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Age group differences in learning-related activity reflect task stage, not learning stage

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Abstract

Healthy aging is accompanied by declines in the ability to learn associations between events, even when their relationship cannot be described. Previous functional magnetic resonance imaging (fMRI) studies have attributed these implicit associative learning (IAL) deficits to differential engagement of the hippocampus and basal ganglia in older relative to younger adults in early and late stages of the task, respectively. However, these task stages have been confounded with age group differences in learning performance that emerge later and to a lesser degree in older adults. To disentangle the effects of task stage from learning stage (i.e., when there is significant evidence of learning) on age group differences in the neural substrates of IAL, we acquired fMRI data while 28 younger (20.8 ± 2.3 years) and 22 older (73.6 ± 6.8 years) healthy adults completed the Triplets Learning Task, in which the location of two cues predicted the location of a target with high (HF) or low (LF) frequency. When matched for task stage, results revealed worse learning performance and increased IAL-related activity in the hippocampus during the early stage and in the globus pallidum during the late stage in older relative to younger adults. However, when matched for learning stage, there were no significant age group differences in learning performance or IAL-related activity. Thus, although learning emerges later for older adults, they are engaging similar brain regions as younger adults when learning the associations, suggesting that previous reports of age group differences reflect effects of age on task stage, but not learning stage.

Keywords

aging; fMRI; associative learning; hippocampus; basal ganglia

Implicit associative learning (IAL) refers to the ability to form associations between events without being able to describe the regularity. It is fundamental to making decisions based on experience, learning and using language, engaging in social interactions, and perceiving the world efficiently [1-4]. Behavioral evidence of IAL is usually seen as faster responses to stimuli that can be predicted based on their relationship to prior events, such as frequently

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occurring cue-target associations. Age group differences in IAL are often seen as learning that emerges at a later stage of the task and to a lesser degree in older than younger adults [5-13]. Of interest here is whether effects of age on IAL reflect differential engagement of the neural substrates that mediate early and late stages of learning in younger and older adults.

Functional magnetic resonance imaging (fMRI) studies in younger adults have reported relatively consistent patterns of IAL-related activity in the hippocampus and dorsal striatum (caudate, putamen) that correspond to behavioral evidence of learning. Specifically, younger adults engage the hippocampus early in a task when learning begins to emerge, whereas they recruit the dorsal striatum throughout the task (for reviews, see [14,15]). There is also recent structural imaging work that indicates globus pallidum involvement in IAL [16,17] and evidence of nucleus accumbens [18,19] and prefrontal cortex [14,15,20] involvement in associative learning. These findings are in line with classic computational models proposing that the hippocampus rapidly forms associations between stimuli and the basal ganglia (including the dorsal striatum) gradually learns associations over time [21,22]. Still, there are reports that the hippocampus remains involved throughout learning [23] or that the basal ganglia is implicated in both rapid, one-shot learning [24] as well as proceduralization (i.e., showing increased involvement with practice)[25-27]. Thus, the specific contributions of these regions to IAL remains unclear, especially in relation to differential engagement in aging.

When examining age group differences in the neural substrates of IAL, only a handful of studies have contrasted learning-related activity in younger and older adults across different stages of the task. Whereas one study found comparable recruitment of the hippocampus in both age groups during the early task stage [9], another study found that older adults increased hippocampal activity across task stages [28]. Similarly, relative to younger adults, older adults also showed comparable [29] or decreased recruitment [9,30] of the dorsal striatum during the late task stage. Importantly, however, these studies either used tasks that revealed no age group differences in learning [28,30] or confounded analyses of task stage with learning stage by examining age group differences in learning-related activity when there were (late task stage) or were not (early task stage) age group differences in learning performance [9,29]. Thus, it remains unknown whether effects of age on learning performance result from differential engagement of these neural substrates as a function of learning stage (where “early learning stage” corresponds to the task stage at which significant learning is first seen), while controlling for the effects of task stage (where “early task stage” corresponds to the first stage of performing the task).

To better understand the neural substrates of age-related associative learning deficits, we acquired fMRI data in 28 younger and 22 older healthy adults during performance of a cue-cue-target (triplet) learning task [16]. We aimed to assess whether previous reports of differential engagement of the hippocampus and basal ganglia in younger and older adults was specific to comparisons of IAL-related activity from task stages in which there were significant differences in learning performance (early task stage for both age groups) or whether they persisted when comparing task stages in which learning performance was matched across age groups (early task stage in younger adults and late task stage in older

adults). We further extended the existing fMRI literature by examining basal ganglia nuclei beyond the dorsal striatum, with additional analyses conducted across the whole brain.

Method

Participants

We recruited 29 younger and 26 older adults from the undergraduate research pool at the University of California, Riverside and surrounding communities, respectively. One younger and three older individuals were excluded for poor task performance (i.e., overall accuracy < 1.5 standard deviations below the mean of all younger and older participants) and one older participant was cut for having corrupted behavioral data files. All participants had normal general cognition (i.e., > 23 on the Montreal Cognitive Assessment, MoCA; [31]. Demographic and neuropsychological data for the final sample of 28 younger (20.8 ± 2.3 years, 20 female) and 22 older (73.6 ± 6.8 years, 8 female) adults can be found in Table 1.

Prior to enrollment in the study, participants were screened for conditions that would affect their ability to complete the computer-based task (e.g., uncorrectable vision, arthritis), prevent them from being able to enter the MRI scanner (e.g., non-MR compliant implants, difficulty lying in the supine position, claustrophobia), or impair their cognitive functioning (e.g., stroke, diabetes, uncontrolled depression). All participants provided informed consent and received course credit or compensation for participation. This study was conducted in compliance with the Institutional Review Board of the University of California, Riverside.

Triplet Learning Task

We developed an abbreviated, deterministic version of an implicit associative learning task (Triplet learning task, TLT; [8]), as previously reported [16]. In the TLT, participants viewed four open circles presented in a row on a white background. Each trial, or triplet, consisted of a cue-cue-target sequence (2000 ms) in which two “cue” circles filled in red (150 ms each) followed by one “target” circle filling in green (800 ms), with inter-stimulus intervals of 150 ms and an inter-trial interval of 600 ms. Participants passively viewed the red cues and were told to respond as quickly and accurately as possible to the location of the green target via MR-compatible button press.

Critically, the locations of the red cues could be used to predict the green target location. Of the 64 possible cue-cue-target combinations, we excluded 40 triplets in which any two events occurred in the same location (e.g., 111, 112, 121; where the number corresponds to the location of the four circles on the screen from left to right), as their performance reflects pre-existing response tendencies [8,32]. Of the 24 triplets that remained, we selected four to occur more often (high frequency, HF) and eight to occur less often (low frequency, LF), ensuring that cues and targets occurred in each location equally often.

Participants completed a total of eight runs. Only the first three and last three runs were performed during fMRI scanning and those will be reported here. Each five-minute run consisted of four blocks of 32 triplets, with the four unique HF triplets presented six times (75% frequency) and eight unique LF triplets presented once (25% frequency).

Mean accuracy and median reaction times were calculated for each block and each triplet type (HF, LF), and then averaged within each run. Mean of median reaction times were logarithmically transformed to control for age-related slowing [16,33]. We then calculated learning scores for each participant as the difference in mean accuracy or in mean of median reaction times between the triplet types (LF – HF) averaged across the first three (early task stage) or last three (late task stage) runs. Accuracy learning scores were multiplied by −1 so that positive values were indicative of better learning for both measures (i.e., a larger trial type difference).

Prior to these calculations, trials were excluded if they contained an artifact produced by the TTL (Transistor-Transistor Logic) pulses during functional scans, in which the same incorrect button response was recorded on every sixth and seventh trial for all participants. Because the artifact occurred systematically and throughout the task, it likely had minimal impact on IAL performance measures.

Outside of the scanner, participants completed a computer-based recognition task followed by a verbal post-test interview to test for awareness of the relationship between the cues and target, particularly for HF triplets (see [16] for more details). For the former, participants indicated via keyboard responses whether a series of HF, LF, or never presented (no frequency, NF) triplets occurred “frequently”, “infrequently”, or “not at all” during the scanned version of the TLT. For the latter, a trained researcher asked participants a series of verbatim questions about their strategy and whether they noticed any relationship between the first two “lights” and the third [8]. As in our study using the same subset of participants [16], examination of these data revealed that no participant was able to differentiate between HF and LF triplets or to accurately describe any relationship between the cues and targets, providing confidence that participants were not aware of the regularities learned here.

Imaging Data Acquisition

Imaging data were collected at the Center for Advanced Neuroimaging at the University of California, Riverside on a 3 Tesla Siemens Prisma MRI scanner (Siemens Medical Solutions, Malvern, PA) equipped with a 32 channel receive-only head coil.

A single T1-weighted magnetization prepared rapid acquisition gradient echo (MP-RAGE) sequence was acquired with the following parameters: repetition time (TR) / echo time (TE) = 2400 / 2.72 ms, field of view = 256 x 256 x 208 mm, flip angle = 8 degrees, and spatial resolution = 0.8 mm^3.

Six separate echo-planar imaging (EPI) pulse sequences were acquired during performance of the TLT task with the following parameters: TR / TE = 1750 / 32 ms, field of view = 221 × 190.4 mm, flip angle = 77 degrees, spatial resolution = 1.7 mm^3, 72 slices with no gap, AP phase encoding direction, GRAPPA acceleration factor = 2, and multiband factor = 3. To correct for susceptibility distortions in each participant’s functional data, two sets of spin echo EPI images with phase-encoding directions of opposite polarity were acquired using parameters identical to the EPI sequence in the functional runs, except TR / TE = 7700 / 58 ms.

Functional Imaging Data Analysis

Preprocessing.—Raw functional imaging data were preprocessed using FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). First, the data were corrected for susceptibility-induced distortions using TOPUP [34]. Next, distortion-corrected data were subjected to the following preprocessing steps in FEAT (FMRI Expert Analysis Tool): motion correction with MCFLIRT (Motion Correcting FMRIB's Linear Image Registration Tool), skull stripping using the brain extraction tool [35], spatial smoothing using a Gaussian kernel with a full width at half maximum of 5 mm, and high-pass filtering (100 s). Data were then registered to the participant's T1-weighted image using FLIRT (Jenkinson and Smith, 2001; Jenkinson et al., 2002), and then to the standard Montreal Neurological Institute (MNI) 152 template (resampled to 1.7 mm^3 resolution) using a combination of FLIRT and FNIRT (FMRIB's Nonlinear Image Registration Tool; Andersson et al., 2007). The final preprocessed data were used as input for the lower-level analyses.

Lower-Level Analyses.—For each participant and each run, we separately modeled each of the five combinations of trial type and response: correct responses to (1) HF or (2) LF targets, (3) incorrect responses to either triplet type, (4) no responses, and (5) trials with the TTL pulse artifact. These explanatory variables were convolved with a gamma-variate hemodynamic response function (standard deviation = 3 s, mean lag = 6 s). One contrast captured IAL-related activity by contrasting correct responses to HF > LF triplets.

Higher-Level Analyses.—To obtain separate estimates of fMRI activity for early and late task stages, two separate mid-level analyses were conducted for each participant to capture their unique variance across runs. Specifically, for each participant, one explanatory variable modeled IAL-related activity from the lower-level analysis separately across the first (early task stage) or last (late task stage) three runs and one contrast was used to combine these data.

Higher-level analyses were then conducted on outputs of the mid-level analyses using FSL's Local Analysis of Mixed Effects (FLAME) stage 1. Separate voxel-wise one sample *t*-tests first captured mean effects of IAL during the early and late task stages, separately for each age group. Separate voxel-wise unpaired *t*-tests then contrasted IAL-related activity between younger and older adults in (1) the early task stage (matched for task stage, but not IAL performance), (2) the late task stage (matched for task stage and IAL performance), and (3) the early task stage in younger adults and late task stage in older adults (matched for learned stage and IAL performance).

Because we had *a priori* hypotheses about the hippocampus and basal ganglia (caudate, putamen, globus pallidum, nucleus accumbens), our primary analyses were spatially restricted to a combined bilateral anatomical mask of these regions with a nonparametric statistical threshold of $p < 0.01$ (uncorrected, $k \geq 10$ voxels). Although liberal [39], this threshold was selected to allow for comparisons with earlier work [9,40] and was applied to a small mask containing only the *a priori* regions of interest. Additional analyses were spatially restricted to a whole brain gray matter mask conducted with a nonparametric

statistical threshold of $p < 0.005$ (uncorrected, $k \geq 40$ voxels). All regions of interest and the gray matter mask were defined by FSL's Harvard-Oxford atlases (> 50% probability).

Results

Learning Performance

Evidence of learning was assessed using separate one sample t-tests for each task stage (early, late) in each age group (younger, older) for each learning score (log transformed mean of median reaction time, mean accuracy), with significant effects indicating that the difference in performance to HF and LF triplets was different than 0 (Figure 1). For reaction time, significant learning was seen for both the early and late task stages in younger adults, ts(27) > 3.45, ps < 0.002, but only the late task stage for older adults, t(21) = 3.99, $p = 0.001$. One-tailed paired t-tests revealed that these learning scores were significantly larger in the late versus early task stage in older adults, $t(21) = -3.01$, $p = 0.004$, with a similar trend in younger adults, $t(27) = -1.46$, $p = 0.079$. For accuracy, learning scores did not differ from 0 for either task stage in any age group, ps > 0.13, and were therefore not used in subsequent analyses with the fMRI data.

Age group differences in learning were then probed using separate unpaired t-tests within and between task stages for the reaction time learning score (Figure 1). Results revealed a significant difference between early task stage learning scores in younger (0.041 ± 0.063 msec) and older (0.004 ± 0.060 msec) adults, $t(48) = 2.13$, $p = 0.038$. However, there were no age group differences between late task stage learning scores in younger (0.064 ± 0.048 msec) and older (0.048 ± 0.057 msec) adults, $p = 0.29$, or between early task stage learning scores in younger adults and late task stage learning scores in older adults, $p = 0.69$.

Mean Effects of IAL-Related Activity

Mean effects of IAL-related activity (HF > LF triplets) within the subcortical mask were assessed using separate voxel-wise one sample t-tests for each age group and task stage (Figure 2 and Table 2). During the early task stage, younger adults had significant activity in the left hippocampus whereas older adults had significant activity in the left hippocampus (directly adjacent to the cluster seen for younger adults) and right putamen. During the late task stage, only older adults showed significant activity in the left globus pallidum.

When assessing these effects across the whole brain during the early task stage (Figure 2 and Table 3), results revealed that younger adults had significant activity in the left angular gyrus, frontal pole, inferior frontal gyrus, and right temporal fusiform/parahippocampal gyrus, whereas older adults only had significant activity in the same left hippocampus cluster as in the subcortical mask analysis. During the late task stage, younger adults had significant activity in the left occipital pole and precuneus whereas older adults had significant activity in the left parahippocampal gyrus.

Age Group Differences in IAL-Related Activity Within Task Stages

We then used voxel-wise unpaired t-tests to separately assess age group differences in IAL-related activity within the subcortical mask during the early and late task stages (Figure

3 and Table 2). Relative to younger adults, older adults had significantly greater activity in two clusters of the left hippocampus during the early task stage and in the left globus pallidum during the late task stage.

When assessing these effects across the whole brain (Figure 3 and Table 3), younger adults had significantly greater activity than older adults in the left lateral occipital cortex during the early task stage, with no age group differences during the late task stage.

Age Group Differences in IAL-Related Activity Between Task Stages

Finally, we used a voxel-wise unpaired *t*-test to assess age group differences in IAL-related activity during the early task stage for younger adults and late task stage for older adults. Results revealed no significant age group differences in activity within the subcortical mask or when assessing these effects across the whole brain.

Effects of Sex

Given that younger adults had a significantly higher proportion of females than older adults (Table 1), all analyses were re-assessed after controlling for sex. Separate univariate ANOVAs were conducted for each dependent measure (learning score, fMRI parameter estimate), with age group as a random factor and sex as a covariate of no interest. Results revealed that the pattern of results remained unchanged.

Discussion

The current study assessed whether previous reports of differential engagement of the hippocampus and basal ganglia in older relative to younger adults during IAL reflect age group differences across early and late stages of the task, or whether they persisted after matching the age groups for learning stage (i.e., the task stage at which significant learning is first seen). When matched for task stage, we observed significant age-related increases (hippocampus) and decreases (occipital cortex) in IAL-related activity during the early task stage when older adults learned significantly less than younger adults, and significant increases (globus pallidum) during the late task stage when there were no age group differences in learning. Importantly, however, when the learning stage was matched across age groups (i.e., when comparing the task stage that first shows evidence of learning at the group level), results no longer revealed significant age group differences in IAL-related activity. Together, these findings suggest that older adults are recruiting the same brain regions as younger adults when learning associations between events, albeit at a later task stage.

Behaviorally, we observed age group differences in IAL during the early, but not late, task stage. Reaction times were significantly faster to HF than LF triplets in younger adults during both task stages, whereas older adults did not show significant learning until the late task stage. This finding is largely consistent with previous behavioral studies using probabilistic versions of the TLT, in which the magnitude of learning increases across trials especially in younger compared to older adults [5,6,8,41]. Finding significant learning effects for reaction time, but not accuracy, were also expected in light of previous implicit associative learning studies [5,8,9,33]. Often, accuracy remains high in the TLT task for both

HF and LF trial types (>80% as in the present study) but specific task parameters (e.g., feedback to maintain specific accuracy levels, amount of training, or response deadlines) may bias the extent to which learning is exhibited in reaction time or accuracy measures. However, our results differ from most previous neuroimaging studies as their IAL tasks did not yield significant age deficits in learning [28,30,40,42]. This is likely due to multiple methodological differences across IAL tasks. For example, the current TLT version may have facilitated learning in younger and older adults and amplified age group differences by using a more deterministic regularity, fewer unique triplets, and more exposures to each triplet. Compared to previous studies that used more probabilistic regularities [9,28], the deterministic structure used here likely contributed to older adults to being able to learn the regularity, albeit at a slower pace [43]. The resulting pattern of age effects was critical for subsequent fMRI analyses aimed at disentangling the effects of task stage and learning stage on the neural substrates of learning cue-target associations in healthy aging.

We first sought to replicate previous reports of older adults differentially engaging the hippocampus and basal ganglia during early and late task stages, respectively. Consistent with prior studies [28,40], during the early task stage we observed significantly greater IAL-related activity in the hippocampus in older adults compared to younger adults. Early recruitment of the hippocampus is consistent with its role in forming associations that are less well-learned, compared to later in the task when the associations may be consolidated into memories [18-20]. Our pattern of results also align with the notion that the hippocampus propagates these initial learning-related signals to the globus pallidum via the nucleus accumbens [21,22,44,45]. Of note, the hippocampus activity was localized to a subfield previously shown to be involved in learning (cornu ammonis 1, CA1)[23]. However, it is unclear why older adults are overrecruiting this region, particularly when they did not exhibit learning during this early task stage, unlike younger adults. One possibility is that the increased hippocampus recruitment is reflective of older adults requiring more effort and time to form, maintain, and respond to the regularities among events [46], thereby resulting in less rapid association formation when compared to younger adults. These findings provide partial support for the notion that IAL-related deficits in aging are due to differential engagement of the neural substrates that mediate early task stages.

Similar to prior studies finding age group differences in basal ganglia recruitment during IAL [9,30], during the late task stage we observed significantly greater IAL-related activity in the globus pallidum in older adults compared to younger adults. As with the early task stage, this finding suggests that older adults differentially recruit the neural substrates of IAL that mediate the late task stage. Finding significant IAL-related activity in the hippocampus and putamen during the early task stage and in globus pallidum during the late task stage is remarkably consistent with predictions based on computational models and other theories proposing that the hippocampus and basal ganglia communicate via a functional loop, especially when associations are less well-learned [21,22]. These results are also consistent with the hypothesis that the hippocampus responds to information not currently stored in long-term memory (e.g., during early learning) and then propagates learning-related signals to the globus pallidum via the nucleus accumbens until the associations are more well-learned [44]. Although often overlooked in earlier IAL studies, the globus pallidum may be involved in maintaining the cue and target locations in working memory as these

associations are being learned [47]. Moreover, this finding extends our recent diffusion imaging work, in which we found that microstructural properties of globus pallidum gray matter related to better IAL performance in younger and older participants from the current study [16], thereby providing converging evidence between structural and functional markers of IAL in adults across the lifespan.

However, a notable limitation of these analyses is that, regardless of whether there were (early task stage) or were not (late task stage) significant age group differences in learning performance, within-task stage comparisons are confounded by younger and older adults being in different learning stages. For example, when comparing age groups within the late task stage, younger adults may be in a later, potentially more automatized learning stage because they had demonstrated significant learning since the early task stage, whereas older adults who first show evidence of learning in the late task stage may still be engaged in processes related to the early acquisition of regularities. To address this confound, we assessed whether age group differences in learning-related activity persisted when the groups were matched for learning stage by comparing IAL-related activity in younger adults during the early task stage to older adults during the late task stage. When matched for learning stage in this way, there were no longer any significant age group differences in IAL-related activity. This finding is comparable to at least one previous study that reported similar patterns of IAL-related activity in younger and older adults [29], although these effects were again confounded by task stage – with no differences in IAL-related activity between task stages, but with age group differences in learning performance during the early (and not late) task stage. Nonetheless, our result supports the notion that older adults recruit a similar network as younger adults when learning associations between events, albeit at a later task stage.

In light of well-documented anatomical connections between the basal ganglia and cortex [48,49] and between the hippocampus and cortex [50,51], we also assessed age group differences in IAL-related activity across the brain. Younger adults had significant activity in the temporal fusiform/parahippocampal gyrus during the early task stage, whereas older adults recruited the parahippocampal gyrus during the late task stage. Finding significant activity in this region for both age groups when behavioral evidence of IAL began to emerge is consistent with previous studies [18,28,52] and theories [21,22] implicating medial temporal structures beyond the hippocampus in early associative processes. It also further supports the notion that younger and older adults recruit similar regions to learn associations between events, but that this recruitment is delayed in aging. As with studies using other IAL tasks [14,15,20], younger adults also had significant activity in the prefrontal cortex during the early task stage, which may reflect its role in mediating the interaction between the hippocampus and basal ganglia [53,54] or working with the globus pallidum to maintain associations in working memory [47]. Together, these findings suggest that the medial temporal and prefrontal cortices contribute to IAL processes occurring in the hippocampus and basal ganglia. Future studies, particularly those combining structural and functional imaging, will be important for understanding how these interconnected regions interact throughout learning.

In closing, this study is the first to disaggregate task stage and learning stage effects on the engagement of neural substrates of IAL in younger and older adults by comparing IAL-related activity at each task stage when behavioral performance was (early) and was not (late) significantly different between age groups and when the groups were matched at the early stage of learning. Results revealed differential recruitment of the hippocampus and globus pallidum in younger and older adults in the early and late task stage, respectively, but comparable recruitment of these learning systems across age groups in their respective early learning stage. Together, these findings demonstrate that although IAL and its neural substrates are delayed in aging, older adults are not differentially engaging the hippocampus and basal ganglia when matched for learning stage.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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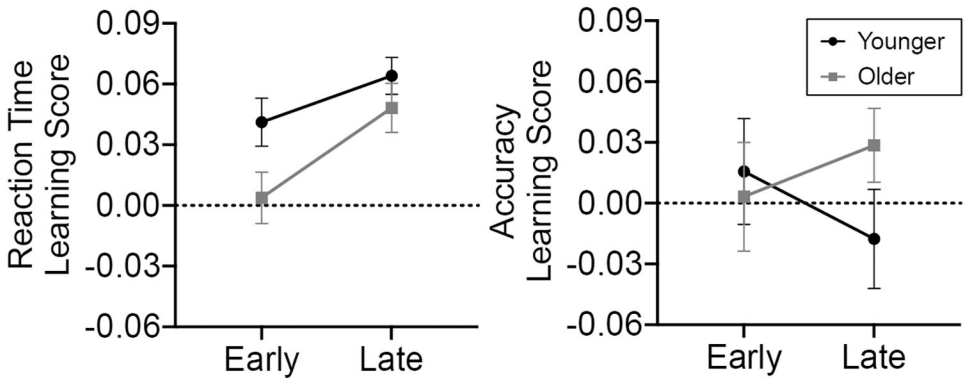

Figure 1.

IAL learning scores (i.e., difference scores between high and low frequency triplets) are shown for log transformed mean of median reaction time (left) and mean accuracy (right) for each task stage (early, late) in younger (black) and older (gray) adults. For both measures, more positive values are indicative of better learning. Error bars represent the standard error of the mean.

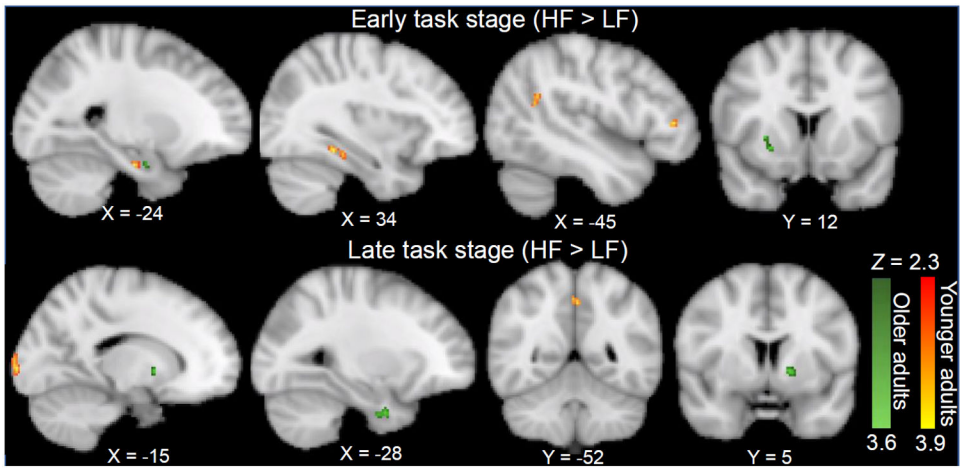

Figure 2.

Significant mean effects of IAL-related activity during early (top) and late (bottom) task stages are displayed separately for younger (red-yellow) and older (green-light green) adults. Displayed results were thresholded at $p < 0.01$ (uncorrected) and presented in Montreal Neurological Institute (MNI) 152 space (right = left).

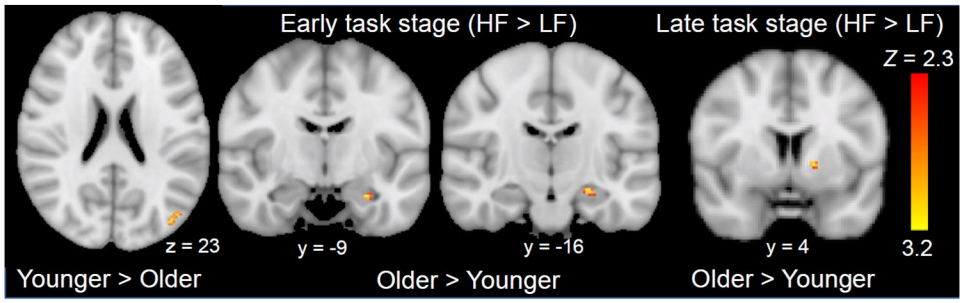

Figure 3.

Significant age group differences in IAL-related activity are shown for the comparison when learning performance was (early task stage) or was not (late task stage) significantly different between younger and older adults. No differences were observed when comparing task stages in which learning performance was matched across age groups. Displayed results were thresholded at $p < 0.01$ (uncorrected) and presented in Montreal Neurological Institute (MNI) 152 space (right = left).

Table 1.

Demographic information and neuropsychological test results.

	Younger Adults	Older Adults	t / χ^2
Age (years)	20.8 (2.3)	73.6 (6.8)	**38.15**
% Female	71%	36%	**6.15**
Education (years)	13.7 (1.4)	16.5 (3.6)	**3.75**
% Non-Hispanic[a]	64%	100%	**8.12**
% White[b]	29%	81%	**12.07**
% Right-Handed	86%	77%	0.59
MoCA	27.3 (1.4)	27.2 (1.9)	0.30
RAVLT Total Recall	49.9 (7.3)	37.6 (11.1)	**4.77**
RAVLT Recognition	13.5 (2.9)	12.7 (2.0)	1.37

Notes. Scores are presented as mean (standard deviation) or percent (%) for each age group. Significant group differences at $p < 0.05$ are indicated by bolded t (mean scores) or χ^2 (% scores) statistics. RAVLT = Rey Auditory Verbal Learning Test, MoCA = Montreal Cognitive Assessment.

[a]One older participant did not provide ethnicity data.

[b]Four younger participants did not provide race data.

Table 2.

Voxel-wise IAL-related activity from the subcortical analyses.

	Region	*x*	*y*	*z*	z-max	Voxels
Early task stage						
Younger adults	L hippocampus	−24	−16	−24	3.85	38
Older adults	L hippocampus	−27	−9	−24	3.57	74
	R putamen	25	12	−6	2.83	27
Older > younger	L hippocampus	−24	−16	−16	3.07	23
	L hippocampus	−26	−9	−23	3.01	14
Late task stage						
Older adults	L globus pallidum	−15	5	−1	3.40	28
Older > younger	L globus pallidum	−15	5	−1	3.01	15

Notes. Clusters that exhibited significant mean effects or age group differences in IAL-related activity during each task stage (early, late) are described with their peak voxel (x, y, z coordinates in Montreal Neurological Institute 152 space), corresponding maximum z-statistic (*Z*-max), and spatial extent (number of voxels). R = right, L = left.

Table 3.

Voxel-wise IAL-related activity from the whole brain analyses.

	Region	*x*	*y*	*z*	z-max	Voxels
Early task stage						
Younger adults	L frontal pole	−12	59	−14	3.22	72
	R temporal fusiform cortex	34	−39	−13	3.55	56
	L angular gyrus	−44	−55	22	3.17	47
	L inferior frontal gyrus	−46	37	6	3.15	47
Older adults	L hippocampus	−27	−9	−24	3.57	65
Younger > older	L lateral occipital cortex	−43	−77	20	3.17	43
Late task stage						
Younger adults	L occipital pole	−15	−102	1	3.44	103
	L precuneus	−7	−44	49	2.97	43
Older adults	L parahippocampal gyrus	−29	0	−35	3.42	50

Notes. Clusters that exhibited significant mean effects or age group differences in IAL-related activity during each task stage (early, late) are described with their peak voxel (x, y, z coordinates in Montreal Neurological Institute 152 space), corresponding maximum z-statistic (*Z*-max), and spatial extent (number of voxels). R = right, L = left.