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**SUCCESSFUL ENCODING WITHIN RETRIEVAL: NEURAL DIFFERENCES
IN YOUNGER AND OLDER ADULTS**

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Abstract

The present study used a three part memory paradigm in order to test the neural activity of younger and older adults during a retrieval phase containing a simultaneous encoding phase. Specifically, age differences in neural activity associated with encoding success were examined while individuals performed a given retrieval task. Behavioral comparisons showed no significant differences in memory for younger and older adults. Neural activation results indicated common areas of successful encoding activation for younger and older adults in the ventrolateral prefrontal cortex, dorsolateral prefrontal cortex, parahippocampal gyrus (bilateral), anterior cingulate cortex, posterior cingulate and occipital regions. The majority of activations were concentrated in the left hemisphere of the brain. A direct comparison between age groups indicated that younger adults activated more posterior regions than older adults, including regions in occipital/temporal, precuneus and posterior cingulate. Older adults activated more anterior regions, including the anterior cingulate cortex, dorsolateral prefrontal cortex and orbital frontal cortex. The results obtained indicate two main conclusions. The increased left lateralized activity seen in common for both younger and older adults is consistent with the hemispheric encoding/retrieval asymmetry (HERA) pattern, indicating that even though participants were taking part in both encoding and retrieval, brain regions predicting successful encoding were largely left-lateralized. Furthermore, results support the theory of a posterior-anterior shift in aging (PASA), indicating that as people age, anterior regions are used more often than posterior regions in order to store and retrieve information.

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Introduction

Learning and remembering new information is a fairly commonplace task that many people often take for granted. On a daily basis we use our memory in order to complete daily tasks, whether it is as simple as recalling items needed at the grocery store, or a task that taps deep into cognitive abilities such as studying for a neurophysiology exam. The intricate workings of our brain, as we try to remember and recall items, have been studied extensively by many experimenters.

Originally, phrenologists hypothesized that the amount of brain tissue devoted to cognitive function was determined by its influence on behavior. Bumps and indentations in the brain were thought to directly correlate to the trait supported by the underlying brain region. However, since the 1990s, technological advancements in functional magnetic resonance imaging (fMRI) have disproved these original hypotheses and allowed for vast advancements in cognitive neuroscience. fMRI uses strong magnetic fields to create images of the brain, so that brain function can be investigated and analyzed over time. Through fMRI techniques, modern researchers now have found that many functions rely on networks throughout the brain, and that single brain regions can have multiple functions. Dominating the field of brain mapping, fMRI is the preferred tool for many experimenters due to its quick speed, low invasiveness and minimal radiation exposure for participants. In relation to cognitive psychology and episodic memory, fMRI has allowed researchers to measure brain activity while participants are performing each phase of an episodic memory task: encoding and retrieval. In both phases, the use of event-related fMRI permits the investigation of brain activations at specific time intervals are coordinated with the remembering and forgetting of words or images (Huettel, 2004).

To date, many memory studies have used encoding and retrieval task paradigms and

fMRI analyses in order to measure differences in behavioral and neural activity while subjects perform various tasks. Specifically, many have focused on differences in memory as it relates to aging. Age-related changes in memory may in part reflect changes in lifestyle, or daily practices as people grow older; however, it is more likely that they reflect biological changes in neural systems that function in memory. fMRI studies allow for direct comparison of brain regions that are active while younger and older individuals are performing memory tasks, providing trends for age-related changes in memory performance in terms of changes in specific memory systems.

As we grow older, are different brain regions being recruited to help us to remember new information? Do younger individuals inevitably remember more details than older individuals in all types of memory? Are different neural regions recruited in older adults in order to compensate for neural degeneration in other areas? Questions such as these, as well as others which scrutinize age related differences in memory do not always provide straightforward answers, but some generalities have been formulated based on a few repeated findings across studies.

Encoding and Memory (Comparing Age Differences)

One of the two most common phases analyzed during memory studies is the encoding phase. Based on numerous studies, both intentional and incidental encoding have been viewed as processes that become impaired with age (Park & Gutchess, 2004). Behavioral findings suggest that older adults may show encoding deficits because they are less likely to elicit effective encoding strategies on the spot (Morcom et al., 2003). Although encoding efficiency has shown to decrease with age, impairment has been found to a lesser degree when the tasks conducted

involve environmental cues to guide encoding. Smaller age differences have been observed between younger and older individuals when the task at hand allows individuals to integrate both target and contextual cues. If older adults do not benefit enough from environmental support, they must rely heavily on working memory and speed (deep engagement of cognitive resources), disabling their ability to effectively encode (Park & Gutchess, 2004). Although older adults seem to show reduction in encoding due to less effective encoding strategies, it is only seen as one of the factors contributing to such age effects. The processes and neural structures that are associated with successful encoding across ages and their changes must also be considered.

Functional differences between age groups can only truly be understood upon understanding age-related atrophy in brain regions. The highest rate of atrophy is observed in the frontal lobes (avg. decline of .9% and 1.5% per year) whereas the fastest decline in function is observed in the parietal lobes (Raz et. al., 2005). Within the medial temporal lobe (MTL), subregions exhibit different rates of decline. Studies have shown that hippocampal atrophy increases with age. Age related shrinkage has also been found in the caudate, and corpus callosum (for a review see Dennis & Cabeza, 2008). The atrophy in brain regions correlates with declines in function, and is taken into consideration when comparing cognitive assessments.

Until recently, encoding related studies have used blocked experimental designs, where neural correlates have been defined by comparing different study tasks (Morcom et al., 2003). The most consistent finding among studies has been an age-related reduction in left prefrontal cortex (PFC) activity. However, the reduction has found to be more prevalent in intentional vs. incidental encoding, suggesting that the environmental support in an incidental encoding task may lessen the reduction in left lateralization. Along with a decrease in left lateralization in older adults, a compensatory mechanism for the loss of this activity has also been observed.

Specifically, age related increases in right PFC activity have been seen, showing a more bilateral pattern of PFC activity for older adults. The PFC pattern of findings in relation to age has been formalized as the ‘hemispheric asymmetry reduction in older adults’ (HAROLD) (Cabeza, 2002).

Along with changes in PFC activity, older adults have also been shown to exhibit reduced medial temporal lobe (MTL) activity during encoding (for a review see Dennis and Cabeza, 2008). Daselaar et al. (2003) found that age-related memory decline was associated with decreased activity in the MTL. Based on these findings, neural activity is seen to be reduced in older adults, along with diminished connection between the PFC and MTL. Gutchess et al. (2005) suggested that the additional observed PFC activity could help compensate for the MTL deficits.

Aside from intentional encoding, which presses participants to actively learn a word or picture, incidental encoding can also be measured where participants are not specifically directed to remember an item. Paired with intentional encoding, subsequent memory studies can be used to measure successful incidental encoding by comparing neural activity for items subsequently remembered to items that are subsequently forgotten, known as ‘difference in memory’ (dm). In one key incidental encoding study (Morcom et al., 2003), activity in the left inferior prefrontal cortex and the left hippocampal formation was greater for subsequently remembered words for both older and younger age groups. However, as consistent with previous findings in intentional encoding, the younger group exhibited more left lateralized PFC activity, while older adults exhibited a more bilateral pattern of activity, showing that the HAROLD pattern extends to incidental encoding studies and subsequent memory tasks. Along with similar activations among age groups, younger adults manifested a greater subsequent memory effect in the left anterior

inferior temporal cortex, whereas older adults showed bilateral anterior prefrontal cortex and left supramarginal gyrus activations (Morcom et al., 2003).

Along with the HAROLD pattern, another common pattern associated with age-related differences in brain activity is a posterior-anterior shift in aging (PASA). Several studies have observed the PASA pattern, which entails age-related decreases in occipital activity along with age-related increases in PFC activity. Researchers who have observed this pattern in their studies have come to the conclusion that the increase in PFC activity could be a potential compensatory mechanism for the decrease in visual processing (occipital decrease) (Anderson et al., 2000; Cabeza, 2002; Schiavetto et al., 2002). In many of these studies, older and younger adults performed the memory tasks with equal accuracy; however, longer retention times were observed with older adults. Therefore, recruiting the PFC could allow older adults to maintain accuracy despite their slow speed in performing the task at hand (Dennis & Cabeza, 2008).

Retrieval (Comparing Age Differences)

Although encoding related studies have found more prominent age related differences in memory, a few trends have been observed and should be noted. Behaviorally, age differences have been larger for explicit memory and recall (Craik & McDowd, 1987). When older adults are forced to recall information, they are more likely to include items that have never been presented before. Although older adults perform better when their minds are prompted through recognition, during this type of retrieval they are also more likely than younger adults to fall into lures, and false alarm to accept old never-presented items as having been shown earlier in the study. Therefore, older adults have been found to perform more poorly on recall tasks than those involving recognition. (Craik & McDowd, 1987). Larger differences in recall over recognition

for younger adults compared to older adults suggests less differentiation of neural activity as a function of the retrieval task performed (Park & Gutchess, 2004).

Neural studies have demonstrated that older adults have shown decreases in occipital and parietal regions coupled with increases in PFC regions (PASA pattern). A few studies have found age-related decreases in right PFC activity, indicating a more bilateral pattern of PFC in older adults than in younger (Dennis & Cabeza, 2008). Although the HAROLD pattern seems to be observed during both encoding and retrieval tasks, it is important to note the contrasting PFC activity during successful encoding and retrieval; successful encoding is associated with left lateralization in the PFC, whereas successful retrieval shows more activation in the right side of the PFC. The lateralization of PFC activity has been described as the hemispheric encoding/retrieval asymmetry (HERA) model in episodic memory (Tulving, 1993).

It is apparent that older adults use different neural networks during retrieval when compared to younger adults, but it is not clear whether this is due to strategy differences or reorganization. Despite this difference, the automatic nature of the retrieval mode has remained relatively unimpaired with age (Park & Gutchess, 2004).

Encoding within Retrieval

When looking into short-term memory, the concept of working memory (WM) is oftentimes considered. Working memory refers to a type of episodic memory where information is held in the mind for a short time, but requires active tasks such as manipulation, storage and transformation of the held material. Age differences have been found to be very significant when looking at working memory. Episodic memory has been shown to decline with age and the

reasons for age-related decline have been debated. Some possibilities that have been suggested include a decrease in mental energy (attentional resources), decline in processing speed or a decline in the ability to inhibit unwanted information (Park & Schwarz, 2000). Episodic memory relies heavily on resources, and with atrophy of key neuron connections in the brain and blood flow, these processes are expected to decline (Park & Schwarz, 2000). Since age-related deficits have been observed while conducting dual task processes and during divided attention conditions (e.g., Anderson, Craik, & Naveh-Benjamin, 1998), it may be very difficult for older adults to incidentally encode information while retrieving information that has already been stored. Three recent studies have taken a new approach to studying incidental encoding, by observing the effects as it is conducted within a simultaneous retrieval mode.

Huijbers et al. (2009), subjected nine young participants (mean age of 24) to an experimental task involving three separate phases: word encoding, word/retrieval/scene encoding, and scene retrieval. During the 2nd phase, words and pictures were shown simultaneously in order to see if incidental encoding of pictures competed with retrieval (I) of words that were shown during part 1 of the study. Finally, a surprise scene retrieval (II) phase was conducted with pictures previously present and completely new scenes. Behaviorally, it was found that remembering old information was associated with impaired learning of new information, and fMRI analyses discovered suppression of learning related activity in visual and medial temporal areas. Despite the reduction in learning processes, a compensatory mechanism was found in the left midventrolateral prefrontal cortex (VLPFC), as it facilitated rapid switching between learning and remembering during the short time period. In correlation with prior studies conducted, an increase in posterior cingulate cortex (PCC) activity for successful retrieval was also found, along with a decrease for successful encoding; thereby coming to the final conclusion

that successful incidental encoding was inhibited due to simultaneous retrieval (Huijbers et al., 2009).

Another similar picture study performed by Stark et al. (2003) focused on MTL activity as it relates to both encoding and retrieval. The paradigm again consisted of three distinct phases. In the first phase, participants were shown color scenes, and explicitly asked to remember them. After a short delay (10 minutes), the first recognition test was performed, where participants were presented with old and new pictures and asked to press a key as to whether they had seen the picture before or not. After removal from the scanner, a surprise recognition test was conducted where the novel items from the second phase were shown along with completely new pictures that had never before been shown during the experiment. Participants responded with a “yes” or a “no” to whether they had seen the picture previously in the experiment. The study demonstrated how failing to observe MTL activity for retrieval success could be a result of activity associated with incidental encoding- verifying the importance of the MTL region of the brain for both tasks. The encoding related activity could explain why retrieval-related activity could be obscured during traditional retrieval studies. In this case, MTL activity during the 2nd phase was consistent with predicting subsequent memory, and the MTL region (perirhinal cortex, bilateral hippocampal region, parahippocampal cortex) activated were the same as for regular intentional encoding.

Perhaps the most relevant to the current study, the third study was conducted by Buckner et al. (2001). The study once again was broken down into three phases. During the first phase (the prescan study phase), participants initially studied a list of words. In the second phase, a scanned recognition test (T1) was performed where participants had to differentiate between old and new words presented. Finally, a surprise postscan recognition test (T2) was given where

subsequent memory was tested for the novel items shown in the second phase. A confidence scale was used and participants were directed to choose definitely old (DO), probably old (PO), guess (G), probably new (PN) or definitely new (DN)- 400 words were tested (200 previously presented words and 200 foils). fMRI analyses revealed greater activity in left frontal regions (inferior frontal gyrus) for those words subsequently remembered when compared to those that were subsequently forgotten. Similar to Stark et al. findings, incidental encoding was found to be just as good as intentional memory encoding. It was also concluded that a retrieval mode can be a very effective in facilitating incidental encoding.

Current Study

Similar to the three studies previously mentioned (Huijbers et al., 2009; Stark & Okado, 2003; Buckner et al., 2001), the following encoding-during-retrieval study used a word paradigm and fMRI techniques to assess successful encoding activity (neural activity associated with words subsequently remembered vs. those forgotten) within a retrieval mode. However, this study is unique in that it specifically focuses on comparing age differences within this forced mode of simultaneous encoding within retrieval. Similar to Buckner et al. (2001), the goal of this study was to analyze behavioral and neural activity by strictly focusing on the encoding of words during a retrieval task.

When conducting this study, the following behavioral questions were asked: Does unintentional encoding during retrieval produce similar success in remembering words in both younger and older adults? Or is there a subsequent difference in memory (dm) between younger and older adults? If so, do older adults exert all of their energy during retrieval, disabling them

from successful encoding? Behaviorally, during intentional encoding, it has been found that older adults tend to have poorer subsequent memory than younger adults because they do not use an effective encoding strategy (Morcom et al., 2003). However, since the following study is looking at incidental encoding with a supportive task (retrieval), it is expected that both younger and older adults will show similar behavioral results in words that are subsequently remembered vs. forgotten (dm). In relation to neural activity, the following questions will be analyzed: Which areas of the brain are predicting subsequent memory in both groups, and is there an observed difference between the neural activations for younger and older adults?

Material and Methods

Participants

In order to conduct the following experiment, forty individuals (twenty one older and eighteen younger) were recruited. Younger adults were all students at Duke University, whereas older adults were recruited from the Durham, NC community. Although forty individuals were recruited, for the purpose of the analysis, a few individuals had to be removed from the study because all of them lacked a minimum number of 10 entries for the four trial types of interest (see below). Specifically, four older individuals and four younger individuals were removed from the study, leaving the analysis with seventeen older adults (mean age= 67.94 (5.92) yrs) and fourteen younger adults (mean age = 21.65 (3.20) yrs). Participants with a history of neurological difficulties or psychiatric illness, alcoholism, drug abuse, and learning disabilities were excluded from the study. All participants completed a battery of neuropsychological tests taken from the Cambridge Neuropsychological Test Automated Battery (CANTABeclipse, version 2.0;

Cambridge Cognition Ltd; see Table 1) designed to measure short term memory. No individuals performed less than 1.5 standard deviations from the calculated value for each age group, thereby verifying all participants as cognitively intact for the experiment at hand. All participants provided written informed consent and received financial compensation for their participation. All experimental procedures were approved by the Duke University Institutional Review Board for the ethical treatment of human participants.

Stimuli and Procedure

The current memory study consisted of three distinct phases conducted in the following order: encoding, retrieval (I) with simultaneous incidental encoding, and retrieval (II). Four hundred concrete nouns were chosen from the MRC Psycholinguistic Database (http://www.psy.uwa.edu.au/MRCDataBase/uwa_mrc.htm) and used as stimuli amongst the three trials. First, in the encoding phase, participants encoded two hundred and forty words equally divided across 4 functional runs. During the encoding phase, participants were asked to make an animacy decision regarding the words (i.e., living/non living).

Following the 1st encoding phase, participants performed a second task during a retrieval phase, which also served as a simultaneous encoding phase for the current analysis. Participants were presented with the two hundred and forty words they had originally responded to during the encoding phase and one hundred and twenty new words. In response to each presented word, participants were asked to make old/new judgments and indicate their memory for the previous presentation of the word and their confidence of this decision (definitely old, probably old, probably new, and definitely new). Words were presented one at a time in the center of a computer screen for 2.5 seconds each. The memory score was displayed below each

word and participants pressed a key corresponding to their recall of the word.

A final second surprise recognition task (retrieval II) was presented outside of the scanner upon completion of the first retrieval phase. During the second retrieval phase, the one hundred and twenty new words presented in the previous retrieval phase were shown along with forty completely new words. The second retrieval task was held in order to measure successful encoding within the first retrieval phase. Participants were directed to make the same old/new judgments as they did before (definitely old, probably old, probably new, and definitely new). Similar to the first two phases, words were presented one at a time in the center of a computer screen. The memory score was displayed below each word and participants pressed a key corresponding to their recall of the word.

Image Acquisition

Images were collected on a General Electric 3.0 Tesla Signa Excite HD short bore scanner (Milwaukee, WI) equipped with an 8-channel head coil. Following acquisition of the high-resolution anatomical images (450-ms repetition time (TR), a 3-ms echo time (TE), a 24-cm field of view (FOV), a 256^2 matrix, and a slice thickness of 1.9-mm), whole-brain functional images were acquired parallel to the anterior–posterior commissure plane using an inverse spiral sequence (direction = interleaved, matrix = 64^2 , FOV = 24 cm, TR = 2000 ms, TE = 30 ms, sections = 34, thickness = 3.8 mm, inter-scan spacing = 0).

Image Processing

Functional data were preprocessed and analyzed with SPM2 (Statistical Parametric Mapping; Wellcome Department of Cognitive Neurology, <http://www.fil.ion.ucl.ac.uk/spm>). Time-series

data were corrected for differences in slice acquisition times and realigned. Functional images were spatially normalized to a standard stereotaxic space using the Montreal Neurological Institute (MNI) templates implemented in SPM2 and resliced to a resolution of 3.75 mm³. The coordinates were later converted to Talairach space (Talairach & Tournoux, 1988). Finally, the volumes were spatially smoothed using an 8-mm isotropic Gaussian kernel. Head motion was assessed prior to pre-processing. No individual moved more than 3 mm in any direction, in any run. Thus, no data were eliminated in either group due to motion artifacts.

fMRI analyses

Encoding success activity (ESA) is neural activity that is modulated by memory performance. Encoding success was defined as activity associated with subsequently remembered items > subsequently forgotten items. Subsequent high hits were categorized as encoding trials that correctly led to a “definitely old” response. Subsequent misses were defined as encoding trials there were old but stated as “probably new” or “definitely new”, and hits made with low confidence. The old words from retrieval (I) were also included in the model, but disregarded when conducting the current analysis.

Three main contrasts were conducted for the purpose of this study. Subsequently remembered (hits) > subsequently forgotten (misses) trials served as the main contrast of interest (ESA). Contrasts were run in order to find 1) common neural activity for both younger and older adults 2) neural activity greater in younger adults than older adults and 3) neural activity greater in older adults than younger adults.

Common ESA activity was assessed by performing a conjunction analysis of both groups, each at $p < .07$ $k=10$ voxels (for a conjoint probability of $p < .005$). Differences in ESA activity

amongst younger and older adults was assessed by examining group differences at $p < .05$ $k=10$, within regions that showed significant within-group effects ($p=.005$, $k=10$). The parameter estimates for subsequent hits and misses were used to plot the bar graphs depicting fMRI effect sizes in the figures.

Results

Behavioral Results

All of the p values derived from the statistical analyses conducted in this experiment were considered significant if less than .05. In order to analyze memory differences in both younger and older individuals, d' values were calculated and compared between groups using an unpaired t -test. No significant difference between age groups was observed, thereby indicating equal memory performance across groups [$t(29) = .047$, $p = .9630$]. Further breaking d' down into its main components (hit rate and false alarm rate), no significant difference was observed between groups for false alarm rate [$t(29) = .144$, $p = .8868$] or for total hit rate [$t(29) = .922$, $p = .3643$]. A one group t -test was performed for each group and both hit rates were significantly different than a mean of .50. Although on average younger (.816) individuals had a slightly higher hit rate than older individuals (.778), based on the results of the t -test, it is apparent that both groups successfully performed the task at hand and are in fact remembering the words shown.

Analyses were also made for reaction times between all misses and all hits within and between groups using paired and unpaired t -tests, respectively. When younger and older groups were compared, no significant difference was observed for reaction times for all misses [$t(29) = 1.765$, $p = .0880$] and all hits [$t(29) = 1.352$, $p = .1867$]. Since imaging analyses were conducted based on high hits, reaction times were also compared for high hits and all other responses

(misses + low confidence hits), and once again no significant difference was observed within either group [$t(29) = 1.551, p = .1318$].

Paired t-tests were also performed within the younger group, and no significant difference was observed between the reaction times for all misses and all hits [$t(13) = 2.057, p = .0603$]. No difference was observed when comparing high hits and all other responses (low confidence + misses) showing that there was no difference in reaction times for low confidence and high confidence hits. A similar paired t-test was conducted for older individuals and no significant difference was observed in reaction times.

fMRI results

Three contrasts were run for the purpose of the study. The first contrast was targeted to find areas of common ESA activity between younger and older adults (table 2). Results show common ESA in the anterior cingulate cortex, bilateral ventrolateral prefrontal cortex/dorsolateral prefrontal cortex, along with bilateral parahippocampal gyrus (PHG). The second contrast looked at ESA that was greater for younger adults when compared to older individuals. Younger adults showed increased activity in the occipital/temporal regions, precuneus and posterior cingulate. The final contrast looked to see where ESA was greater in older adults when compared to younger adults. Increased activity was observed in older adults throughout the prefrontal cortex, including orbital frontal cortex and anterior cingulate cortex, as well as occipital/parietal cortex, when compared to younger adults.

Discussion

The current study focused on assessing both common areas of neural activation and differences in the neural activations between younger and older adults while engaging in a retrieval task with a simultaneous encoding phase. Upon data retrieval and thorough analysis of three contrasts, two main conclusions were drawn from this study. The first contrast, which looked at common ESA for younger and older adults, showed more activity in the left hemisphere of the brain, and supporting the hemispheric encoding/retrieval asymmetry (HERA) pattern. The second two contrasts, which looked at differences between age groups, showed greater ESA in posterior regions for younger adults, and greater ESA in anterior regions for older adults, supporting the posterior-anterior shift in aging (PASA) pattern.

Common Activity

The first contrast (see table 2) showed many brain regions that were commonly activated among both younger and older adults associated with successful encoding during the given retrieval task. Activity was seen in the VLPFC, DLPFC, and parahippocampal gyrus (PHG). ESA was also identified in the anterior cingulate cortex, posterior cingulate, occipital cortex, occipital/temporal and superior parietal regions. When comparing the neural regions that were commonly significant among both sets of individuals to previously published studies, the findings shown to be consistent with previous encoding studies done with younger and older adults (Dennis et al., 2007; Morcom et al., 2003). Similar to Dennis et al. (2007), bilateral activity was observed in the VLPFC/DLPFC, as well as activity in the left PHG, and occipitotemporal cortex. Similar to Morcom et al. (2003), bilateral PHG activity was observed,

along with occipital cortex activity.

However, although predicted regions were activated in this particular contrast, one specific trend must be noted. The majority of regions activated are notably observed in the left hemisphere of the brain (Table 2; Figure 1). Previous studies have found that the left and right prefrontal lobes are part of an extensive neuronal network that involves episodic memories, but the two different hemispheres have been found to play different roles in each phase of memory processing. Specifically, the left hemisphere has been found to be involved more with encoding, and the right hemisphere more with retrieval. Based on analysis of various studies, the hemispheric encoding/retrieval asymmetry (HERA) model of prefrontal activation was established (Tulving et al., 1993). The HERA model suggests that encoding tasks are found to engage the left prefrontal regions, in the absence of comparable right frontal activation, whereas retrieval tasks are found to engage right prefrontal regions, in the absence of comparable left frontal activation. The HERA model also suggests that right prefrontal cortical regions are involved in retrieval of episodic information. On the contrary, left prefrontal cortical regions are involved in retrieval of information from semantic memory and in simultaneous encoding of the retrieved information into episodic memory (Tulving et al., 1993).

Since the current study involves a semantic retrieval task, while simultaneously encoding a set of new words, the left lateralization observed can be explained by the HERA model. Specifically, the semantic retrieval in the second phase of the memory study paradigm was paired with simultaneous encoding of information into episodic memory. When subjects were presented with the word, they were directed to respond with “definitely old”, “probably old”, “probably new” or “definitely new”. While participants were retrieving relevant information from their semantic memory (information that was encoded during the first phase of

the memory test), they were subconsciously involved in a deep, incidental encoding task for the foil or new words presented during retrieval. Even though they were not specifically directed to remember the words for later, they were engaged in an implicit encoding task- a search of semantic and episodic information to guide retrieval success. Therefore, since the common neural activations obtained for both younger and older adults were found to be more left lateralized (table 2), it can be concluded that the second phase of the study served as an effective encoding task, involving encoding-related processing regions albeit while subjects were engaged in a retrieval task. Since a significant amount of left-lateralized activity (associated with encoding) was observed during a retrieval phase, the findings suggest that retrieval processes can successfully support and modulate encoding operations.

Age Differences in Neural Activity

When looking at activity that was greater in younger adults (Table 2; Figure 2), all were posterior, including occipital/temporal regions, posterior cingulate and precuneus. While testing only younger adults, Buckner et al. (2001) showed similar activations in their study, observing significant bilateral activations in the occipital/temporal regions. However, the posterior cingulate and precuneus regions observed in the present study, showed different Brodmann's areas (BA) than those observed in Buckner et al. When looking at activity that was greater in older adults (Table 2; Figure 2), neural activations were concentrated in anterior portions of the brain, including the dorsolateral prefrontal cortex, orbital frontal cortex and anterior cingulate cortex.

Analyzing the neural activations that were greater in both younger and older adults, the findings are consistent with the posterior-anterior shift in aging (PASA) pattern observed in

many age-related studies of cognitive processing including encoding, retrieval and perception (Dennis & Cabeza, 2008).

The PASA pattern is an age-related reduction in occipitotemporal activity coupled with an age-related increase in frontal activity. Since it was first identified (Grady et.al, 1994) through a positron emission tomography (PET) study that investigated perception of faces and locations, the pattern has been observed in a variety of cognitive functions, including episodic memory encoding and episodic memory retrieval. Older adults tend to show greater activity in anterior regions, including the prefrontal cortex. The anterior recruitment displayed by older adults has been shown to arise independently of both task and difficulty, and has been linked to an increase in cognitive performance for older adults (Davis et. al., 2007). The age-related shift towards anterior regions has been postulated as a compensatory mechanism for older adults to overcome the neuroanatomical declines in posterior regions as people grow older (Davis et al., 2007).

In the current study, behavioral results showed that there was no statistically significant difference for remembered vs. forgotten (dm) words in younger and older adults. Since older adults had greater neural activations in anterior regions, the shift in activation could have been a compensatory mechanism to increase overall cognitive performance, allowing them to perform with equal caliber to younger adults.

Conclusion

Consistent with our predictions, no behavioral differences in memory were seen between younger and older adults while participating in a retrieval mode containing simultaneous incidental encoding. As shown, upon thorough analysis of the fMRI imaging data collected, three main neural activation findings were seen in the current study: 1) left lateralization within the

retrieval/encoding mode 2) older adults activated a great number of anterior regions 3) younger adults activated a greater number of posterior regions. The findings support the patterns of hemispheric encoding/retrieval asymmetry (HERA) and posterior-anterior shift in aging (PASA). The HERA pattern observed in this study suggests that incidental encoding can be successfully supported by a simultaneous retrieval phase. The PASA pattern shows that older adults may use more anterior regions than younger adults as a compensatory mechanism due to degenerating posterior regions.

Overall, the results obtained from this study support the theory that younger and older adults can subsequently remember items with equal success, but use different neural mechanisms in order to remember that information.

Appendix

Table 1. Overall Dm Performance and Retention Times for Younger and Older Adults during Retrieval Phase (I)

	Young	Old
Dm Performance		
High Confidence Hits (HCH)	0.702 (.137)	0.537(0.223)
Misses	0.184 (.095)	0.222 (0.128)
False Alarms (FA)	0.080(0.0601)	0.077 (.050)
Difference in Memory (dm)	2.48 (0.623)	2.50(1.034)
Encoding RT's		
High Confidence Hits (HCH)	1567.74 (204.70)	1662.84 (160.68)
Misses	1505.48(234.56)	1631.535(161.99)

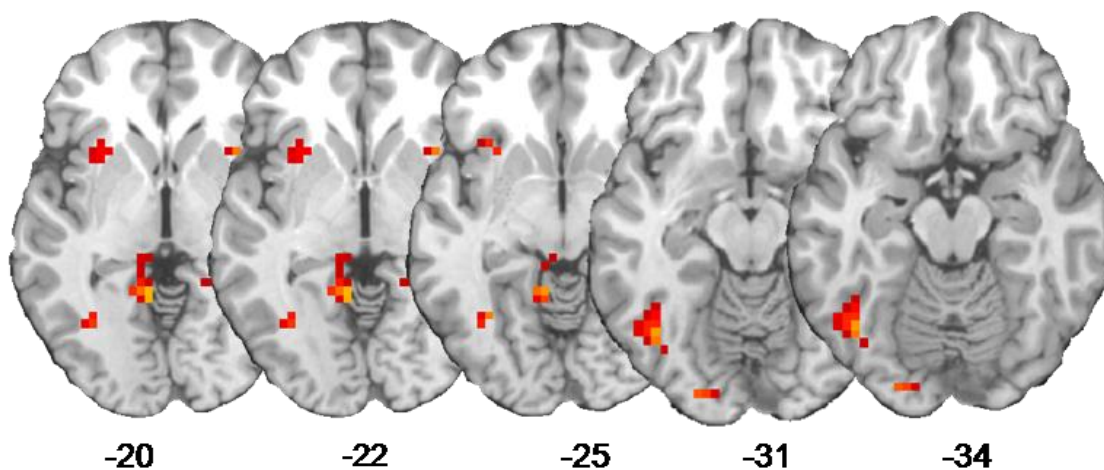
* The table above shows the mean high confidence hit rate, miss rate, false alarm rate and the difference in Hits vs. False Alarms (d') for both younger and older adults. The mean retention times observed for both high confidence hits and misses were also recorded. Standard deviations are shown in parentheses beside the mean.

Table 2. Brain Regions Showing Significant Neural Activity Predicting ESA during Retrieval Phase (I)

Common Areas of Activity (Y=O)	BA	H	X	Y	Z	T	Voxels
Anterior Cingulate Cortex	32, 24	M	-4	31	37	6.13	73
Left Parahippocampal Gyrus	29,30	L	-11	-47	6	4.3	44
Ventral/Lateral Prefrontal Cortex (VLPFC)	47	R	37	22	-1	4.23	25
Dorsolateral/Ventrolateral Prefrontal Cortex	45,44,46	L	-48	16	20	4.22	77
Superior Parietal	7	L	-30	-56	45	4.08	11
VLPFC	47	L	-37	21	-11	3.89	15
Occipital Cortex	17	L	-22	-88	-12	3.78	27
Occipital/Temporal	19,37	L	-41	-62	-10	3.69	46
Right Parahippocampal Gyrus	30	R	15	-44	2	2.52	19
Posterior Cingulate	31	L	-11	-42	27	2.28	18
Activity Greater in Younger Adults (Y>O)							
Occipital/Temporal	37,19	L	-45	-51	-4	3.61	33
Occipital/Temporal	37,19	R	45	-66	-16	3.52	21
Precuneus	7	M	4	-44	65	3.41	23
Posterior Cingulate	29,30	M	0	-47	6	2.33	11
Activity Greater in Older Adults (O>Y)							
Dorsolateral prefrontal cortex	46,10	R	30	37	16	3.63	10
Fusiform gyrus	19	L	-26	-55	-4	3.61	13
Orbital frontal cortex	10	L	-11	54	-3	3.46	10
Anterior cingulate cortex	32,9	R	11	48	19	3.41	10
Anterior cingulate cortex	32,24	M	-7	31	37	3.19	22
Occipital/parietal cortex	19	L	-30	-68	28	2.76	10
	21	R	45	-1	-16	2.67	13
Cerebellum	N/A	R	11	-56	-36	2.64	11

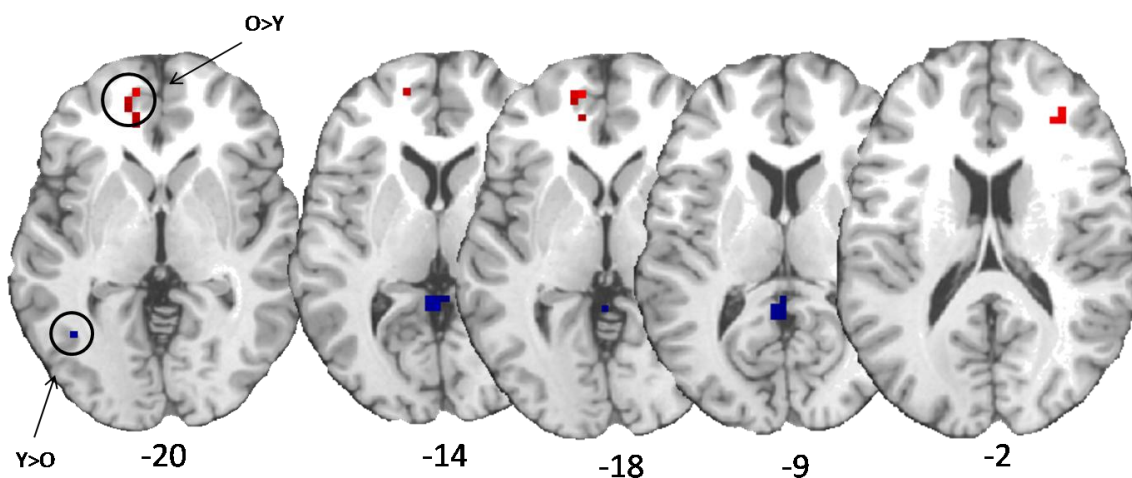
*The table above shows activity observed in brain regions for areas significant in both younger and older adults, areas where younger adults showed greater activity than older adults, and where older adults showed greater activity than younger adults (top to bottom).

Figure 1. Common Areas of Neural ESA for Younger and Older Adults



* The figure above displays several five separate axial views of the brain in order to depict the left lateralization of activity when looking at neural activity that is common for both younger and older adults. The Z coordinate values are listed under each corresponding image in order to show which slice of the brain is being depicted.

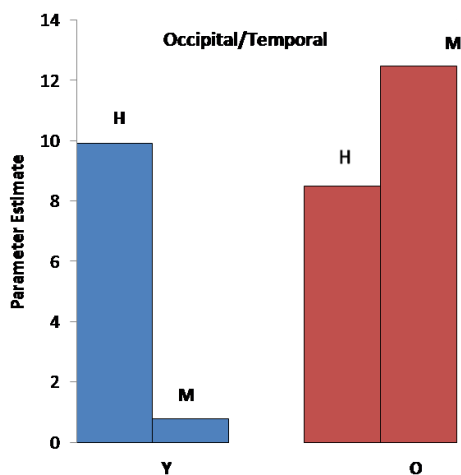
Figure 2. Age Differences Seen in Neural ESA for Younger and Older Adults



*The figure above depicts the ESA where Older or Younger group activity is significantly greater than the other on five different axial slices of the brain. The voxels shown in red depict neural activity where $O > Y$ in the anterior portion of the brain, whereas the voxels shown in blue depict neural activity where $Y > O$ in the posterior region of the

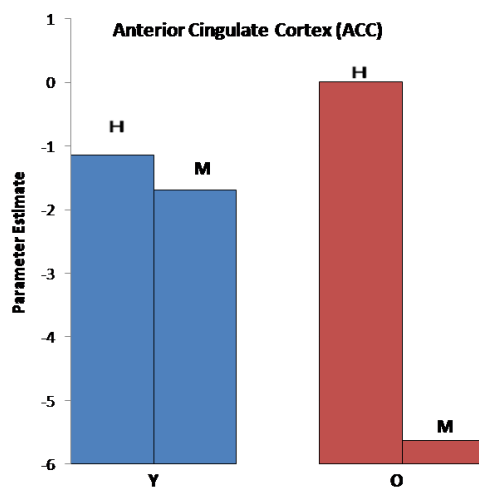
brain. The voxels displayed clearly show the posterior anterior shift in aging (PASA) pattern. The Z coordinate values are listed below the images in order to show which slice of the brain is being depicted.

Figure 3. Younger Adults Showing Greater Activation than Older Adults in Posterior Region



*The bar graph above depicts the hits vs. miss activity for younger and older adults where younger neural activity is greater than old (figure 2- axial slice (-20)). The graph indicates that while younger adults exhibit ESA in the occipital-temporal cortex (greater activity for hits and misses) older adults do not.

Figure 4. Older Adults Showing Greater Activation than Younger Adults in Anterior Region



The bar graph above depicts the hit vs. miss activity for younger and older adults where older neural activity is greater than young (figure 2- axial slice (-20)). The graph indicates that while older adults exhibit ESA in the ACC (greater activity for hits than misses, younger adults' ESA is significantly reduced).

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Academic Vita of Deepa Ramasamy

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Education

Major: Biology

Honors: Biology

Thesis Title: Successful Encoding within Retrieval: Neural Differences in Younger and Older Adults

Thesis Supervisor: Dr. Nancy Dennis, Assistant Professor of Psychology

Awards/Honors

Schreyer Honors College Summer Research Scholarship <i>The Pennsylvania State University</i>	Summer '09
Schreyer Honors College College Study Abroad Scholarship <i>The Pennsylvania State University</i>	Summer '09
Jean Phillips Shibley Memorial Scholarship <i>Biology Department, The Pennsylvania State University</i>	2008-2009
Gerald L. Memorial Scholarship <i>The Pennsylvania State University</i>	2006-2009
Hartz, R. Academic Excellence Scholarship <i>The Pennsylvania State University</i>	2006-2009
Guthrie Scholarship <i>Guthrie Scholarship Committee</i>	2006-2009
Robert C. Byrd Scholarship <i>PHEAA</i>	2006-2009
Dean's List <i>The Pennsylvania State University</i>	2006-2009

Work/Research Experience

Honors Undergraduate Research Assistant **Fall '08-Spring '10**
The Pennsylvania State University (Psychology Department), University Park, PA
Senior Thesis Supervisor: Dr. Nancy Dennis

- ❖ Studying the effects of cognitive aging by observing the behavioral and neural differences in younger and older adults upon completion of a memory task
- ❖ Learned how to operate an fMRI scanner and analyze neural images
- ❖ Administered weekly cognitive behavioral tests to older and younger individuals for various piloted studies

Organic Chemistry II Teaching Assistant (Grader)**Fall '08***The Pennsylvania State University (Chemistry Department), University Park, PA*

- ❖ Selected by Dr. Raymond Funk (Organic Chemistry II Professor) to grade Organic Chemistry II exams

Research Assistant**(10 week internship) Summer '08***Future Talent Program, Merck & Co, Inc., Rahway, NJ*

Supervisor: Dr. Naoki Yoshikawa, PhD

- ❖ Conducted analyses for my own project and learned how to operate chemistry laboratory equipment including NMR and HPLC
- ❖ Practiced basic lab techniques including recrystallizations, product isolation, Thin Layer/Column Chromatography and proper record-keeping procedures

Student**(2 week experience) Summer '08***Primary Care Scholars Program (Selected and Attended), Penn State Milton S. Hershey Medical Center, Hershey, PA*

- ❖ Gained a broad knowledge of primary health care, including general medicine, pediatrics and internal medicine (1 week)
- ❖ Shadowed Dr. Robert D. Baker (Pediatrician) in his clinic and observed patient's appointments (1 week)

Undergraduate Research Assistant**Spring '08***The Pennsylvania State University (Evolutionary Genomics), University Park,*

Supervisor: Dr. Kateryna Makova

- ❖ Reviewed basic lab techniques such as preparation of stock solutions, running gels, conducting PCR's and DNA purifications
- ❖ Learned how to operate computer program, 'Quantity One' for analyzing gel bands

Research Assistant**Summer '07***Mansfield University (Biology Department), Mansfield, PA*

Supervisor: Dr. John Sternick

- ❖ Researched bacterial protein synthesis with the American partner of a larger research collaboration with LAAS-CNRS, France
- ❖ Extracted proteins and plasmids from *E. coli* bacteria to study the function of the *E. coli* nanomotor of the flagellum

Extracurricular

Global Medical Brigades

Fall '08-Spring '10

The Pennsylvania State University

- ❖ Raised money throughout the semester and traveled to Honduras during Spring Break '09 to conduct medical brigades in the surrounding towns of the underprivileged area of Gracias Lempira
- ❖ The brigades consisted of three main stations: triage, consultation and pharmacy
- ❖ Accompanied by 3 doctors (OBGYN, Pediatrician, Internist) and treated a little over 1,800 patients in 4 days

HOINA (Homes of the Indian Nation)

Spring '09- Fall '09

Schreyer Honors College

- ❖ Selected to take part in a 3 week service learning project (Summer '09) working at an orphanage (HOINA) located in Andhra Pradesh, India
- ❖ Took part in activities such as helping the founder with labor work around the orphanage (cooking, construction etc.), taught English lessons to the Indian staff, and helped students with their homework
- ❖ Took a 2 credit course in Spring '09, and 1 credit course in Fall '09 in order to prepare for the trip and reflect on it after returning

Pre-Dental Society (PDS)

Fall '09-Spring '10

The Pennsylvania State University

- ❖ Attended meetings, listened to guest speakers, learned more about the process of applying to dental school, and went on dental school visits

Alpha Epsilon Delta (Pre-Medical Honors Society- AED)

Fall '08-Spring '09

The Pennsylvania State University

- ❖ Inducted honors member (Sp '09); participated in service events and learned more about the health care field through guest speakers

THON- Annual Dance Marathon

Fall '06-Spring '08

The Pennsylvania State University

- ❖ Member of ATLAS thon
- ❖ Helped to raise money for the families of children suffering from pediatric cancer by attending canning events