Neurobiology of Aging 90 (2020) 1–12

Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging

Frontostriatal functional connectivity supports reward-enhanced memory in older adults

Holly J. Bowen [a,*], Jaclyn H. Ford [b], Cheryl L. Grady [c,d], Julia Spaniol [e]

[a] Department of Psychology, Southern Methodist University, Dallas, TX, USA
[b] Department of Psychology, Boston College, Chestnut Hill, MA, USA
[c] Rotman Research Institute, Baycrest Centre, Toronto, Ontario, Canada
[d] Departments of Psychiatry and Psychology, University of Toronto, Toronto, Ontario, Canada
[e] Department of Psychology, Ryerson University, Toronto, Ontario, Canada

ARTICLE INFO

Article history:
Received 1 April 2019
Received in revised form 10 February 2020
Accepted 12 February 2020
Available online 21 February 2020

Keywords:
Memory
Reward
Motivation
Aging
Functional connectivity

ABSTRACT

Both younger and older adults prioritize reward-associated stimuli in memory, but there has been little research on possible age differences in the neural mechanisms mediating this effect. In the present study, we examine neural activation and functional connectivity in healthy younger and older adults to test the hypothesis that older adults would engage prefrontal regions to a greater extent in the service of reward-enhanced memory. While undergoing MRI, target stimuli were presented after high- or low-reward cues. The cues indicated the reward value for successfully recognizing the stimulus on a memory test 24 hours later. We replicated prior findings that both older and younger adults had better memory for high- compared to low-reward stimuli. Critically, in older but not younger adults, this enhanced subsequent memory for high-reward items was supported by greater connectivity between the caudate and bilateral inferior frontal gyrus. The findings add to the growing literature on motivation-cognition interactions in healthy aging and provide novel findings of the neural underpinnings of reward-motivated encoding.

Reward-associated stimuli receive prioritized attention (Anderson, 2017; Williams et al., 2018, 2017), encoding (Adcock et al., 2006; Castel, 2007; Castel et al., 2002; Cohen et al., 2014; Hennessee et al., 2017; Shigemune et al., 2014, 2010), and consolidation (Spaniol et al., 2014). Although there is some evidence that the influence of reward on memory is preserved in healthy aging (e.g., Castel, 2007; Castel et al., 2002; Mather and Schoeke, 2011; Spaniol et al., 2014), there has been little research on age differences in the neural mechanisms mediating this effect. The goal of the present study was to compare reward-enhanced memory in healthy younger and older adults using functional magnetic resonance imaging (fMRI).

Behavioral and fMRI studies have shed light on the influence of reward motivation on declarative memory formation and its neural circuitry in younger adults (for reviews, see Miendlarzewska et al., 2016; Shohamy and Adcock, 2010). For example, using an incidental memory paradigm, Wittmann and colleagues (2005) found that images serving as reward-predicting cues during a numbers comparison task activated regions of the dopaminergic reward network, including the bilateral putamen, right caudate, and bilateral nucleus accumbens, as well as insula and thalamus. Furthermore, greater neural response in midbrain regions to reward-predicting images was linked to successful recognition of these images 3 weeks after encoding. Similar findings have been reported for intentional memory tasks. Adcock and colleagues (Adcock et al., 2006) used a Monetary Incentive Encoding (MIE) task in which reward was contingent on successful (intentional) encoding of scene stimuli. After a 24-hour delay, high-reward scenes were better remembered than low-reward scenes. This behavioral effect was associated with enhanced connectivity between the hippocampus and regions of the reward network during the presentation of reward cues that preceded the to-be-remembered scenes at encoding.

A small body of work has revealed that healthy older adults also demonstrate reward-enhanced memory (but see Geddes et al., 2018, described in more detail below). Using an incidental memory paradigm, Mather and Schoeke (2011) found a small effect indicating that both younger and older adults showed better memory for positively valenced objects that had been encoded after a reward anticipation cue. Furthermore, they found a much larger effect indicating that objects of any valence that were encoded

* Corresponding author at: Department of Psychology, Southern Methodist University, P.O. Box 750442, Dallas, TX 75275-0442, USA. Tel.: +1 214 768 3442; fax: +1 214 768 0821.
E-mail address: hbowen@smu.edu (H.J. Bowen).

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https://doi.org/10.1016/j.neurobiolaging.2020.02.013

following positive monetary gain feedback were better remembered than objects encoded following loss or neutral feedback. Reward also modulates intentional memory formation in older adults. Studies by Castel and colleagues (Castel, 2007; Castel et al., 2002; Cohen et al., 2016; Hennessee et al., 2017) have demonstrated that both younger and older adults are more likely to remember high-value information more than low-value information. Finally, in a study using an MIE task similar to that of Adcock et al. (2006), we showed reward-enhanced scene memory in both younger and older adults on a delayed recognition test (Spaniol et al., 2014).[1]

The finding of a preserved reward-memory interface in healthy aging is intriguing when considered against the backdrop of age-related decline in the component processes of reward-motivated memory. First, healthy aging is associated with well-documented decline in episodic memory (Cabeza et al., 2018; Grady, 2012; Nilsson, 2003; Nyberg et al., 2012; Shing et al., 2010), so the finding that reward motivation can boost episodic memory performance in older adults is an important discovery. Second, dopaminergic neuromodulation—thought to play a critical role in reward processing (Arias-Carrión et al., 2010; Berridge, 2007; Berridge and Robinson, 1998; Chowdhury et al., 2013; Ridderinkhof et al., 2012)—undergoes age-related decline (Bäckman et al., 2010; Li et al., 2010). Accordingly, age-related deficits have been reported in stimulus-reward learning (Bäckman et al., 2010; Eppinger et al., 2011), reward-based attention (Williams et al., 2018), and reward-based decision making (Samanez-Larkin et al., 2014, 2011). Interestingly, results of a meta-analysis (Karrer et al., 2017) suggest that although dopamine receptors and transporters are reduced, dopamine synthesis appears largely spared in healthy aging. This combination of factors may reduce dopamine reuptake in older adults and may partially explain why older adults are able to engage dopaminergic midbrain regions during gain and loss anticipation (Spaniol et al., 2015; but see Samanez-Larkin et al., 2007, for evidence of reduced loss sensitivity in older adults), as well as in response to gain and loss feedback (Bowen et al., 2019). As Karrer et al. (2017) note, it is still not clear, due to a lack of empirical work, why age-related changes in the dopamine system appear to have more impact in some cognitive domains than in others.

Most fMRI studies on reward-motivated behavior have focused on activity within the reward network, with relatively little attention paid to reward-based modulation of other brain regions. In one study, whole-brain analyses of fMRI data acquired during an incentive processing task revealed that older adults, but not younger adults, recruited the lateral prefrontal cortex during processing of high-value gain and loss cues (Spaniol et al., 2015). The extent of lateral frontal recruitment in older adults was associated with higher response speed, possibly reflecting the engagement of cognitive control mechanisms in the service of goal-directed behavior (Braver, 2012; Miller, 2000; Nyberg, 2018). Engagement of the prefrontal cortex often accompanies tasks that require cognitive control (for reviews, see Miller, 2000; Miller and Cohen, 2001) and that tap into executive functions such as goal-directed attention or working memory (Balota et al., 2000; Owen et al., 2005; Vallesi et al., 2011). Age-related over-recruitment of frontal regions is commonly reported in the fMRI literature and in some cases may serve to compensate for age-related decline in tasks that demand high levels of cognitive control (Cabeza et al., 2018; Grady, 2012). However, few published studies have examined age differences in reward-based modulation of behavior and corresponding brain activity in tasks with high control demands, such as episodic memory. In particular, only 2 studies have looked at fMRI correlates of reward-modulated long-term memory encoding in younger and older adults (Cohen et al., 2016; Geddes et al., 2018).

The goal of the study by Cohen et al. (2016) was to examine possible age-related differences in neural recruitment during the presentation of high and low point values (reward anticipation phase) that preceded the to-be-remembered words (target stimulus phase). In line with previous behavioral studies detailed previously, both younger and older adults showed greater recall for high-value words compared to low-value words, but the fMRI data revealed age differences in the underlying neural patterns. Activity in the reward network during the reward anticipation phase was modulated by reward value in younger adults, but not older adults, and in neither group was this activation associated with value-based memory selectivity. These neural findings are in contrast to other work with younger adults showing that engagement of the reward network during the reward anticipation phase leads to greater memory for the subsequent to-be-remembered stimulus (e.g., Adcock et al., 2006). Instead, Cohen and colleagues found that for younger adults, activity within the reward network during this later target stimulus phase correlated with value-directed memory selectivity, but not in older adults. A whole-brain activation analysis revealed that both younger and older adults engaged lateral prefrontal and temporal cortex, and this activation contributed to value-based memory selectivity during learning. The authors interpreted this finding as evidence for engagement of semantic strategies to prioritize high-value words at encoding. Additional evidence for this interpretation comes from an investigation of structure-function relationships in older adults (Hennessee et al., 2019). Structural integrity of the fronto-occipital fasciculus correlated with older adults' memory performance in a value-directed memory paradigm. This correlation suggests that older adults may rely on strategic control processes, rather than reward-related processes, to support memory for reward-related information.

In the study by Geddes et al. (2018), older and younger adults completed the MIE task while undergoing fMRI. In contrast to the behavioral findings detailed previously (e.g., Castel et al., 2002; Cohen et al., 2016; Spaniol et al., 2014), older adults did not show evidence of reward motivation effects on behavioral memory performance. Only younger adults demonstrated modulation of memory performance as a function of reward motivation (both gain and loss), and this effect was limited to recollection-based (rather than familiarity-based) memory. Similar to the findings reported by Cohen et al. (2016), activation in the reward network during the target stimulus phase was associated with motivation-related memory gains, but this effect was limited to younger adults. Both age groups activated the reward network as well as memory-related regions during anticipation of gains and losses, but unlike findings from Adcock et al. (2006) who tested a sample of younger adults, this activity was not correlated with memory performance in either the younger or older adult group.

In sum, the 2 existing fMRI studies on aging and reward-modulated memory obtained contradictory behavioral results, but neither of these studies found a link between reward-related brain regions and memory performance in older adults. Cohen and colleagues replicated the behavioral effect of reward-modulated memory discussed previously, but activity in the reward network during the target stimulus phase, not the anticipation phase, predicted behavioral performance, and only in younger adults. Activation in the prefrontal and temporal cortex predicted older adults'

[1] The behavioral study, Spaniol et al. (2014), included a different sample of participants than the sample reported in the present study. Participants in two prior neuroimaging studies—Spaniol et al. (2015) and Bowen et al. (2019)—are the same participants included in the present study and where we report results of the MID task.

memory performance. Geddes and colleagues did not replicate the behavioral findings in older adults although older adults showed intact reward network responses to anticipatory reward cues. There were many differences between these 2 studies that could potentially account for the discrepant findings. For example, differences in the type of motivation (i.e., points vs. monetary rewards), motivation valence (Geddes and colleagues included both gains and losses, whereas Cohen et al. only examined gains), retention interval (immediate vs. delayed), and how the reward network was defined for analyses (i.e., derived from neurosynth.org vs. functional localizer from the study participants).

1. The present study

In the present study, younger and older adults completed the MIE task during fMRI scanning, similar to Adcock et al. (2006) and Geddes et al. (2018). We hypothesized that we would replicate our prior behavioral findings of reward-based memory enhancement in both age groups (Spaniol et al., 2014). However, in the present study, we analyzed the neural activity using an approach that differed from the one chosen by Adcock et al. (2006) and Geddes et al. (2018). In addition to probing activation within regions of the reward network, we also examined the functional connectivity between a reward-related region and the rest of the brain. This is the first investigation into age-related differences in functional connectivity associated with reward-motivated memory. Moreover, we hypothesized that in addition to the reward network, older adults would show increased connectivity to prefrontal regions in the service of reward-enhanced memory. This hypothesis was based on our previous observations in the context of a monetary incentive delay task with the same participants included in the present study (Spaniol et al., 2015), and evidence that engagement of prefrontal regions may serve older adults in tasks that require high levels of cognitive control (Cabeza et al., 2018; Grady, 2012) to maintain goal relevant information (Braver, 2012; Chiew and Braver, 2013; Fröber and Dreisbach, 2014). Whether this neural pattern would occur during the reward anticipation phase or during the target stimulus phase was an open question given mixed findings in the literature regarding the timing of activation that supports memory performance (Adcock et al., 2006; Cohen et al., 2016; Geddes et al., 2018).

2. Method

2.1. Participants

Ethics approval for all procedures was obtained from Baycrest Hospital and Ryerson University. Younger adults were recruited from Ryerson University and the Toronto area via community web sites (Craigslist.ca and Kijiji.ca) and older adults were recruited from both the Baycrest Hospital and Ryerson University older adult participant pools. Study eligibility was established before scheduling and determined with a screening questionnaire to assess past and current medical conditions (e.g., psychiatric illness, depression, head injury, stroke), and medications that may affect cognition (e.g., sleep aids, prescription pain medication). Contraindications to the MRI procedure (e.g., metal implants) were assessed with an MRI safety questionnaire. Sixteen young adults (9 females) and 17 older adults (9 females) completed the study. Two older adult males were excluded from all analyses: one due to an incidental MRI finding, and one for failing to follow instructions resulting in a sample of 15 older adult participants. One additional older adult male was excluded from the connectivity analyses due to extreme outlier percent signal change values in the brain data, leaving a sample of 14 older adults in that analysis. Participants were compensated $80 for participation over the 2 sessions, in addition to task-based earnings.

Table 1
Demographics, background measures (cognition, personality, and mood), and proportion of remember/know responses by age group

Characteristic	Young adults	Older adults
Age	25.4 (0.94)	68.5 (1.39)
Education	16.7 (0.71)	16.5 (0.51)
Mill-Hill Vocabulary Test	18.4 (0.81)	23.0 (1.07)
Mini-Mental State Examination	29.3 (0.27)	28.9 (0.37)
NEO Five-Factor Inventory		
Neuroticism	19.0 (1.9)	16.6 (1.86)
Extraversion	27.6 (1.81)	16.6 (1.86)
Openness	33.4 (1.45)	34.1 (1.42)
Agreeableness	32.9 (2.34)	33.4 (1.61)
Conscientiousness	31.9 (1.83)	34.0 (1.83)
Positive and Negative Affect Schedule		
Positive Mood	28.3 (1.43)	33.1 (1.82)
Negative Mood	11.6 (0.39)	11.5 (0.54)
Proportion of each response type to target items by reward value		
High Reward—Remember	0.21 (0.04; 1–36)	0.10 (0.02; 1–19)
High Reward—Know	0.10 (0.02; 1–15)	0.08 (0.02; 0–13)
High Reward—Pretty Sure	0.15 (0.02; 2–16)	0.22 (0.02; 2–21)
High Reward—Guess	0.05 (0.01; 0–9)	0.09 (0.02; 0–15)
Low Reward—Remember	0.17 (0.04; 1–35)	0.09 (0.02; 0–18)
Low Reward—Know	0.10 (0.02; 0–15)	0.09 (0.02; 0–16)
Low Reward—Pretty Sure	0.13 (0.02; 2–15)	0.19 (0.02; 6–23)
Low Reward—Guess	0.05 (0.001; 0–7)	0.10 (0.02; 0–16)

For demographic and background measures, standard errors are provided in parentheses. For the recognition data, standard error and the range in the number of trials is indicated in parentheses.

Older adults were 68.4 years old on average (SD = 5.38, range = 60–78) and younger adults 25.44 (SD = 3.79, range = 20–33) years old. All older adults scored 27 or higher on the Mini–Mental State Examination (Folstein et al., 1975), with the exception of one with a score of 26, but this individual was not excluded from the analyses because no other measures showed evidence of impairment, and excluding the participant did not change the pattern of results. The 2 groups did not differ on years of education, nor on any subscales of the revised 60-item NEO Five-Factor Inventory (Costa and McCrae, 1989). Older adults scored higher than younger adults on the positive mood scale of the Positive and Negative Affect Schedule (PANAS; Watson et al., 1988), $t(29) = 2.09$, $p = 0.05$, $\eta^2 = 0.13$, and on the Mill-Hill vocabulary scale, $t(28) = 3.50$[2], $p = 0.002$, $\eta^2 = 0.30$. See Table 1 for the means of all demographic and questionnaire data by age group.

2.2. Stimuli

The experimental stimuli were 240 color photographs consisting of 120 indoor scenes and 120 outdoor scenes (see Fig. 1 for examples), taken from a picture database in CorelDraw. Stimuli were devoid of people or animals. The scenes were divided into 4 sets of 60 stimuli (half indoor, half outdoor). The sets contained approximately equal proportions of specific types of indoor scenes (e.g., kitchens, living rooms) and outdoor scenes (e.g., deserts, mountains). Sets of stimuli were counterbalanced across reward value and participants. An additional 12 stimuli were used for the practice runs.

2.3. Paradigm

The paradigm closely followed the procedures from prior work (Adcock et al., 2006; Spaniol et al., 2014). While in the MRI scanner,

[2] Due to time constraints during the experiment, one older adult did not complete the Mill-Hill vocabulary scale.

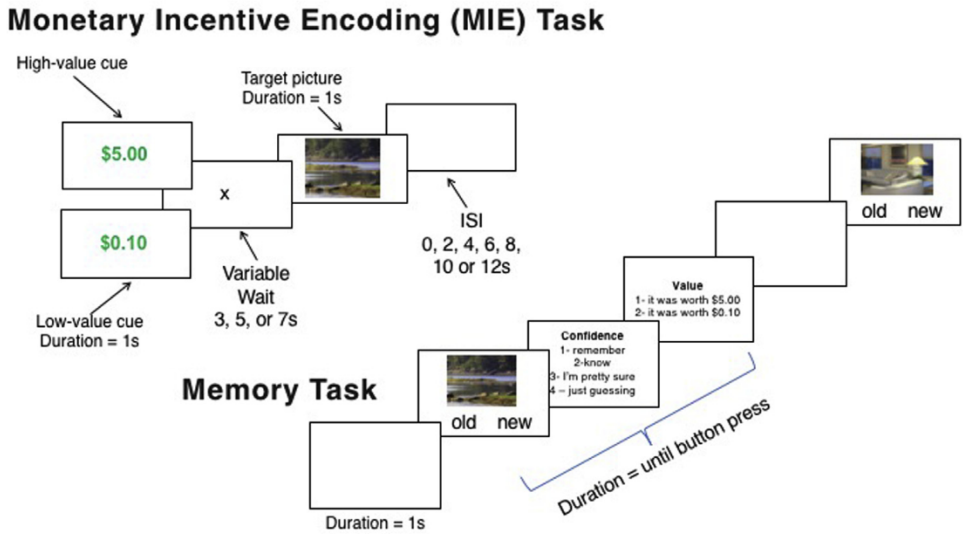

Fig. 1. Trial procedure in the Monetary Incentive Encoding (MIE) task and recognition memory task. The MIE task was completed in the fMRI scanner, and the duration of each element of the procedure is reported. The memory task depicts a trial resulting in an "old" response followed by a confidence rating and value judgment. Abbreviations: fMRI, functional magnetic resonance imaging.

participants completed 3 runs of the Monetary Incentive Encoding (MIE) task (Adcock et al., 2006). This was an event-related design and each run was 7 minutes and 36 seconds. During this task, participants were asked to intentionally encode 120 scene stimuli (40 trials per run). The target images remained onscreen for 2000 ms and were preceded by a reward cue. The reward cue indicated how much money the participant could earn if the image was correctly recognized on the memory test the following day. Cues indicated either a high value ($5.00) or low value ($0.10) and remained onscreen for 1000 ms. The cue was followed by a fixation that remained onscreen for a variable length of 3,000, 5000, or 7000 ms. Optseq was used to create a randomized schedule of between-trial interstimulus interval lengths of 2,000, 4,000, 6,000, 8,000, 10,000, and 12,000 ms based on the study parameters (e.g., number of time points, repetition time). See Fig. 1 for a depiction of the MIE task.

After completing the MIE task and while still in the MRI scanner, participants then completed a functional localizer task—the Monetary Incentive Delay (MID) task—well established to localize the reward network of the brain (Dugré et al., 2018; Knutson et al., 2001b, 2000). We have described the details of this task in prior publications (Bowen et al., 2019; Spaniol et al., 2015), but briefly, a participant's reaction time to a fast-paced target is incentivized with monetary gains and losses. Like the MIE task, each trial begins with a reward cue (reward anticipation phase) indicating how much money the participant can gain or avoid losing if the target stimulus—a star—is responded to in the allotted amount of time. The duration that the target remains on screen is calibrated to speed-up and slow-down so participants maintain a hit rate of approximately 66%.

The day after completing the MIE task, participants completed a recognition test with the 120 stimuli previously encoded in the MRI scanner and 120 new stimuli. For each image, participants were asked to first indicate old or new; if new was selected, the next image was presented. If old was selected, participants were asked to rate their confidence in their memory for the image on a scale of 1–4. Participants were told to respond "1" if "you remember the moment that you encountered the picture" ("remember"); respond "2" if "you feel sure that the picture was presented, but you have no specific memory" ("know"); respond "3" if "you are pretty sure, but not certain, that the picture was old" ("pretty sure"); respond "4" if "you were just guessing" ("guess"). Following the confidence rating, participants were asked a value judgment and to indicate whether they thought the image was worth a high ($5.00) or low reward ($0.10) value. See Fig. 1 for a depiction of the recognition memory task.

During the recognition test, if participants correctly identified an image as "old," they earned either the $5 or $0.10 the image was worth; however, if they incorrectly identified a new image as old, they lost $2.55. This penalty for false alarms was included to reduce liberal responding on the memory test.

2.4. Procedure

2.4.1. fMRI and behavioral procedures

Session 1 took place at Baycrest Hospital, and after obtaining informed consent, participants spent the first 30 minutes reading instructions and practicing the MIE task. Practice took place in the MRI simulator to ensure that participants were comfortable with the MRI environment and the necessary responses. After setup in the MRI, data for the MIE task were collected first, followed by the MID task. After completion of the MRI session, participants were paid for their participation and earnings on the MID task.

Session 2 took place approximately 24 hours after encoding, at Ryerson University. Participants completed the questionnaires followed by the recognition task described previously, which took approximately 40 minutes. At the end of the session, participants were paid for participation and earnings on the MIE memory test.

2.4.2. fMRI data acquisition

MRI scanning was conducted on a Siemens Trio 3.0 T whole-body scanner using a 32-channel "matrix" head coil. Anatomical imaging protocol included three-dimensional T1-weighted imaging (MPRAGE, FOV = 25.6 cm^2, 1 × 1 × 1 mm voxels, TI/TE/TR = 1100/2.63/2000 ms, flip angle = 9 deg, averages = 2, 160 slices, scan time = 5:44) and fluid-attenuated inversion recovery imaging (interleaved axial multislice FLAIR, FOV = 22.4 cm^2, 0.9 × 0.9 × 5 mm voxels, bandwidth = 315 Hz/Px, TI/TE/TR = 2200/96/9000 ms, averages = 1, concatenations = 3, 32 slices, 5 mm thickness, scan time = 3:38). Functional (MIE task) scans were acquired using an interleaved multislice EPI sequence (oblique axial orientation

intercallosal line, 228 volumes; FOV = 19.2 cm^2, 64x64 acquisition matrix, 40 slices 3 × 3 × 3.5 mm in-plane resolution, bandwidth = 2604 Hz/Px, TE/TR = 27/2000 ms, flip angle = 70 deg). Stimulus presentation and image acquisition was synchronized with a trigger pulse sent by the scanner at the beginning of each experimental run. Using an LCD projector (NEC Model MTI065) with a 2.75–5 zoom lens (Navitar, Inc), visual stimuli were projected on a screen at the back of the magnet bore and viewed by the participant through a mirror attached to the head coil. Responses to the stimuli were made via a Fiber-Optic Response Pad System (Current Designs Inc.; 4 buttons available per hand). fMRI-compatible prescription glasses were available to correct for visual acuity (SafeVision LLC., −6 to +6 diopters available in 0.5 increments). To reduce movement, foam sponges were used to restrain the participant's head and physiological data (heart rate, respiration, pulse) were also collected. To allow magnetic stabilization, the first 4 TRs of the functional runs were discarded.

2.5. Data analysis

SPSS (Statistical Package for Social Sciences 24.0, SPSS Inc., Chicago) was used to analyze the behavioral data and connectivity estimates of the fMRI data. All post hoc test *p*-values are reported using the Bonferroni corrected values.

2.5.1. Analysis logic

Overall, we were interested in both activation in a region of the reward network and functional connectivity patterns between that region and the rest of the brain. We examined these neural patterns during encoding in both younger and older adults with trial types defined based on subsequent memory for high- and low-reward items. To this end, we first established an region of interest (ROI) in the reward network using an activation analysis from the functional localizer MID task. From this analysis, the highest maximum activation was in the caudate—a well-established region of the reward network—and it was subsequently chosen as the ROI. Activation patterns with this caudate seed were examined during the anticipation and target stimulus phase of the MIE task. A whole-brain generalized psychophysiological interaction (gPPI) functional connectivity analysis using the caudate as a seed was conducted at the anticipation phase of the MIE task. These results are presented below.

2.5.2. Preprocessing of fMRI data

Using SPM12 software (Wellcome Department of Cognitive Neurology, London, United Kingdom), preprocessing steps of functional images included reorienting realignment, as well as coregistration of image volumes to a standard MNI-space template, resampling to 2 mm^3 voxels (EPI.nii) and spatial smoothing with a 4-mm Gaussian kernel. To detect motion and global mean intensity outliers, we used Artifact Detection Tools (ART; available at www.nitrc.org/projects/artifactdetect). The parameters for outlier detection were the following: (1) more than 3 standard deviations above the global mean intensity, (2) more than ±5 mm translation motion, and (3) ±1° rotation. A run was considered problematic if more than 10 TRs were detected as outliers. No run or trials were removed for any participants based on these criteria.[3] These preprocessing steps and artifact detection parameters were used for both the MIE and MID task.

2.6. MID task

2.6.1. General Linear Model

The functional localizer MID task was used to find a ROI within the reward network. After the data were preprocessed, at the first (subject) level of analysis, an event-related design matrix was created. It was modeled around the onset of the reward cue, contained 4 columns of interest (high gain, low gain, high loss, low loss) and 3 columns to regress out linear drift for the 3 concatenated runs. Contrasts were then created comparing each condition of interest to baseline (e.g., high gain cue > baseline). A full-factorial ANOVA was used at the second (group) level to examine activation during the reward anticipation phase of the experiment. Reward (high, low) and valence (gain, loss) were entered as within-subjects variables and age (young, old) was entered as a between-subjects variable.

2.6.2. ROI

To identify an ROI to be used in subsequent analyses, we used the results from the General Linear Model of the functional localizer MID task. Activation during the high > low value anticipation cue (across young and older adults) was used to isolate the reward network. This analysis revealed widespread activity[4] in the mesolimbic reward network (see Fig. 2) with the most significant cluster in the left caudate (MNI: X = −8, Y = 6, Z = 2), a region that has previously been implicated in reward processing (Knutson et al., 2001a; Wilson et al., 2018; Zink et al., 2004). Using the SPM toolbox MarsBaR (Brett et al., 2002), a 6 mm sphere around this left caudate voxel was used to create an ROI (rightmost panel of Fig. 2 in pink highlight) for subsequent analyses of data from the MIE task.

2.7. MIE task

2.7.1. Activation analysis

In line with prior work examining activation associated with reward-modulated memory in younger adults (Adcock et al., 2006), the current fMRI analysis of the MIE task contains only high-confidence trials, combining "remember" and "know" responses. At the first level of analysis, a design matrix was modeled around the onset of the reward cue and the onset of the target stimulus. A 13-column regression matrix included 8 conditions of interest (subsequent hit and subsequent miss, for both high and low reward, at cue and at target), 2 nuisance regressor columns of low confidence trials, and 3 columns to regress out linear drift for the 3 concatenated runs. Contrasts were then created comparing each condition of interest to baseline (e.g., subsequent high-reward hits > baseline at cue). Consistent with prior work (Adcock et al., 2006; Cohen et al., 2016; Geddes et al., 2018), we examined activation within the reward-related region as a function of age, memory status, and reward[3]. Specifically, activation within the caudate ROI created from the MID task was extracted from each participant's first-level models using the REX toolbox (downloaded from http://web.mit.edu/swg/software.htm) and entered into a mixed ANOVA. A full description of the whole-brain activation analysis and results is reported in the Supplementary Material.

2.7.2. Connectivity analysis

The ROI analysis described previously was used to determine whether age influenced the extent to which a reward-related

[3] When linear motion values (x, y, z) and rotational values (pitch, yaw and roll) from the ART toolbox were included as covariates in the random-effects gPPI model, the pattern of results did not change. We therefore chose to report analyses that do not include these covariates.

[4] The contrast High > Low value anticipation cue of MID task revealed a large contiguous cluster (k = 3423) that included not only the caudate, but nucleus accumbens, ventral tegmental area, as well as thalamus and inferior frontal gyrus. An ROI of this entire cluster was created to examine subsequent memory analyses with the MIE task. This analysis, reported in the supplementary material, using the large cluster revealed generally the same activation pattern as those using the 6 mm sphere surrounding the caudate.

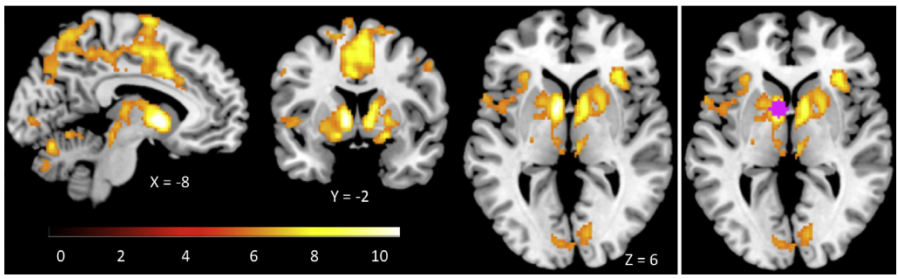

Fig. 2. Left panel: the activation from the Monetary Incentive Delay (MID) task during the reward anticipation (cue) phase with the contrast high > low value across younger and older adults. The T-values indicated by the color bar were familywise error corrected to $p = 0.05$ with a cluster threshold of k = 20. Right panel: the pink circle indicates the 6 mm sphere created around the left caudate (MNI: X = −8, Y = 6, Z = 2) to use as an ROI in all other analyses. Abbreviations: MNI, Montreal Neurological Institute. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

region preferentially supported memory for high-reward versus low-reward items. When age invariance was identified, we conducted follow-up connectivity analyses to determine whether this reward-related region supported memory for high-reward versus low-reward items in the same way in young and older adults. In other words, we examined whether the network associated with reward region activation would differ as a function of age, despite the age invariance of the reward region activation itself. These connectivity analyses thus probed for possible age-variant networks supporting high- compared to low-reward memory through their connections with an age-invariant reward region. The gPPI toolbox (http://brainmap.wisc.edu/PPI; McLaren et al., 2012) was used to compare functional connectivity with a single seed region across task conditions. Specifically, we examined functional connectivity between the caudate ROI and the rest of the brain during the presentation of the reward cues of the MIE task. During the target stimulus phase, the caudate did not exhibit greater subsequent memory effects for high- versus low-reward items, as would be expected if the caudate was contributing to reward-related memory enhancements. Because there was no evidence that younger or older participants relied on this region to enhance memory for high-reward stimuli during the target phase, it was not necessary to examine how additional regions might be recruited during this phase. As a result, we performed functional connectivity analyses for the anticipation phase only. We first created a 6 mm volume of interest around the caudate ROI peak (MNI: X = −8, Y = 6, Z = 2) for each participant. The gPPI toolbox estimated the functional connectivity with this volume of interest across the entire brain in the 5 memory conditions (high-reward hit, high-reward miss, low-reward hit, low-reward miss, low-confidence hit) to calculate the 4 contrasts of interest compared to baseline. At the group level, all participants' gPPIs entered full-factorial ANOVAs with reward (high, low) and memory (hit, miss) as within-subjects factors and age as a between-subjects factor. To better understand the direction of significant effects, we extracted beta estimates for a theoretically motivated subset of regions. We were interested in areas of the frontal lobe to test the hypothesis that older adults would show increased engagement of prefrontal regions in the service of reward-enhanced memory. We were also interested in occipital regions because studies of neurocognitive aging have shown an age-related reduction in posterior neural activity and increased frontal activity (Davis et al., 2008; Grady et al., 1994; Li et al., 2015), a pattern often referred to as the posterior-anterior shift in aging. The voxel threshold for these analyses was set at $p < 0.005$ (uncorrected). We ran Monte Carlo simulations (https://www2.bc.edu/sd-slotnick/scripts.htm) with the normalized voxel size of 2 × 2 × 2 and determined that a 17-voxel extent-corrected results to $p < 0.05$. We report all clusters that reach this threshold. We converted MNI coordinates from SPM12 to Talairach Coordinates using GingerAle (http://www.brainmap.org/ale), and we assigned anatomical labels in the cluster report tables using the Talairach Daemon (Lancaster et al., 1997). Each label was also visually checked using an anatomy atlas (Talairach and Tournoux, 1988).

3. Results

3.1. Behavioral results

Reaction-time results from the MID functional localizer task have been reported in prior publications (Bowen et al., 2019; Spaniol et al., 2015).

3.1.1. Reward earnings

On average, younger adults earned higher memory-based rewards ($M = \$101.17$, $SE = \$15.10$) than older adults ($M = \$63.62$, $SE = \$6.91$), $t(29) = 2.21$, $p = 0.05$, $\eta^2 = 0.14$.

3.1.2. Reaction time for recognition hits

Median reaction times for correctly recognized items (i.e., recognition hits) were submitted to a 2 (reward magnitude: high [$5], low [$.10]) × 2 (age: younger, older) mixed ANOVA. There was no main effect of either variable, nor a significant interaction, $F(1, 29) \leq 3.17$, $p \geq 0.09$, $\eta_p^2 \leq 0.10$. The average median reaction time across groups and conditions was 2647 ms (SE = 194 ms). This pattern held even when only high confidence trials (collapsed across "remember" and "know") were analyzed.

3.1.3. Memory accuracy

Hit rates were first calculated collapsing across confidence level and submitted to a 2 (reward: high, low) × 2 (age: younger, older) mixed ANOVA. This revealed a significant main effect of reward, $F(1, 29) = 4.35$, $p = 0.05$, $\eta_p^2 = 0.13$, such that hit rates were higher for high ($M = 0.50$, $SE = 0.03$), compared to low reward ($M = 0.46$, $SE = 0.03$), items. The main effect of age was not significant, $F(1, 29) = 0.001$, $p = 0.98$, $\eta_p^2 < 0.001$, nor was the reward × age interaction, $F(1, 29) = 0.98$, $p = 0.33$, $\eta_p^2 = 0.03$. Because new items were never paired with a reward value, only a single false alarm rate could be calculated which did not differ significantly for younger adults ($M = 0.18$, $SE = 0.03$) and older adults ($M = 0.28$, $SE = 0.02$), $t(29) = 2.58$, $p = 0.02$, $\eta^2 = 0.18$.

To align with prior work (e.g., Adcock et al., 2006) and the fMRI analyses reported in the following, the memory accuracy results were also analyzed restricting hit rates to high confidence trials only (collapsed across "remember" and "know") and excluding low confidence trials ("pretty sure" or "guessing" responses). Hit rates were submitted to a 2 (reward: high, low) × 2 (age: younger, older) mixed ANOVA. The previously reported main effect of reward failed

to reach significance, $F(1, 29) = 2.96$, $p = 0.10$, $\eta_p^2 = 0.09$, as hit rates for high-reward items ($M = 0.25$, $SE = 0.03$) were not significantly different from low-reward items ($M = 0.22$, $SE = 0.03$). A significant main effect of age emerged, $F(1, 29) = 4.08$, $p = 0.05$, $\eta_p^2 = 0.12$, such that hit rates were higher for younger adults ($M = 0.29$, $SE = 0.04$) compared to older adults ($M = 0.18$, $SE = 0.04$). Critically, like the analyses reported previously, the reward × age interaction was not significant, $F(1, 29) = 1.68$, $p = 0.21$, $\eta_p^2 = 0.06$. The false alarm rate did not differ significantly for younger adults ($M = 0.07$, $SE = 0.02$) and older adults ($M = 0.07$, $SE = 0.01$), $t(29) = 0.40$, $p = 0.97$, $\eta_p^2 = 0.005$. See Supplementary Fig. 4 for a graph of the mean hit rates for each condition, as well as the false alarm rates, for each age group.

3.1.4. Memory confidence

To examine whether older and younger adults differed in their use of "high" (remember/know) versus "low" (pretty sure/guess) confidence levels for recognition hits, the proportion of high and low confidence levels were submitted to a 2 (confidence level: high, low) × 2 (reward: high, low) × 2 (age: younger, older) mixed ANOVA. There was a significant main effect of confidence, $F(1, 29) = 39.21$, $p < 0.001$, $\eta_p^2 = 0.57$, qualified by a significant reward × confidence level interaction, $F(1, 29) = 8.41$, $p = 0.01$, $\eta_p^2 = 0.23$. Bonferroni-corrected pairwise comparisons revealed that hit rates were statistically equivalent ($p = 0.10$) for high-confidence high-reward ($M = 0.25$, $SE = 0.03$) and high-confidence low-reward trials ($M = 0.26$, $SE = 0.02$), but hit rates were higher ($p < 0.001$) for low-confidence high-reward trials ($M = 0.22$, $SE = 0.03$) compared to low-confidence low-reward trials ($M = 0.15$, $SE = 0.03$). The reward × age interaction was also significant, $F(1, 29) = 9.04$, $p = 0.005$, $\eta_p^2 = 0.24$, and pairwise comparisons revealed that younger adults had higher ($p = 0.01$) hit rates for high confidence responses ($M = 0.29$, $SE = 0.04$) compared to low confidence ($M = 0.15$, $SE = 0.30$), but older adults' hit rates did not significantly differ ($p = 0.14$) for high ($M = 0.18$, $SE = 0.04$) and low confidence responses ($M = 0.26$, $SE = 0.03$). There were no other significant interactions nor main effects, $F(1, 29) \leq 3.35$, $p \geq 0.08$, $\eta_p^2 \leq 0.10$. The proportion of remember and know, as well as pretty sure and guess, responses to target items is reported in Table 1.

3.1.5. Memory for reward value

Accuracy of reward value judgments was calculated for correctly identified target items (given a remember or know response). Accuracy values were submitted to a 2 (reward: high, low) × 2 (age: younger, older) mixed ANOVA. There was a main effect of reward, $F(1, 29) = 11.83$, $p = 0.002$, $\eta_p^2 = 0.29$, such that the accuracy of value judgments was higher for high reward ($M = 0.15$, $SE = 0.02$) compared to low reward ($M = 0.09$, $SE = 0.02$), but the main effect of age and the reward × age interaction were not significant, $F(1, 29) \leq 3.45$, $p \geq 0.07$, $\eta_p^2 \leq 0.11$.

3.2. fMRI results

To align with the behavioral analyses, the fMRI analyses reported in the following include only high-confidence trials. We first report the results of activation within the caudate ROI followed by the gPPI functional connectivity analysis. Whole-brain activation analyses are presented in the Supplementary Material.

3.2.1. Activity in the ROI during MIE task

Activity within the 6 mm sphere created around the caudate (MNI: X = −8, Y = 6, Z = 2) was extracted at the anticipation phase and the target stimulus phase of the MIE task. Activity (reported as percent signal change) from these phases was then entered into separate repeated-measures ANOVAs with reward (high, low) and subsequent memory (hit [recognized], miss [forgotten]) as within-subjects variables and age (young, old) as a between-subjects variable.

3.2.2. Anticipation phase

A main effect of reward, $F(1, 29) = 4.10$, $p = 0.05$, $\eta_p^2 = 0.12$, was qualified by a reward × memory interaction, $F(1, 29) = 5.39$, $p = 0.03$, $\eta_p^2 = 0.16$. Follow-up paired samples t-tests indicated a marginally significant subsequent memory effect (hit > miss) for high-reward, but no effect for low-reward items. Activity was greater for subsequently recognized ($M = 0.43$, $SE = 0.15$) compared to subsequently forgotten high-reward items ($M = 0.15$, $SE = 0.09$), $t(30) = 1.81$, $p = 0.07$, $\eta^2 = 0.10$. There was no difference in activity within the caudate for subsequently recognized ($M = -0.04$, $SE = 0.14$) compared to subsequently forgotten ($M = 0.16$, $SE = 0.11$) low-reward items, $t(30) = 1.54$, $p = 0.14$, $\eta^2 = 0.07$. No effects involving the age variable, nor any other main effects or interactions, were significant, $F(1, 29) \leq 1.59$, $p \geq 0.22$, $\eta_p^2 \leq 0.05$.

3.2.3. Target phase

There were no significant main effects of reward, $F(1, 29) = 2.40$, $p = 0.13$, $\eta_p^2 = 0.08$, subsequent memory, $F(1, 29) = 0.04$, $p = 0.85$,

Table 2
Regions exhibiting a 3-way interaction in neural connectivity with the caudate

Lobe	Region	Hem	BA	MNI Coordinates			T-value	k
				X	Y	Z		
Positive Reward × Memory × Age Interaction								
Frontal	Inferior frontal gyrus	R	38	52	26	−4	3.99	48
			47	40	36	−8	3.21	17
		L	9	−50	4	20	3.42	46
			47	−52	22	−6	3.18	24
	Medial frontal gyrus	R	6	14	10	50	4.1	17
	Middle frontal gyrus	L	9	−34	16	26	3.55	18
	Precentral gyrus	R	4	34	−24	52	3.36	27
	Precentral gyrus	L	6	−34	2	38	3.65	33
Limbic	Posterior cingulate	R	30	28	−70	10	3.98	41
Occipital	Inferior occipital gyrus	R	19	36	−80	0	3.25	25
Parietal	Postcentral gyrus	R	40	50	−24	50	3.4	38
Temporal	Superior temporal gyrus	L	38	−48	8	−30	3.91	27
		L	30	−12	−44	−22	4.28	21
Other	Nucleus accumbens	R	*	8	0	−10	3.92	32
	Insula	L	13	−40	6	10	4.18	74

We report all clusters with at least 17 contiguous voxels in the tables.
Key: Hem, hemisphere; L, left; R, right; BA, Brodmann's Area; *, no Brodmann Area; MNI, Montreal Neurological Institute; k, cluster extent.

$\eta_p^2 = 0.001$, or age, $F(1, 29) = 0.001$, $p = 0.98$, $\eta_p^2 = 0.001$. There was also no significant reward × age interaction, $F(1, 29) = 0.69$, $p = 0.41$, $\eta_p^2 = 0.02$, memory × age interaction, $F(1, 29) = 3.97$, $p = 0.06$, $\eta_p^2 = 0.12$, reward × memory interaction, $F(1, 29) = 0.25$, $p = 0.62$, $\eta_p^2 = 0.009$, nor a reward × memory × age interaction, $F(1, 29) = 2.62$, $p = 0.12$, $\eta_p^2 = 0.08$.

3.2.4. Generalized psychophysiological interaction

Despite the activation analysis showing age invariance of the caudate, we used gPPI to examine whether functional connectivity between the caudate and the rest of the brain would show age variant patterns during reward anticipation. Critically, the gPPI analysis revealed a significant reward × memory × age interaction in connectivity between the caudate and several regions, including bilateral inferior frontal gyrus, middle and medial frontal gyrus, precentral and postcentral gyrus, superior temporal gyrus, posterior cingulate, inferior occipital gyrus, and insula. See Table 2 for all regions that showed the three-way interaction, and Supplementary Fig. 3 for a visual depiction of these regions. A list of regions that showed effects of reward, memory, and age on caudate connectivity is presented in the Supplementary Table 3.

To clarify the direction of these effects, beta estimates were extracted from all frontal clusters implicated in the significant interaction. Analyses for a left and a right inferior frontal gryus (IFG) cluster were chosen to highlight here, but the pattern is the same for all frontal regions that emerged in this interaction. The three-way interaction within a left IFG cluster (MNI: X = −52, Y = 22, Z = −6) was driven by significant reward × memory interaction for both younger adults, $F(1, 15) = 7.21$, $p = 0.02$, $\eta_p^2 = 0.33$, and older adults, $F(1, 13) = 5.84$, $p = 0.03$, $\eta_p^2 = 0.21$. In younger adults, connectivity between these regions did not differ for subsequently recognized versus forgotten high-reward items, $t(15) = 1.24$, $p = 0.24$, $\eta^2 = 0.09$, but connectivity was greater for subsequently recognized compared to forgotten low-reward items, $t(15) = 2.47$, $p = 0.03$, $\eta^2 = 0.29$. For older adults, connectivity between the caudate and left IFG was significantly greater for subsequently recognized versus forgotten high-reward items, $t(13) = 2.23$, $p = 0.04$, $\eta^2 = 0.28$, but not for subsequently recognized compared to forgotten low-reward items, $t(13) = 1.36$, $p = 0.20$, $\eta^2 = 0.12$. The right IFG cluster (X = 40, Y = 36, Z = −8) did not show a reward × memory interaction for younger adults, nor any other effects, $F(1, 15) \leq 3.67$, $p \geq 0.08$, $\eta_p^2 \leq 0.20$. For older adults, the reward × memory interaction was significant, $F(1, 13) = 7.91$, $p = 0.02$, $\eta_p^2 = 0.38$. This interaction was driven by a significant subsequent memory effect in connectivity between these regions for high-reward items, $t(13) = 2.63$, $p = 0.02$, $\eta^2 = 0.27$, but significantly less connectivity between these regions during subsequently recognized compared to forgotten low-reward items, $t(13) = 2.20$, $p = 0.05$, $\eta^2 = 0.27$. See Fig. 3 left panel for a depiction of the IFG brain regions and Fig. 3 right panel for a graphical representation of this pattern.

The three-way interaction with posterior regions including the inferior occipital gyrus and the posterior cingulate (extending into lingual gyrus) was driven by a pattern different from the one in the frontal regions. The interaction in the inferior occipital gyrus was driven by a reward × memory interaction in younger adults, $F(1, 15) = 12.37$, $p = 0.003$, $\eta_p^2 = 0.45$, such that there was greater connectivity with the caudate during low-reward hits compare to low-reward misses, $t(15) = 3.88$, $p = 0.001$, $\eta^2 = 0.50$, but there was no subsequent memory effect for high-reward items, $t(15) = 1.77$, $p = 0.10$, $\eta^2 = 0.17$. For older adults, the reward × memory interaction was not significant, $F(1, 13) \geq 2.65$, $p \leq 0.13$, $\eta_p^2 \geq 0.17$. In the posterior cingulate, there was a reward × memory interaction for young adults, $F(1, 15) = 5.79$, $p = 0.03$, $\eta_p^2 = 0.28$. Follow-up paired t-tests revealed the subsequent memory simple main effects were nonsignificant for both high-reward and low-reward items, $t(15) \leq 1.56$, $p \geq 0.14$, $\eta^2 \leq 0.14$. For older adults, the interaction was also significant, $F(1, 13) = 6.95$, $p = 02$, $\eta_p^2 = 35$. This interaction was driven by decreased connectivity with the caudate during subsequently recognized compared to forgotten high-reward items, $t(13) = 2.96$, $p = 0.01$, $\eta^2 = 0.40$. There was no subsequent memory effect for low-reward items, $t(13) = 1.49$, $p = 0.16$, $\eta^2 = 0.16$. See Fig. 4 left panel for a depiction of the brain regions and Fig. 4 right panel for a graphical representation of this pattern for the posterior cingulate.

4. Discussion

In the present study, we examined neural activation and functional connectivity patterns associated with reward-enhanced memory in healthy younger and older adults. In line with our hypothesis, both age groups showed better memory for high-reward items than for low-reward items. Furthermore, both age groups showed greater activity in the left caudate, a reward-network region, during high-reward cues that preceded subsequently remembered items. In line with our second hypothesis, functional connectivity between the caudate and bilateral frontal gyri was associated with reward-enhanced memory in older adults. These results provide further evidence of a preserved influence of reward

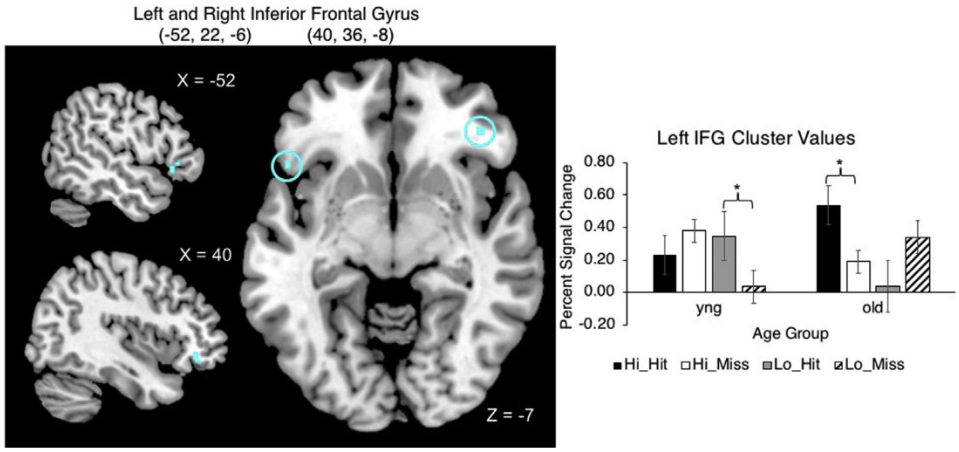

Fig. 3. Left panel: left and right inferior frontal gyrus showing a three-way interaction in connectivity with the caudate ROI. Right panel: graph of the percentage signal change depicting the pattern of connectivity of the three-way interaction. Values in the graph are from the left IFG cluster, but the pattern is the same for right IFG. Abbreviations: IFG, inferior frontal gryus; Yng, younger adults; old, older adults.

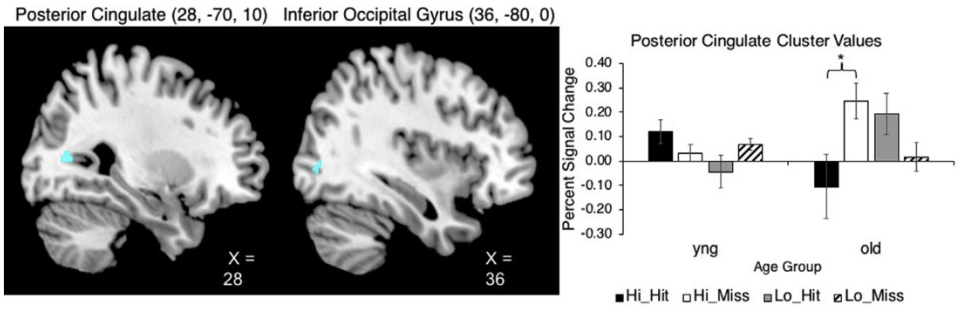

Fig. 4. Left panel: posterior cingulate and inferior occipital gyrus clusters that showed a three-way interaction in connectivity with the caudate ROI. Right panel: graph of the percentage signal change depicting the pattern of connectivity of the three-way interaction. Values in the graph are from the posterior cingulate cluster. Abbreviations: Yng, younger adults; old, older adults.

on memory formation in healthy aging, but they also point toward age differences in the nature of the link between reward and memory. In particular, increased frontostriatal connectivity during high reward cues that precede the presentation of target stimuli during encoding suggests that older adults may be engaging cognitive control processes to bolster memory for reward-related information (Braver, 2012; Chiew and Braver, 2013; Fröber and Dreisbach, 2012). The finding also aligns with the theoretical and empirical literature in neurocognitive aging of over-recruitment of prefrontal regions to support behavior in cognitively demanding tasks (Cabeza et al., 2018; Grady, 2012).

4.1. Reward-motivated memory in younger and older adults

Compared with younger adults, older adults earned lower performance-based rewards in the MIE task. However, like younger adults, older adults demonstrated better memory for items associated with high-reward compared to items associated with low-reward. This replicates findings from our 2 previous experiments with a separate group of younger and older participants where we used this same paradigm (Spaniol et al., 2014) as well as other findings of preserved value-based memory selectivity in aging (Castel et al., 2011, 2002; Cohen et al., 2016; for a review, see Castel, 2007). Of note, when analyses were restricted to trials given a high confidence rating of remember or know, memory was no longer statistically different for high-reward versus low-reward items. Reward effect on memory likely failed to reach statistical significance due to lower statistical power when low confidence trials were removed. Evidence that healthy older adults are sensitive to motivational incentives fits with theories of aging postulating that reward processes do not show the same age-related decline as other cognitive domains but remain intact or even improve in healthy aging (Mather, 2016).

4.2. Activity in caudate associated with reward motivated memory

The pattern of behavioral results for younger and older adults was generally similar, but these results do not explain how younger and older adults engage neural mechanisms to prioritize high-reward items at encoding. Using a functional task to localize the reward network, we found extensive activation in the dopaminergic midbrain and reward network, choosing the left caudate, part of the dorsal striatum, to create an ROI. To align with prior studies (Adcock et al., 2006; Cohen et al., 2016; Geddes et al., 2018), we first investigated the level of activation within the ROI during the anticipation and target stimulus phase of the MIE task. Activation within the ROI during the anticipation phase was greater for subsequently remembered compared to forgotten high-reward items, across both older and younger adults. This region was not differentially activated by memory status (hit vs. miss) for low-reward items, nor was activity in this region sensitive to the task conditions during the target stimulus phase, in either younger or older adults. Our results are consistent with those of Adcock et al. (2006) who found that activation in the ventral striatum during reward anticipation was associated with reward-motivated memory in younger adults. Only 2 prior studies have been focused on age differences in neural activation during reward-motivated memory. Cohen and colleagues (Cohen et al., 2016) investigated activity in a much larger ROI of the reward network and found that activity was modulated by reward cue, but this did not predict value-directed memory selectivity. Instead, activity in that ROI during the target stimulus phase correlated with value-directed memory selectivity, but only in younger not older adults. Of note, similar to Cohen and colleagues, we also conducted an analysis of the memory effects within a large ROI that included many regions within the reward network, but found the pattern of results to be the same as those we report using a 6 mm caudate sphere[3]. Geddes et al. (2018) did not report significant effects of reward on memory in older adults, despite evidence that the reward network was engaged to the same extent in their older and younger adults during processing of incentive cues during the MIE task. We speculate about reasons for the varied results across these 3 studies in a section below.

4.3. Frontal-striatal functional connectivity supports reward-motivated memory in older adults

The present study is the first to investigate age-related differences in functional connectivity associated with reward-motivated memory. Prior studies with older adults (Cohen et al., 2016; Geddes et al., 2018) have examined reward and age effects on activation within a priori reward network ROIs, or whole-brain activation. One study with younger adults (Adcock et al., 2006) reported that greater connectivity between the ventral tegmental area and hippocampus during reward anticipation predicted superior memory performance. This connectivity analysis focused on 2 a priori regions of interest and did not encompass the rest of the brain. Based on our prior findings that older adults recruit a network of regions during incentive processing, including bilateral prefrontal cortex (Spaniol et al., 2015), an area often associated with control processes (Miller, 2000; Miller and Cohen, 2001) and that has been implicated in motivated behavior (Braver, 2012), we hypothesized that older adults would show greater connectivity between the reward network and frontal regions during reward-motivated encoding. Our connectivity analysis indeed supported this hypothesis with greater connectivity between the caudate and bilateral inferior frontal gyrus that was associated with high-reward

items that were subsequently remembered versus forgotten. In younger adults, connectivity between these regions was associated with subsequent memory for low-reward items. Regions in posterior sensory cortices also showed connectivity with the caudate, but the pattern underlying the interaction was different. Greater connectivity between the caudate and posterior cingulate/lingual gyrus was associated with high-reward items that were later forgotten versus remembered, akin to a negative subsequent memory effect (Kim, 2011) for older adults. For younger adults, in contrast, connectivity between the caudate and posterior regions was not significantly modulated by task conditions. Interestingly, a whole-brain activation analysis conducted by Geddes and colleagues during reward anticipation revealed activation in visual association cortex during the anticipatory cue period for motivational compared to neutral trials. They proposed that this reflects heightened visual attention in both age groups during the presentation of the gain and loss cues. Other work with younger adults (Murty et al., 2017) has indicated that increased postencoding connectivity between the visual cortex, ventral striatum, and hippocampus predicted associative memory for high but not low-reward items. The present study could not address postencoding connectivity, but it appears that connectivity between the reward network and visual cortex during reward anticipation may actually hurt memory for high-reward items, at least for older adults.

4.4. Comparing findings from three studies examining neural recruitment in older adults

Behaviorally, both Cohen et al. (2016) and the present study report that older adults are sensitive to reward and have better memory for items associated with high versus low reward. In Cohen et al.'s (2016) study, rewards were points, whereas in our study, they were monetary incentives. Our behavioral findings generally do not align with those from Geddes et al. (2018), who found no effect of monetary reward on memory in older adults (although see behavioral results restricted to high-confidence trials only), although Geddes et al. (2018) also used the MIE task. A possible explanation is that Geddes et al. (2018) intermixed monetary gains, losses, and neutral zero-dollar trials. It is possible that the presence of intermixed loss trials may have dampened reward effects on memory for older adults. The preponderance of existing evidence from studies of reward-motivated memory in younger and older adults (e.g., Castel, 2007; Cohen et al., 2016; Spaniol et al., 2014) suggests that older adults' memory is responsive to reward. The nonsignificant reward effect on older adults' memory reported by Geddes et al.'s (2018) forms an exception, but given that reward effects on memory are typically small (e.g., $\eta^2 = 0.13–0.28$, Spaniol et al., 2014), occasional null findings are not unexpected.

There were some other notable differences between the paradigms. Like the study by Geddes et al. (2018), the present study featured a longer encoding session as well as a 24-hour delayed recognition test outside the scanner, whereas participants in Cohen et al.'s (2016) study recalled the words directly after each encoding block. Despite similarities in the overall behavioral findings between our results and those of Cohen et al., these task differences may have encouraged different encoding strategies by older adults and thereby different neural engagement. Indeed, Cohen and colleagues (Cohen et al., 2019, 2016) have proposed that the experimental conditions of the value-directed remembering paradigm, which involve encoding verbal stimuli coupled with multiple study-test blocks, encourage older adults to engage semantic encoding strategies leading to recruitment of the left frontal and temporal cortex as evidenced during presentation of the target stimulus. Furthermore, it is these strategies that enable reward effects on memory performance. According to Cohen et al. (2016), the MIE task, which involves a single long encoding session before a single delayed retrieval session, may not promote the use of semantic encoding strategies. Our results, both in the present study and in a prior study that used the same paradigm (Spaniol et al., 2014), are at odds with this proposal. Younger and older adults in both our studies generally exhibited a reward-motivated memory enhancement, although both employed a long encoding session and a delayed memory test. In the present study, we also report that reward anticipation cues lead to reward network activation, and connectivity between the reward network and lateral prefrontal regions was associated with successful memory for high-reward items for older adults. This set of results is in line with other evidence suggesting that reward cues in the MIE task may trigger reward-network activation and dopaminergic modulation of hippocampal long-term consolidation processes. These processes may strengthen delayed memory for target stimuli encoded during reward anticipation (Adcock et al., 2006; Lisman and Grace, 2005; Shohamy and Adcock, 2010). Younger adults may engage these processes in a relatively automatic manner, but our connectivity findings suggest that older adults may recruit not only reward-network regions but also additional frontal regions associated with cognitive control to carry out this cognitively demanding task (Cabeza et al., 2018; Grady, 2012).

The temporal characteristics of reward-network engagement and its link to memory performance also varied across the 3 studies. Differential task demands and participant strategies may play a role here. In the present study, caudate activation during the anticipation phase, but not during the target presentation, was linked to subsequent memory performance in both younger and older adults. By contrast, Cohen et al. (2016) observed activation in reward regions that was predictive of value-directed memory selectivity during the target phase only and in younger adults only. Geddes et al. (2018) did not find activation at either stage that supported reward-motivated memory in older adults but also did not find a behavioral reward effect on memory in older adults. Perhaps, future research using methods with better temporal resolution (e.g., event-related potentials) could help elucidate the temporal characteristics of reward-related memory in these tasks.

4.5. Limitations and future directions

One of the limitations of the present study is its small sample size. Accordingly, both the crossover effects reported from the gPPI analysis and lack of age differences in overall behavior and reward network activity in our sample should be interpreted with caution as these effects may be exaggerated or not reliable. However, it should also be noted that the current findings replicate prior behavioral findings of better memory for high-reward compared to low-reward stimuli (Adcock et al., 2006; Castel et al., 2002; Cohen et al., 2014, 2016; Shigemune et al., 2010, 2014; Spaniol et al., 2014). Relatedly, despite a lack of age differences in overall behavior, age differences in the functional connectivity results are consistent with the idea that incentives may have mobilized different encoding strategies in younger and older adults. We speculate that during the MIE task, both younger and older adults use automatic dopaminergic modulation of consolidation processes, but that older adults additionally engage cognitive control processes that lead to better memory for high-reward stimuli. Investigating individual differences in older adults' cognitive control abilities in relation to MIE task performance, or manipulating encoding strategies (rather than leaving them unconstrained), may

be fruitful ways to test this hypothesis. Another possibility is separating remember and know responses to better understand the cognitive and neural processes underlying these results. Although we employed a remember/know paradigm in the present study, we had too few trials to do this type of comparison between age groups. A second potential limitation is that the present study included only gain cues, not punishments or monetary losses. Whether valence plays a role in behavior or neural recruitment is an important theoretical question. Prior work has shown that monetary gains and losses do not have the same effects on incidental episodic memory in younger adults (Bowen and Spaniol, 2017) or older adults (Mather and Schoeke, 2011) and that monetary gains may lead to better performance than punishments for younger adults in a spatial memory task (Murty et al., 2011). In addition, healthy aging is often associated with a motivational shift that can manifest as a positivity bias in attention and memory (Carstensen, 1995; Mather and Carstensen, 2005) and differences in neural processing of gain compared to loss anticipation (Samanez-Larkin et al., 2007) and gain and loss feedback (Bowen et al., 2019). Geddes and colleagues included both gain and loss trials in their paradigm but did not observe valence effects on memory in older adults. The presence of loss cues might have undermined effort in older adults, but this remains speculative in the absence of a separate assessment of effort. An empirical test of this question may help clear up discrepancies across studies. Finally, the results of Cohen et al. (2016) indicated that frontal and temporal lobe activation is related to older adults' performance in the value-directed remembering paradigm, and the results of the present study revealed that functional connectivity between frontal lobe and reward regions supported reward-related memory in older adults. An interesting next step in this line of work is to understand the direction of these relationships using effective connectivity analysis.

5. Conclusion

We examined reward-motivated memory and its neural correlates in younger and older adults using whole-brain functional connectivity with a region in the reward network during reward-modulated encoding. Although there were no age differences in ROI activation levels during the reward anticipation phase, older and younger adults showed different functional connectivity patterns. For older adults, greater connectivity between the caudate and bilateral inferior frontal gyrus was positively associated with reward-motivated memory, whereas connectivity between the caudate and posterior regions was negatively associated with reward-motivated memory. These findings add to the growing literature on motivation-cognition interactions in healthy aging, and provide novel evidence of the neural underpinnings of reward-motivated encoding.

Acknowledgements

This work was supported by a Canadian Institutes of Health Research grant IAP 107854 awarded to JS.

Authors' contributions: HJB conceived and designed the study, collected the data, performed the analysis, and wrote the paper. JHF performed the analysis and wrote the paper. CLG conceived and designed the study and wrote the paper. JS conceived and designed the study, collected the data, and wrote the paper.

Disclosure statement

The authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.neurobiolaging.2020.02.013.

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