing and pattern completion operations.

RTs for the associative memory judgments were significantly faster in the dual relative to the single task condition. This finding was somewhat surprising, with others reporting increased RTs for both the memory test and the secondary task under conditions of divided attention (e.g., Craik et al., 2018). However, a potentially important difference between the present study and that of Craik et al. (2018) is while the primary and secondary tasks shared a modality in the prior study, here we combined a visually presented retrieval task with an auditory tone detection task. We conjecture that the present decrease in associative memory RTs in the dual task condition reflects the requirement for attention switching between the two sensory modalities – that is to say, participants allocated less time to the memory test in the dual task condition because of the requirement also to monitor and respond to the tones (Craik et al, 2000). Tone detection RTs, on the other hand, were slower during the dual task than the baseline condition and, as might be expected, this slowing was more pronounced in older than in young adults (although, as previously noted, we do not consider the attentional demands of the baseline tone detection practice phase and the single task retrieval phase to be equivalent). The finding of slower RTs to tones in the dual task condition (compared to baseline) is in keeping with prior reports of RT costs for secondary tasks in similar settings (e.g., Craik et al., 1996; Craik et al., 2000; Naveh-Benjamin et al., 2005).

4.2 fMRI results

4.2.1 Monitoring-related activity

The magnitudes of the monitoring effects in the three frontal ROIs did not significantly differ between the task conditions in either age group. Additionally, across-trial variability in the BOLD activity associated with the items placing most demand on post-retrieval monitoring (i.e., rearranged pairs) was not reliably modulated by the task manipulation in either group (although across trial variability of the responses elicited by both rearranged and intact pairs was higher in the dual task condition in the young group). Together, these findings are inconsistent with our predictions that monitoring-related activity in the dual task condition would be lower and more variable in older than in young adults. Monitoring effects were however larger in magnitude in the young relative to the older adults in the single task condition (Figure 4C). This finding contrasts with the results of a prior study employing the same associative recognition procedure, when the magnitude of frontal monitoring effects was age-invariant (de Chastelaine et al., 2016; see also Wang et al., 2015). The retrieval demands in the present study were likely considerably heavier than those in our prior study, however; even in the single task condition, there was a requirement to ignore the potentially distracting tones (a requirement that we suspect was more onerous for the older adults). Perhaps as a consequence, the effects of age on memory performance in the present study were somewhat greater than those reported previously (Cohen's d = 1.32 in the present single task condition, as opposed to 0.99 in de Chastelaine et al., 2016). Thus, in light of the robust age-invariant relationship that exists between memory performance and monitoring-related activity (at least under single task conditions, see below and de Chastelaine et al., 2016), the present age-related reduction in monitoring effects in the single task condition is perhaps unsurprising. Consistent with this argument, the effects of age on the magnitude of the single task monitoring effects were eliminated by controlling for associative memory

performance. That is, the magnitudes of these effects in the older adults approximated those that would be expected in young adults demonstrating equivalent levels of memory performance (see Figure 5).

4.2.2 Relationship between monitoring-related activity and memory performance

As mentioned above, and replicating prior findings (de Chastelaine et al., 2016; Wang et al., 2015), there was a robust and age-invariant relationship between the magnitude of frontal monitoring effects and associative recognition performance in the single task condition. In striking contrast, whereas a similarly robust relationship was evident for the young group in the dual task condition, the correlation between monitoring effects and memory performance in this condition for the older group was weakly (and non-significantly) negative. This pattern of findings is consistent with our pre-experimental prediction that the across-participant relationship between monitoring effects and memory performance would break down in older adults with the imposition of the secondary task. As already noted, however, the lack of a secondary task effect on the magnitude of the older adults' frontal monitoring effects is inconsistent with another of our pre-experimental predictions.

How can the combination of a null secondary task effect on the size of monitoring effects and the elimination of their association with memory performance be explained? Some potential clues come from an examination of the across-participant simple correlations between key variables. First, while monitoring effects in the dual task condition did not reliably predict older adults' memory performance in that condition (r = -0.03), monitoring effects in the *single* task condition did do so (r = 0.46, p = .013). Second, the across-participants correlation between the magnitude of the monitoring effects in the two conditions was robust for the young group (r = 0.60, p < .001) but weak and non-significant for the older group (r = 0.21, p = .28). And last, the correlation between memory performance in the two task conditions was significantly greater in the young than in the older group (respectively, r = 0.81, p < .001, r = 0.52, p < .004, difference p < .05). Together, these findings suggest that, to varying extents, older, but not young, adults, were influenced during the secondary task by a factor that both reduced the accuracy of their memory performance and 'decoupled' performance from concurrently measured monitoring effects. The nature of this factor is presently a matter of speculation – potential candidates include the requirement to task switch, the need to engage cross-modal attention, or perhaps something as simple as auditory acuity. According to the first of these accounts, individual differences in the ability of our older adults to switch between the retrieval test and the secondary task played such a large role in mediating memory performance that they overshadowed monitoring as an important determinant of performance. By the second, closely related, account, it was individual differences in the ability to switch attentional focus between the visual and auditory modalities that mediated memory performance. According to the third of these accounts, despite our best efforts to equate the perceptibility of the tone stimuli across participants, residual differences remained, such that memory performance suffered to a greater extent in those older participants who required the most attentional resources to discriminate the stimuli (cf. Peele and Wingfield, 2016). Adjudicating between these and other possible accounts will require further research but, regardless, the data suggest that individual differences in the ability to cope with the demands of the secondary

task were uncorrelated with individual differences in the ability to efficiently engage post-retrieval monitoring, at least as this is operationalized by the magnitude of frontal monitoring effects.

4.2.3 Monitoring-related modulation of functional connectivity

To our knowledge, the present study is the first to examine monitoring-related modulation of functional connectivity between frontal and other cortical regions in samples of either young or older adults. We caution that these PPI analyses were exploratory, and hence that the findings should be treated as provisional until replicated. We identified regions in bilateral occipital cortex and left IPS where functional connectivity with frontal seed regions increased with monitoring demand regardless of secondary task load (Figure 7). An overlapping cluster in bilateral occipital cortex was identified for all three seed regions (ACC, left DLPFC, and right DLPFC). We conjecture that this finding might reflect enhanced attention to perceptual features of retrieved information in an attempt to resolve an ambiguous memory signal (cf. King et al., 2015; see also Watrous & Ekstrom, 2014). Alternately, the finding might reflect enhanced attention to the retrieval cues themselves. By contrast, the left IPS preferentially increased connectivity with the left and right DLPFC seeds, but not the ACC. We think it is not a coincidence that the IPS and DLPFC are prominent members of the 'fronto-parietal control network' held to support goal directed cognition (Cocchi et al, 2013). It is also worth noting that the left IPS cluster overlaps with the parietal cluster that demonstrated monitoring-related activity in the mass univariate analysis (Supplementary Materials, Table S1). The monitoring-related increase in connectivity between bilateral DLPFC and left IPS thus likely reflects the engagement of cognitive control mechanisms supporting the monitoring of retrieved information and its employment in service of behavioral goals (here, choice between an 'intact' and a 'rearranged' response). While we also observed univariate monitoring effects in the right IPS, no monitoring-related modulation of connectivity was identified for that region. We have no ready explanation for this apparent asymmetry in monitoring-related functional connectivity between DLPFC and IPS.

The monitoring-related increases in functional connectivity between seed regions in frontal cortex and target regions in visual cortex (for all three seeds) and left IPS (for left and right DLPFC seeds) were invariant with respect to both age group and task condition. Together with the finding that monitoring-related increases in BOLD signal in frontal ROIs were similarly age-invariant, at least after controlling for memory performance, these null findings support the proposal that the young and older adults were equally able to recruit a common network of regions in support of post-retrieval monitoring, even when attentional resources were divided between the retrieval test and a secondary task.

4.3 Limitations

An important caveat to our findings stems from the cross-sectional design of the experiment. Consequently, as discussed in more detail elsewhere (e.g., de Chastelaine et al., 2016; for review see Rugg, 2016), it is not possible to determine the extent to which the present age-related differences in neural activity and memory performance should be attributed to aging rather than to confounding factors such as cohort effects. A

second caveat is that, as is well recognized, caution is always warranted before accepting a null result. Notably, while we make liberal use of the term 'age-invariant' when describing null effects of age, we acknowledge that more highly powered studies might reveal subtle but theoretically significant age differences. A third caveat arises from evidence indicating the existence of systematic age differences in the transfer function mediating between neural activity and the fMRI BOLD response (e.g., Lu et al., 2011). Thus, age differences in the hemodynamic transfer function (HTF) are a potentially confounding factor in the present study. That said, it is difficult (although not impossible) to see how generic age differences in the HTF could fully explain our results, most notably the finding of a condition-specific breakdown in the relationship between monitoring effects and memory performance in our older group. Relatedly, we note that, as in all prior studies of the effects of age on the neural correlates of retrieval monitoring (see Introduction), monitoring effects were operationalized in terms of differences in a univariate measure of BOLD signal change. It remains to be established whether appropriately designed studies allowing monitoring to be examined with multivariate analysis approaches will yield convergent findings. Finally, we note that our secondary task manipulation was limited to a contrast between only two points on the hypothetical 'performance-resource function' for associative recognition (cf. Norman & Bobrow, 1975). Future research could usefully examine the relationships between age, retrieval monitoring effects (both univariate and multivariate), and performance over a wider range of secondary task loads (and a wider range of tasks) than those employed here.

4.4 Conclusion

In summary, we replicated prior findings that young and older adults engage a common set of frontal regions when monitoring mnemonic signals during episodic retrieval (de Chastelaine et al., 2016; Wang et al., 2015). Contrary to our prediction, there was no evidence that older adults' monitoring effects were disproportionately impacted by the imposition of a secondary task, or that an impaired ability to engage monitoring operations accounted for age differences in memory performance. Rather, it appears that when attentional demands during retrieval were increased, other factors came into play that affected older adults' ability to cope with the concurrent demands of the associative recognition and secondary tasks. The nature of these factors is currently unclear, although we conjecture that they may have been related to the requirement for cross-modal task switching.

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Declarations of Interest: None

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Bilateral occipital cortex

Increased connectivity with seed regions as a function of retrieval monitoring



Left intraparietal sulcus (IPS)

- Frontal retrieval monitoring effects were not modulated by attentional demands
- There was a positive relationship between monitoring effects and memory performance
- The monitoring-performance relationship broke down for older adults in dual task

Verification

- 1. No declarations of interest.
- 2. This work was supported by the National Institute on Aging [grant numbers R21AG054197, RF1AG039103].
- 3. The data contained in the manuscript being submitted have not been previously published, have not been submitted elsewhere and will not be submitted elsewhere while under consideration at Neurobiology of Aging.
- 4. Experimental procedures were approved by the Institutional Review Boards of The University of Texas at Dallas and The University of Texas Southwestern Medical School.
- 5. All authors have reviewed the contents of the manuscript being submitted, approve of its contents, and validate the accuracy of the data.