The Effects of Aging on the Neural Basis of Implicit Associative Learning in a Probabilistic Triplets Learning Task

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Abstract

■ Few studies have investigated how aging influences the neural basis of implicit associative learning, and available evidence is inconclusive. One emerging behavioral pattern is that age differences increase with practice, perhaps reflecting the involvement of different brain regions with training. Many studies report hippocampal involvement early on with learning becoming increasingly dependent on the caudate with practice. We tested the hypothesis that the contribution of these regions to learning changes with age because of differential age-related declines in the striatum and hippocampi. We assessed age-related differences in brain activation during implicit associative learning using the Triplets Learning Task. Over three event-related fMRI runs, 11 younger and 12 healthy older adults responded to only the third (target) stimulus in sequences of three stimuli ("triplets") by corresponding key press. Unbeknown to participants, the first stimulus' location predicted one target location for 80% of trials and another target location for 20% of trials. Both age groups learned associative regularities but differences in favor of the younger adults emerged with practice. The neural basis of learning (response to predictability) was examined by identifying regions that showed a greater response to triplets that occurred more frequently. Both age groups recruited the hippocampus early, but with training, the younger adults recruited their caudate whereas the older adults continued to rely on their hippocampus. This pattern enables older adults to maintain near-young levels of performance early in training, but not later, and adds to evidence that implicit associative learning is supported by different brain networks in younger and older adults. ■

INTRODUCTION

Implicit associative learning refers to the acquisition of information without intent or explicit knowledge of what has been learned (Frensch, 1998). Such learning is ubiquitous in daily life, underlying our sensitivity to routines and our ability to gain professional expertise (Cleeremans, 2002). Here, we examined the neural bases of implicit associative learning and how these vary with adult age. Despite the importance of implicit learning in adapting to the world, it has been studied much less than its explicit counterpart in the context of aging.

This neglect is likely because of the dominant view that implicit learning is relatively unaffected by age (Dennis & Cabeza, 2008; Hedden & Gabrieli, 2004). Yet, this assumption is misleading; although older adults can acquire new implicit associations, evidence from a range of tasks suggests that older adults rarely attain the level of performance of younger adults and further that the magnitude of age differences increases with training (Maddox, Pacheco, Reeves, Zhu, & Schnyer, 2010; Filoteo & Maddox, 2004; Raz, Williamson, Gunning-Dixon, Head, & Acker, 2000).

This finding is particularly true for probabilistic tasks, in which older adults' learning asymptotes while younger adults continue to learn (Simon, Howard, & Howard, 2011; Howard, Howard, Dennis, & Kelly, 2008; Bennett, Howard, & Howard, 2007; Ciomek, Song, Howard, & Howard, 2007; Howard & Howard, 1997). The current study asks why this is the case by examining the neural bases of this form of learning in aging.

Research with younger adults suggests that implicit associative learning involves two interactive learning systems: one based on the medial-temporal lobes (MTLs) and the other based on the striatum. Specifically, studies show that the hippocampus is important for rapid association formation early in training, whereas the caudate is involved in integrating probabilistic information gradually over an extended temporal window (Poldrack & Packard, 2003). This pattern has been reported in the motor-based serial RT task (Nissen & Bullemer, 1987), in which people learn to make faster motor responses to repeating sequences versus those that are randomly determined (Schendan, Searl, Melrose, & Stern, 2003; Rose, Haider, Weiller, & Buchel, 2002) as well as in the judgment-based weather prediction task (Knowlton, Squire, & Gluck, 1994), in which people learn to classify stimuli into two contrasting categories when given probabilistic

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feedback (Shohamy, Myers, Kalanithi, & Gluck, 2008; Poldrack et al., 2001).

Of note, healthy older adults have pronounced volume declines in the caudate (Raz et al., 2003; Gunning-Dixon, Head, McQuain, Acker, & Raz, 1998), whereas the hippocampus shows relatively little decline (Head, Snyder, Girton, Morris, & Buckner, 2005; Sullivan, Marsh, & Pfefferbaum, 2005; but see also Raz, Rodrigue, Head, Kennedy, & Acker, 2004). Because studies show that Parkinson's patients and animals with striatal damage have increased reliance on their intact hippocampus to support striatal-based learning (Moody, Bookheimer, Vanek, & Knowlton, 2004; Poldrack & Packard, 2003), we propose that age deficits in implicit associative learning appear with practice because of the relative aging of the hippocampus and caudate and the functional reorganization of neural learning systems that occurs as a result. Early in training, older adults learn implicit associative regularities just as well as younger adults because the hippocampus, which is efficient at the rapid association formation needed early in training, is relatively spared with aging. However, age deficits emerge later because older adults continue to engage the hippocampus throughout training, and this structure is not as well suited as the caudate for the gradual integration of complex, probabilistic associations (Ashby, Turner, & Horvitz, 2010).

To our knowledge, only five functional imaging studies have examined the effects of aging on the neural bases of implicit associative learning. One study found no age group differences in behavioral performance or in task-related brain activations, including striatal regions (Daselaar, Rombouts, Veltman, Raaijmakers, & Jonker, 2003). This age equivalence was likely because of the use of a "young" adult sample (aged 30–35 years) that is older than the 20-year-old groups used in other studies, which is important because the striatum shows linear declines starting in early adulthood (e.g., Raz et al., 2003). Of the remaining studies, each reported that older people had reduced striatal activation and increased reliance on regions elsewhere in the brain during learning relative to younger adults. In two studies, increased MTL activation was observed in older adults consistent with our hypothesis here (Dennis & Cabeza, in press; Rieckmann, Fischer, & Backman, 2010), whereas in two other studies, older adults recruited frontal or parietal cortices (Aizenstein et al., 2006; Fera et al., 2005). However, none of these studies yielded age-related deficits in behavioral learning. This may be a result of brief training and/or that event timing was slowed down to fit the imaging protocol, which resulted in minimal learning effects in the younger adults that made it hard to detect age deficits. Likewise, some of the above studies used deterministic regularities, which may not produce age differences in learning (Howard & Howard, in press). Thus, it is not yet known which neural regions contribute to observed age differences in learning implicit probabilistic associations with practice.

Here, we used the Triplets Learning Task (TLT; Howard et al., 2008), which uses event timing that is more condu-cive to learning and provides ample training to examine the time course of behavioral learning and brain activations in younger and older adults. Importantly, studies using this task have shown that both age groups learn equally well early in training but that age deficits appear over time (Simon, Howard, et al., 2011; Howard et al., 2008). Moreover, the TLT has been found to be sensitive to individual differences in striatal function in healthy younger adults (Simon, Stollstorff, et al., 2011). In this task, participants view open circles that become red or green in discrete three-event sequences or "triplets." On each trial, participants observe two red cues and respond only to a third green target via corresponding button, providing a continuous, performance-based learning measure. Unbeknown to participants, triplets have a probabilistic second-order structure, in that the first cue's location predicts one target location for a majority of the trials and another location for the remaining trials. Such complex probabilistic sequences minimize spontaneous explicit awareness (Reber, 1976), rendering it possible to study the evolution of implicit associative learning with training. In fact, people reveal such learning with practice by faster responses on more predictable trials despite having no explicit knowledge of the embedded regularities, even after 3 hr of training (Howard et al., 2008).

The present study used event-related functional imaging of the TLT to investigate the neural bases of implicit associative learning in healthy younger and older adults to examine why older adults rarely attain the level of learning of practiced younger adults. Our hypotheses focused on the hippocampus and caudate and predicted that younger and older adults rely on these brain regions differently. Early on, hippocampal activation will be common to both age groups, but older adults will reveal reduced caudate activity compared with younger adults. With more training, younger adults will continue to recruit the caudate whereas older adults will not, but will instead continue to recruit the hippocampus because of age-related striatal declines. We expect that this pattern of brain activity will result in age-equivalent behavioral learning early on, but not later.

To ensure that learning was implicit, we performed a separate behavioral experiment in younger adults who completed this identical TLT task outside the scanner, followed by two sensitive measures of explicit knowledge.

METHODS

Participants

For the fMRI study, 11 younger adults (18.8 ± 0.60 years old, six women) and 12 healthy, older adults (67.5 ± 3.2 years old, nine women) received either course credit or monetary compensation for their participation. The younger adults were all students at Georgetown University, and the older adults responded to advertisements in the *Washington Post* Health Section. All participants, but

one, were right-handed. Because of scanner malfunction, data were lost for one younger adult and one older adult in the final scan run (late training). The Georgetown University Institutional Review Board approved the experimental procedures, and all participants gave informed consent. Before participation, adults were screened for conditions that would prevent them from being able to enter the MRI environment. Participants were also screened for neurological disease or disorder, drugs known to influence cognition, and/or meeting criteria for dementia (i.e., a score of below 27 on the Mini-Mental State Examination) or abnormal intelligence status (i.e., scores outside the expected age range on neuropsychological measures of processing speed, cued recall, free recall, verbal memory, vocabulary, and reading ability; see Table 1 for results).

Participants in this imaging study completed 3 days of testing, although data from only the first day are reported here. On the first day, they completed the MRI scanning protocol, and the second and third testing days included two additional implicit learning tasks as well as a comprehensive neuropsychological test battery.

We did not include any probes of explicit awareness after the TLT in the fMRI study so as to keep learning implicit in the subsequent two implicit learning tasks. This decision was based on earlier evidence that neither younger nor older adults develop explicit knowledge in

the TLT with more training than in the present study (Bennett, Romano, Howard, & Howard, 2008; Howard et al., 2008). However, to ensure that there was no explicit knowledge of the statistical regularities in the modified version of the TLT used here, we performed a separate behavioral experiment in younger adults, which included both a postexperimental interview and a recognition task. For this separate behavioral study, 11 younger adults (20.1 ± 1.0 years old, six women) received either monetary compensation or course credit for their participation. None had participated in the fMRI study.

Experimental Paradigm

The TLT was a shortened and simplified version from that reported in Howard et al. (2008). Participants viewed three open circles on a computer screen, displayed against a gray background (Figure 1). Each trial or "triplet" consisted the sequential presentation of two cue events (circles filling in red) followed by the target (a circle filling in green). Each red event was displayed for 200 msec, and the green target remained in view for 850 msec, with 250 msec separating events (a total of 2000 msec per trial). Participants observed the first two red events and responded to only the third, green target event location as quickly and as accurately as possible via corresponding button (one of three buttons

Table 1. Neuropsychological Test Results

	Cognitive Processing	Younger Adults	Older Adults	t
MMSE	Screen for dementia	30 (0.0)	29.3 (.8)	−2.84*,a
WAIS-III vocabulary	Vocabulary	62.4 (6.7)	67.9 (5.7)	2.14*
WAIS-III digit symbol coding	Processing speed	93.6 (14.8)	60.7 (13.7)	−5.55**
WAIS-III digit symbol pairing	Cued recall	15.5 (3.5)	10.4 (5.0)	−2.77*
WAIS-III digit symbol recall	Free recall	8.0 (1.3)	7.0 (1.4)	ns
WAIS-III logical memory (unit)	Verbal memory	49.6 (11.0)	45.8 (6.4)	ns
WAIS-III logical memory (thematic)	Verbal memory	18.7 (2.8)	19.0 (2.0)	ns
WAIS-III digit span forward	Working memory	12.4 (2.5)	11.8 (2.0)	ns
WAIS-III digit span backward	Working memory	7.4 (2.6)	9.0 (2.6)	ns
COWAT-FAS Sum	Verbal fluency	47.6 (12.2)	46.0 (12.5)	ns
USC-REMT free recall correct	Free recall	33.1 (4.9)	24.9 (5.1)	−3.68*
USC-REMT free recall repetitions	Free recall	2.6 (2.6)	2.7 (3.6)	ns
USC-REMT free recall intrusions	Free recall	.6 (1.0)	1.0 (.9)	ns
WJ-III Word Attack SS	Reading ability	27.8 (2.4)	27.5 (1.4)	ns
WJ-III Word Identification SS	Reading ability	72.7 (2.8)	74.2 (1.7)	ns

All scores are given as mean (SD), with neuropsychological test scores based on raw data except where standard scores (SS = age-adjusted standard scores with a mean of 100 and an SD of 15) are noted. Independent sample t tests sow group effects (*p < .05, **p < .001, ns = not significant). Two younger participants did not complete the WAIS-III logical memory, COWAT-FAS, and USC-REMT tests. MMSE = Mini-Mental State Examination; WAIS-III = Wechsler Adult Intelligence Scale, 3rd ed.; COWAT-FAS = Controlled Oral Word Association Test-FAS; USC-REMT = University of Southern California-Repeatable Episodic Memory Test; WJ-III = Woodcock-Johnson, 3rd ed.

[a]In the Mini-Mental State Examination, all younger adults scored a perfect score (30), whereas older adults' scores ranged from 28 to 30.
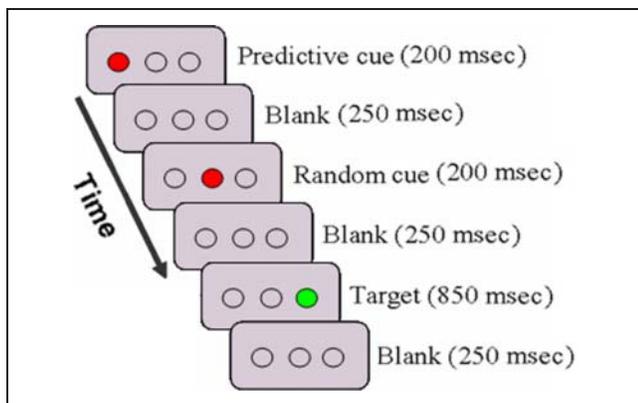
Figure 1. Sample presentation of one triplet in TLT.

on a button box held in the right hand). Unbeknown to participants, the first cue's location probabilistically predicted the target event's location as described below and the second cue's location was unrelated, thereby creating second-order structure.

Eighteen triplets (of a possible 27) were presented: nine occurred with high probability (HP) and nine with low probability (LP). The frequency of HP to LP triplets was 4:1. Event locations were counterbalanced, such that cue and target events occurred equally often in each location. Trial order was presented in fixed, pseudorandomized sequence, optimized using OptSeq2 (Dale, 1999). Participants completed three runs, with breaks between each run. Each run of 6 min 30 sec included 108 HP and 27 LP trials that were presented in a rapid event-related design with a temporally jittered intertrial interval (0.5–6 sec, mean = 1.36 sec).

The behavioral sample performed the identical task as above. Again, participants were instructed to make behavioral responses by pressing one of three buttons in the right hand (using a keypad) that corresponded to the location of the target as quickly and accurately as possible. After testing, explicit knowledge was probed immediately in two ways. First, participants completed a postexperimental recognition task, in which they observed each of the 27 possible triplets (only 18 of which had actually occurred during the TLT task), and they were instructed to judge if each triplet had occurred frequently, infrequently, or never during training by responding 2, 1, or 0, respectively. Second, participants were interviewed about strategy and their declarative knowledge of triplet structure. Questions ranged from general inquiries about strategies used to improve performance to more specific questions that asked participants to describe any patterns or relationships between red and green events that they might have noticed.

fMRI Acquisition

Imaging data were acquired using a 3.0-T MRI system (Siemens Magnetom Trio, Erlangen, Germany). A technician positioned participants in the supine position with a circularly polarized head coil. A mirror mounted on the head coil allowed participants to view stimuli during scanning. Fitted padding minimized head movement.

A high-resolution T1-weighted structural scan (MPRAGE) was acquired first, using a 3-D MPRAGE sequence with a scan time of 7:23 min and the following parameters: repetition time (TR) = 2300 msec, echo time = 2.94 msec, inversion time = 900 msec, flip angle = 90°, 1 slab, 160 sagittal slices with a 1.0-mm thickness, field of view = 256×256 mm^2, matrix = 256×256, resulting in an effective resolution of 1.0-mm^3 isotropic voxels. A neurologist later reviewed these images and identified no clinically significant structural abnormalities (e.g., lesions or abnormal growths). Functional imaging was acquired on the same equipment while participants completed the TLT. Functional data were acquired along the AC–PC line using T2*-sensitive gradient EPI pulse sequence with the following parameters: TR = 2500 msec, echo time = 30 msec, field of view = 256×256 mm, acquisition matrix = 64×64, flip angle = 90°, and a 0.3-mm gap for an effective resolution of $4.0 \times 4.0 \times 4.0$ mm^3. Forty-two contiguous 3.7-mm-thick axial slices were acquired descending in the transverse plane for 154 time points for each run.

Behavioral Analysis

To determine if participants showed implicit associative learning, we compared performance on HP versus LP triplets. Repetitions (e.g., 111 and 222) and trills (e.g., 121 and 232) were excluded from the analyses reported below because they reflect preexisting response tendencies (Boyer, Destrebecqz, & Cleeremans, 2005). Median RTs were determined for correct responses on each triplet type in each block of 27 trials. These medians were averaged to obtain a single mean RT for each individual and the two triplet types. A similar procedure was used to calculate the mean accuracy for each person for the two triplet types.

fMRI Processing and Data Analysis

We focused our neuroimaging results only on Run 1, which will be referred to as *early training*, and Run 3, which will be referred to as *late training*. Our choice to analyze Runs 1 and 3 was driven by cognitive theories that have proposed distinct stages in learning, characterized as early training (i.e., fast encoding and rapid improvements) and late training (i.e., when performance reaches asymptote after associations are relatively well learned; e.g., Doyon, 2008; Karni & Bertini, 1997). Research has shown that different brain regions are involved for these distinct training stages, with early training involving the hippocampus and later learning involving the caudate (e.g., Poldrack et al., 2001). This choice was also based on previous work that has shown that older adults can acquire new implicit associations quickly and as well as younger adults (i.e., Run 1) but that age differences emerge with practice in favor of younger adults (i.e., Run 3; e.g., Simon, Howard, et al.,

2011). Thus, based on this previous literature, we did not have specific predictions for Run 2, nor did we know whether it should be considered early or late training.[1]

Functional images were analyzed in SPM5 (www.fil.ion.ucl.ac.uk/spm). The first two TRs were discarded from the analysis, as they had been included for signal stabilization. All participants displayed less than 3 mm of motion in any direction within each run, so no data were eliminated because of motion artifact. Images were slice-timed, motion corrected, and spatially normalized to the Montreal Neurological Institute template using each subject's high-resolution structural MPRAGE. Normalized image volumes were then smoothed (8-mm FWHM Gaussian kernel) and temporally filtered (128-sec high-pass filter). fMRI responses for correct responses on HP and LP triplets were modeled by a canonical hemodynamic response function, and autocorrelations removed signal related to biorhythms. The remaining trial types (trills, repetitions, and incorrect trials) were excluded from analysis.

For each participant, an activation map was generated using a linear contrast identifying regions that showed greater response to predictable events (HP > LP) in the first run (early training) and in the third run (late training). Individual-level contrasts were entered into second-level analysis with subjects as a random factor. Given the study's primary focus on the hippocampus and caudate, these areas were targeted as ROIs using one mask including both regions in both hemispheres, defined anatomically by the automated anatomic labeling library (Tzourio-Mazoyer et al., 2002). Correction for multiple comparisons was performed using 3dClustsim (a function from AFNI), based on Monte Carlo simulation of random correlated noise distribution to estimate the probability of false positive detection at $p < .05$ ($p < .005$) with a cluster extent of 19 voxels for the gray matter mask of the bilateral hippocampus and caudate combined (Ward, 2000; afni.nimh.nih.gov/pub/dist/doc/manual/AlphaSim.pdf). Two second-level analyses were performed separately for early and late trainings: (1) To test our hypothesis of age group differences in the caudate and not the hippocampus, we compared the response to predictability between younger and older adults using a two-sample t test. (2) To examine whether the hippocampus and caudate engagement varied with the magnitude of behavioral learning, we ran correlations between individual implicit associative learning scores and the response to predictability (activation associated with the HP > LP contrast) within each age group in a voxel-wise manner with the combined anatomical mask. Learning scores were calculated as the difference in performance between HP and LP triplets at both early and late trainings (i.e., LP triplet RT minus HP triplet RT).

Finally, as an exploratory analysis, we examined whether any regions in the rest of the brain differed by age group, using a two-sample t test similar to that in (1) above, but without any mask, using an uncorrected threshold, $p < .001$.

All reported coordinates were converted from Montreal Neurological Institute to Talairach space using the algorithm mni2tal (imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach).

RESULTS

Behavioral Results

fMRI Study

Data were analyzed using a Group (fMRI young, fMRI old) × Triplet Type (HP, LP) × Training Stage (early, middle, late) mixed design ANOVA. Group varied between subjects, and Triplet Type and Training Stage varied within subjects. Overall accuracy was high (younger: $M = 99.0\%$, $SD = 0.03\%$; older: $M = 98.4\%$, $SD = 0.04$), and the ANOVA for accuracy revealed no significant main effects or interactions ($ps > .24$). This aids interpretation in that there were no age-related speed–accuracy trade-offs. As expected, the ANOVA for RT produced a main effect of Group, $F(1, 19) = 36.22$, $p < .0001$, revealing that younger adults responded significantly faster than older adults (younger: 368.31 ± 49.96, older: 482.72 ± 41.76). A main effect of Training Stage, $F(1, 19) = 9.39$, $p = .0005$, revealed significantly faster responses over time (early: 439.64 ± 71.71, middle: 423.59 ± 75.68, late: 420.34 ± 72.66), and a main effect of Triplet Type, $F(1, 19) = 47.19$, $p < .0001$, revealed associative learning or significantly faster responses to HP than LP triplets (HP: 416.66 ± 72.08, LP: 439.50 ± 73.33). The Triplet Type × Training Stage interaction was not significant, $F(1, 19) = 1.43$, $p = .25$[2]; however, the Critical Group × Triplet Type × Training Stage interaction was significant, $F(1, 19) = 3.95$, $p < .05$, showing age group differences in associative learning over time. RT difference scores, shown in Figure 2, revealed that younger adults had significantly higher learning scores than older adults only late in training (i.e., Run 3), $t(19) = 2.05$, $p = .05$.

We further evaluated this age deficit in late learning by examining each individual's implicit associative learning scores in Run 3, that is, LP triplet RT minus HP triplet RT. Using a median split, we classified any subject with a difference score of ≥20.2 msec as being a high learner and any other subject as a low learner. Of the high learners, eight were younger adults and three were older adults, whereas of the low learners, two were younger adults and eight were older adults, $\chi^2(2) = 5.8$, $p = .02$. Thus, late in training, most younger adults were classified as high learners and most older adults as low learners.

Although neuropsychological measures had been collected to characterize our sample as normal, we also correlated these scores with individual implicit associative learning scores from early and late trainings to determine whether age-related differences in processing speed, free recall, or cued recall were related to age differences observed in late associative learning. There were no significant correlations between individual RT difference scores at early or late training and any of the

neuropsychological measures, either within or across groups ($ps > .21$).

Behavioral Study

Participants were highly accurate for both the HP and LP triplets across training stages (mean = 99.2%, SE = 002%). To assess potential differences in implicit associative learning inside and outside the scanner, mixed design ANOVAs were conducted separately for RT and accuracy: Group (fMRI young, Lab young) × Triplet Type (HP, LP) × Training Stage (early, late). As expected, there were no significant main effects of experiment or interactions between the studies for either behavioral measure ($ps > .51$), indicating similar learning between the two experiments (see Figure 2).
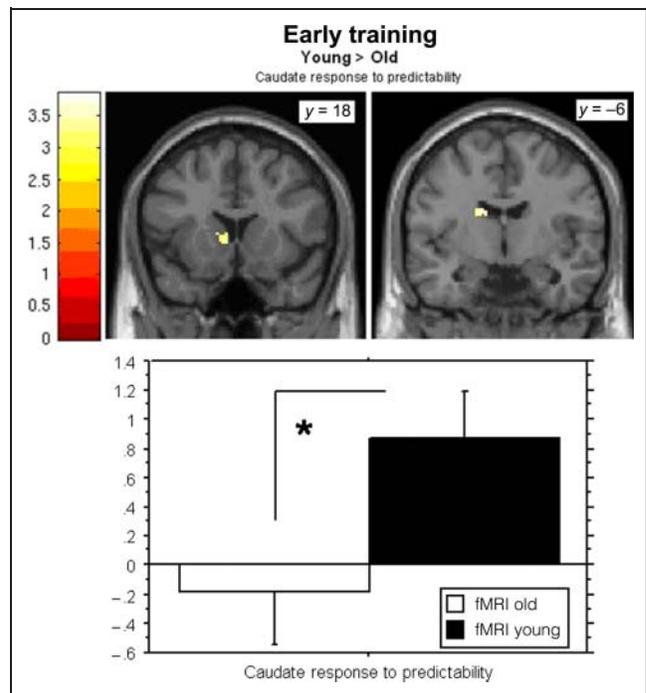
Measures of Explicit Knowledge

Younger adults in the separate behavioral study also completed two sensitive measures of explicit knowledge after testing. Postexperimental interviews revealed no strategies related to learning and no evidence of explicit knowledge, in that no one reported that the first cue predicted the target or that some triplets occurred more often than others. To assess explicit judgments of triplet frequencies on the recognition task, a one-way repeated measures ANOVA was conducted on the mean recognition ratings for each triplet type (HP, LP, and those that never occurred). Data were lost for one participant, leaving 10 participants in this analysis. There was no relationship between judgment and triplet category, $F(2, 18) = .46, p > .05$, such that all triplet types were rated as having occurred equally often during training (HP: 1.19 ± 0.17, LP: 1.14 ± 0.20, never occurred: 1.21 ± 0.25).

To examine individuals, 3×3 chi-square analyses for each person compared judgments (more often, less often,
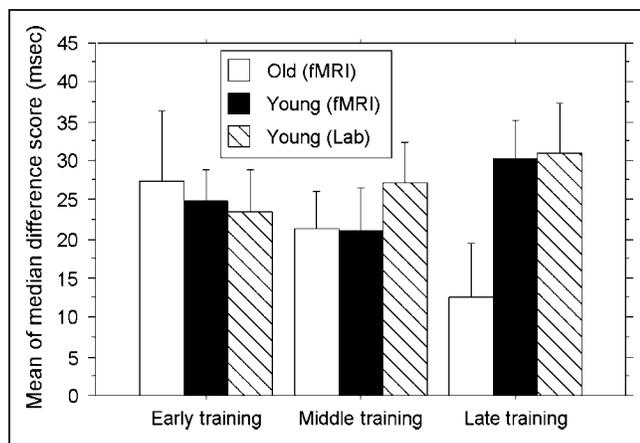
Figure 3. Clusters of activity in the left caudate in which younger adults show a greater response to predictability than older adults in early training. Graph shows contrast estimates, extracted from the mean of activated clusters using MARSBAR ($\pm SE$) in younger and older adults (*$p < .05$).

and never) for the three triplet categories (HP, LP, and never occurred). As expected, no individual had explicit knowledge of triplet frequencies, in that ratings did not vary with triplet type ($ps > .09$). Moreover, associative learning was independent of recognition task judgments; triplet ratings on the recognition task (i.e., HP–LP ratings) did not correlate with individual RT difference scores in early or late training ($ps > .12$). In summary, participants unknowingly learn regularities of the sort studied here.

fMRI Results

Age Group Differences in the Hippocampus and Caudate

Consistent with our predictions and as seen in Figure 3, in early training, we observed two clusters of activity in the left caudate that were significantly greater in younger versus older adults ($x, y, z = -14, -11, 25; z = 3.31, k = 33$ voxels; $x, y, z = -8, 15, 6, z = 3.21, k = 32$). Of note and also as predicted, there were no significant age-related differences in the hippocampus in early training.

The previous analysis does not reveal whether the hippocampus showed a response to predictability in each group, so we examined this using one-sample t tests separately for younger and older adults using the same corrected threshold as above. As predicted, at early training, hippocampal involvement was observed, in the left hemisphere in younger adults ($x, y, z = -19; -38, 9; z = 3.50$,

Figure 2. Difference of mean of median RTs for LP–HP triplets in milliseconds over early, middle, and late learning for younger (black) and older (white) adults in the fMRI study and younger adults in the separate behavioral study (cross-hatch). Error bars represent the SEM.

$k = 24$ voxels) and bilaterally in older adults ($x, y, z = 32,$ $-16, -6; z = 3.90, k = 47$ voxels; $x, y, z = 25, -34, 7; z =$ $3.60, k = 44$ voxels).

In late training, the response to predictability in the hippocampus and caudate did not differ significantly for younger and older adults.

Correlations with Implicit Associative Learning

Using the aforementioned anatomical mask of the bilateral hippocampus and caudate, in early training no significant correlations were observed between the neural response to predictability and individual implicit associative learning scores for either age group.

Late training, however, revealed the predicted dissociation, such that individual differences in learning were related to individual differences in caudate response for younger adults and in hippocampal response for older adults. That is, as shown in Figure 4A, for younger adults two clusters were observed in the bilateral caudate ($x, y,$ $z = 12, 10, -4; z = 4.44, k = 37$ voxels; $x, y, z = -16,$ $2, 20; z = 3.17, k = 43$ voxels), both showing positive correlations with learning, whereas for older adults no significant clusters were observed in the caudate. In contrast, older adults revealed a positive correlation between learning scores and the hippocampus ($x, y, z = -27, -37, 3; z =$ $3.23, k = 19$ voxels), as shown in Figure 4B, that was not observed in younger adults. Contrast estimates were then extracted from the mean of activated clusters using MARS-BAR (Brett, Anton, Valabregue, & Poline, 2002) in younger and older adults (see Figure 4C and D) to examine whether these correlations differed significantly between the age groups; the correlation between learning and the response to predictability was significantly larger in younger than older adults for the caudate, $z = 1.98, p < .05$, but the age group difference was not significant for the hippocampus, $z = -.64, p > .05$.

Whole-brain Age Group Differences

Early in training, younger adults showed a greater response to predictability than older adults in regions often observed during associative learning, including the bilateral caudate, the left dorsolateral pFC, and the bilateral cerebellum (see Table 2). In contrast, older adults showed a greater response to predictability than younger adults in parietal regions, including the inferior parietal lobule and the precentral and postcentral gyri (Table 2). This is consistent with a previous study of aging and associative learning that showed compensatory parietal activation in healthy older adults that was related to deficient neural responses in the pFC and caudate (Fera et al., 2005).

In late training, younger adults showed a greater response to predictability than older adults in the occipito-temporal

Figure 4. Regions showing significant correlations between implicit associative learning scores and neural response to predictability in (A) younger adults and (B) older adults at late training, using a combined mask of the bilateral caudate and bilateral hippocampus (anatomically defined). The scatter plot is presented to visualize how individual differences in the (C) caudate and (D) hippocampus relate to individual differences in late implicit associative learning within each age group. Contrast estimates were extracted from the mean of activated clusters using MARSBAR (Brett et al., 2002) in younger and older adults.
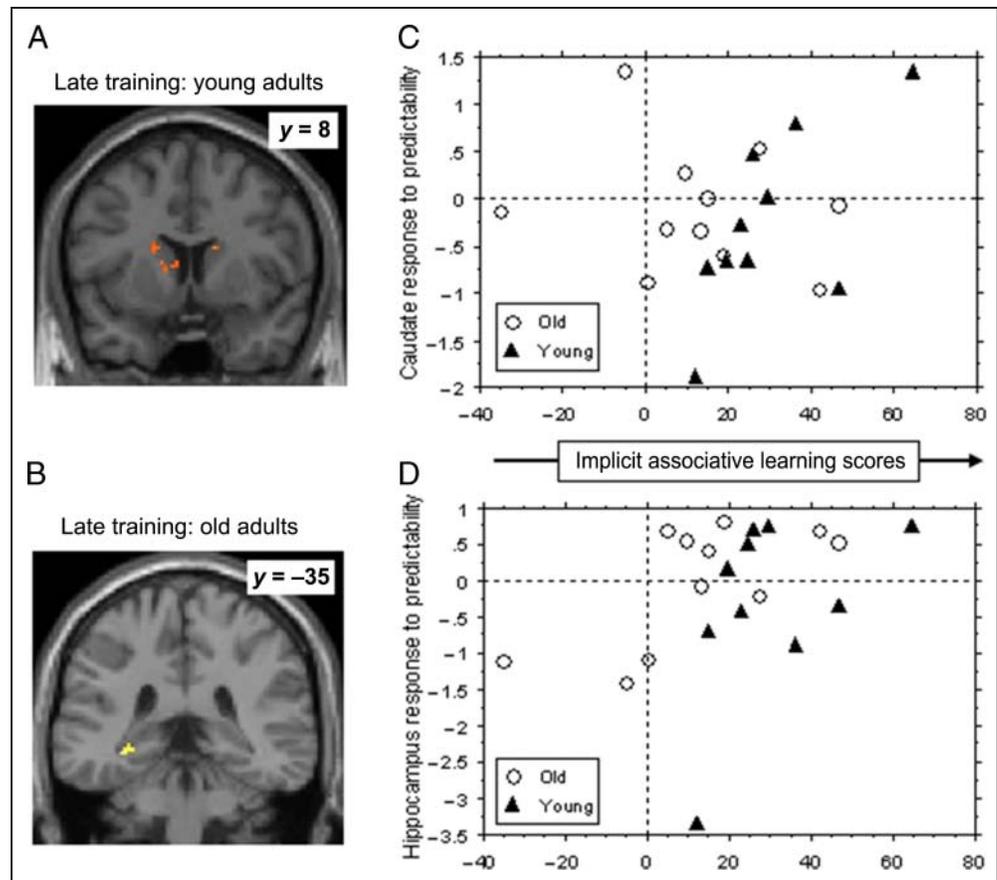
Table 2. Age Group Differences in the Neural Response to Predictability (HP > LP Contrast) at Early Training

Region	Hemisphere	BA	Talairach (mm)			Peak z	Volume (mm³)
			x	y	z		
Younger > Older							
DLPFC	Left	46	−29	29	20	3.74	528
Caudate	Left		−14	−11	25	3.26	344
Caudate	Left		−8	15	6	3.19	232
Cerebellum	Right		11	−46	−45	3.17	192
Cingulate	Left	24	−16	35	13	3.06	176
Caudate	Right		10	20	10	3.05	96
Cerebellum	Left	19	−20	−58	−14	2.98	88
Older > Younger							
Precentral gyrus	Right	6	47	5	19	3.85	232
Inferior parietal lobule, postcentral gyrus	Right	1/2/40	50	−26	37	3.54	600
	Right		39	−21	30	3.24	
Cingulate/precuneus	Right	7/23/31	21	−39	33	3.24	136
	Right		13	−38	31	2.88	
Precentral gyrus	Right	1/2	30	−14	29	3.05	88

cortices, whereas older adults showed a greater response than younger adults in bilateral frontal regions (see Table 3). This is consistent with findings that older adults show an age-related reduction in occipito-temporal activity coupled with an age-related increase in frontal activity (Davis, Dennis, Daselaar, Fleck, & Cabeza, 2008).

DISCUSSION

This study is the first to examine age differences in hippocampal and caudate involvement during early and late phases of learning of implicit associations. Results revealed three main findings. First, implicit associative learning is not spared in healthy aging but is rather characterized by age-related deficits evident later with practice. Second, this type of learning is supported by different neural regions in younger and older adults. Early in training, both age groups showed a similar response to predictability in the hippocampus, but younger adults showed a greater response to predictability than older adults in the caudate. Later in training, we observed systematic individual differences in the neural response to predictability that related to variation in the amount of learning within each age group; younger adults who showed greater implicit associative learning showed a greater caudate response to predictability, whereas for older adults, the hippocampus showed this relationship. The hippocampus is not as well suited as the caudate to the gradual acqui-

sition of probabilistic associations over time (Ashby et al., 2010), so we argue that age deficits in learning emerge with practice because of age-related declines in the striatal learning system. To our knowledge, this is the first functional imaging study to examine the neural bases of implicit associative learning in aging when behavior is both spared (early) and impaired (late).

Age Differences in Behavioral Learning

Younger and older adults both demonstrated learning of probabilistic associations in the TLT (i.e., faster responses to triplet events that occur more often), but age differences in learning emerged with practice in favor of the younger adults despite no changes in task demands (Simon, Howard, et al., 2011; Howard et al., 2008). On the basis of previous research from our laboratory, we originally expected older adults' learning to asymptote while younger adults' would continue to increase across runs, but in the present study, older adults' learning scores appeared to decline from early to late training ($p = .05$). The underlying cause for this drop in performance is a matter for further investigation. However, from the present study, we know that this age-related learning deficit cannot be attributed to age differences in event timing within a triplet, because this did not depend on participant response rate and, therefore, could not be influenced by older adults' longer and more variable response times (Howard, Howard, Dennis, &

Yankovich, 2007). Nor could it be because of age deficits in explicit associative learning (Old & Naveh-Benjamin, 2008), because no explicit knowledge was revealed on separate recognition tests. This age-related learning deficit also cannot be attributed to age differences on neuropsychological measures, as these scores did not correlate with learning in either age group. Finally, age deficits in learning are not a result of fatigue arising from longer training, because training was relatively short in comparison with behavioral studies, and furthermore, age deficits have been observed in studies that had extended training via short sessions occurring over a number of days (Howard et al., 2004). Instead, from our neuroimaging results, we argue that age differences in learning result from a fundamental deficit in the striatal learning system in older adults—a deficit that impairs learning of probabilistic associations of the sort embedded in the triplets task studied here.

Age Differences in Neural Bases of Learning

Early in training, older adults learn implicit associative regularities just as well as younger adults, and the hippocampus reveals a similar response to predictable events in both age groups. The hippocampus is efficient at forming new stimulus representations that compress redundant information while differentiating predictive information (Gluck & Myers, 2001) and is likely involved early on as sequences are initially acquired to flexibly bind the three

events that occur within each triplet (Schendan et al., 2003). Early in training, we also observed a greater response to predictability in the caudate in younger adults as compared with older adults, although the groups did not differ behaviorally. This result replicates reports of reduced striatal activation in older adults in associative learning tasks when behavioral learning was age equivalent (Dennis & Cabeza, in press; Rieckmann et al., 2010; Aizenstein et al., 2006; Fera et al., 2005). Although there is this initial learning period when age groups perform similarly behaviorally, but not neurofunctionally, our study extends previous work by providing additional training that reveals age-related differences in both learning-related brain activity and behavior. This suggests that a caudate response to predictable events is necessary for the gradual acquisition and integration of triplet frequencies over time or, more generally, for learning implicit probabilistic associative events that occur more often with practice (Ashby et al., 2010).

Yet, when older adults showed impaired implicit associative learning later in training, we surprisingly did not see group-level age differences in the hippocampus or the caudate. The fact that we could only observe learning-related correlations late in training, but not group activations, is likely because of the variability in the amount of learning between individuals as training progresses. In late training, the caudate response to predictability was related to learning in younger adults only. Across subjects, greater learning scores were associated with greater caudate activation to

Table 3. Age Group Differences in the Neural Response to Predictability (HP > LP Contrast) at Late Training

| Region | Hemisphere | BA | Talairach (mm) | | | Peak z | Volume (mm³) |
			x	y	z		
Younger > Older							
Cingulate	Right	24/32	17	35	17	3.95	264
Occipital gyrus	Left	17/18	−14	−80	20	3.93	392
Lingual gyrus	Right	36	29	−42	−10	3.69	872
Inferior temporal gyrus, middle occipital gyrus	Right	36/37	36	−71	2	3.45	992
		19	36	−74	14	3.43	
Lingual gyrus	Left	18	−25	−86	−2	3.28	248
Middle temporal gyrus	Right	37	43	−59	12	2.97	88
Superior frontal gyrus	Right	6	2	−4	67	2.93	104
Older > Younger							
Inferior frontal gyrus	Right	45/47	36	32	3	3.86	1304
	Right		42	21	5	3.05	
	Right		47	26	2	2.94	
Cingulate	Left	23	−14	−39	24	3.77	608
Inferior frontal gyrus	Left	44	−34	17	22	3.07	168

more predictable events. Unlike younger adults, the hippocampus was associated with later learning in older adults only, such that older individuals who demonstrated greater learning in late training also showed a greater hippocampal activity in response to triplets that occurred more frequently. Reduced involvement of the caudate, but not the hippocampus, in older adults confirmed our predictions, which were based on evidence that the hippocampus exhibits less age-related morphological change than the caudate (Raz et al., 2005). Indeed, this claim is further supported by a diffusion tensor imaging study from our laboratory, which used the same sample of participants studied here. Importantly, Bennett, Madden, Vaidya, Howard, and Howard (in press) found age group differences in the integrity of white matter connections (assessed by fractional anisotropy) for bilateral caudate–dorsolateral prefrontal cortex (DLPFC) tracts, but not for bilateral hippocampus–DLPFC tracts.

Taken altogether, our results reveal age-related preservation of hippocampal function (e.g., Johnson, Schmitz, Asthanaab, Gluck, & Myers, 2008; Rand-Giovannetti et al., 2006) that accompanies striatal underactivation (Dennis & Cabeza, in press). This pattern is akin to how Parkinson's patients and brain lesion animals compensate for their striatal deficits (Moody et al., 2004; Poldrack & Packard, 2003). In fact, Rieckmann and Backman (2009) have argued that increased MTL activity in older adults might explain why some behavioral studies have observed no age deficits in implicit learning (e.g., Salthouse, McGuthry, & Hambrick, 1999). It is likely that older adults were able to maintain striatal-dependent behavioral learning via the hippocampus in these cases, because the embedded regularities were deterministic, rather than probabilistic. Consistent with this view, behavioral age deficits were observed in the present study and in an implicit motor-based task that each had a complex second-order *probabilistic* structure (e.g., Howard & Howard, 1997), but not in a similar task that contained a complex second-order *deterministic* structure (Gaillard, Destrebecqz, Michiels, & Cleeremans, 2009). Because the striatum is better suited for learning complex, probabilistic associations over time than the hippocampus (Hartley & Burgess, 2005), age-related functional reorganization of learning systems may be unable to adequately compensate for striatal losses when learning probabilistic regularities, thereby producing age deficits in some forms of implicit associative learning. Future work should address this possibility empirically by directly comparing the learning of deterministic versus probabilistic regularities in younger and older adults.

No Explicit Knowledge

Despite having responded faster to HP than LP triplets during training, younger adults in the separate behavioral study were unable to discriminate between triplet frequencies in a postexperimental recognition task, consistent with work that had trained younger and older participants on up to 6000 trials (Simon, Howard, et al., 2011; Bennett et al., 2008; Howard et al., 2008). This indicates that it is possible to test implicit learning in the TLT without use of a dual task, such as counting tones simultaneously, which is often used to foster implicit learning in other studies (e.g., Grafton, Hazeltine, & Ivry, 1995). Training without a secondary task is better suited for isolating neural regions associated with implicit associative learning as opposed to those imposed by dual task demands, in addition to being less taxing and more practical for older adults.

Moreover, a post-training interview from this separate behavioral study revealed that people did not adopt conscious, deliberate strategies for stimulus selection in the TLT. This stands in contrast to other probabilistic associative learning tasks, like weather prediction, in which participants often use hypothesis-testing strategies that make it difficult to dissociate implicit from explicit learning (Meeter, Myers, Shohamy, Hopkins, & Gluck, 2006). Because age differences in strategy are not likely in the TLT, our results suggest that neural compensation with age can be nonstrategic and does not always reflect deliberate changes in learning strategy (Reuter-Lorenz & Cappell, 2008).

Nonetheless, we cannot definitively establish that no explicit knowledge of triplet structure developed in our fMRI sample, although our separate behavioral findings from younger adults suggest that it was unlikely. In fact, one possible interpretation of the finding that hippocampal activity is associated with better performance in older adults is that older adults were explicitly aware of the triplet regularities. However, this is not likely for three reasons. First, as stated above, learning in the TLT has consistently been reported to be implicit for both younger and older adults, even with extended training (Simon, Howard, et al., 2011; Bennett et al., 2008; Howard et al., 2008). Second, younger adults are more likely to gain explicit knowledge than older adults in a range of learning/memory tasks, and typically, if younger adults do not become aware, then older adults are not likely to either (e.g., Gaillard et al., 2009; Dennis, Howard, & Howard, 2006). Third, the hippocampus does not necessarily align with declarative awareness; recent work has divided memory systems based on processing modes rather than explicit knowledge (e.g., Henke, 2010), such that the same task, whether implicit or explicit, can involve either the MTLs or the striatum (e.g., Sadeh, Shohamy, Levy, Reggev, & Maril, 2011; Turk-Browne, Scholl, Chun, & Johnson, 2009). Thus, the most probable explanation is that the hippocampus is supporting learning of implicit associative contingencies throughout training in older adults, consistent with previous work in patients and younger adults (Moody et al., 2004; Schendan et al., 2003; Rose et al., 2002; Chun & Phelps, 1999).

Conclusions

In summary, older adults show declines in implicit associative learning, contrary to popular belief, and these

deficits likely reflect age differences in the contribution of the hippocampus and caudate to implicit associative learning. Early on, when responding involves the relatively preserved hippocampus, there is age invariance in behavior, but when responding is dominated by the age-impaired striatum later in training, age differences emerge. Because the ability to acquire new implicit associations is essential throughout the life span, especially later in adulthood when little time is spent in formal schooling, our findings suggest that older adults may face challenges in acquiring new skills or adapting to new environments (e.g., graduated assisted living facilities and internet) even after extended exposure. Thus, future research should focus on understanding of the cognitive and neural bases of implicit learning to foster independent and successful aging.

Notes

1. We did examine the neural response to predictability from Run 2, and the pattern of results was consistent with what is reported for Run 3, only at an uncorrected threshold.
2. Because of the lack of Triplet Type × Training Stage interaction, we conducted a separate ANOVA across epochs (1–3) within the first session only to ensure that the observed main effect of triplet type was reflecting learning. This additional test revealed a significant Triplet Type × Epoch interaction, $F(2, 42) = 7.42, p < .0005$ and no interactions with group ($ps > .08$), indicating that associative learning occurred quickly for both age groups.

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