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Effects of aging on transient and sustained successful memory encoding activity

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Abstract

Event-related fMRI studies have investigated age-related changes in encoding by identifying greater activity for items that are later remembered than for those that are forgotten (difference in memory, or Dm). The present study used hybrid blocked/event-related analyses to distinguish between *transient Dm* versus *sustained Dm*. Dm was identified as parametric increases in encoding activity as a function of a combined subsequent memory/confidence scale. Dm was measured in each trial (transient activity) and in blocks of eight trials (sustained activity). Transient Dm analyses showed age-related reductions in the left hippocampus but increases in left prefrontal cortex (PFC). Sustained Dm analyses showed age-related reductions in right PFC, but no region showing increased activity in older adults. These findings suggest that during semantic classification older adults show less spontaneous hippocampal-mediated encoding processes, but greater PFC-mediated semantic processes. Additionally, the decline in sustained Dm in PFC may involve age-related deficits in sustained attention that impact encoding processes. The results underscore the importance of investigating aging effects on both transient and sustained neural activity.

Keywords

Aging; Hybrid analysis; Subsequent memory; Encoding; fMRI

1. Introduction

Memory for personally experienced past events, or episodic memory, is one of the cognitive functions most affected by aging [16]. Older adults' difficulties with episodic memory may reflect deficits occurring during the initial storage of the information (encoding), the maintaining of information (storage), as well as recovery of the stored information (retrieval). Behavioral studies that manipulated attention during these two phases suggest that encoding deficits play a major role in older adults' episodic memory deficits [1,15,27]. Unfortunately, it is difficult to isolate encoding from retrieval differences using behavioral paradigms. The ideal methods to investigate this issue are functional neuroimaging techniques, such as functional MRI (fMRI), which provide a measure of the effects of aging on encoding activity. Moreover, using event-related paradigms, these techniques can isolate neural activity specifically associated with successful encoding processes and determine how this activity changes as a function of aging. This was the goal of the present study.

To isolate successful encoding activity, event-related fMRI studies have used the *subsequent memory paradigm* [37], which identifies brain regions showing greater study-phase activity for items that are remembered than for those that are forgotten in a subsequent memory test. The difference between remembered and forgotten items is known as difference in memory or Dm. In fMRI studies, Dm has usually been found in medial temporal lobe (MTL) and prefrontal cortex (PFC) regions (e.g., [5,19], e.g., [34,43,51]). To our knowledge, only two event-related fMRI studies have applied the subsequent memory paradigm to investigate the effects of aging on encoding processes. First, a word encoding study by Morcom et al. [33] found that both young and older adults showed Dm in left MTL and PFC regions, and that Dm activity in PFC regions was more bilateral in older adults. The latter finding is consistent with abundant evidence of increased bilaterality in older adults [11]. Second, a picture encoding study by Gutchess et al. [25] found that, compared to young adults, older adults showed reduced Dm in bilateral MTL regions but greater Dm in bilateral PFC regions. Thus, taken together, these studies suggest that older adults may show reduced Dm in MTL and increased Dm in PFC. According to Gutchess et al., additional PFC recruitment in older adults could help compensate for the deficits in MTL recruitment. Consistent with this idea, they found in older adults a negative correlation between encoding activity in these two regions.

However, older adults do not always show greater encoding-related PFC activity than younger adults. Actually, several studies using positron emission tomography (PET) found age-related decreases in encoding activity in left and right PFC regions [1,8,24]. An important difference between these earlier PET studies and the recent fMRI studies described above is that the former used blocked designs, which are sensitive to both transient (trial-related) and sustained (blocked-related) activity, whereas the latter used event-related designs, which measure mainly transient activity. Thus, a potential explanation of inconsistent PFC findings is that, compared with younger adults, older adults show increased transient activity but decreased sustained activity. One possibility is that older adults are successful in engaging certain cognitive processes in response to the specific demands of each trial, but unsuccessful in sustaining attention throughout the whole encoding block. This hypothesis fits with the notion that *environmental support* attenuates age-related cognitive decline [17]: the concrete task performed in each trial guides processing, whereas maintaining attention throughout the task is more dependent on self-initiated processing. Moreover, when the encoding task requires semantic retrieval, which is a cognitive function relatively well preserved in older adults (e.g., [40]), older adults may rely on this preserved ability and recruit PFC regions that partly compensate for MTL deficits. In contrast, sustained attention is a cognitive function significantly impaired in old age [32,38], and this deficit could have contributed to the age-related PFC decreases observed in blocked PET studies. To investigate the hypothesis that, during encoding, older adults show compensatory recruitment of transient PFC activity but deficits in sustained PFC activity we conducted a subsequent memory fMRI study using a hybrid event-related/blocked analysis.

Several fMRI studies have used hybrid event-related/blocked designs to distinguish transient versus sustained activity [7,20,36,50]. The typical method is to separate blocks of trials by an inter-block fixation period, in order to allow block-related analyses, and, simultaneously separate the trials within each blocked by jittered inter-trial fixation intervals, in order to allow trial-related analyses (see Fig. 1A). fMRI data is typically analyzed using the general linear model (GLM) that include regressors for the blocks as well as regressors for the trials, and that compares block-related activity to the inter-block fixation baseline and trial-related activity to the inter-trial fixation baseline. Although inter-block fixation intervals are critical if one wishes to compare memory-related block activity to a non-memory baseline, they are not necessary when the focus is on a “tighter” memory-related contrast. Thus, because we

were interested in changes in activity as a function of subsequent memory, we eliminated inter-block intervals, and included only jittered inter-trial intervals, as in a standard event-related paradigm (see Fig. 1B). Thus, in our study the term hybrid applies specifically to the GLM analyses, which included both block and trial regressors. The block regressors corresponded to groups of eight trials.

Another innovation in our subsequent memory paradigm is that instead of coding each encoding trial as either remembered or forgotten, we measured both accuracy and confidence at test and scored each encoding trial in a three-level subsequent memory scale: forgotten, remembered with low confidence, and remembered with high confidence. Thus, instead of subtracting forgotten from remembered trials, we used a parametric approach to identify encoding activity that increased as a function of subsequent memory scores. The subsequent memory score for each block was the average of the scores of the trials within the block (see Fig. 1B). Using GLM, transient Dm was identified as trial-related activity that varied with subsequent memory scores, and sustained Dm was identified as blocked-related activity that varied with subsequent memory scores. Finally, we compared activity in young and older adults to identify the effects of aging on transient and sustained Dm. This is the first fMRI study distinguishing age-related changes on transient versus sustained Dm.

Based on previous subsequent memory studies of aging [25,33], we predicted older adults would show reduced transient Dm in MTL regions but increased transient Dm in PFC regions. The critical question was whether the effects of aging on PFC activity would be similar or different for transient versus sustained Dm. Based on the results of blocked PET studies, we predicted that the sustained Dm in PFC would be reduced in older adults. Thus, we predicted that in PFC regions aging would increase the transient Dm but reduce the sustained Dm. Age-related reductions in sustained Dm may reflect deficits in sustained attention, which has been found to be impaired by aging [32,38] and to involve deficits in frontal function [13]. If age-related decreases in sustained Dm in PFC are due to sustained attention deficits, then these decreases are likely to be right-lateralized, given that PFC activity related to sustained attention is usually greater in the right than in the left hemisphere (or a review, see [47]).

2. Methods

2.1. Participants

Twelve healthy younger (eight males), with an average age of 22.2 years (S.D. = 3.5) and 12 healthy older adults (seven males), with an average age of 67.4 years (S.D. = 6.7) were scanned and paid for their participation. See Table 1 for older participant characteristics. Younger adults were all students at Duke University and older adults were recruited from the Durham, NC community. Written informed consent was obtained from all participants for a protocol approved by the Duke University Institutional Review Board.

2.2. Stimuli

The stimuli consisted of 304 words equally divided into four categories, animal, place, object, and job. All words could be categorized into one, and only one, of the four categories. Two hundred and twenty-four words were used for the encoding task, inside the scanner, and an additional 80 words were presented at retrieval only, outside of the scanner.

2.3. Procedure

During two fMRI scans, participants performed a category classification task, which served as the encoding phase for a surprise memory test after the scanning session. During three other scans, they performed an unrelated motor learning task, results of which are not

reported in this article. Each fMRI scan began with a 15-s fixation period in order to allow image stabilization, and there was another 15-s fixation period in the middle of the scan. Each run consisted of 112 words, displayed individually for 1500 ms and followed by an inter-trial fixation period, which varied randomly between 500 and 1250 ms. This random jitter allowed for words to be analyzed in both an event-related and a blocked manner. Eight words (four following each fixation block) were regarded as practice trials and removed from analysis. Each encoding run lasted 4.8 min and alternated with a second unrelated motor learning task (run order: motor learning–encoding–motor learning–encoding–motor learning).

During the encoding phase in the scanner, participants were asked to make a semantic judgment pertaining to each word. On each trial, a single word was displayed in the center of the screen. Below the word, the first letter of the four category alternatives (a, p, o, j) was displayed in order to remind participants about the possible responses. Participants were instructed to respond as quickly and accurately as possible with a button press corresponding to the category to which the word belonged. Encoding was incidental, as participants were unaware of a subsequent memory test.

During the recognition test, which followed approximately 20 min after the scanning session, participants were presented with the 208 old words intermixed with 80 new words, from the same four categories. They were asked to make old/new judgments and indicate their confidence (definitely old, probably old, probably new, definitely new). Again, words were presented one at a time in the center of a computer screen. The memory score was displayed below each word. Words were presented for 3 s, during which time participants pressed a key corresponding to their recall of the word.

3. fMRI methods

3.1. Scanning

Images were collected using a 4T GE scanner. Stimuli were presented using liquid crystal display goggles (Resonance Technology, Northridge, CA) and behavioral responses were recorded using a four button fiber optic response box (Resonance Technology). Scanner noise was reduced with earplugs and head motion was minimized using foam pads and a headband. Anatomical scans began by first acquiring a T1-weighted sagittal localizer series. The anterior (AC) and posterior commissures (PC) were identified in the mid-sagittal slice and 34 contiguous oblique slices were prescribed parallel to the AC-PC plane. High resolution T1-weighted structural images were acquired with a 12 ms repetition time (TR), a 5 ms echo time (TE), 24 cm field of view (FOV), 68 slices, 1.9 mm slice thickness, 0 mm spacing, and 256×256 matrix. Echoplanar functional images were acquired using an inverse spiral sequence with a 1500 ms TR, 31 ms TE, 24 cm FOV, 34 slices, 3.8 mm slice thickness, resulting in cubic 3.8 mm^3 isotropic voxels, and 64×64 image matrix.

3.2. fMRI analyses

All image preprocessing and statistical analyses were performed using Statistical Parameter Mapping software implemented in Matlab (SPM2; Wellcome Department of Cognitive Neurology, London, UK). After discarding the first six volumes, images were corrected for slice-timing and motion, then spatially normalized to the Montreal Neurological Institute (MNI) template and smoothed using a Gaussian kernel of 8 mm FWHM. For each subject, item-related activity was modeled with a stick function corresponding to stimulus onsets, convolved with a canonical hemodynamic response function (HRF) within the context of the GLM, as implemented in SPM2. Confounding factors (head motion, magnetic field drift) were also included in the model. According to our motion parameters no participant moved more than 3 mm in any direction either within or across runs. Thus, no data was eliminated

in either age group due to motion artifacts. To further address this issue we calculated both the mean and maximum value for each motion parameter for each subject for each direction (x , y , z , pitch, roll, and yaw). We then performed unpaired t -tests on each motion parameter across age groups. No test approached significance (p ranged from 0.1 to 0.96 across all tests).

In order to identify regions associated with both transient and sustained activity, a parametric approach was used involving three steps. As a first step, we created a three-point transient Dm scale by combining subsequent memory scores with confidence ratings (1 = subsequently forgotten, 2 = subsequently remembered with low-confidence, 3 = subsequently remembered with high-confidence). Next, we created a sustained Dm scale by averaging the transient Dm scores within a given block of eight words. Parametric weightings were applied in order to use a common method for assessing both item and block-related Dm activity. Since the average memory score of the blocks was a composite score of individual items within the block it followed more or less a continuous scale. Thus, the use of parametric weighting and analysis allowed for assessing the full range of scores.

As a second step, a GLM was constructed in which trial-related activity was modulated simultaneously by the transient and sustained Dm scales using the first order parametric modulation option integrated in SPM2. The correlation between the transient and sustained regressors did not exceed 0.5 in any individual. The average correlation was 0.39 (S.D. = 0.05) in the young adults and 0.39 (S.D. = 0.04) in the older group. While overlap between regressors is always a concern in mixed models, these correlations are in accord with the ones found in published fMRI studies using hybrid analyses (e.g., [36]).

For assessing common areas of activation associated with transient Dm across age groups, a conjunction map was created thresholding each age group's random effects of the transient parametric regressor at $p = 0.05$ and eight voxels. A similar analysis was conducted for sustained Dm. Due to the lack of overlap in sustained Dm activity across groups, a second analysis was conducted assessing within-group effects in sustained functioning in each group ($p < 0.005$ with an extend threshold of eight voxels). These results are reported in Table 3.

For assessing age effects, we used a region-of-interest approach. First, we identified those regions that show significant within-group effects at $p < 0.005$ with minimum cluster size of eight voxels. Within that restricted set of regions, we tested for group differences at $p < 0.05$, again, with a minimum cluster size of eight voxels. (The voxel-wise probability for false positive activation within these regions is $p = 0.00033$ for the within-group effects and $p = 0.021$ for the group differences [22].) For illustrative purposes a second set of analyses were conducted. For each age group subsequent memory scores for each trial were categorized into two bins—high memory (all hits) and low memory (all misses). Each bin was entered as a separate trial type in the model. A similar analysis was repeated for blocks, based upon the average block score. The difference in the parameter estimates for subsequent high and low memory scores – for events and blocks – were used to plot the bar graphs depicting fMRI effect sizes shown in Figs. 2 and 3.

4. Results

4.1. Behavioral results

Subjects responded incorrectly during encoding less than 1% of the time, leading to the inclusion of all trials in the analyses. Table 2 lists the proportion of hits and false alarms (FAs) within each confidence level for both age groups, as well as encoding reaction times (RTs) for subsequently remembered and forgotten items. A 2 (group: young, old) \times 2

(memory: hits, false alarms) \times 2 (confidence: high, low) ANOVA revealed a significant main effect of memory, $F(1, 1) = 172.47$, $p < 0.001$, with participants showing significantly more hits than FAs overall, and a significant main effect of confidence, $F(1, 1) = 19.53$, $p = 0.002$, showing greater high (versus low) confidence responding overall. Furthermore, results revealed a memory \times confidence interaction, $F(1, 21) = 115.69$, $p < 0.001$, indicating that participants made significantly more hits than FAs associated with high confidence, than with low confidence. Neither the main effect of group, nor any interaction involving group reached significance. Additionally, two-sample t -tests comparing the groups in Hits, FAs, and Hits–FAs revealed no significant differences, either for high or for low confidence responses. To ensure that activation differences between remembered and forgotten trials were not confounded with differences in time-on-task, two-sample t -tests were conducted to compare encoding RTs for subsequently remembered versus forgotten words. These tests also revealed no significant differences within either group. Furthermore, a 2 (group: young, old) \times 2 (subsequent memory: remembered, forgotten) ANOVA on encoding RTs revealed no significant main effects or interactions. Thus, activation differences between subsequently remembered and forgotten words cannot be a result of greater looking time or exposure during encoding. Furthermore, the data was examined for evidence of primacy and recency effects. No evidence for either was detected—either within the individual trial or the block Dm measure.

4.2. fMRI results

Table 3 reports common areas of activation for young and old adults associated with transient and sustained Dm. As previously noted, Dm was identified as parametric increases in encoding activity as a function of the three-level subsequent memory score. Transient Dm showed typical subsequent memory effects across both age groups, including significant activations in left PFC and left MTL regions. Sustained Dm showed only one common area of activation across groups, left parietal. Assessed separately, sustained Dm was associated with bilateral PFC, bilateral temporal, caudate, and visual areas in younger adults and anterior cingulate, caudate, and visual cortex in older adults. Table 4 lists brain regions that showed significant age-related differences in activation, specific to the transient Dm or the sustained Dm. Transient Dm showed age-related reductions in a number of brain regions, including the left hippocampus (see Fig. 2B). The only region in which older adults showed increased transient Dm activity compared to young adults was left dorsolateral and anterior PFC (see Fig. 2A). Sustained Dm activity showed age-related reductions in right PFC (see Fig. 3), as well as in anterior temporal and insula regions. No region showed greater sustained activity in older adults.

To confirm that the age-related reduction in right PFC reflected sustained rather than misapplied transient activity, we conducted two separate sets of ancillary SPM analyses. First, using the assumed hrf as done in the original analyses we conducted two additional analyses: one including only the event-related regressor and the other, only the block-related regressor. In the first analysis, using the event-related regressor only, the right PFC region in Fig. 3 did not show a significant age-related difference (nor significant activation in younger adults). The second analysis, using only the block regressor alone, did produce a significant age-related difference in right PFC (as well as significant activation in this region in younger adults). These results confirm the sustained nature of the age-related difference in right PFC activity. Second, using a finite impulse response (FIR) model, we modeled the block regressor—for both high and low memory blocks, for both younger and older adults. We assessed the time-courses for the peak voxel within each of the right PFC ROIs identified in the in the Y > O group analysis. Results indicated that while younger adults showed a clear difference in sustained activity between high and low memory blocks, the older adults did not. Thus, we conclude that the age-related difference in memory (HighvLow) in the right

PFC is indeed captured by the block regressor and is not a result of misattributed transient activation. The finding of qualitatively similar transient activity for young and old (only quantitative differences) but qualitatively different sustained activity underscores the importance of looking at the effects of aging on sustained activity.

In order to confirm that the aforementioned findings result from transient and sustained Dm effects and are not an analysis-specific finding two follow-up analyses were conducted. In each, the hybrid analysis was re-run with both blocks of 6 or 10 items. While the activations in each analysis differed slightly, the main findings were replicated (i.e., peak coordinates of main findings fell within the cluster reported in the original analysis). We therefore conclude that the reported results are generalizable to blocks of varying length and are not analysis-specific.

5. Discussion

The present study utilized a mixed design analysis to assess the effects of aging on transient and sustained activity associated with successful encoding (Dm). The results provided two main findings. First, consistent with our predictions, event-related analyses yielded an age-related reduction in transient Dm in left MTL coupled with an age-related increase in transient Dm in left PFC. This finding is consistent with previous event-related fMRI studies of aging, and with the idea that older adults compensate for MTL deficits by recruiting PFC functions. Second, also consistent with our predictions, block-related analyses yielded an age-related decrease in sustained Dm in right PFC. This finding is consistent with evidence that older adults have difficulty in sustained attention and context maintenance. The two main findings are discussed in separate sections below.

5.1. Transient Dm: age-related reduction in left MTL, age-related increase in left PFC

Subsequent memory paradigms show item-specific subsequent memory effects associated with both frontal and MTL activity [5,26,51]. In the current study older adults showed reduced transient Dm activity in left MTL but increased transient Dm activity in left PFC (see Fig. 2). These findings extend the results of Gutchess et al. [25] by demonstrating that these effects are specific to transient Dm activity. The age-related reduction in MTL activity we found in high-performing older adults challenges the popular idea that cognitive deficits in older adults reflect mainly a decline in PFC function [52]. Early functional neuroimaging studies of memory and aging tended to support this frontal hypothesis because they usually found age-related activity reductions in PFC but not in MTL [10]. This pattern was consistent with cross-sectional volumetric MRI data suggesting that MTL atrophy in healthy aging is modest when compared to PFC atrophy [45]. It has also been suggested that, whereas healthy aging is primarily associated with PFC dysfunction, MTL dysfunction is a feature of pathological aging [6]. Consistent with this idea, Daselaar et al. [18] found reduced MTL activity during encoding in low-performing but not in high-performing older adults. In contrast with the emphasis on PFC as the main cause of older adults' memory deficits, the present study demonstrated a significant reduction in MTL activity associated with successful encoding in a group of high-performing older adults, who performed as well as young adults in a subsequent memory test. The reduction in MTL activity is consistent with recent volumetric MRI evidence based on longitudinal contrasts which clearly shows a significant MTL atrophy in healthy older adults, particularly in the hippocampus [46]. Thus, the present study suggests that MTL dysfunction plays an important role in normal aging, even among high-functioning individuals.

However, in the present study, the age-related reduction in MTL encoding activity was not associated with a reduction in memory performance. A possible explanation is that the age-related deficit in MTL function was offset by the observed age-related increase in left PFC

activity (see Fig. 2). As previously noted, left frontal activity is associated with semantic processes. Thus, additional recruitment of the left dorsal lateral PFC in older adults could reflect deeper or more elaborate semantic processing on their parts while executing the semantic classification task. The fact that this activation is associated with remembered words, in turn supports a role of increased semantic processing in successful memory performance in older adults [8]. Furthermore, increased activity in areas associated with semantic processing has been found to facilitate memory performance in young adults after a 48 h delay [49] additional to that supporting memory after only a 30 min delay. Difficulty associated with this longer delay, may be analogous to that experienced by older adults after a shorter delay (e.g., [33]). Alternatively, it is possible that the increased activity in left PFC results from greater phonological processing or rehearsal in older adults. However, given the semantic nature of the encoding task coupled with the rate of presentation of the words the authors feel that it is more likely that semantic elaboration is a more plausible explanation. Increased activity in older adults is often regarded as compensatory [11]. A recent meta-analysis of pre-frontal function and aging concluded that left dorsal PFC was often recruited to a greater extent in older compared to younger adults, and reflect functional compensation [44]. The strength of this functional argument in the current study is augmented by the fact that no performance difference exists between the age groups. Though the encoding task is incidental, later memory in older adults is supported by the engagement of additional semantic processing during encoding compared to that undertaken by younger adults. Thus, the increased activity may represent deeper semantic processing undertaken by the older group, facilitating encoding and subsequent memory in a way that offsets deficits in hippocampal functioning. Furthermore, Dm-related compensation occurs despite the incidental nature of the encoding task. Unaware of the later memory task, differential successful Dm activity between age groups is a corollary of differential processes undertaken to perform the semantic classification task at hand. Thus, results indicate that altered neural processing undertaken by older adults in one task can be compensatory when executing future cognitive functions.

5.2. Sustained Dm: age-related reduction in right PFC

Like previous work by Otten and colleagues [34,35], the current study also found subsequent memory effects for words in right PFC. Furthermore, younger adults demonstrate increased activation in right PFC associated with sustained Dm compared to older adults (see Fig. 3). Right PFC activation has been associated with attentional processes, among other cognitive operations [14,39]. As such, results indicate that younger adults, able to maintain attentional focus across an encoding set, showed enhanced memory for those items within the set; whereas an attentional dysfunction in older adults impedes sustained Dm in this area.

Age deficits in attentional processes may be linked to age deficits in context processing resulting from age-related changes in PFC and dopamine function [4]. In the current task, maintaining a contextual representation of the four categories and task instructions may help to focus attentional processes and response criteria. When context maintenance fails, so do encoding processes that aid in successful subsequent memory. Dopamine projections within PFC are posited to regulate context processes, maintaining attention on current task demands and filtering out interfering noise [4]. Thus, age-related decreases in dopamine function within PFC [2] could severely alter this system. Though increased LPFC activations during transient Dm in older adults do not support this conclusion, it is possible that dopamine functioning may be more critical for sustained than transient functioning.

5.3. Other findings

In addition to left MTL, older adults showed reduced transient Dm activity in bilateral visual cortex, dorsal precuneus, and sensorimotor cortex. Reduced visual activity during remembered items was also observed by Gutchess et al. [25], and is consistent with evidence of age-related deficits in sensory processes. Age-related reductions in occipital activity coupled with increased prefrontal were also observed across several other cognitive tasks (working memory, visual attention, and episodic retrieval) [12]. These findings are consistent with the view that occipital reductions are indicative of a common factor theory of aging, positing that sensory deficits form the basis of cognitive deficits [28]. Furthermore, prefrontal increases are regarded as functionally compensatory in aging, and have been associated with age-related decreases in both MTL [25] and occipital activity [23,31].

Precuneus activity during episodic retrieval [9,29,30] has been attributed to the retrieval of item–context associations. Activation of the precuneus in the current study was associated with successful encoding and may have arisen from the need to retrieve category–word associations. Following, the strength of the associations aided in a more durable memory trace leading to better memory in younger adults.

Older adults also exhibited decreased sustained Dm in anterior lateral temporal and insular regions. Previous research has linked the anterior lateral temporal lobe to semantic processing [21], indicating that this region may reflect deep semantic encoding aiding memory performance in younger adults. Additionally, previous studies have shown the insula to be activated during a wide variety of tasks, including the evaluation of emotional outcomes [3,41]. Recently insula activation has been more generally associated with the action selection stage of decision making [42]. Specifically, right insula was more activated when participants switched their response from that given on a previous trial. In the current study, age-related decreases in the insula may reflect deficits in response switching.

6. Conclusions

In summary, the current study used a mixed design approach to examine the separable effects of transient and sustained processing on age-related difference in subsequent memory performance. Results showed that successful incidental encoding requires both transient and sustained processes. Furthermore, these processes are recruited differently in young and older adults. Where young show increased activity in hippocampal and visual areas associated with transient Dm and in right PFC associated with sustained Dm, older adults show compensatory recruitment of left PFC associated with transient Dm. Thus, while older adults show age deficits in activation at both levels, they are able to compensate for these deficits with increased activation associated with item-specific processing.

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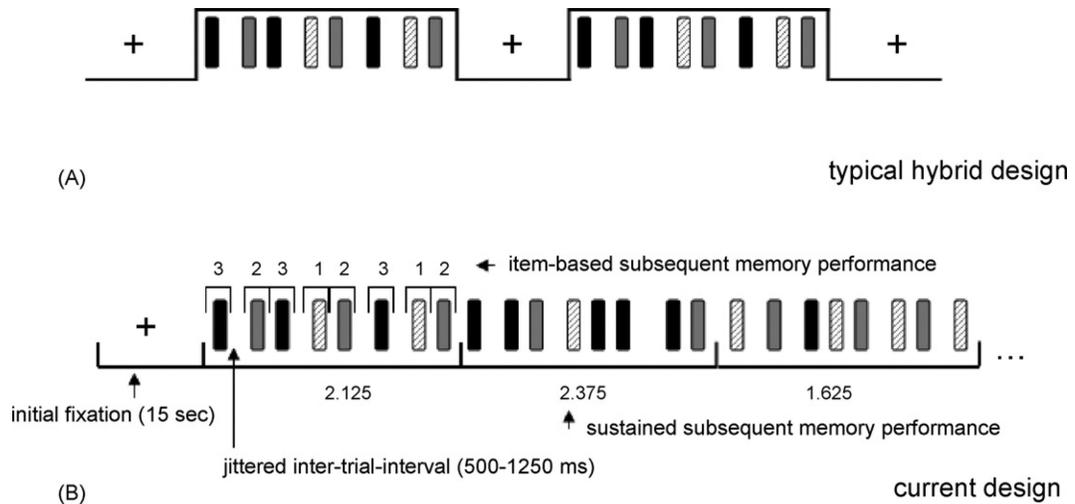
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**Fig. 1.**

A typical hybrid design (A) compares individual trials to a resting baseline state. Whereas our hybrid design (B), excludes the resting baseline condition, a condition that is not necessary in subsequent memory analysis. Rather, it separates trials into contiguous blocks (of eight in this case). Furthermore, trials are coded both individually based upon their subsequent memory score and as a block, based upon the average subsequent memory score of all individual trials within that block.

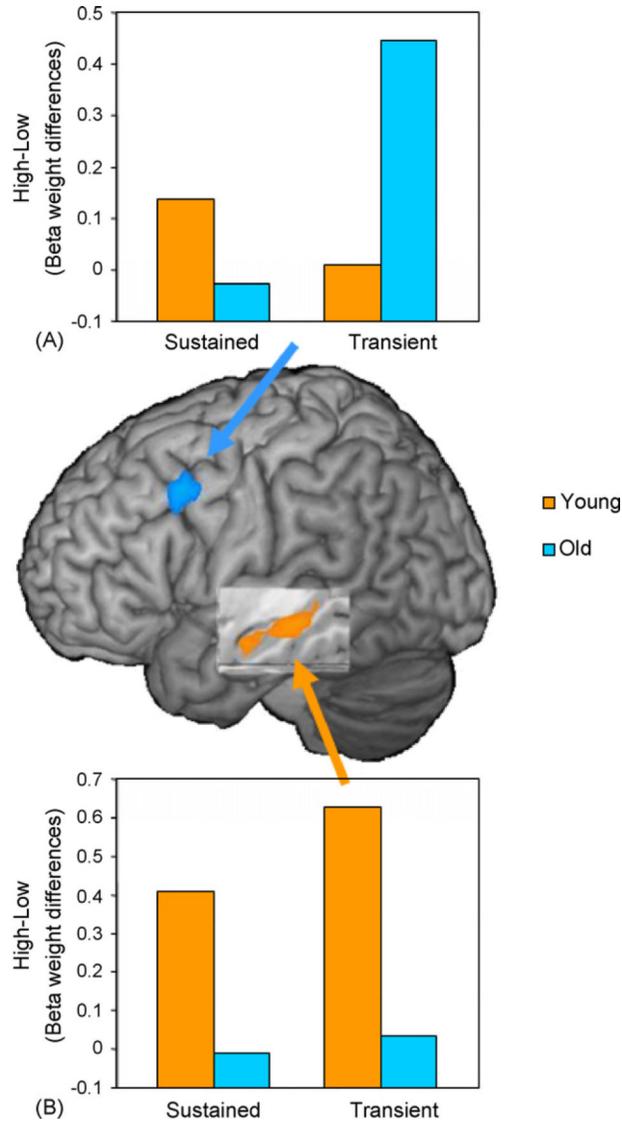


Fig. 2. Age differences associated with transient Dm. See Table 4 for coordinates. Younger adults show greater left medial temporal lobe (MTL)/hippocampal activity compared to older adults whereas older adults show greater left dorsolateral prefrontal cortex (DLPFC) activation compared to younger adults. The bar graphs represent the difference in functional activation (e.g., beta weights) between high and low memory condition for sustained and transient Dm activity in both younger and older adults-for left DLPFC (A) and left MTL/hippocampus (B).

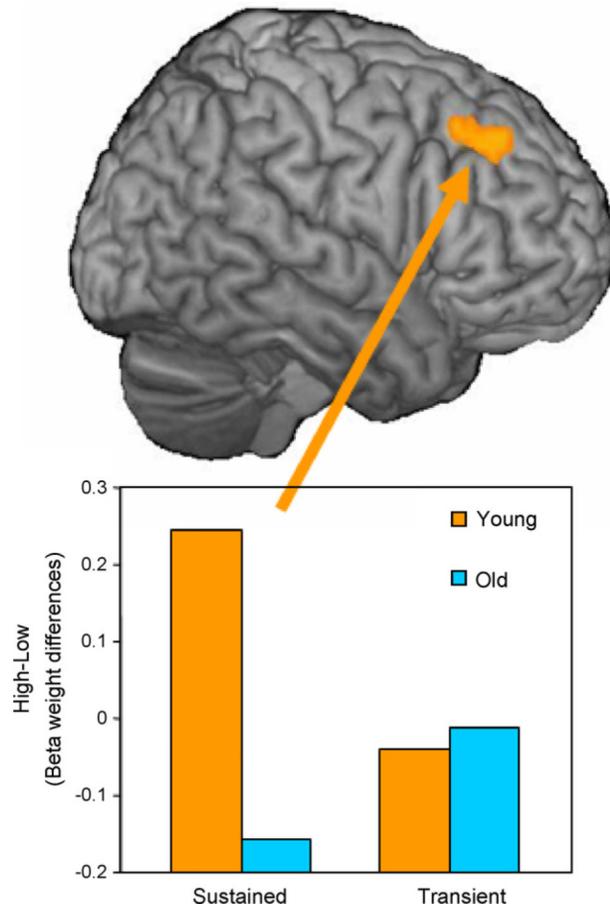


Fig. 3. Age differences in right PFC activity associated with sustained Dm, with younger adults showing greater activation in this region compared to older adults. See Table 4 for coordinates. The bar graph represents difference scores of functional activation (e.g., beta weights) between high and low memory conditions for sustained and transient Dm activity in both younger and older adults.

Table 1

Older participant characteristics

	Older group score	Age-matched norm	Young norm
BVMT-R (TR)	26.67 (6.37)	21.44 *	28.74
HVLT-R (TR)	30.50 (25.54)	26.65 **	29.14
MMSE	29.83 (0.39)	29 **	30
Education (years)	18.25 (0.75)	N/A	N/A

Notes: BVMT-R, brief visuospatial memory test-revised; HVLT-R, Hopkins verbal learning test-revised; MMSE, mini-mental state exam; TR, total recall. As noted, older adults in the current study performed significantly better than age-matched norms on all cognitive measures. Furthermore, the older group does not significantly differ from young norms (based upon the age of our young group).

* $p = 0.016$.

** $p < 0.001$.

Table 2

Behavioral results

	<u>High confidence</u>		<u>Low confidence</u>	
	Young	Old	Young	Old
Dm performance				
Hits	0.83 (0.13)	0.81 (0.15)	0.48 (0.12)	0.43 (0.11)
FAs	0.16 (0.16)	0.26 (0.25)	0.26 (0.13)	0.24 (0.14)
Hits–FAs	0.67	0.55	0.22	0.19
Encoding RTs				
Hits	842 (91)	878 (71)	827 (92)	871 (80)
Misses	829 (85)	892 (97)	841 (100)	875 (68)

Percent of total high and low confident responses that were responded to as either hits or false alarms (FAs) for both young and older adults. Average reaction time (RT) in ms for subsequently remembered (hits) and forgotten (misses) items for young and old, broken down by confidence level.

Table 3

Task specific activations across groups

	H	BA	Voxels	Coordinates (T&T)											
				Young						Old					
				x	y	z	T	x	y	z	T	x	y	z	T
Transient (common areas)															
Frontal															
Ventrolateral/dorsolateral PFC	L	45/47	120	-41	26	-4	3.35	-49	33	2	4.81				
Dorsal lateral PFC	L	9	75	-41	9	31	3.62	-49	9	31	4.31				
Sensorimotor	L	4/6	8	-45	-5	49	3.67	-45	-5	49	2.55				
Temporal															
Fusiform/PHG	L	36/37	123	-26	-45	-11	5.6	-26	-41	-14	7.06				
Hippocampus/PHG/fusiform	L		32	-11	-4	-16	6.12	-11	-4	-13	3.72				
Hippocampus/PHG	R		25	26	-4	-16	4.07	26	-19	-12	3.87				
Anterior temporal	L	20	13	-56	-45	-11	3.02	-56	-41	-11	2.7				
Sustained (common areas)															
Parietal	L	7	13	-11	-53	55	2.95	-11	-56	59	3.97				
Young sustained															
Frontal															
Orbital frontal	R	11	22	30	44	-9	5.73								
	R	6/44	18	45	1	24	3.95								
Dorsal lateral PFC	R	10	10	11	56	22	4.48								
	R	9	29	34	39	37	4.13								
Caudate	R		32	19	19	6	4.42								
Anterior lateral temporal	L	21/38	12	-41	0	-10	3.36								
Old sustained															
Caudate	M		11					-8	22	-1	4.88				

Notes: PFC, prefrontal cortex; PHG, parahippocampal gyrus; BA, Brodmann area; T, statistical t-value, Talairach and Tournoux [48] coordinates reported. The table reports common areas of activation for both young and old groups associated with transient Dm and sustained Dm (conjunction analysis at $p = 0.05$ with an extend threshold 8 in each age group). Additionally, table reports areas associated with sustained Dm in each individual age group ($p < 0.005$ uncorrected, with an extent threshold 8).

Table 4

Activation differences amongst groups

	H	BA	Coordinates (T&T)				Voxels
			x	y	z	T	
Y > O (transient)							
Hippocampus/PHG	L		-15	-16	-18	3.51	69
Sensorimotor	L	4/6	-45	-10	28	3.38	42
Dorsal precuneus	L	7	-15	-45	58	5.68	12
Visual cortex							
Lateral occipital	R	19	41	-63	3	3.56	16
Primary visual	M	17	4	-81	8	3.36	10
Cuneus	L	18	-11	-73	14	4.57	13
Occipitotemporal	R	19	34	-65	28	4.98	35
O > Y (transient)							
Anterior PFC	M	10	0	63	14	3.38	13
Dorsal lateral PFC	L	9	-45	17	38	4.43	17
Y > O (sustained)							
Midposterior PFC	R	6	45	1	28	3.31	18
Dorsal lateral PFC	R	9	34	42	36	4.56	20
Anterior lateral temporal	L	21/38	-41	-4	-9	3.39	11
Insula	R		26	12	13	3.18	17
O > Y (sustained)		No significant areas of activation					

Notes: Y, young; O, old; PHG, parahippocampal gyrus; PFC, prefrontal cortex; BA, Brodmann area; H, hemisphere; T, statistical *t*-value. Talairach and Tournoux [48] coordinates reported. Age differences in regions significant at $p < 0.05$ uncorrected, with a minimum cluster size > 10 ; inclusively masked with the primary activation (e.g., young event, old event, or young blocked) at $p > 0.005$.