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NEURAL CORRELATES UNDERLYING THE EFFECT OF TEMPORAL PROXIMITY ON
ASSOCIATIVE MEMORY RETRIEVAL FOR OLDER VERSUS YOUNGER ADULTS

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ABSTRACT

Associative memory is a vital component of everyday memory, and success in this form of memory is dependent on one's ability to limit attention and inhibit irrelevant information. Previous behavioral research has shown that older adults exhibit deficits in this ability compared to younger adults (Dennis and McCormick-Huhn, 2018), and this age-related discrepancy is exacerbated as the two target items are presented closer together in time (Campbell and Hasher, 2014). In this study, we aimed to replicate these behavioral findings as we hypothesized that when completing an associative memory task, older adults would exhibit higher false alarm rates than younger adults for near re-pairings ($n \leq 9$ positions apart) compared to far re-pairings ($n > 9$ positions apart), and that younger adults would exhibit lower overall false alarm rates. The current study utilized functional magnetic resonance imaging (fMRI) to determine the neural correlates underlying the effect of temporal proximity on associative memory retrieval for older versus younger adults. Due to the role of the medial temporal lobe in the retrieval of associative memories and the role of the prefrontal cortex in the inhibition of irrelevant information, we hypothesized that older adults would exhibit increased brain activity in these regions compared to younger adults for near versus far re-pairings. We found that younger adults did in fact exhibit lower overall false alarm rates than older adults ($p < 0.001$). However, the age-related behavioral difference associated with the effect of temporal proximity was insignificant. Nonetheless, we did find differences in neural activity between the near and far temporal proximity conditions in older and younger adults, suggesting that older adults utilize different neural strategies than younger adults when overcoming the effect of

temporal proximity on associative memory retrieval.

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Chapter 1

Introduction

Memory for day-to-day activities involves associative memory, and associative memory is more complex than memory for a single item. Associative memory is defined as the binding of individual items or items within a context. A few examples of associative memories include face-name associations, medicine dosage and symptom associations, and class and room location associations. In comparison to younger adults (YA), older adults (OA) exhibit deficits in associative memory. In order to exhibit optimal associative memory, individuals must be able to successfully limit their attention, and older adults have been shown to have impairments in this ability. Therefore, older adults typically form more associations than younger adults. Additionally, associative memory requires the ability to bind different aspects of an event together, and this activity relies on the hippocampus. Hippocampal activity and the ability to bind event details show age related decline (Dennis and McCormick-Huhn, 2018).

In addition to this, temporal proximity has been shown to play a role in associative memory (Campbell and Hasher, 2014). The following example elucidates the effect of temporal proximity on associative learning: At a party, one would be more likely to confuse the names of people they met at the same time than they would be to confuse the names of two people they met 20 minutes apart. Campbell and Hasher (2014) found that older adults are more likely than younger adults to make false alarms (FA) for item pairs that are presented closer together in time. It is critical to understand the neural correlates underlying this behavioral

difference in order to determine the best strategies to address the effect of temporal proximity on associative memory.

Theories and Past Behavioral Research

In the past, researchers have shown that attentional demands relating to the processing of associative memories have significantly impaired this form of memory as opposed to item memory. Impairments exhibited by younger adults under compromised attention conditions resemble the performance of older adults under full attention conditions, highlighting the attention limitation impairments exhibited by older adults (Dennis and McCormick-Huhn, 2018).

In regards to the effect of temporal proximity on paired-associate learning, researchers have shown that older adults exhibit greater false-alarm rates for near re-pairings than for far re-pairings, with re-pairings referring to the recombination of face-name associations to create novel pair combinations. Younger adults' false alarm rates were not affected by the temporal proximity of the re-pairings (Campbell and Hasher, 2014). Campbell and Hasher (2014) attribute this impairment in older adults to deficits in their ability to inhibit irrelevant information or limit their attention within a tight temporal window. In other words, when a re-paired lure is composed of parts of target items that were presented in close proximity to one another (compared to parts of target items that were presented across a larger gap of time), it is more challenging for older adults to reject the irrelevant lure as opposed to when the lure is presented further apart in time (Campbell and Hasher, 2014).

Previous Neuroimaging Research

The main brain regions found to be involved in the retrieval of associative memories include the hippocampus within the medial temporal lobe (MTL) and the prefrontal cortex (PFC) (Dennis and McCormick-Huhn, 2018). Research examining age-related differences in hippocampal activity vary depending on whether studies are measuring task-related or success-related activity. In regards to success-related activity for face-name associations, Persson and colleagues (2011) did not find a significant difference between behavioral recruitment of the bilateral hippocampus during retrieval in younger and older adults. Another study found that both older and younger adults showed significant hippocampal activity supporting successful associative memory. However, younger adults performed better than older adults and showed greater hippocampal recruitment (Tsukiura et al., 2011). In addition to this, Dulas and Duarte (2011) found that the difference in hippocampus activity across age groups was insignificant, yet older adults showed greater perirhinal cortex activity compared to younger adults during associative memory. Authors believe that this age-related difference, correlated with performance, relates to the need for older adults to overcompensate or over-recruit brain regions in order to successfully complete associative memory tasks. The fact that there are no main conclusions that can be drawn across studies, suggests not only that there is a need for additional research in this area but also that behavior and task design must be considered when investigating age-related differences in neural functioning (Dennis and McCormick-Huhn, 2018).

Many studies have found a negative correlation between PFC activity and age-related deficits in associative memory retrieval. For example, Dulas and Duarte (2011) found that older adults tend to under-recruit the right lateralized PFC regions compared to younger

adults. Due to the fact that decreased behavioral success was observed in older adults, and the PFC is responsible for inhibiting irrelevant information and monitoring retrieval processes, the researchers believed that older adults have an impaired ability to successfully monitor and assess the retrieval of source information. Tsukiura and colleagues (2011) found similar results with older adults showing age-related decreased activation of the right middle frontal gyrus, and these researchers believed that their findings were attributed to age-related impairments in the older adults' ability to successfully monitor retrieval output required for associative memory achievement. Finally, in a study by Perssons et al. (2011), older adults showed increased activation of left dorsolateral frontal cortices, and this activity was correlated with erroneous associative memory performance. The researchers suggest that this finding represents a failed attempt at compensating for the older adults' lower performance, compared to younger adults. Collectively, the results indicate that, older adults have an impaired ability to engage PFC regions to successfully meet the needs of demanding associative memory tasks.

The Present Study

The present study aims to determine the neural correlates underlying the behavioral effects of temporal proximity on paired-associate learning outlined by Campbell and Hasher (2014). The independent variable, temporal proximity, consists of two conditions: near and far. This study analyzes behavioral data obtained from a previous study that observed how different forms of associative encoding induce differential processing in both younger and older adults. In the present study, we hypothesized that older adults would exhibit greater false alarm rates for near versus far re-pairings compared to younger adults. We also hypothesized that younger adults would have lower overall false alarm rates. In addition to this, we hypothesized that

older adults would exhibit greater activity in the MTL and PFC for near re-pairings as opposed to far re-pairings due to the behavioral impairments associated with the more difficult near condition.



Figure 1. Millennium Scholars Program, Est. 2013

Chapter 2

Methods

Participants

A total of 30 right-handed, English-speaking participants were recruited from the State College, PA community, and each individual received monetary compensation for their participation. Each participant was screened for a history of neurological disorders and psychiatric illness, alcoholism, drug abuse, and/or learning disabilities, as well as contraindications for MRI. Two older adults and one young adult displayed head movement in excess of 4 mm, and they were therefore excluded from the data. One young adult was excluded due to failure to comply with test instructions. Two young adults withdrew from the scanner due to claustrophobia. One older adult was excluded because they had received the incorrect task version. Thus, data from 26 young participants [19 females; $M_{\text{age}} = 20.5$ years, $SD_{\text{age}} = 1.95$] and 27 older adults [20 females; $M_{\text{age}} = 71.19$ years, $SD_{\text{age}} = 6.19$] were analyzed. All participants provided written informed consent, and The Pennsylvania State University's Institutional Review Board for the ethical treatment of human participants approved all procedures. Prior to the study, older adults participated in a 1-hour cognitive assessment battery, consisting of MMSE, GDS, Letter-Number Sequencing, WAIS-III Vocabulary, Symbol Coding, Symbol Copy, and Digit Span. Results are reported in Table 1.

Stimuli

The stimuli used in this study were created by Dennis et al. (2019) for a previous study investigating how different types of associative encoding evoke differential processing in both younger and older adults. This study consisted of face and scene stimuli. Face stimuli included 170 color photographs of male and female faces which displayed neutral expressions, and the images were retrieved from the Color FERET database (Phillips, Moon, Rizvi, & Rauss, 2000), adult face database from Dr. Denise Park's lab (Minear & Park, 2004), the AR face database (Martinez & Benavente, 1998), and the FRI CVL Face Database (Solina, Peer, Batageli, Juvan, & Kovac, 2003). Scene stimuli included 170 color photographs of outdoor and indoor scenes retrieved from an Internet image search. Adobe Photoshop CS2 version 9.0.2 and Irfanview 4.0 (<http://www.irfanview.com/>) were used to give the face stimuli a uniform size (320 x 240 pixels) and background (black). Scene stimuli were standardized to 576 x 432 pixels.

During the associative encoding task, participants were shown 170 face-scene pairs in one of two presentations—either with the pairs organized as an item (face) embedded within a context (scene) or organized as two independent items (face and scene side-by-side). Therefore, the focality of scenes were manipulated across the item-context (IC) and item-item (II) conditions. In IC associations, scenes were displayed as contexts as they were arranged behind the faces (reduced focality of the scene). In II associations, scenes were presented as items as they were arranged beside the faces with a small white gap separating the two photographs. For the purposes of this study, we collapsed across these conditions.

The encoding process consisted of 5 encoding blocks. During each block, 17 item-context and 17 item-item associations were randomly presented. Each retrieval block consisted of 17 congruent pairings, meaning that they match the same visual configuration as encoding, and

17 incongruent pairings, meaning that they are the opposite visual configuration from encoding. 5 item-item and 5 item-context pairings in the retrieval condition were lures, meaning that the face-scene pair was a rearranged version of what was presented at encoding. Each image presentation was separated by a jittered interstimulus interval (2-8s), and each encoding and retrieval block had a duration of 4 minutes and 18 seconds.

For the purpose of the current analysis, we focused on rearranged pairs at retrieval, classifying them with respect to the temporal distance between the pairs at the time of encoding. Rearranged pairs were labeled as “near,” if the items in the pair were $n \leq 9$ positions apart at encoding, while rearranged pairs were labeled as a “far,” if the items in the pair were $n > 9$ positions apart. Our near and far proximity definitions were inconsistent with past research, as Campbell and Hasher defined near temporal proximity as $n + 1$, and classified far re-pairings as $n + 9$ (Campbell and Hasher, 2014). However, because the stimuli were not originally presented with the purpose of observing temporal proximity, it was necessary to classify $n \leq 9$ as near re-pairings, and $n > 9$ as far re-pairings in order to ensure that each experimental condition consisted of approximately the same number of pairs.

Procedure

Participants were given verbal instructions prior to entering the scanner. Before scanning, all participants practiced both the encoding and retrieval practice block procedures. During the practice, participants were encouraged to ask questions. A 7-minute structural scan (MPRAGE)

initiated the scanning session, and participants were prompted to remain as still as possible throughout this scan. After the structural scan, participants completed 5 encoding and 5 retrieval blocks in an alternating order, and instruction screens that repeated the verbal instructions were presented before each block. The instruction screens were self-paced with the participants pressing “1” on the handheld button box after they had finished reading the instructions and were ready to progress to the next screen. In order to confirm that the participants had a thorough understanding of the instructions, they were asked to verbally explain the instructions presented on the screen before beginning the experimental task.

Once the encoding block began, a sequence of face and scene pairings were presented on the screen in either an II or IC configuration. Each pair was shown for 4 seconds with the question: “How welcoming are the scene and face?” displayed under each pair. During the 4 seconds, participants answered the question by pressing the keys that coordinated with a 1-4 rating scale (1=not at all; 4=very). In order to ensure that the face and scene were encoded together, the instructions emphasized that the participants should rate the pairs based on how welcoming they believed the face and scene were together, rather than as individual items. This question was utilized in order to prevent the scene from being incidentally encoded while the face was intentionally encoded, as the question helped guarantee that participants paid attention to the scene, even when it was arranged behind the face in the IC condition.

In order to counter-balance the experiment, two task versions were created. In each version, faces and scenes were counter-balanced for their inclusions in either an II or IC pair. Analyses were collapsed across versions, and there were no differences between versions. A retrieval block followed each encoding block, and like encoding, each face-scene pair presented during retrieval was shown for 4 seconds. The statement: “Please identify the pairings that have been presented previously” was shown below each pair, and participants were prompted to

respond by pressing “1” for ‘Remember,’ “2” for ‘Know,’ and “3” for ‘New’ on the button box. Participants were asked to base their choices on the co-occurrence of the face and scene rather than the display arrangement. They were asked to respond ‘Remember,’ if they remembered exact details about the face and scene that were presented together during encoding. The Remember-Know-New design helped to distinguish recollection activity linked to ‘Remember’ responses, from the familiarity linked to ‘Know’ responses. In regards to analyzing memory-related activity especially in the MTL, this difference has been shown to be vital (Yonelinas, 2002; Yonelinas, Otten, Shaw, & Rugg, 2005; Yonelinas et al., 2007). For the purposes of classifying lures as false alarms, we also collapsed across both levels of memory specificity (remember and know).

Image Acquisition

Siemens 3T scanner with a 12-channel head coil, parallel to the AC-PC plane was used to acquire structural and functional images. Structural images were acquired with a 1,650 ms TR, 2.03 ms TE, 256 mm field of view (FOV), 2562 matrix, 160 axial slices, and 1.0 mm slice thickness for each participant. Echo-planar functional images were acquired using a descending acquisition, 2,500 ms TR, 25 ms TE, 240 mm FOV, a 802 matrix, 90 degree flip angle, 42 axial slices with 3.0 mm slice thickness resulting in 3.0 mm isotropic voxels.

Image Processing

For univariate analyses, raw anatomical and functional images were first skull stripped using the Brain Extraction Tool (Smith, 2002) in the FMRIB Software Library (FSL) version

5.0.10 (www.fmrib.ox.ac.uk/fsl). FSL's MCFLIRT function (Jenkinson, Bannister, Brady, & Smith, 2002) was then applied for realignment and motion correction within each functional run. All volumes were aligned to the middle volume of the middle run of encoding. The realigned functional images were then processed by FSL's fMRI Expert Analysis Tool (FEAT; Woolrich, Ripley, Brady, & Smith, 2001), where they were high-passed filtered and spatially smoothed at 6mm FWHM. These data were then prewhitened to account for temporal autocorrelations within voxels. Lastly, the structural data underwent non-linear transformation into the standardized Montreal Neurological Institute (MNI) space by using the warping function in FSL's FNIRT (Andersson, Jenkinson, & Smith, 2010).

Behavioral Analysis

Re-pairings that were correctly identified as 'New' during retrieval were identified as correct rejections (CR). Re-pairings that were incorrectly identified as 'Remembered' or 'Know' were identified as false alarms (FA). The ratios of CR near, FA near, CR far, and FA far were calculated for both older and young adults. These ratios were calculated as follows: 1) $CR\ near = \#CR\ near / \text{Total count of near re-pairing responses}$ 2) $FA\ near = \#FA\ near / \text{Total count of near re-pairing responses}$ 3) $CR\ far = \#CR\ far / \text{Total count of far re-pairing responses}$ 4) $FA\ far = \#FA\ far / \text{Total count of far re-pairing responses}$. Since the CR and FA rates are inverses of one another, only the FA rates were subjected to behavioral analyses (all 4 trial types were examined using fMRI analyses). FA rates were analyzed by 2x2 between and within group ANOVA designs. The between group factor was age (older versus young adults), while the within group factor was temporal proximity (near versus far). Ratios were used rather than counts because not all participants had equal total near and far

response counts due to the fact that some participants did not respond to every pair.

fMRI Analysis

Univariate

At the first level, trial-related activity was modeled using the general linear model (GLM) with a stick function corresponding to trial onset convolved with a canonical hemodynamic response function. A second-level random effects GLM was created, and one sample t-tests were conducted to investigate contrasts of interest for each age group. The current analyses focused on 6 trial types of interest: 1) All CR 2) All FA 3) Near CR 4) Near FA 5) Far CR 6) Far FA. In order to identify the neural correlates underlying the effect of temporal proximity on paired associate learning for older and younger adults, ten contrasts of interest were used: All FA > All CR, Far CR > Near CR, Far FA > Near FA, Near CR > Near FA, Far CR > Far FA, and the inverse of each. We also analyzed Hit > Miss activity as a way to show that the tasks functioned properly. Hits referred to the identification of non-recombined pairs shown previously in encoding as ‘Remembered’ or ‘Know’ while misses referred to the identification of these pairs as ‘New.’

We examined the activity in each of the above contrasts across the whole brain at $p < 0.005$ and $k \geq 100$ voxels. Based on our *a priori* hypotheses regarding the role of the MTL with relation to associative memory, we investigated all contrasts within the MTL using a reduced threshold of $p < 0.05$ and $k \geq 10$ voxels.

Chapter 3

Results

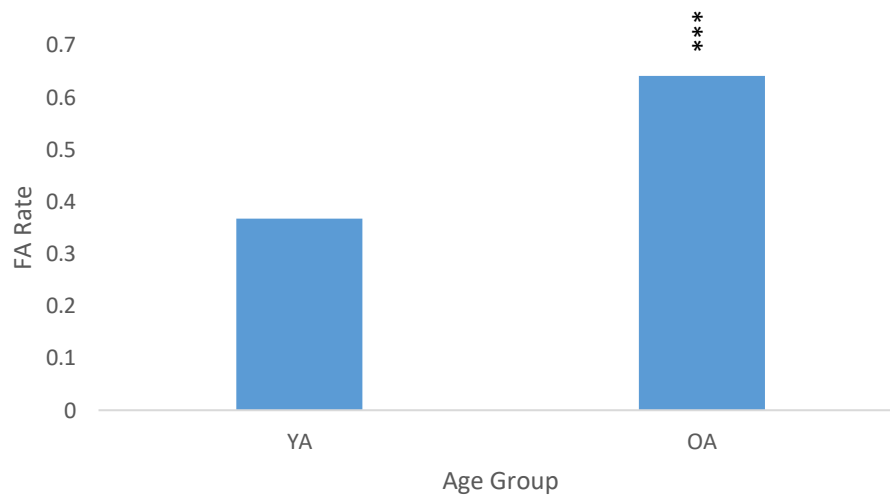


Figure 2. False alarm (FA) rates for younger versus older adults. *** = $p < 0.001$.

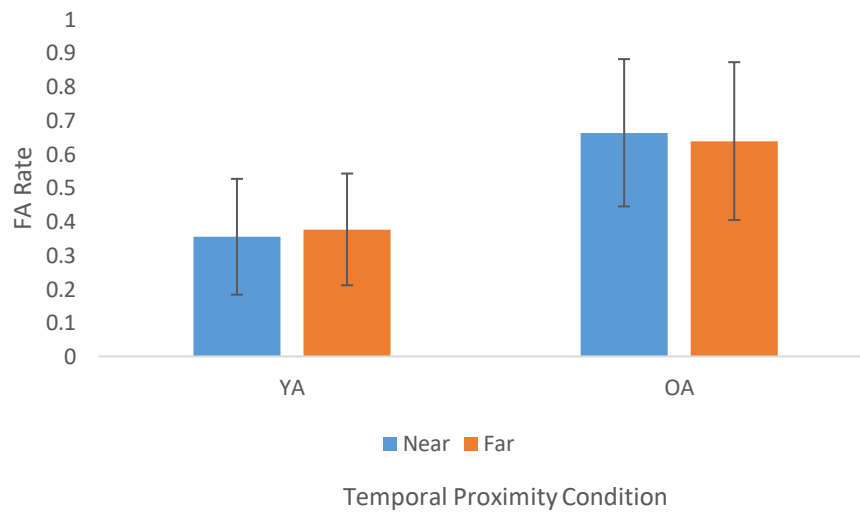


Figure 3. False alarm rates for near versus far re-pairings for younger ($SD_{\text{near}}=0.172$, $SD_{\text{far}}=0.166$) and older adults ($SD_{\text{near}}=0.252$, $SD_{\text{far}}=0.234$).

Table 1. YA Brain Activation for Paired Associate Memory with Near and Far Conditions

		MNI coordinates			t	mm ³
	H	BA	x	y	z	
Hit > Miss						
Ant cingulate cortex (ACC)	L	11/32/10/24	-6	26	-10	6.93 233790
Parietal cortex	L	40	-54	-46	32	5.78 2142
Cuneus	R	19	10	-86	40	5.63 1129
MTL (Hippocampus/PHG)	R	36	26	-6	-22	5.95 754
MTL (Hippocampus/PHG)	L	27	-12	-38	4	5.43 712
Cerebellum	R		22	-86	-34	5.02 677
Temporal Mid	R	21	62	-8	-20	4.49 172
Temporal Pole Sup	L	38	-46	16	-16	4.06 160
Cerebellum	L		-22	-57	-38	4.25 123
All FA > All CR						
No significant areas of activation						
All CR > All FA						
Lingual gyrus	R	18	12	-80	-2	6.21 2070
Angular gyrus	R	39	46	-62	38	4.77 801
Hippocampus/PHG	L	35	-14	-12	-10	5.99 730
Angular	L	39	-44	-66	38	3.59 347
Hippocampus/PHG	R	34	6	-8	-14	4.06 207
Postcentral	L	40	-64	-20	22	3.88 124
Far CR > Near CR						
Cerebellum	L	19	-18	-60	-46	5.26 671
Cerebellum	R	37	34	-48	-42	5.34 378
Sup frontal gyrus	R	32	16	18	42	4.22 270
Caudate	R	48	22	16	22	3.73 182
Postcentral gyrus	L	6	-52	-6	48	3.2 119
Near CR > Far CR						
No significant areas of activation						
Far FA > Near FA						
Occipital cortex	R	18	20	-92	6	5.68 643
Inf parietal cortex	R	40	42	-24	28	4.84 229
Occipital Mid	R	19	40	-78	10	3.84 221
Cuneus	R	18	6	-76	26	3.92 199
Near FA > Far FA						
No significant areas of activation						
Near CR > Near FA						
Lingual gyrus	R	18	20	-70	-6	6.51 4285
Hippocampus	L	20	-26	-18	-10	4.31 322
Hippocampus/PRC	L	30	-14	-22	-10	4.71 187
Amygdala /PRC	R	48	26	8	-16	3.79 164
Lingual	L	19	-20	-56	2	3.68 102
Near FA > Near CR						
No significant areas of activation						
Far CR > Far FA						
Precentral gyrus	L	6	-52	6	34	4.15 152
Hippocampus	L	20	-26	-10	-8	3.92 137
Inf frontal gyrus	R	46	26	44	6	5.42 132
Occipitoparietal	L	39	-50	-66	16	4.51 109
Far FA > Far CR						
No significant areas of activation						

This table reports the brain regions in younger adults (YA) associated with paired associate memory at $p < 0.005$ and $k \geq 100$ voxels.

Key: BA: Broadmann area, FA: false alarm, CR: correct rejection, Ant: anterior, Inf: inferior, Mid: medial, MTL: medial temporal lobe, PHG: parahippocampal gyrus, PRC: perirhinal cortex, Sup: superior

Table 2. OA Brain Activation for Paired Associate Memory with Near and Far Conditions

		MNI coordinates					
		H	BA	x	y	z	t
							mm ³
Hit > Miss							
	Cerebellum	L		-10	-70	-14	4.66
	Postcentral	L	40	-40	-18	30	4.43
	Cingulum Ant	L	10	-12	48	4	4.16
	Cerebellum	L		-20	-44	-34	4.25
	Temporal Inf	L	20	-46	6	-36	4.35
All FA > All CR							
	Lingual	L	18	-8	-74	-4	3.83
All CR > All FA							
	Precentral L	L	6	-26	-16	62	6.41
	Parietal Inf	L	40	-38	-42	42	5.18
	Sup frontal gyrus	R	32	8	20	42	6.4
	Precentral L	L	6	-50	4	28	4.33
	Supramarginal gyrus	R	2	52	-28	46	4.31
	Precentral	R	6	34	-8	56	4.1
	Insula	R	47	28	22	-8	4.79
	Frontal Mid	R	8	30	8	60	3.91
Far CR > Near CR							
	Occipital Mid	R	19	34	-76	32	3.75
Near CR > Far CR							
No significant areas of activation							
Far FA > Near FA							
	Occipital Sup	R	19	28	-88	32	4.98
	Temporal Inf	L	37	-46	-60	-6	4.23
	Cingulum Ant	R	25	16	34	12	4.57
	Thalamus	R	27	8	-14	0	4.51
	Temporal Inf	R	37	48	-66	-8	5.74
	Hippocampus/PHG	L	37	-12	-24	-14	4.08
	Putamen	L	48	-22	6	10	4.46
	Postcentral gyrus	R	43	56	-2	24	4.22
Near FA > Far FA							
No significant areas of activation							
Near CR > Near FA							
	Precentral	L	6	-28	-18	56	5.65
	Parietal cortex	R	32	10	20	44	5.84
	Postcentral	R		52	-26	44	4.86
	Parietal Inf	R	3	-42	-46	48	4.36
Near FA > Near CR							
	Temporal Sup	R	37	34	-34	-16	4.32
Far CR > Far FA							
	Precentral	L	6	-26	-6	48	4.69
	Parietal Inf	L	40	-38	-42	40	4.29
Far FA > Far CR							
	Cuneus	L	19	8	-84	38	3.78

This table reports the brain regions in older adults (OA) associated with paired associate memory at $p < 0.005$ and $k \geq 100$ voxels.

Key: BA: Broadmann area, FA: false alarm, CR: correct rejection, Ant: anterior, Inf: inferior, Mid: medial, MTL: medial temporal lobe, PHG: parahippocampal gyrus, Sup: superior

Table 3. MTL Mask: YA Brain Activation for Paired Associate Memory with Near and Far Conditions

			MNI coordinates						
			H	BA	x	y	z	t	mm^3
Hit>Miss									
	Precuneus	L	27	-12	-38	4	5.43	1331	
	Temporal Pole Sup	R	34	26	6	-22	5.95	1195	
	Temporal Pole Sup	R	38	38	8	-18	2.9	26	
All FA > All CR									
No significant areas of activation									
All CR > All FA									
	Hippocampus	L	30	-16	-10	-12	5.16	515	
	Hippocampus	R	28	22	-6	-20	3.84	258	
	Fusiform	R	37	30	-34	-14	2.57	46	
	Hippocampus	L	36	-32	4	-26	2.22	26	
	Lingual	R	30	18	-42	-10	2.22	26	
	Parahippocampal	L	36	-26	-4	-30	2.44	16	
Far CR > Near CR									
	Hippocampus	R		34	-14	-22	3.03	169	
	Ant Parahippocampal/PRC	L	36	-30	-8	-28	3.58	51	
	Parahippocampal Gyrus	L	30	-28	-26	-20	2.1	19	
Near CR > Far CR									
	Posterior PHG	L	36	-28	-40	-8	2.99	61	
	Posterior PHG	L	36	-18	-34	-2	1.97	10	
Far FA > Near FA									
	PHG	L	30	-26	-26	-24	2.9	104	
	Hippocampus/PHG	R	30	24	-22	-24	2.81	67	
	Hippocampus	R		38	-8	-20	2.91	54	
	Hippocampus	L		-34	-14	-20	2.43	45	
	PHG	R	20	34	-22	-8	2.71	30	
	PHG	R	30	18	-40	-8	3.01	18	
	PHG	L	34	-14	2	-18	3.13	13	
	PHG	R	20	48	-18	-24	3.33	13	
	PHG	L	20	-30	-26	-8	2.6	11	
	PHG	L	34	-32	2	-20	2.22	10	
Near FA>Far FA									
No significant areas of activation									
Near CR > Near FA									
	Hippocampus/PHG	L	20	-28	-8	-14	4.18	477	
	Hippocampus/PHG	R	37	32	-34	-14	4.07	308	
	PHG/PRC	L	36	-32	2	-26	2.94	43	
	PHG/PRC	L	34	-14	2	-18	3.61	16	
Near FA>Near CR									
No significant areas of activation									
Far CR>Far FA									
	Ant Hippocampus	L		-18	-10	-12	3.6	140	
	Ant Hippocampus	R		20	-10	-12	3.25	114	
	Hippocampus	L		-20	-24	-10	2.33	25	
Far FA>Far CR									
No significant areas of activation									

This table reports the brain regions in younger adults (YA) associated with paired associate memory indicated by the MTL mask at $p < 0.05$ and $k \geq 10$ voxels.

Key: BA: Broadmann area, FA: false alarm, CR: correct rejection, Ant: anterior, Mid: medial, MTL: medial temporal lobe, PHG: parahippocampal gyrus, PRC: perirhinal cortex, Sup: superior

Table 4. MTL Mask: OA Brain Activation for Paired Associate Memory with Near and Far Conditions

		MNI coordinates						
		H	BA	x	y	z	t	mm^3
Hit>Miss								
	Hippocampus/PHG	L	30	-22	-18	-26	3.47	423
	Hippocampus	R		32	-8	-22	4.43	165
	Hippocampus	R		40	-32	-12	3.1	127
	PHG	L	27	-12	-38	4	2.22	10
All FA > All CR								
	Hippocampus/PHG	L	20	-30	-16	-20	3.72	816
	Hippocampus/PHG	R	20	32	-18	-18	3.46	575
	Amygdala	L	36	-28		-26	2.54	18
	Cingulum Post	L	29	-14	-40	10	2.93	11
All CR > All FA								
No significant areas of activation								
Far CR > Near CR								
	Hippocampus/PHG	R	30	20	-24	-26	3.2	133
	Hippocampus	R		2	-6	-22	2.19	20
Near CR > Far CR								
No significant areas of activation								
Far FA > Near FA								
	Hippocampus/PHG	R	20	26	-8	-16	3.87	566
	Hippocampus/PHG	L	35	-18	-16	-20	4.18	304
	Hippocampus	L		-30	-6	-18	2.96	36
	PRC	R	36	34	2	-38	2.25	32
Near FA>Far FA								
No significant areas of activation								
Near CR > Near FA								
No significant areas of activation								
Near FA>Near CR								
	Hippocampus	L		28	-30	-10	3.04	292
	Hippocampus	L		-26	-20	-16	2.67	212
	Posterior PHG	L	37	-28	-38	-12	3.58	67
	PRC	L	36	-38	-6	-40	2.17	36
	PRC	L	36	-40	-2	-24	2.52	27
Far CR>Far FA								
No significant areas of activation								
Far FA>Far CR								
	Hippocampus/PHG	L	20	-38	-8	-30	2.38	142
	Hippocampus/PHG	L	30	-18	-30	-14	2.81	118
	Hippocampus	L	20	-38	-18	-16	2.31	111
	Hippocampus	R		34	-18	-16	3.54	100
	PHG	R	30	20	-34	-12	2.29	78
	PRC	R	36	26	-4	-22	2.52	18

This table reports the brain regions older adults associated with paired associate memory indicated by the MTL mask at $p < 0.05$ and $k \geq 10$ voxels.

Key: BA: Broadmann area, FA: false alarm, CR: correct rejection, MTL: medial temporal lobe, PHG: parahippocampal gyrus, PRC: perirhinal cortex

Chapter 4

Discussion

In this study, older adults showed a larger ratio of false alarms than younger adults, which is consistent with our behavioral hypothesis. However, in contrast to our hypothesis regarding the effect of temporal proximity on associative memory retrieval, a behavioral difference was not found within age groups in neither near nor far proximity with respect to false memories, as the difference between near and far false alarm rates in both age groups was insignificant. Although we did not find a behavioral difference in either age group regarding this effect, we found differences in brain activity between near and far proximity in older and younger adults, and this activity is explained below. These findings suggest that older adults were able to compensate for difficulties associated with near re-pairings by recruiting neural strategies that differed from those of younger adults.

Hit>Miss

Although this was not a contrast of interest in regards to our hypothesis, the activity shown for older and younger adults for hits compared to misses indicates that the task worked properly and the neural activity within each age group was typical. For hit compared to miss activity, younger adults exhibited greater activation in the MTL, PFC, and visual, parietal, and temporal cortices. These areas of activation are part of the typical memory success network. Older adults also showed increased activity in the temporal and parietal lobes. However, older adults did not differentially recruit the MTL or visual cortex, which is indicative of the age-related deficits associated with memory retrieval. Older adults also exhibited increased cerebellum activity. The cerebellum has been shown to be involved in motor learning

(Kawashima et al., 2000). This increased activity may correlate to the process of learning the correct buttons to press in order to accurately indicate 'Remember,' 'Know,' or 'New.'

All CR>All FA

After examining all CR and all FA activity for each age group, we found that overall, brain activity is greater for CR than FA. Older adults showed greater brain activation in the bilateral precentral gyrus, right superior frontal gyrus, left inferior parietal lobe, right insula, right supramarginal gyrus, and the right mid frontal lobe. For younger adults, greater brain activity for CR compared to FAs was found in the bilateral hippocampus/parahippocampal gyrus (PHG), the visual cortex (localized in the right lingual gyrus), and the parietal lobe (localized in the bilateral angular gyrus and the left postcentral gyrus). These findings are consistent with past research (Bowman et al., 2019), suggesting that over-recruitment of brain activity has a direct relationship with successful memory retrieval.

Correct rejection success relies on one's ability to identify information as novel as well as the ability to avoid false recognitions (Bowman and Dennis, 2015). The fact that younger adults were found to differentially recruit hippocampal/PHG regions and the lingual gyrus (part of the visual cortex) for all CR compared to all FA is consistent with previous studies on novelty processing (Bowman and Dennis, 2015). This activity suggests that younger adults were able to successfully rely on familiarity or gist processing of visual information. In addition to this, Bowman and Dennis (2015) found that older adults did not differentially recruit the early visual cortex nor the anterior hippocampus, which is consistent with our findings and suggests that older adults struggle with using item-specific details to achieve novelty processing success. Our finding that older adults differentially recruit the insula when engaging in novelty processing supports our hypothesis regarding PFC activity.

This is supported by Bowman and Dennis (2015), as they found that in order to achieve successful novelty processing, older adults were found to differentially recruit the bilateral ventrolateral PFC.

In addition to this, our findings also indicate that older adults differentially recruit additional frontal lobe regions when making CRs, suggesting that older adults utilize higher level cognitive processing to compensate for the difficulties linked to associative memory and novelty processing, leading to the achievement of successful pattern completion. Lastly, both older and younger adults showed increased activity in the sensory regions of the parietal lobe. This finding is consistent with typical memory success networks (Baddley et al., 2015).

All FA>All CR

In older adults, all false alarm versus all correct rejection activity was associated with increased visual cortex activity localized in the lingual gyrus. Meanwhile, younger adults did not exhibit differential brain activation. Consistent with Bowman and Dennis (2015), these findings suggest that visual cortex activity is associated with erroneous novelty processing in older adults, indicating that older adults exhibit flawed visual analysis of re-pairings. Younger adults did not show any significant areas of activation. This represents typical brain activity as past research has shown that an under-recruitment of brain regions has a direct relationship with retrieval failure (Baddley et al., 2015).

Far CR>Near CR

The data indicates that both older and younger adults exhibit more brain activity for far CR compared to near CR, contrasting our hypothesis. Past research has shown that older adults exhibit behavioral impairments when assessing near re-pairings, we hypothesized that near CR

activity would be associated with an over recruitment of brain regions in an attempt to compensate for this difficulty.

For far CR compared to near CR, older adults exhibited increased visual cortex activity that encompassed the mid occipital region. Bowman et. al (2015) showed that older adults typically under-recruit this region when engaging in novelty processing. The fact that older adults were able to achieve successful recruitment of the visual cortex for the far compared to near condition, suggests that increasing the temporal distance between the presentation of two unrelated items may appease the older adults' deficits in utilizing item-specific details.

Younger adults exhibited over recruitment of the right superior frontal gyrus, left postcentral gyrus, right caudate, and bilateral cerebellum for far CR compared to near CR. Again, the increased cerebellum activity is likely associated with motor learning (Kawashima et al., 2000). The increased parietal and frontal lobe activity is typical and suggests that younger adults do not exhibit a struggle in analyzing sensory details and engaging in higher-level cognitive process for far compared to near re-pairings, highlighting the easier task nature of the far condition. Also, in support of the easier nature of the far condition, the younger adults' increased caudate activity is consistent with normal memory function, as the caudate is linked to stimulus-response associations (Nils et al, 2017).

Near CR > Far CR

For both older and younger adults, there were no significant areas of activation for near CR compared to far CR. This finding does not support our hypothesis. We propose that the temporal range for near ($n \leq 9$) and far ($n > 9$) re-pairings may have been too large to observe the neural strategies underlying the increased task difficulty of the near compared to far conditions at a significance level of $p < 0.005$ and $k = 100$. Past research has defined near re-pairings as $n + 1$

pairs apart and far re-pairings as $n + 9$ pairs apart (Campbell and Hasher, 2014). In this study, the maximum n -value for near re-pairings was $n=9$, while the largest value for far re-pairings was $n=28$. These n -value differences may indicate why we were able to observe neural differences for far CR compared to near CR as opposed to near CR compared to far CR, for it is possible that the temporal distance is so large in the far condition compared to the near, that it elicits significant differences in the brain activity. Meanwhile, the temporal proximity in the near condition is not small enough to elicit significant differences in the reverse direction.

Far FA > Near FA

Contrary to what was hypothesized, brain activity exhibited by older adults was greater for far FA compared to near FA. This pattern was also shown in younger adults. When experiencing far FA, older adults differentially recruited regions that spanned the whole brain including the hippocampal/PHG regions, while younger adults differentially recruited regions responsible for visual/spatial processing.

The increased whole brain far FA activity shown by the older adults may represent mental searching for items that were presented temporally further apart, for it is possible that the presentation of far re-pairings may elicit attempts to recall both the original pair and the pair presented further apart in time, in order to correctly reject the recombined pair. This recollection attempt may have failed due to deficits in utilizing the hippocampus for successful novelty processing completion (Bowman and Dennis, 2015).

The increased visuospatial activity shown by younger adults suggests that the far re-pairings induced erroneous sensory processing, leading younger adults to believe that they had seen the re-pairings in the past. In contrast, it may be more challenging for younger adults to recruit sensory regions for near re-pairings, as the presentation of items closer together in time

may elicit a decreased assessment of sensory characteristics, pointing to the increased task difficulty of the near condition. Therefore, while far FA activity is associated with erroneous sensory processing, near FA activity may result from a lack of sensory processing.

Near FA > Far FA

There were no significant areas of activation for near FA compared to far FA for neither older nor younger adults. This finding may have resulted from the fact that the range for the near and far conditions were too large to observe significant differences at $p < 0.005$ and $k = 100$. In contrast, being that FA activity is typically associated with an under-recruitment of brain regions, this finding may suggest that errors in near re-pairings compared to far re-pairings result from decreased brain activation (Bowman et al. 2019). The latter theory would suggest that when unrelated items are paired closer together in time it is more difficult to recruit the necessary retrieval processes.

Near CR > Near FA

For near CR compared to near FA, young adult CR rates were associated with the hippocampus and PHG, amygdala, perirhinal cortex, and lingual gyrus. These findings indicate that when successfully completing near re-pairings, younger adults utilize the MTL and visual processing regions, and these results are consistent with past research highlighting younger adults' brain activity underlying associative memory success and novelty processing. However, the fact that younger adults did not utilize the PFC for near re-pairing success, may suggest that it may be so difficult to discriminate between items presented closer together in time that neural strategies outside of inhibition must be utilized in order to achieve associative memory success.

Near CR rates in older adults were associated with activity in the parietal cortex, precentral gyrus, postcentral gyrus, and inferior parietal lobe. These findings support our claim

that older adults struggle with item-specific details as they under-recruit the MTL and visual cortex when executing novelty processing. However, older adults were able to compensate for this deficit by utilizing additional sensory regions and higher-level cognitive processes.

In contrast to our hypothesis, older adults did not utilize the MTL and PFC for near re-pairing success. These findings have likely resulted from the fact that compared to younger adults, older adults typically show deficits in these regions when engaging in novelty processing and paired associate learning. Therefore, with the increased task difficulty associated with the near condition, older adults likely needed to recruit different neural strategies in order to achieve associative memory success.

Near FA > Near CR

Both older and younger adults showed decreased activity for near FA compared to near CR, which is consistent with past research indicating that decreased brain activity is directly related to retrieval failure. For younger adults, near FA compared to near CR activity was not associated with any significant areas of activation. However, for older adults, near FA compared to near CR activity was correlated with increased activity of the right superior temporal gyrus. Being that the superior temporal gyrus is responsible for auditory processing, this activity may be indicative of an erroneous attempt to assess the sensory details of the images, for auditory processing is not required for the assessment of visual images. This finding taken together with our older adult findings for near CR > near FA, suggest that older adults struggle with the near condition because they are unable to recruit the sensory regions required for visual processing.

Far CR > Far FA

Similarly to our findings for near CR activity compared to near FA activity in younger adults, younger adult activity for far CR compared to far FA activity was associated with increased hippocampal activity, which again, is consistent with past research on the MTL's role in associative memory retrieval. Our findings indicate that, regardless of the temporal proximity of the re-paired items, younger adults are able to successfully recruit the hippocampus in associative memory retrieval, and this finding may be indicative of the fact that in comparison to older adults, younger adults typically do not show deficits in hippocampal recruitment. In addition to this, far CR activity compared to far FA activity in younger adults was associated with increased activity in the left precentral gyrus, right inferior frontal gyrus, and left occipitoparietal cortex. These findings suggest that younger adults utilize the inhibition of irrelevant information as well as sensory processing to successfully assess far re-pairings. This activity is consistent with typical younger adult activity for successful associative memory and novelty processing. In other words, when younger adults achieve successful pattern completion for far re-pairings, typical associative memory and novelty processes remain intact.

Also similarly to near CR compared to near FA activity in older adults, older adults' far CR activity compared to far FA activity was associated with increased activity in the precentral gyrus and the inferior parietal lobe. These findings suggest that older adults are able to achieve sensory processing recruitment for both near and far re-pairings, and this is consistent with past research showing that parietal lobe activity is a typical part of the memory success network (Baddley et al., 2015). These findings also suggest that accurate parietal sensory processing in older adults may be resistant to the effects of temporal proximity on paired associate learning.

Far FA > Far CR

Similarly to near FA compared to near CR activity, far FA compared to far CR activity was not associated with differential recruitment of brain activity in younger adults. However, the older adults' far FA activity was correlated with increased activity of the left cuneus, suggesting that far FA compared to far CR activity is associated with erroneous processing of visual information. This finding is consistent with our claim that older adults face deficits in processing item-specific details.

MTL Mask

Our analysis of the MTL at lower significance threshold may help to compensate for the limitation in our data related to the large temporal ranges in the near and far conditions. Although it was observed at a lower significance level, the MTL Mask has helped to shed additional light on our *a priori* hypothesis relating to the role of the MTL in associative memory completion.

Hit > Miss

Activity in this contrast ensured that the tasks worked properly. Both older and younger adults showed increased MTL activity, which is typical for successful associative memory retrieval.

All CR > All FA

Younger adults over-recruited MTL regions for all CR compared to all FA, whereas older adults did not show increased areas of activation. These findings indicate that the younger adults exhibit MTL activity typical for associative memory retrieval, while older adults show MTL deficits and must utilize different neural strategies to achieve CR success.

All FA > All CR

At a lower significance threshold, the MTL mask revealed that older adults differentially recruit MTL regions for all FA compared to all CR, while younger adults do not show any significant areas of activation. These findings suggest that older adults, who on average made more false alarms than younger adults, engaged in erroneous MTL processing, further supporting our claim that older adults experience MTL deficits. The younger adults' lack of brain activation is typical for erroneous memory retrieval.

Far CR > Near CR

Far CR activity was greater than near CR activity for younger adults. Both older and younger adults exhibited increased MTL activity in the hippocampus and PHG for far CR compared to near CR. These findings suggest that both age groups were able to engage in both recollection and familiarity success for far CR compared to near CR. Being that our findings for all FA > all CR suggest that older adults engage in erroneous MTL recruitment during associative memory retrieval, the fact that older adults were able to successfully recruit the MTL for far re-pairing success compared to near re-pairing may be indicative of the easier nature of the near condition.

Near CR > Far CR

For near CR compared to far CR, younger adults showed increased MTL activity in only the posterior PHG, while older adults did not exhibit significant areas of activation. These findings suggest that younger adults exhibit increased familiarity processing for near compared to far re-pairing success. This may represent the difficulty associated with the near condition in the way that the younger adults needed to rely on gist processing, as they were unable to achieve recollection processing for near re-pairing success as opposed to far. However, the fact that younger adults still had a level of MTL activity sufficient enough for success in the harder near

condition suggests that MTL activity in younger adults is robust, and this activity may explain why younger adults showed greater task performance over all.

Meanwhile, older adults show deficits in both familiarity and recollection processing, which may be indicative of increased task difficulty in the near condition for older adults. These findings are consistent with our data indicating that older adults do not successfully utilize the MTL for novelty processing.

Far FA > Near FA

MTL activity was greater for far FA than near FA in both older and younger adults. Both older and younger adults exhibited increased activation of the hippocampus and PHG. Older adults also experienced increased activation in the perirhinal cortex (PRC), another region responsible for familiarity. Therefore, far FA compared to near FA activity in both age groups is associated with erroneous familiarity and recollection processing.

Near FA > Far FA

Neither younger nor older adults exhibited significant areas of MTL activation for near FA compared to far FA, suggesting that the more difficult nature of the near re-pairings is associated with under-recruitment of the MTL for both older and younger adults. These findings may suggest that the near re-pairing task difficulty is associated with an inability to over-recruit the MTL.

Near CR > Near FA

For near CR compared to near FA, younger adults showed greater MTL activation, while older adults did not show significant areas of activation. This finding further suggests that younger adults engage in more accurate MTL processing for successful analysis of near re-pairings, while older adults do not utilize the MTL as a strategy.

Near FA>Near CR

For near FA compared to near CR, older adults showed greater MTL activation, while younger adults did not show significant areas of activation. This finding suggests that while younger adults show a reduction of MTL activity typical for false alarms, older adults tend to erroneously recruit the MTL when making near re-pairing errors, which is likely indicative of the increased task difficulty associated with the near condition and hippocampal deficits associated with novelty processing in older adults.

Far CR>Far FA

For far CR compared to far FA, younger adults showed greater MTL activation, while older adults did not show significant areas of activation. This finding suggests that younger adults engage in more accurate MTL processing for successful analysis of far re-pairings, while older adults do not. Therefore, when accurately assessing far re-pairings, younger adults successfully recruit the MTL, showing typical activity for associative memory success. The older adult activity is consistent with past findings indicating that older adults do not utilize the hippocampus as a strategy for novelty processing success.

Far FA>Far CR

For far FA compared to far CR, older adults showed greater MTL activation, while younger adults did not show significant areas of activation. This finding suggests that the younger adults engaged in typical false alarm activity, while the older adults erroneously recruited the MTL during associative memory retrieval, which further highlights our claim that older adults experience deficits in MTL activation.

Chapter 5

Conclusion

As we hypothesized, older adults showed greater total false alarm rates than younger adults. However, the behavioral difference between age groups regarding the effect of temporal proximity on associative memory retrieval was insignificant as there were no significant differences between near and far false alarm rates in either age group. Nevertheless, we did find differences in brain activity between near and far proximity in older and younger adults, suggesting that older adults elicit neural strategies that differ from those of younger adults in order to achieve associative memory success for far compared to near re-pairings.

In contrast to our hypothesis, our findings did not indicate that older adults over-recruit the MTL and PFC for near compared to far re-pairing success, as we found that older adults tend to erroneously recruit the MTL. However, older adults were able to successfully recruit the MTL for far CR compared to near CR completion, pointing to the easier nature of the far condition, as the far temporal distance seemed to appease the older adult's MTL deficits.

The MTL mask allowed us to observe that increased MTL activity in older adults was associated with all FA compared to all CR, further suggesting erroneous MTL recruitment. In contrast, younger adults showed typical MTL recruitment success for all CR compared to all FA. These findings suggest that older adults face deficits in MTL recruitment during associative memory retrieval, which could be explained by their deficits in hippocampal recruitment in novelty processing (Bowmen and Dennis, 2015).

In contrast, younger adults were able to successfully recruit the MTL for both the near and far conditions, and this might suggest that successful MTL recruitment is more robust in younger adults than older adults, helping to explain their overall better task performance.

Both older and younger adults recruited greater brain activity for far re-pairings compared to near re-pairings. Older adults were able to recruit the visual cortex for far condition success compared to the near condition success. Older adults typically face visual cortex defects in novelty processing, so this finding further suggests that increasing the temporal distance between the presentation of two unrelated items may appease older adult's deficits in utilizing item-specific details.

Meanwhile, younger adults used greater cerebral, parietal and frontal lobe activity for far CR success compared to near CR success. This activity is typical and suggests that younger adults do not exhibit a struggle in analyzing sensory details, utilizing motor learning skills, and engaging in higher-level cognitive processes for far compared to near re-pairings, highlighting the easier task nature of the far condition.

Younger adult activity for far re-pairing errors compared to near re-pairing errors were associated with erroneous visuospatial processing. We propose that it may be more difficult for younger adults to recruit sensory regions for near re-pairings as opposed to far, being that the presentation of items closer together in time may elicit a decreased assessment of sensory characteristics, highlighting the increased task difficulty of the near condition. Thus, far FA activity may be associated with erroneous sensory processing, while near FA activity may result from a lack of sensory processing in younger adults.

In contrast, older adult far FA activity compared to near FA activity spanned the whole brain, and we believe that this activity may represent a failure in mental searching for items previously presented further apart in time due to deficits in hippocampal recruitment.

We propose that we did not observe increased brain activity for near versus far re-pairings because the maximum n-value for near re-pairings was $n=9$, while the largest value for far re-pairings was $n=28$. It is possible that the temporal distances in the far condition were so much greater than the near distances, that contrasts in the far>near direction were able to elicit significant differences in the brain activity. Meanwhile, the temporal proximity in the near condition likely was not small enough to elicit significant differences in the reverse direction. However, being that the memory failures are associated with reduced brain activity, it is also possible that older and younger adults showed reduced brain activity for near FA compared to far FA because the greater task difficulties in the near condition are associated with an under-recruitment of brain regions.

Within both the near and far conditions, we found that that both older and younger adults showed increased brain activity for CR than for FA, this is consistent with past research that has shown that increased brain activity has a direct relationship with successful memory retrieval.

For near CR compared to near FA, younger adults utilize the MTL for recollection, familiarity, and emotional processing, and this is consistent with past research on successful memory retrieval. Younger adults also utilize visual cortex processing, while older adults utilize higher level cognitive processes and sensory processing outside of the visual cortex, which is consistent with past research on novelty processing (Bowmen et. al). Our data further suggests that older adults were able to achieve success within the near condition by recruiting additional sensory regions to compensate for difficulties associated with novelty processing.

For far CR activity compared to far FA activity, younger adults showed increased hippocampal activity, which again is consistent with past research highlighting the MTL's role in associative memory retrieval and novelty processing. Also, for far CR compared to far FA, younger adults showed increased activity in the left precentral gyrus, right inferior frontal gyrus, and left occipitoparietal cortex, suggesting that younger adults engage in the inhibition of irrelevant information and sensory processing to successfully assess far re-pairings which is typical for associative memory success.

For older adults, far CR activity compared to far FA activity was associated with increased activity in the precentral gyrus and the inferior parietal lobe, suggesting that older adults engage in accurate sensory processing in order to achieve success for far re-pairings.

For far FA compared to far CR, older adults erroneously recruited the cuneus, which is consistent with our claim that older adults experience deficits in processing item-specific details. Meanwhile, younger adults did not show any significant areas of activation, and this reduced activation is typical for false alarm compared to correct rejection rates.

The MTL mask allowed us to take a deeper look at the recollection and gist or familiarity processes. We found that younger adults utilize increased PHG activity in order to successfully assess near compared to far re-pairings, while older adults did not show any increased areas of activation. This suggests that younger adults rely on familiarity processing in order to accomplish near compared to far-re-pairing. In contrast, for far CR compared to near CR both younger and older adults utilize both recollection and familiarity, suggesting that difficulties in the near condition may be associated with an inability to recruit recollection processes.

This theory is supported by the MTL activity associated with far FA compared to near FA and near FA compared to far FA as both younger and older adults erroneously recruited

recollection and familiarity processes. Whereas, for near FA compared to far FA, neither older adults nor younger adults exhibited significant areas of activation, suggesting that difficulties in the near re-pairing condition compared to the easier far condition may be associated with an inability to successfully recruit the MTL.

Within both the near and far conditions, CR activity compared to FA activity in younger adults was associated with increased MTL activity consistent with typical novelty processing and memory retrieval success. In contrast, within both the near and far conditions, older adults showed increased MTL activity for FA compared to CR, which is consistent with our claim and past research indicating that older adults show deficits in recruiting the MTL for novelty processing success.

Although we have been able to deduce the neural strategies that older and younger adults utilize to compensate for the effect of temporal proximity on associative memory, our findings indicate the need for researchers to replicate this experiment with the same near and far definitions as Campbell and Hasher (2014). This replication is necessary in order to 1) determine whether their behavioral findings can be replicated and 2) determine whether the more discrete parameters for the near and far conditions will elicit increased significant areas of activation for near compared to far re-pairings. In the future, researchers may use these neural correlates to determine the best strategies to address associative memory impairments in older adults.

BIBLIOGRAPHY

- Andersson, J. L. R., Jenkinson, M., & Smith, S. (2010). Non-linear registration, aka spatial normalisation. FMRIB technical report TR07JA2.
- Baddeley, A., Eysenck, M. W., & Anderson, M. C. (2014). *Memory* (2nd ed.). Psychology Press.
- Bowman, C. R., & Dennis, N. A. (2015). Age differences in the neural correlates of novelty processing: The effects of item-relatedness. *Brain Research*, 1612, 2–15. doi: 10.1016/j.brainres.2014.08.006
- Bowman, C. R., Chamberlain, J. D., & Dennis, N. A. (2019). Sensory Representations Supporting Memory Specificity: Age Effects on Behavioral and Neural Discriminability. *The Journal of Neuroscience*, 39(12), 2265–2275. doi: 10.1523/jneurosci.2022-18.2019
- Campbell, K. L., Trelle, A., & Hasher, L. (2014). Hyper-binding across time: Age differences in the effect of temporal proximity on paired-associate learning. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 40(1), 293–299. doi: 10.1037/a0034109
- Dennis, N. A., & McCormick-Huhn, J. M. (2018). Item and Associative Memory Decline in Healthy Aging. *Stevens Handbook of Experimental Psychology and Cognitive Neuroscience*, 1, 1–40. doi: 10.1002/9781119170174.epcn110
- Dulas, M. R., & Duarte, A. (2011). The effects of aging on material-independent and material-dependent neural correlates of contextual binding. *NeuroImage*, 57(3), 1192–1204. doi: 10.1016/j.neuroimage.2011.05.036

- Jenkinson, M., Bannister, P., Brady, M., & Smith, S. A. (2002). Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage*, 17(2), 825-841.
- Kawashima, R., Okuda, J., Umetsu, A., Sugiura, M., Inoue, K., Suzuki, K., ... Yamadori, A. (2000). Human Cerebellum Plays an Important Role in Memory-Timed Finger Movement: An fMRI Study. *Journal of Neurophysiology*, 83(2), 1079–1087. doi: 10.1152/jn.2000.83.2.1079
- Martinez, A. M., & Benavente, R. (1998). The AR face database. CVC Technical Report #24.
- Minear, M., & Park, D. C. (2004). A lifespan database of adult facial stimuli. *Behavior Research Methods, Instruments, & Computers*, 36(4), 630-633.
- Persson, J., Kalpouzos, G., Nilsson, L.G., Ryberg, M., & Nyberg, L. (2011). Preserved hippocampus activation in normal aging as revealed by fMRI. *Hippocampus*, 21(7), 753–766. doi:10.1002/hipo.20794
- Phillips, P. J., Moon, H., Rizvi, S. A., & Rauss, P. J. (2000). The FERET evaluation methodology for face-recognition algorithms. *Ieee Transactions on Pattern Analysis and Machine Intelligence*, 22(10), 1090-1104. doi:10.1109/34.879790
- Smith, S. M. (2002). Fast robust automated brain extraction. *Human Brain Mapping*, 17(3), 143-155.
- Solina, F., Peer, P., Batageli, B., Juvan, S., & Kovac, J. (2003, March 10-11). Color-based face detection in the "15 seconds of fame" art installation. Paper presented at the Conference on Computer Vision / Computer Graphics Collaboration for Model-based Imaging, Rendering, Image Analysis and Graphical Special Effects, INRIA Rocquencourt, France.
- Tsukiura, T., Sekiguchi, A., Yomogida, Y., Nakagawa, S., Shigemune, Y., Kambara, T.,...
Kawashima, R. (2011). Effects of aging on hippocampal and anterior temporal activations during

successful retrieval of memory for face-name associations. *Journal of Cognitive Neuroscience*, 23(1), 200–213. doi:10.1162/jocn.2010.21476

Woolrich, M. W., Ripley, B. D., Brady, M., & Smith, S. M. (2001). Temporal autocorrelation in univariate linear modeling of FMRI data. *Neuroimage*, 14(6), 1370-1386.

Yonelinas, A. P. (2002). The nature of recollection and familiarity: A review of 30 years of research. *Memory and Language*, 46, 441-517.

as, A. P., Otten, L. J., Shaw, K. N., & Rugg, M. D. (2005). Separating the brain regions involved in recollection and familiarity in recognition memory. *Journal of Neuroscience*, 25(11), 3002-3008.

Yonelinas, A. P., Widaman, K., Mungas, D., Reed, B., Weiner, M. W., & Chui, H. C. (2007). Memory in the aging brain: doubly dissociating the contribution of the hippocampus and entorhinal cortex. *Hippocampus*, 17(11), 1134-1140.

ACADEMIC VITA

Academic Vita of Bianka Onwumbiko

Education

The Pennsylvania State University, 2020
B.S. Biology, Psychology Minor,
Honors: Millennium Scholar

Thesis Title:

Neural Correlates Underlying the Effect of Temporal Proximity on Associative Memory Retrieval for Older Versus Younger Adults
Thesis Supervisor: Dr. Nancy A. Dennis

Research Experience:

Dr. Nancy Dennis, The Cognitive Aging and Neuroimaging Lab: The Pennsylvania State University, University Park

January 2018-present

Studied age-related deficits in memory.

Dr. Anuska Zochowska Laboratory: University of Michigan Pathology Department

May 30th, 2017-August 17th, 2017

Studied the Role of Nox1 in ROS generation and Blood Brain Barrier Permeability

Dr. Michelle Newman Clinical Psychology Laboratory: The Pennsylvania State University, University Park

February 8th, 2017-May 4th, 2017

Conducted experiments to study how positive and negative reinforcement influence generalized anxiety disorder.

Dr. Gong Chen Neuroscience Laboratory: Penn State University, University Park

August 21st, 2017- October 17th, 2017

Investigated neuron regeneration from endogenous glial cells for CNS repair.

Professional Memberships:

President and co-founder of The National Organization for the Professional Advancement of Black Chemists and Chemical Engineers (NOBCCChE at Penn State)

Presentations:

The role of Nox1 in ROS generation and Blood-Brain Barrier permeability in Diabetic Ketoacidosis

August 17th, 2017

Location: University of Michigan; Ann Arbor, MI (SURP Symposium)

November 3rd, 2017

Location: Phoenix, Arizona: ABRCMS 2017

Community Service Involvement:

Clinical Volunteering

August 2016; May-August 2019

Shadowed and volunteered at a Pediatrician's office in Greenbelt, MD

May 2018-June 2018

Shadowed and volunteered at a Psychiatrist's office in Columbia, MD

Penn State Alternative Breaks

November 16th-20th, 2018

Volunteered at a shelter for people experiencing homelessness in Niagara Falls, NY, and learned about mental health in underserved communities.

Fall 2019

Led a community service trip to Washington, D.C. focused on housing access and food security