

Research Article

Effects of Aging on Functional Connectivity of the Amygdala for Subsequent Memory of Negative Pictures

A Network Analysis of Functional Magnetic Resonance Imaging Data

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ABSTRACT—Aging is associated with preserved enhancement of emotional memory, as well as with age-related reductions in memory for negative stimuli, but the neural networks underlying such alterations are not clear. We used a subsequent-memory paradigm to identify brain activity predicting enhanced emotional memory in young and older adults. Activity in the amygdala predicted enhanced emotional memory, with subsequent-memory activity greater for negative stimuli than for neutral stimuli, across age groups, a finding consistent with an overall enhancement of emotional memory. However, older adults recruited greater activity in anterior regions and less activity in posterior regions in general for negative stimuli that were subsequently remembered. Functional connectivity of the amygdala with the rest of the brain was consistent with age-related reductions in memory for negative stimuli: Older adults showed decreased functional connectivity between the amygdala and the hippocampus, but increased functional connectivity between the amygdala and dorsolateral prefrontal cortices. These findings suggest that age-related differences in the en-

hancement of emotional memory might reflect decreased connectivity between the amygdala and typical subsequent-memory regions, as well as the engagement of regulatory processes that inhibit emotional responses.

Emotion enhances memory in young adults, likely because of the modulatory effects of the amygdala on the hippocampus (for a review, see LaBar & Cabeza, 2006). Whether emotion also benefits older adults' memory is debatable, as some behavioral studies have reported relative preservation of emotional memory in older adults (e.g., Denburg, Buchanan, Tranel, & Adolphs, 2003), whereas others have reported age-related reductions in memory for negative stimuli (e.g., Comblain, D'Argembeau, Van der Linden, & Aldenhoff, 2004; Mather & Carstensen, 2003). Moreover, little is known about the neural networks underlying age-related changes in emotional memory. Therefore, examining the neural correlates underlying such changes was the goal of the present study.

There is accruing evidence that healthy aging is characterized by preserved emotional function and greater emotional regulation (for a review, see Mather & Carstensen, 2005). However, there is also evidence that aging is associated with alterations in the responses to emotional stimuli (Mather et al., 2004). On the one hand, the idea of preserved emotional function is supported by anatomical evidence that healthy aging does not markedly impair the structural integrity of the amygdala (e.g., Good et al.,

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2001). On the other hand, evidence from functional neuroimaging suggests that aging is associated with altered amygdala responses to emotional stimuli (Mather et al., 2004), reduced activity in posterior brain regions (e.g., Tessitore et al., 2005), and additional recruitment in frontal cortical control regions (e.g., Gunning-Dixon et al., 2003). Thus, although overall underlying amygdalar function seems to be preserved in aging, older adults might regulate emotional responses to a greater extent than younger adults (e.g., St. Jacques, Dolcos, & Cabeza, in press), so that amygdala activity and its modulatory effects on memory are reduced (cf. Mather, 2006). These findings are consistent with socioemotional selectivity theory, according to which aging is associated with motivational changes in allocating attention to emotional stimuli because of a limited perspective on time (for a review, see Mather & Carstensen, 2005). Socioemotional selective theory suggests that, compared with young adults, older adults are more likely to attend to positively valenced stimuli and less likely to attend to negatively valenced stimuli (i.e., the *positivity effect*; Mather & Carstensen, 2005). However, previous studies have not examined the influence of emotion on the neural correlates underlying memory in aging.

Only a few functional magnetic resonance imaging (fMRI) studies have examined age-related effects on activity predicting *subsequent memory* for neutral stimuli (Dennis, Daselaar, & Cabeza, 2007; Gutchess et al., 2005; Morcom, Good, Frackowiak, & Rugg, 2003). In such studies, activity during encoding is segregated by whether the stimulus is remembered or forgotten on a later test of memory, and remembered versus forgotten trials are compared to examine brain activity predictive of subsequent memory (for a review, see Paller & Wagner, 2002). In general, subsequent-memory studies of aging have found that subsequent memory is associated with reductions in medial temporal lobe (MTL) activity coupled with increases in frontal cortical activity in older adults. This pattern is consistent with the *posterior-anterior shift in aging* (PASA), which involves reduced activity in posterior regions of the brain coupled with increased activity in anterior regions in a variety of tasks, including encoding (for a review, see Dennis & Cabeza, 2008). Moreover, there is also evidence of an age-related dorso-ventral shift (e.g., Dennis et al., 2007; Gutchess et al., 2005); during encoding, older adults recruit greater activity in dorsolateral prefrontal cortices (DLPFC) involved in strategic processes, and less activity in ventrolateral prefrontal cortices (VLPFC) involved in semantic processing. Consistent with the dorso-ventral shift, an fMRI study of neutral memory encoding (Grady, McIntosh, & Craik, 2003) found that older adults showed functional connectivity between DLPFC and the hippocampus, whereas young adults showed functional connectivity between VLPFC and the hippocampus. However, previous studies have not examined the influence of emotion on the network of regions involved in subsequent memory.

Thus, the goals of the study we report in this article were threefold: (a) to identify activity related to preserved emotional

function in aging, (b) to identify age-related differences in brain activity predicting better subsequent memory for negative than for neutral stimuli, and (c) to investigate age-related differences in the neural network underlying subsequent memory for negative stimuli. To address these issues, we employed fMRI recording in conjunction with a subsequent-memory paradigm, to identify brain activity predicting memory for negative versus neutral pictures in young and older participants. We tested three main predictions. First, given the evidence of preserved anatomical and functional integrity of the amygdala in aging (e.g., Good et al., 2001), along with evidence supporting its involvement in the modulation of memory encoding (e.g., Dolcos, LaBar, & Cabeza, 2004b), we predicted that the amygdala would be engaged by subsequent memory for negative stimuli in both age groups. Second, given the evidence of a PASA pattern of activity associated with subsequent memory for neutral stimuli (e.g., Dennis et al., 2007), we predicted a similar pattern would be found for emotional stimuli; that is, we expected that relative to young adults, older adults would show greater subsequent-memory activity in anterior regions but less subsequent-memory activity in posterior regions for emotional stimuli. Third, given the evidence that the network underlying the encoding of neutral stimuli changes with aging (e.g., Grady et al., 2003), and the evidence that activity in frontal control regions during emotional evaluation is enhanced with aging (e.g., Gunning-Dixon et al., 2003; for a review, see Mather & Carstensen, 2003), we predicted age-related reductions in the functional connectivity of the subsequent-memory network for negative stimuli.

METHOD

Participants

Fifteen young (mean age = 24.80 years, $SD = 4.71$) and 15 older (mean age = 70.23 years, $SD = 5.31$) women participated in the experiment. All were healthy, right-handed, and without history of neurological or psychiatric episodes. Participants gave written informed consent for a protocol approved by the Duke University Institutional Review Board.

Materials

The stimuli were 180 pictures from the International Affective Picture System (Lang, Bradley, & Cuthbert, 1997); equal numbers of positive, negative, and neutral pictures (based on normative arousal and valence scores in young adults) were chosen. To equate pictures for content, we replaced some of the neutral pictures with neutral pictures from other sources (Yamasaki, LaBar, & McCarthy, 2002). The exact number of pictures per valence category differed depending on participants' ratings during the scanning task (see Procedure). For young adults, the mean numbers of pictures were as follows: 61.80 positive pictures ($SD = 12.38$), 60.23 negative pictures ($SD = 10.60$), and 57.93 neutral pictures ($SD = 20.31$). For older adults, the

corresponding means were 58.13 positive pictures ($SD = 20.14$), 53.00 negative pictures ($SD = 7.99$), and 66.53 neutral pictures (19.77). Positive pictures were excluded in the age-group analysis we report here because a large number of these pictures contained radical sport and erotic content, which is processed differently in older adults compared with young adults (see Backs, da Silva, & Han, 2005); these pictures were included for separate analyses of the young adults' data (reported in Dolcos et al., 2004b, and in Dolcos, LaBar, & Cabeza, 2004a, 2005).

Procedure

We created six study blocks that were randomly assigned to participants. Each block contained 30 pictures (10 of each valence), presented for 3 s and followed by a 12-s intertrial interval. To avoid long-lasting moods, we pseudorandomized the order such that no more than two identically valenced pictures were presented consecutively. Functional magnetic resonance images were recorded while participants encoded each picture and made a concurrent valence rating (negative, neutral, or positive). A surprise cued-recall task followed scanning after a delay. To avoid overall performance differences between the age groups, while also providing enough delay for the enhancing effect of emotion (e.g., Hamann, Ely, Grafton, & Kilts, 1999), we used different delay periods for young (45 min) and older (30 min) adults. On the recall task, participants were provided with a one- or two-word cue for each picture (e.g., "snake") and asked to describe the pictures they remembered in as much detail as they could, so that an outsider could identify and discriminate those pictures from similar studied pictures (e.g., a brown snake vs. several green snakes; Dolcos et al., 2004b). Two raters evaluated the descriptions, and only pictures whose description allowed both identification and discrimination were classified as remembered. All other pictures were considered forgotten.

fMRI Methods

Scanning

Scanning was conducted using a 1.5-T GE magnet. Stimuli were presented using LCD goggles, and behavioral responses were recorded using a four-button response box (Resonance Technology, Northridge, CA). Anatomical and functional images consisted of 34 contiguous slices parallel to the anterior commissure–posterior commissure plane. High-resolution T1-weighted structural images were acquired with a 450-ms repetition time, 9-ms echo time, 24-cm field of view, 3.75-mm slice thickness, and 256^2 matrix. Functional scanning employed an echoplanar image sequence with a 3,000-ms repetition time, 40-ms echo time, 24-cm field of view, 64^2 image matrix, and 90° flip angle. Slice thickness was 3.75 mm, resulting in 3.75-mm^3 isotropic voxels.

fMRI Analyses

Image processing and analyses were performed using Statistical Parametric Mapping software in Matlab (SPM99 and SPM5, respectively; Wellcome Department of Cognitive Neurology, London, United Kingdom). Functional images were corrected for slice-acquisition order, realigned to correct for motion artifacts, and spatially normalized to standard stereotactic space, using the SPM99 template. Subsequently, the functional images were spatially smoothed with an 8-mm isotropic Gaussian kernel. For each subject, evoked hemodynamic responses to event types were modeled with a delta (stick) function corresponding to stimulus presentation convolved with a canonical hemodynamic response function within the context of the general linear model (GLM), and proportional scaling was used to remove individual differences in the global signal.

Preserved Memory-Related Amygdala Activity

To examine brain activity commonly engaged by young and older adults during memory formation for negative versus neutral pictures, we employed a subsequent-memory procedure. In each age group, we generated contrasts to examine differences between activity associated with remembered items and activity associated with forgotten items. These contrasts were used to calculate subsequent-memory effects, known as D_m (differential neural activity based on memory; i.e., greater activity for remembered than for forgotten pictures). On the basis of participants' own emotional ratings during encoding, we calculated D_m effects separately for negative and neutral pictures (i.e., $D_{m_{\text{negative}}} = \text{activity for negative pictures that were subsequently remembered minus activity for negative pictures that were subsequently forgotten}$; $D_{m_{\text{neutral}}} = \text{activity for neutral pictures that were subsequently remembered minus activity for neutral pictures that were subsequently forgotten}$). The areas associated with enhancement of memory for negative pictures were identified as those areas for which $D_{m_{\text{negative}}}$ was greater than $D_{m_{\text{neutral}}}$. To examine our a priori hypothesis regarding the amygdala, we used a region-of-interest approach (cluster size ≥ 5 voxels). For assessing common areas of activation, we created a conjunction map of the two age groups' maps of areas for which $D_{m_{\text{negative}}}$ was greater than $D_{m_{\text{neutral}}}$, using a threshold p value of .05. Thus, the conjoint probability of the conjunction map was .0025.

Age-Related Differences in the Enhancement of Negative Memory

For assessing brain areas showing age-related differences in the enhancement of negative memory, we used a two-sample t test that compared the activation in areas where $D_{m_{\text{negative}}}$ was greater than $D_{m_{\text{neutral}}}$ ($p = .05$, cluster size ≥ 5 voxels). In order to confirm that the interaction was driven by the expected differences between $D_{m_{\text{negative}}}$ and $D_{m_{\text{neutral}}}$ within each age group, we inclusively masked the resulting map with the corresponding statistical maps showing, separately for each group, areas in which D_m effects were greater for negative than for

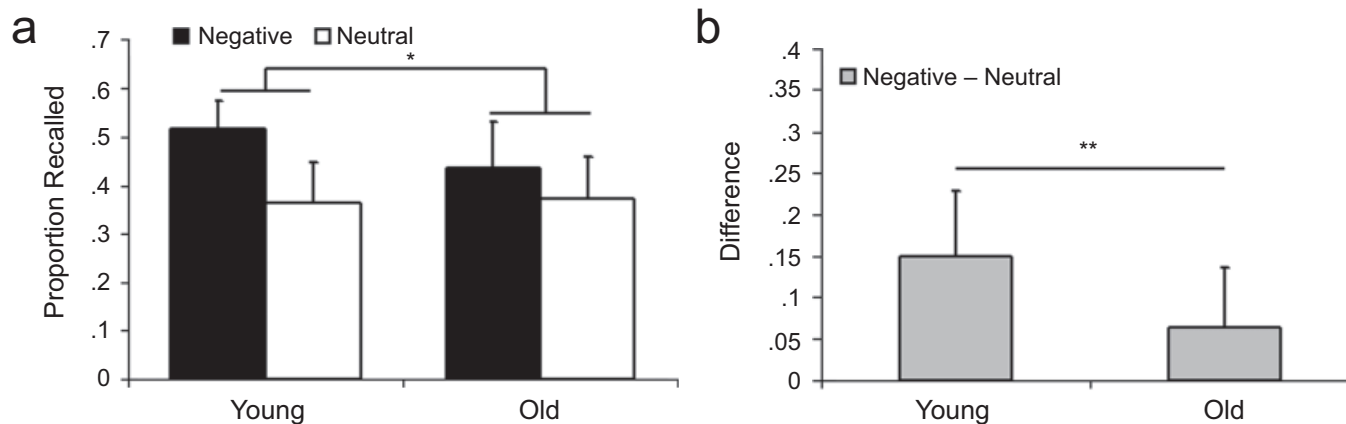


Fig. 1. Behavioral results depicting memory performance for the young and older age groups: (a) mean proportion of negative and neutral pictures recalled correctly during cued recall and (b) extent of the memory enhancement for negative pictures (i.e., proportion of recall for negative pictures minus proportion of recall for neutral pictures). Categorization of pictures as negative and neutral was based on participants' own ratings. Error bars represent standard deviations. Asterisks indicate a significant difference, * $p < .005$, ** $p < .0001$.

neutral pictures and areas in which Dm_{negative} effects were greater than baseline activity (both at $p = .05$, cluster size ≥ 5 voxels). Thus, the resulting pattern of activity had to be confirmed by real differences, observed in each group, that showed greater Dm_{negative} effects not only in the comparison with the corresponding control condition ($Dm_{\text{negative}} > Dm_{\text{neutral}}$), but also in the comparison with the implicit baseline ($Dm_{\text{negative}} > \text{baseline}$); the conjoint probability of these three contrasts can be estimated as .000125.

Age-Related Differences in the Functional Network for Negative Memory

Seed voxels in the amygdala that were identified in our previous analysis for young and older adults, respectively, were further examined to investigate the network of brain regions functionally connected with activity in the amygdala. To create these functional-connectivity maps, we employed a second analysis based on activity on each individual trial (e.g., Rissman, Gazzaley, & D'Esposito, 2004). Specifically, we first created a GLM in which each individual trial was modeled by a separate covariate, so that we obtained different parameter estimates for each individual trial and for each individual subject. Then, as a second step, we employed the GLM to generate a mixed-design analysis of variance in SPM5 using the individual functional-connectivity maps associated with the seed voxel. To examine age-related differences in functional connectivity related to the Dm_{negative} network, we examined the Dm_{negative} (remembered, forgotten) \times Age Group (young, old) interaction ($p = .05$, cluster size ≥ 5 voxels). In order to confirm that this interaction was driven by the expected differences between Dm_{negative} and Dm_{neutral} within each age group, we inclusively masked this interaction image with the corresponding statistical correlational maps showing areas with greater Dm_{negative} than Dm_{neutral} effects ($p = .05$, cluster size ≥ 5 voxels). Thus, the resulting

activity related to the interaction showing age-related differences in the functional connectivity with the amygdala had to be confirmed by real differences, observed in each group, that showed greater Dm effects for the negative pictures than for the corresponding control condition ($Dm_{\text{negative}} > Dm_{\text{neutral}}$); the conjoint probability following this inclusive masking was .0025.

RESULTS

Behavioral Results

Analysis of the behavioral data revealed a main effect of emotion, $F(1, 28) = 59.68, p < .0001$. Memory for negative pictures was better than memory for neutral pictures in both young adults (negative: $M = .52, SD = .06$; neutral: $M = .37, SD = .08$) and older adults (negative: $M = .44, SD = .10$; neutral: $M = .37, SD = .09$; see Fig. 1a). However, there was also a significant Age Group (young, old) \times Emotion (negative, neutral) interaction, $F(1, 28) = 10.11, p < .005$, with older adults showing a reduction in the amount of emotional enhancement (young adults: $M = .15, SD = .08$; older adults: $M = .06, SD = .07$; see Fig. 1b). There was no main effect of age, $F(1, 28) = 2.00, p = .17$. Thus, although both groups recalled a greater proportion of negative pictures than neutral pictures, older adults showed a reduction in the enhancement of memory for negative pictures.

fMRI Results

Preserved Memory-Related Amygdala Activity

Results were consistent with our first prediction. Both young and older adults recruited the amygdala more for subsequent memory of negative pictures than for subsequent memory of neutral pictures. However, there were age-related differences in lateralization: Whereas young adults recruited the left amygdala, older adults recruited the right amygdala (see Table 1 and Fig. 2). Thus, the conjunction analysis showing the brain

TABLE 1
Brain Regions With Greater Subsequent-Memory Activity for Negative Than for Neutral Stimuli

Region	BA	Number of voxels	Hemisphere	Talairach coordinates			<i>t</i> (28)	<i>p</i>
				<i>x</i>	<i>y</i>	<i>z</i>		
Differential activity greater for young than for older adults								
Superior frontal gyrus	6	41	Left	-26	-1	45	2.77	.005
Medial frontal cortex	9	6	Left	-15	38	26	1.87	.035
	6	8	Right	11	24	51	2.81	.005
	6	9	Right	15	-4	59	2.60	.007
Precentral gyrus	9	10	Right	37	9	38	2.35	.013
Somatosensory cortex	5	5	Right	19	-38	50	2.21	.018
Insula	13	12	Right	45	-14	21	2.65	.007
	13	10	Right	33	14	-10	3.25	.002
Clastrum		7	Left	-26	11	10	1.91	.033
Middle temporal cortex	21	15	Left	-37	-1	-25	3.55	.001
Posterior parietal cortex	40	132	Left	-52	-35	33	4.36	<.0001
	40	19	Right	45	-38	33	2.58	.008
	40	5	Right	52	-50	27	2.05	.025
Angular gyrus	39	15	Right	33	-57	34	2.18	.019
Hippocampus		46	Left	-26	-26	-8	2.66	.006
Amygdala		46	Left	-22	-12	-12	2.01	.027
Parahippocampus	19	16	Left	-26	-55	-4	2.56	.008
Cingulate	24	5	Right	7	-20	39	2.50	.009
Visual cortex	18	11	Left	-26	-91	-5	2.28	.015
	19	20	Right	30	-66	0	2.56	.008
Putamen		5	Left	-19	4	0	1.94	.031
Differential activity greater for older than for young adults								
Dorsolateral prefrontal cortex	9	6	Left	-45	34	33	2.93	.003
Amygdala		5	Right	26	3	-19	2.98	.003
Precuneus	7	8	Left	-4	-74	49	2.55	.008
Posterior parietal cortex	40	5	Right	33	-52	58	2.51	.009
Cerebellum		6	Left	-4	-77	-9	4.73	<.0001
		8	Left	-26	-81	-24	2.70	.006

Note. The table presents results from two-sample *t* tests. BA = Brodmann's area.

areas associated with greater $Dm_{negative}$ than $Dm_{neutral}$ did not reveal an overlap in the peak response in the amygdala, even when a more liberal threshold was used (e.g., $p = .05$). When we extended the conjunction analysis to the whole brain, only two regions were commonly engaged: right DLPFC (Brodmann's area, or BA, 9; Talairach coordinates: 37, 24, 37) and right parietal cortex (BA 40; Talairach coordinates: 59, -21, 22).

Age-Related Differences in the Enhancement of Negative Memory
Confirming our second prediction, the two-sample *t* test examining age-related differences in $Dm_{negative}$ versus $Dm_{neutral}$ revealed a pattern of activation consistent with a PASA pattern. Whereas young adults recruited greater *Dm* activity for negative than for neutral pictures in bilateral visual cortices, older adults showed similar effects in the left DLPFC (see Table 1 and Fig. 3). (For other regions showing an age-related difference between $Dm_{negative}$ and $Dm_{neutral}$, see Table 1.)

Age-Related Differences in the Functional Network for Negative Memory

For examining functional connectivity, we used the peak voxels identified in the left and right amygdala regions engaged by young and older adults, respectively, as seed voxels in individual-trial-based analyses. Confirming our third prediction, these analyses revealed age-related differences in the functional connectivity associated with enhanced subsequent memory for negative stimuli relative to neutral stimuli. Specifically, there was an age-related decrease in the functional connectivity of the amygdala with typical subsequent-memory regions in young adults (i.e., left hippocampus and bilateral VLPFC), but an age-related increase in coactivation with regions involved in control processes (i.e., bilateral DLPFC; see Table 2 and Fig. 4). Supporting the idea that the older adults were regulating their emotional response, the analyses showed that the functional coupling between DLPFC and right amygdala was in the positive

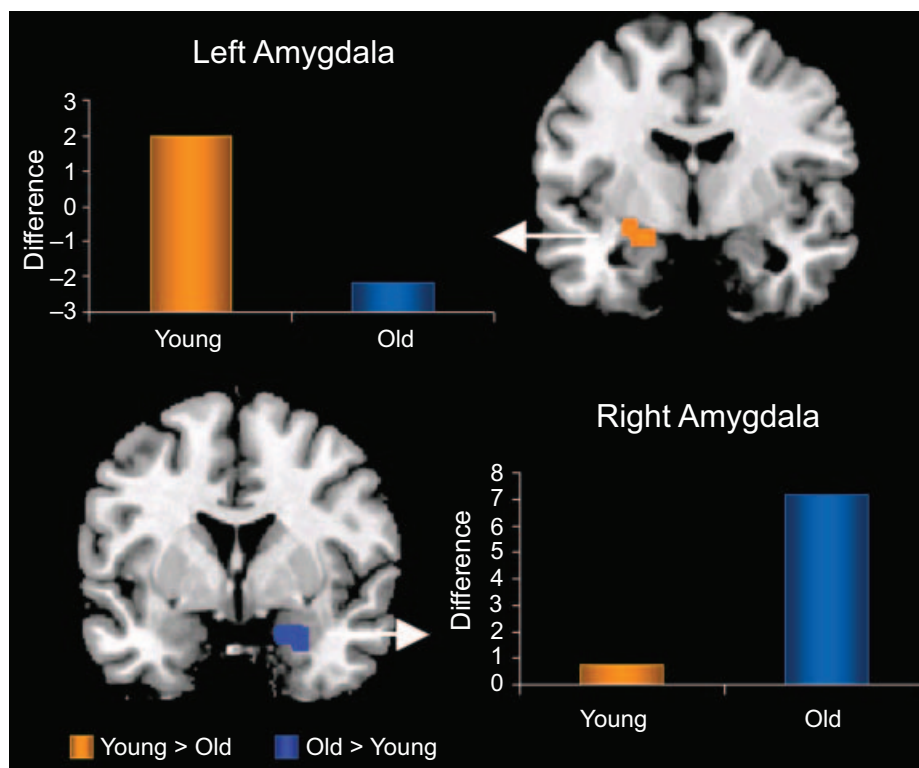


Fig. 2. Areas of the amygdala exhibiting greater subsequent-memory (Dm) effects (i.e., greater activation for remembered than for forgotten pictures) for negative than for neutral pictures. The top panel shows the Dm effects for young and older adults in an area of left amygdala (illustrated in the brain map on the right). The bottom panel shows the Dm effects for young and older adults in an area of right amygdala (illustrated in the brain map on the left). Units reflect the difference in the parameter estimates of the activation. The color key refers to the brain maps only.

direction, such that Dm activity in DLPFC increased as Dm activity in the amygdala increased (see Fig. 4). (For other regions showing an age-related difference in the functional network for negative memory, see Table 2.)

DISCUSSION

Our study yielded three main findings. First, older adults exhibited preserved enhancement of amygdala activity associated with subsequent memory for negative pictures versus subsequent memory for neutral pictures. Second, we found a PASA pattern in brain areas showing greater subsequent-memory activity for negative than for neutral pictures: Compared with young adults, older adults exhibited reduced subsequent-memory activity for negative pictures in visual cortices, but increased subsequent-memory activity for negative pictures in frontal regions. Third, analyses of the functional connectivity of the amygdala revealed age-related differences in the network for negative emotional memory. Whereas in young adults the amygdala was functionally connected to regions typically involved in subsequent memory—specifically, the hippocampus and bilateral inferior frontal cortices—in older adults the amygdala was functionally connected to bilateral DLPFC, a region involved in emotion regulation. Thus, we found preserved

function in the amygdala in older adults, but also age-related differences in brain activity associated with subsequent memory for negative pictures and in the network for negative emotional memory; we discuss these findings in this section.

Preserved Amygdala Activity in Aging

Although some fMRI studies have investigated age-related differences in subsequent memory for neutral stimuli (Dennis et al., 2007; Gutchess et al., 2005; Morcom et al., 2003), to our knowledge this is the first study to examine age-related differences in subsequent memory using emotional stimuli. Our findings show that young and older adults recruited the amygdala more for subsequent memory for negative pictures than for subsequent memory for neutral pictures, and are consistent with evidence that aging is associated with structural preservation (e.g., Good et al., 2001) and robust functional activation (Wright, Wedig, Williams, Rauch, & Albert, 2006) in this region. Preserved amygdala activity in older adults might explain the similarity in the behavioral patterns observed in young and older participants and is consistent with growing evidence that the enhancement in memory for emotional stimuli observed in young adults is also observed in older adults (e.g., Denburg et al., 2003).

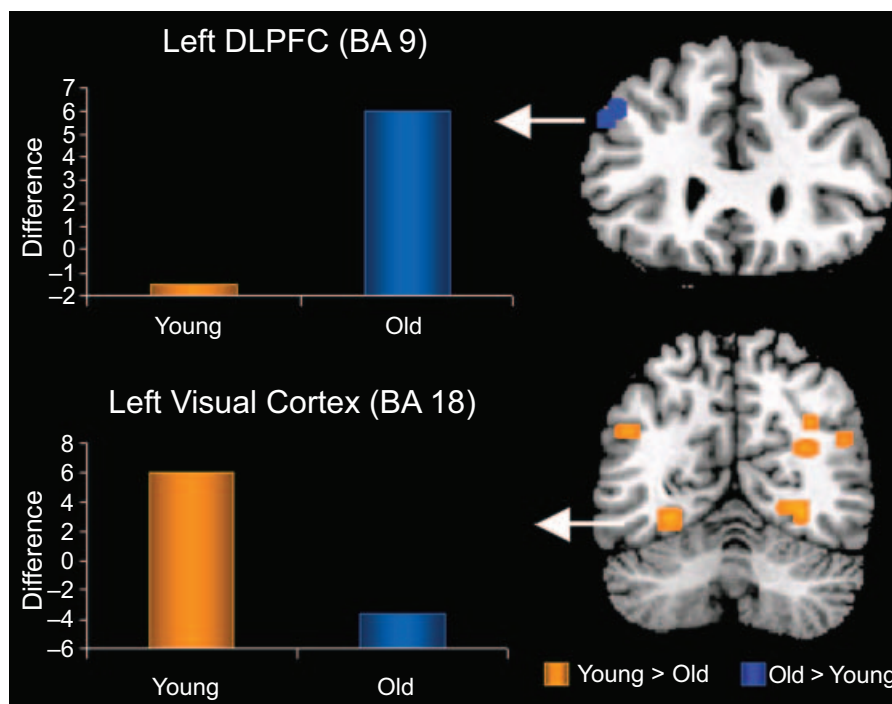


Fig. 3. Age-related differences in brain areas exhibiting greater subsequent-memory (Dm) effects (i.e., greater activation for remembered than for forgotten pictures) for negative than for neutral pictures. The top panel shows the Dm effects for young and older adults in an area of dorsolateral prefrontal cortex (DLPFC, illustrated in the brain map on the right). The bottom panel shows the Dm effects for young and older adults in an area of left visual cortex (illustrated in the brain map on the right along with other areas showing greater Dm effects for young than for older adults). Units reflect the difference in the parameter estimates of the activation. The color key refers to the brain maps only. BA = Brodmann's area.

Although both age groups showed a greater subsequent-memory effect in the amygdala for negative than for neutral pictures, there were also age-related differences in lateralization. Young adults recruited the left amygdala, whereas older

adults recruited the right amygdala. There are several hypotheses regarding lateralization differences in amygdala function across studies (for a review, see Baas, Aleman, & Kahn, 2004), but it is not clear whether there are age-related effects on lat-

TABLE 2
Brain Regions Showing Greater Functional Connectivity With the Amygdala for Subsequent Memory of Negative Stimuli Than for Subsequent Memory of Neutral Stimuli

Region	BA	Number of voxels	Hemisphere	Talairach coordinates			<i>F</i> (1, 56)	<i>p</i>
				<i>x</i>	<i>y</i>	<i>z</i>		
Differential functional connectivity greater for young than for older adults								
Ventrolateral prefrontal cortex	47	5	Left	-41	22	2	9.00	.001
	47	12	Right	33	26	2	12.43	.003
Hippocampus		5	Left	-33	-15	-12	5.96	.016
Differential functional connectivity greater for older than for young adults								
Dorsolateral prefrontal cortex	45	7	Left	-52	12	20	9.67	.002
	46	31	Left	-45	33	9	9.59	.002
	46	24	Right	52	33	9	11.50	.001
Fusiform gyrus	37	5	Left	-33	-48	-7	9.58	.002
Posterior parietal cortex	40	7	Left	-52	-49	48	13.03	<.0001
Cerebellum		22	Right	7	-67	-22	8.69	.004

Note. BA = Brodmann's area.

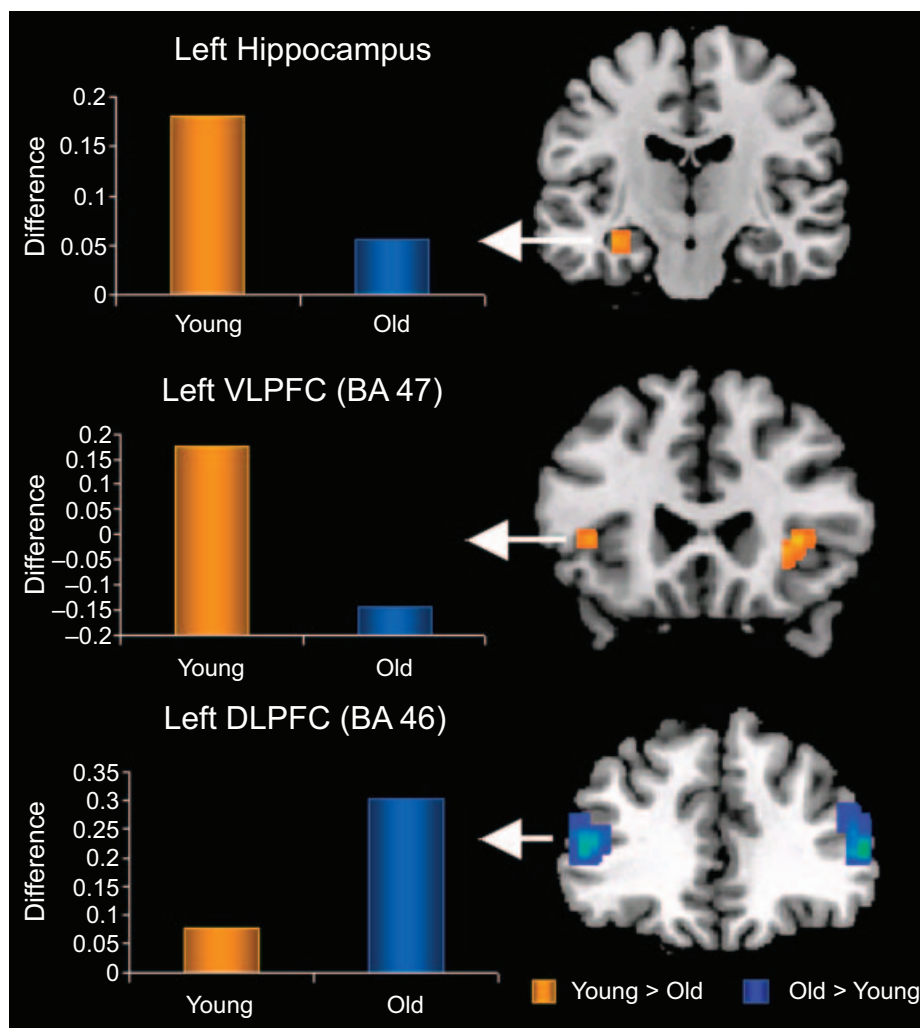


Fig. 4. Age-related differences in the subsequent-memory network for negative stimuli. In the graphs, the y-axes represent the difference between activation associated with subsequent memory for negative pictures and activation associated with subsequent memory for neutral pictures. Results are shown for the left hippocampus (top panel), left ventrolateral prefrontal cortices (VLPFC; middle panel), and left dorsolateral prefrontal cortices (DLPFC; bottom panel). The brain maps show areas of left hippocampus and bilateral VLPFC where functional connectivity with the amygdala was greater for young than for older adults and areas of bilateral DLPFC where functional connectivity with the amygdala was greater for older than for young adults. The color key refers to the brain maps only; brighter areas of color represent a higher level of activation. BA = Brodmann's area.

eralization in the amygdala (e.g., Mather et al., 2004). Sex might influence amygdala lateralization during memory processes for emotional stimuli (e.g., Cahill et al., 2001), with females preferentially recruiting the left amygdala. Our finding that young adults recruited the left amygdala is consistent with this idea, as the young adults in our study were all females; however, the older adults in our study were also all females. In young adults, activity tends to be observed more frequently in the left amygdala than in the right amygdala across a variety of emotional tasks, including encoding of emotional stimuli (Baas et al., 2004). Thus, one intriguing possibility is that aging leads to hemispheric asymmetry in the amygdala similar to the age-related hemispheric asymmetry that has been found in other

MTL regions, such as the hippocampus (e.g., Maguire & Frith, 2003). Future research is needed to examine lateralization in amygdala activity and how this is related to age-related effects on emotional memory.

Age-Related Differences in the Enhancement of Negative Memory

Previous subsequent-memory studies using neutral stimuli have found that aging leads to reduced MTL activity coupled with increased frontal activity (Dennis et al., 2007; Gutchess et al., 2005; Morcom et al., 2003), and are consistent with the PASA (for a review, see Dennis & Cabeza, 2008). In an investigation

restricted to examining emotional perception, we found that aging was associated with reduced activity in visual cortices coupled with increased activity in frontal regions (St. Jacques et al., in press); there were no age-related differences in amygdala activity, which might also influence visual activity (e.g., Anderson & Phelps, 2001). Consistent with evidence for the PASA, the present investigation found that older adults had reduced Dm effects for negative versus neutral pictures in bilateral visual cortices, but increased Dm effects for negative versus neutral pictures in left DLPFC. This pattern of differential activity was potentially augmented by the sensitivity of the cued-recall test to visual details and hence age-related deficits in sensory processing (e.g., Lindenberger & Baltes, 1994) and in memory for visual details (e.g., Koutstaal, 2003; but see Kensinger, Garoff-Eaton, & Schacter, 2007).

Other studies reporting the PASA (e.g., Davis, Dennis, Daselaar, Fleck, & Cabeza, 2007) found that age-related differences in activity in some regions did not fit the shift from visual to frontal activation. In the present study, we also found that young adults recruited greater Dm activity than older adults in medial prefrontal cortex, and older adults recruited greater Dm activity than young adults in parietal cortices (see Table 1). However, the medial prefrontal cortex is not associated with top-down control, but rather is part of the default network, the brain regions that are active during rest (e.g., Raichle et al., 2001), and is a region where there is greater deactivation, or decrease in task-related activity relative to a standard baseline, in older than in young adults (e.g., Davis et al., 2007). Furthermore, parietal cortices have strong links with frontal cortices, and the age-related increases in activation often found in this brain region (e.g., Cabeza et al., 2004) might reflect these fronto-parietal networks. At any rate, the present results extend the available evidence by showing a PASA pattern in the formation of memory for negative stimuli, under conditions in which the amygdala is equally engaged in young and older adults.

Age-Related Differences in the Functional Network for Negative Memory

The findings from the functional-connectivity analysis suggest that, despite the common engagement of the amygdala, there are age-related differences in the functional networks recruited for subsequent memory of negative stimuli, relative to neutral stimuli. Older adults showed reduced functional connectivity between the amygdala and typical subsequent-memory regions found in young adults, such as the hippocampus. Previous studies in young adults have found that amygdalar-hippocampal interactions enhance subsequent memory (Dolcos et al., 2004b), and the current results suggest that this modulation is reduced in aging.

Trial-based analyses also showed that older adults had increased functional connectivity with the DLPFC, a region that is functionally connected with other subregions of the MTL in

older adults during neutral memory encoding (Grady et al., 2003). In tasks using neutral stimuli, the DLPFC is thought to subserve increased strategic or control processes that compensate for reduced memory encoding in aging (e.g., Dennis et al., 2007), whereas in tasks involving emotional stimuli, the engagement of lateral prefrontal cortices is typically thought to be involved in the cognitive control of emotion (for a review, see Ochsner & Gross, 2005; see also Dolcos, Kragel, Wang, & McCarthy, 2006). Our finding of increased functional connectivity between the DLPFC and the amygdala is more consistent with the latter interpretation, because Dm activity in DLPFC increased as Dm activity in the amygdala increased.

In a previous investigation on emotional perception and aging (St. Jacques et al., in press), we found evidence consistent with the idea that older adults automatically regulate emotional responses to negative pictures, and the present findings suggest that increased emotional regulation during encoding improves subsequent-memory performance for negative stimuli. Indeed, in young adults, emotional regulation via reappraisal improves recall performance, likely because of increased attention directed toward the emotional stimuli (e.g., Dillon, Ritchey, Johnson, & LaBar, 2007). The present results suggest that one by-product of older adults' increased motivation to regulate emotions (Mather & Carstensen, 2005) might be a boost in memory for emotional stimuli. However, the increased attentional resources directed toward emotional stimuli as the result of emotion regulation during encoding might be less effective at improving memory than is the modulation of the hippocampus by the amygdala, which boosts consolidation processes and is likely to persist over time (e.g., Ritchey, Dolcos, & Cabeza, 2008).

Conclusions

In this study, we examined age-related changes in the functional connectivity of the amygdala with the network associated with subsequent memory for negative pictures. There were three main results. First, amygdalar activity associated with subsequent memory for negative pictures was preserved in older adults. This finding is consistent with an overall preservation of the enhancement of emotional memory in aging. Second, activity predicting subsequent memory for negative pictures, relative to neutral pictures, showed a PASA pattern. Third, there were age-related differences in the Dm network for negative emotional stimuli, and these differences were consistent with an age-related reduction in memory for negative stimuli. Compared with young adults, older adults had greater functional connectivity between the right amygdala and bilateral DLPFC, a possible reflection of increased emotional regulation of negative pictures, but decreased functional connectivity between the amygdala and typical subsequent-memory regions such as the hippocampus, a possible reflection of decreased modulation by the amygdala and decreased memory retrieval for negative pictures.

These findings advance understanding of the age-related alterations in the neural networks underlying subsequent memory for negative stimuli when affective function is preserved. Future research should examine the generalizability of these findings using a broader range of emotional stimuli, to establish whether these findings are specific to highly arousing negative stimuli and to dissociate possible valence- versus arousal-related effects.

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