Brain Volume Differences and Proactive Interference: A VBM Investigation of Healthy Cognitive Aging

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Research on aging and memory has consistently demonstrated decreased memory performance in older adults, specifically on tasks measuring verbal and spatial memory. Memory decline in aging is partially related to interference from competing information. In older adults, the learning of new information is more adversely affected by already-formed memories (i.e. proactive interference) than in younger adults. However, interference of new information on already-formed memories (retroactive interference) is less affected by age. The present investigation examined the association between proactive and retroactive interference, and brain volume in young and older adults. Proactive and retroactive interference were assessed with a Modified modified free recall (MMFR) test. Participants (n=39) first studied AB and DE word pairs three times before undergoing a cued recall test. Following AB-DE testing, participants had only one study-test cycle of AC and FG word pairs. Finally, participants completed the MMFR test to evaluate their memory for all previously studied and tested words. Results revealed that older adults experienced significantly more proactive interference than younger adults (performance on MMFR-AC minus MMFR-FG), but both age groups performed similarly on the retroactive interference measures. It was hypothesized that brain volume, and specifically Hippocampal and prefrontal volume, would be significantly correlated to memory performance; however no significant correlations were found with any specific brain regions.

Keywords: Memory, memory interference, sleep, exercise, aging, MMFR, recall

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1.0 INTRODUCTION

The study of memory and its relation to cognition is one of the oldest topics in experimental psychology (for review see Lechner, Squire, & Byrne, 1999). Ebbinghaus (1885) highlighted the imperfections of human memory when he described his rapid and exponential memory loss for previously learned nonsense syllables. While many factors contribute to forgetting, memory interference has been identified as a fundamental cause (Wixted, 2004). Proactive interference (PI) is experienced when the learning of new material is adversely affected by previously formed memories. In contrast, when new information disrupts previously learned information, this is defined as retroactive interference (RI). A plethora of research regarding the study of memory interference and its underlying causes has been published over the last 50 years (Dudai, 2004; McKenzie & Eichenbaum, 2011). Moreover, there seems to be specific types of memory that are differentially affected as we age; long-term episodic and working memory are adversely affected in older adults, while procedural and semantic memory are seemingly preserved (Buckner, 2004).

Previous research indicates that older adults experience greater memory disturbances than younger adults concerning both retroactive (Hedden & Park, 2001; Ebert & Anderson, 2009) and proactive (Puglisi, 1980; Schonfield, Davidson, & Jones, 1983; Mistler-Lachman, 1977; Ebert & Anderson, 2009) interference. Results have been mixed, though, and some studies reported no age-related differences in memory abilities, especially concerning retroactive interference (Puckett & Stockburger, 1988; Dobbs, Aubrey, & Rule, 1989; Puckett &

Lawson, 1989). The discrepancy in findings could be a result of the vast variety of memory tasks and testing procedures, which are rarely consistent across studies. For example, Jacoby (1999) demonstrated that older adults are impaired in recollection tests, but not recognition/familiarity tests (Jennings & Jacoby, 1993). Likewise, high-functioning older adults performed similar to young adults on subjective recall tests that employed 'remember' judgments; however, diminished performance was seen using objective source memory recall tests (Duarte, Henson, & Graham, 2008). Another reason for contradictory findings could be attributed to individual differences. Rajah et al. (2010) used differences in regional volumes of the HC to predict contextual memory performance in young adults. Similarly, Shing et al. (2011) also suggested that individual differences in subfield volumes of the HC might contribute to performance on an associative memory task. Due to the rapidly growing aging population (Administration on Aging, 2005), the identification of modifiable risk factors for memory and cognitive decline are of extraordinary importance. The discovery of specific measures associated with memory performance could be a useful diagnostic tool for determining at-risk older adults, as well as an important marker of treatment outcome for patients with mild cognitive impairment (MCI), Alzheimer's disease (AD), and other dementias.

Ebert and Anderson (2009) examined the differences regarding PI and RI between healthy young adults, healthy older adults, and older adults with amnestic MCI (aMCI). Participants underwent two different memory tasks to assess memory interference: the California Verbal Learning Test (CVLT; Delis et al., 1987) and an AB-AC memory interference paradigm. Results showed that both older adults and adults with aMCI experienced more PI and RI than young adults; however, performance differences could not differentiate between the older adults and adults with aMCI. In the second session of the experiment, the modified AB-AC memory

interference task was performed. This test was comprised of 12 semantically related AB-AC word lists. First, participants learned the AB word pairs and were tested via stem-cued recall until participants could recall all word pairs. After a 20-minute delay, participants then learned the AC word pairs that contained the same A term as the AB pairs, but introduced an interfering C term. After participants could complete stem-cued recall of all AC pairs, a final stem-cued recall test was administered on the initial AB word pairs. Results showed that significant performance differences in PI existed between all groups, such that young adults performed significantly better than older adults, who in turn performed significantly better than adults with aMCI. Regarding RI, significant differences were found between young adults and both older adult groups; however, no differences were seen between the two older adult groups. These results suggest that the modified AB-AC task is sensitive enough to detect differences in PI between healthy older adults and adults with aMCI.

Further research regarding susceptibility to memory interference has yielded similar results. Emery, Hale, and Myerson (2008) used a modified release-from-PI operation span task (for review, see; Bunting, 2006) that demonstrated specific age effects in working memory, which suggests susceptibility to PI may play a pivotal role in working memory performance. Relatedly, Hedden and Park (2001) reported that older adults experienced greater RI when performing a verbal working memory task, supporting the notion that interference is partially responsible for working memory deficits in aging. Determining the underlying causes of memory impairments in aging is of incredible importance and for this reason, studies investigating age-related changes in brain activity, volume, and structure have been an exciting area of focus that could help to explicate differences in healthy and pathological cognitive aging.

A meta-analysis by Verhaeghen et al. (1993) reported age-related changes in episodic memory, but relatively intact semantic processing. Studies investigating the HC, an integral structure in episodic memory (Squire, 1987; Deweer et al., 2001), have described increased susceptibility to neurodegeneration (Jack et al., 2000; Raz et al., 2005) and volumetric decreases of 1-2% per year in healthy adults aged 50 years or older (Raz et al., 2004a; 2005; Mungas et al., 2005) and even greater rates of deterioration around 3-5% per year in patients with MCI and AD (Jack et al., 1998; Mungas et al., 2005). Additional studies have replicated these well-documented age-related declines in hippocampal and MTL volume (Pruessner et al., 2001; Raz et al., 2005; Kennedy et al., 2009). Interestingly, Erickson et al. (2011) reported that exercise-training interventions could reverse the typical patterns of hippocampal volume loss in older adults and actually yield volumetric increases of roughly 2%, which were accompanied by corresponding improvements in spatial memory. In contrast, another 6-month exercise intervention study did not report significant volume increases in any MTL structures; however, researchers did find increased gray matter volume in the prefrontal cortex (PFC) and cingulate cortex, and corresponding increases in episodic memory performance (Ruscheweyh et al., 2011). Additional work concerning the relationship between cognitive performance and volume of the MTL, and more specifically the HC, suggests that reduced volume is associated with memory impairments (Raz et al., 1998; Peterson et al., 2000; Lupien et al., 2005; Persson et al., 2006; Kramer et al., 2007; Meyer et al., 2013) and other widespread cognitive deficits (Wolk et al., 2011; Rosano et al., 2012).

Investigations into the specific regions of the HC that undergo deterioration showed volume decreases in the CA1 region of the HC (Mueller et al., 2007) and additional reductions in the CA3/CA4 and dentate gyrus (DG) regions (Mueller et al., 2008; Mueller and Weiner, 2009)

in healthy older adults. Similarly, Shing et al. (2011) found decreased volume in CA1 and CA2 of older adults compared to young adults; however, it was suggested that these differences were likely due to hypertension in the older adults. Additional analyses were conducted on the older adults to investigate the relationship between hippocampal subfield volumes and associative memory; results indicated a significant correlation between CA3/CA4/DG regions and memory performance such that increased volume was linked to better memory (Hit-FA rate) and decreased false alarms. These documented reductions in hippocampal subfield volumes, specifically in the CA1, CA3 and DG regions, have also been reported in individuals with aMCI when compared to healthy older adults (Yassa et al., 2010b).

Additional differences between specific regions of the HC and corresponding associations with memory performance were revealed by Rajah et al. (2010), who reported significant correlations between anterior HC volume and spatial and temporal memory performance in young adults, suggesting an important functional role of the anterior HC (hippocampal head and hippocampal body). Furthermore, age-related differences were found in the anterior HC, but not the hippocampal tail, showing that older adults had decreased volume in the anterior HC and decreased context memory performance, but the two were not predictive of each other.

Although much research has investigated age-related brain changes that may underlie age differences in memory performance, additional questions remain regarding the relationship between brain changes in young and older adults and how these changes relate to verbal memory interference specifically.

1.1 CURRENT STUDY

In the current study, the relationship between brain volume and memory interference was examined. As reported in previous research (Ebert & Anderson, 2009), it was hypothesized that older adults would experience greater amounts of both proactive and retroactive interference than young adults, but that larger differences would be seen for proactive interference measures. In addition to decreased memory performance, it was hypothesized that older adults would show decreased brain volume compared with young adults, specifically regarding the HC and Pre-Frontal Cortex (PFC; Rajah et al., 2010). Furthermore, older adults who performed similar to young adults on memory performance measures were expected to have significantly increased volume in the aforementioned regions compared to older adults that were more impaired in memory interference tasks. Lastly, it was hypothesized that both Hippocampal and PFC volume would be significantly correlated with susceptibility to memory interference (Rajah et al., 2010).

2.0 METHODS

2.1 PARTICIPANTS

There were 41 participants included in the study; however, two participants were excluded from the analyses due to corrupted data and/or not following study instructions. The remaining 39 participants who completed the study were right-handed, English speaking, healthy adults, ranging in age from 21-75 years (mean age= 40.85 years, SD= 19.97). Participants were recruited from the greater Pittsburgh area via Craigslist, Penny Saver, and Pittsburgh news advertisements. Compensation for participation in the experiment was as follows: $10/hour for paper-and-pencil and computer-based portion of the experiment, $25 for the MRI component of the experiment, and $5 for wearing an accelerometer for the entire week (with a bonus $50 if the participant wore the accelerometer every day for at least 20 hours each day). All participants gave informed consent as reviewed and approved by the Institutional Review Board. Participants were divided into two age groups: older adults aged 55-75 years (n = 18, mean age = 61.72 years, SE = 1.28) and young adults aged 21-28 years (n = 21, mean age = 22.95 years, SE = .47). The older adult group (OA) had 5 males and 13 females, while the young adult group (YA) had 8 males and 13 females. Independent t-tests were performed to determine differences regarding demographic characteristics of age and years of education. Obviously, there were significant differences in age, $t(37) = 30.212$, $p < .001$. There were no significant differences found

between older and young adults concerning years of education, which ranged from 12-21 years of education in the YA group and from 12-20 years of education in the OA group, $t(37) = -1.021$, $p = .314$. A chi-square test was performed to examine the relation between age group and race, which showed that there was no significant relationship, $X^2 = 3.993$, $p = .136$. There was also no significant relationship found between age group and gender, $X^2 = .464$, $p = .496$. Demographic information is reported in Table 1 (See Below).

Table 1. Subject Demographics

Characteristic	Older Adults	Young Adults	t (p-value)
# of Subjects	18	21	
Mean Age (years)	61.72 (1.28)	22.95 (.47)	30.212 (<.001)***
Mean Education (years)	15.194 (.562)	15.857 (.360)	-1.021 (.314)
Race			**X^2 (p-value)**
White	12	18	3.993 (.136)
Black	6	2	
Asian	0	1	
Gender			**X^2 (p-value)**
Male	5	13	.464 (.496)
Female	13	8	

Numbers in parentheses are SE of mean *** Significance at .001

2.2 MATERIALS

The memory interference assessment consisted of 2 different word-pair lists (AB- DE and AC-FG). In session 1, participants studied 48 word pairs consisting of 18 semantically related A-B word pairs and 28 D-E word pairs, 18 of which were related and 10 that were unrelated, at a rate of 1500ms for each word pair. Following the study phase, participants were tested by cued-recall, in which the first word of each pair was presented and the participant was required to type in the second word. Participants repeated this study-test cycle 3 times for the AB and DE pairs.

This concluded session 1, which was immediately followed by session 2. To begin session 2, participants were presented 1 time with the AC and FG word pairs, which consisted of 18 semantically related A-C word pairs and 28 F-G word pairs, 18 of which were related and 10 that were unrelated, at a rate of 1500ms for each word pair. Following the AC-FG study-test cycle, participants completed a modified modified free recall (MMFR) test (Ekstrand, 1967).

The MMFR consisted of a cued-recall test of all word pairs, in which participants were given the first word of each pair and required to type in the 2nd word (target) of the pair. Since some words (A words) were paired with 2 different words (B and C words), participants were instructed to type in both words, separated by a comma, if they could recall both. The MMFR contained 74 cued prompts, consisting of 18 A words, 28 D words, and 28 F words. Scoring in the MMFR was as follows: proactive interference (PI) was calculated by subtracting the percentage of related F-G word pairs recalled from the percentage of A-C word pairs recalled during the MMFR. Retroactive interference (RI) was calculated by subtracting the percentage of related D-E word pairs recalled from the percentage of A-B word pairs recalled during the MMFR. Higher PI and RI scores are indicators of proactive and retroactive facilitation; respectively, and therefore correspond with decreased memory interference. Intrusions could not be calculated on the MMFR test because the instructions did not specify to denote the order or each paired word.

Participants were asked to answer a brief sleep questionnaire to assess basic sleep patterns and behaviors; however, these results will not be discussed, as they are not integral to the analyses. Participants were also required to wear a Body Media Accelerometer for one week, which recorded physiological data (e.g. body temperature, steps taken, calories burned, energy expenditure, intensity of activity levels, total time lying down, total time asleep, etc.). To

supplement the data recorded by the accelerometer, participants were asked to keep a journal regarding daily activities and participant changes in temperature and sweat; however, the subjective journal reports and accelerometer data will not be discussed in this paper either.

2.3 IMAGE ACQUISITION AND ANALYSIS

Structural MRI was acquired with a 3 Tesla magnetic resonance scanner (Siemens Trio) at the University of Pittsburgh Medical Center Presbyterian Hospital. For each participant, a T1-weighted gradient echo Magnetization prepared rapid gradient echo (MP-RAGE) sequence (TR=2300, TE=2.98, flip angle 9°, FOV: 256x240 mm, voxel size 1.0 mm x 1.0 mm x 1.2 mm, 160 sagittal slices) was acquired.

Voxel-based morphometry (VBM; Ashburner et al., 2000) was applied to the structural MR data and correlational analyses between memory performance and brain volume values were used to investigate the relationship between these variables of interest. VBM was used to highlight volumetric differences between the two age groups, as the contrasts used were Young > Old, and Old > Young. Due to the automated processing in VBM and its rater-independent method, repeated results are possible (Busatto, 2008). Data pre-processing and analysis were performed using an optimized VBM procedure (Good et al., 2001) and FSL-VBM tools (Smith et al., 2004), starting with skull stripping and brain-extraction (BET; Smith, 2002). This was followed by tissue segmentation using FMRIB's automated segmentation tool (FAST; Zhang, Brady, & Smith, 2001), which divides the image into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF). Each participant's brain was segmented into separate

partial volume estimates (PVE) for the three different types of tissue. Next, a study-specific template was created and a linear affine transform was performed (FLIRT), followed by a non-linear registration algorithm, which was applied (FNIRT) before normalization to the Montreal Neurological Institute (MNI) template occurred. The normalization step provided a matrix (Jacobian determinants), which was used for the modulated VBM data in order to correct for local expansion and contraction. Individual GM images were smoothed using an isotropic Gaussian kernel of 2 mm full-width at half-maximum before entering them into statistical analyses. Global volumes of GM, WM, and CSF were assessed from FAST segmented images (see figures 1 & 2 below for OA and YA, respectively).

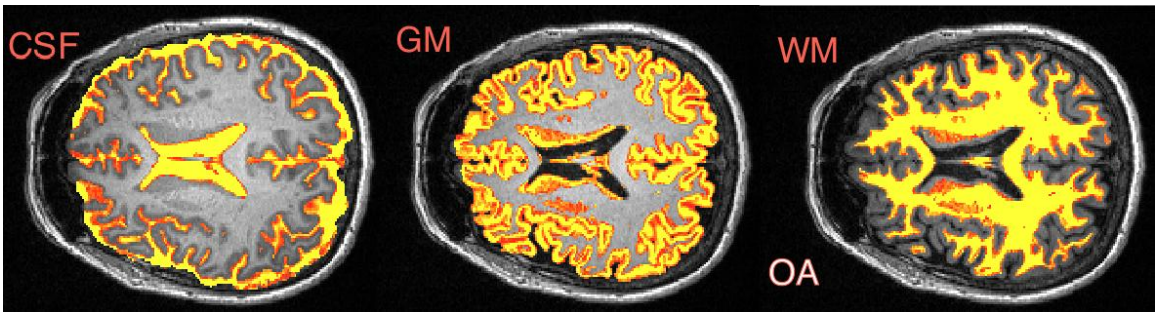

Figure 1. FAST Segmentation of an Older Adult subject

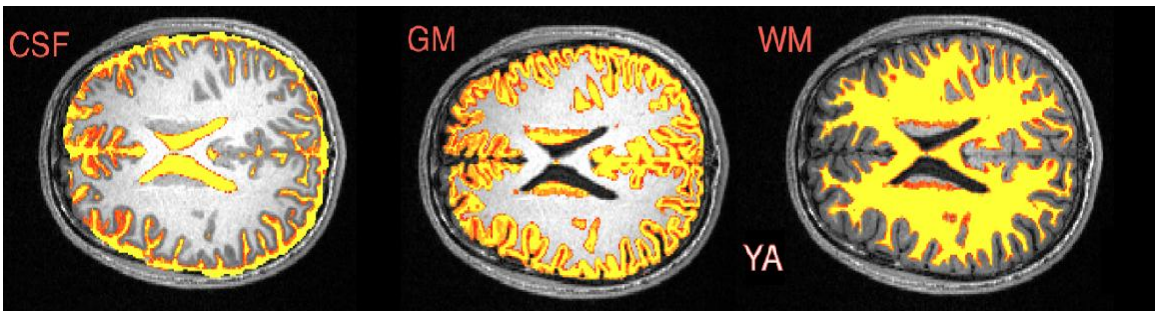

Figure 2. FAST Segmentation of a Young Adult subject

Due to age not being a continuous variable, correlational analyses for brain volume and memory performance were performed separately on young adults and older adults. This was done using centered PI scores as explanatory variables, and entering them into the FSL-VBM

general linear model (GLM). Threshold-free cluster-enhanced (TFCE) images were used to identify significant regions that survived corrections for multiple comparisons at the $p < .05$ level.

2.4 PROCEDURE

On day 1, participants were given an explanation regarding the study's tasks and procedures. First, participants gave informed consent. Following some basic demographic questionnaires, the memory interference assessment was explained and performed (see Figure 3 below).

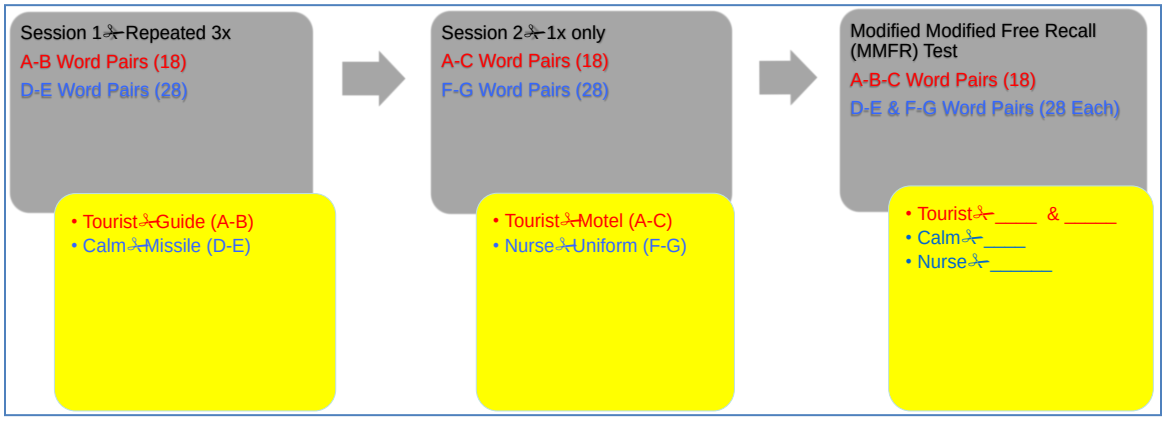

Figure 3. Task Diagram of Procedure

Participants started with the AB-DE list (3x study-test cycle) followed by the AC-FG list (1x study-test cycle). Following the study portion, participants were administered the final MMFR test. After this task was finished, participants answered the sleep questionnaire and were given instructions regarding the accelerometer. Participants were requested to keep a daily log to record activities. After wearing the accelerometer for one week, participants returned to the lab

in order to upload their accelerometer data. To end the study, subjects were debriefed and paid for their participation.

2.5 ANALYTIC PLAN

One-way ANOVAs were run to investigate age group differences in memory interference scores. Additional one-way ANOVAs were also conducted in order to investigate age-related differences in global CSF, GM, and WM volumes. To account for individual differences in head size, all tissue types were added together to calculate a measure of total brain volume (TBV). Next, percentages of each tissue type in regards to TBV were calculated separately for all participants; this percentage was used in the statistical analyses to look for a correlation with proactive interference and GM within each individual age group.

3.0 RESULTS

3.1 MEMORY PERFORMANCE

Memory performance results on the MMFR test are reported in Table 2 (see below).

Table 2. Memory Performance Measures in Young and Older Adults on the MMFR

Measure	Young Adults	Older Adults	*F-stat*	p-value
PI	.138 (.036)	-.068 (.036)	**16.004	<.001
RI	.029 (.029)	-.043 (.036)	2.503	0.122
MMFR AB	.929 (.020)	.682 (.059)	**17.39	<.001
MMFR AC	.437 (.027)	.255 (.059	**8.624	0.006
MMFR ABC	.683 (.016)	.455 (.043)	**27.482	<.001
MMFR DE	.876 (.031)	.704 (.049)	**9.163	0.004
MMFR FG	.310 (.030)	.281 (.035)	0.401	0.530
MMFR DEFG	.593 (.026)	.492 (.039)	*4.911	0.033
AB No Response	.045 (.019)	.099 (.028)	2.619	.114
AC No Response	.400 (.040)	.707 (.053)	**22.540	<.001
DE No Response	.071 (.029)	.086 (.028)	.135	.715
FG No Response	.331 (.064)	.272 (.067)	.407	.527

The results indicated that there was a significant difference in PI, $F(1, 38) = 16.004$, $p < .001$, with young adults ($n = 21$, *mean PI* $= .138$, $SE = .036$) experiencing less PI than older adults ($n = 18$, *mean PI* $= -.068$, $SE = .036$; see figure 4 below).

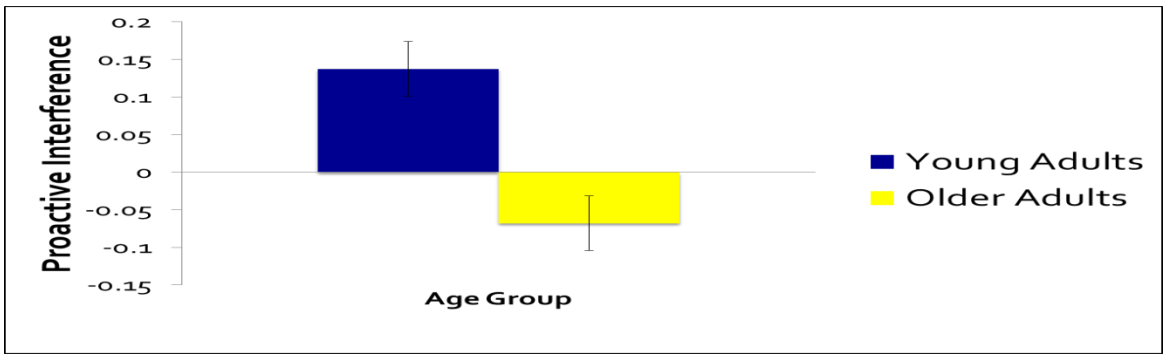

Figure 4. Proactive Interference of Young and Older Adults

There was no significant difference between RI performance, *F(1,38) = 2.503, p = .122*, showing that young adults (*mean RI = .029, SE = .029*) experienced similar amounts of RI when compared to older adults (*mean RI = -.043, SE = .036*; see figure 5 below).

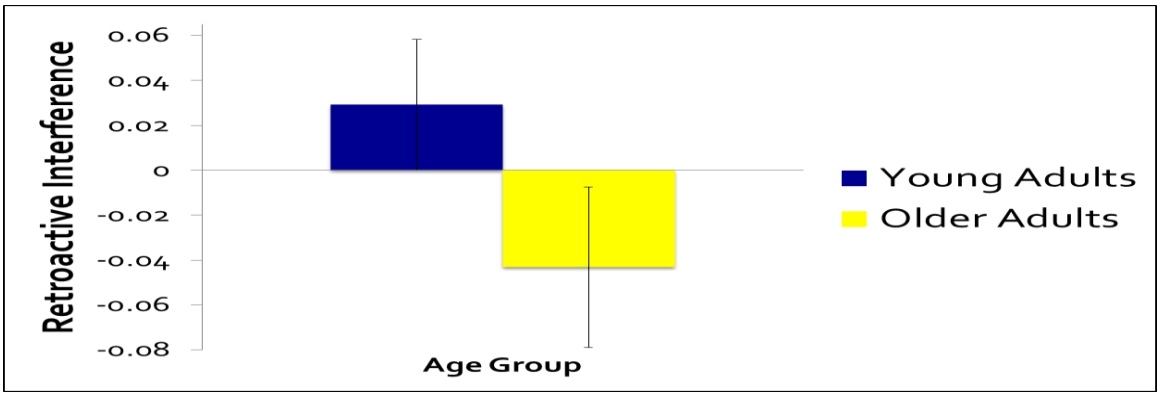

Figure 5. Retroactive Interference of Young and Older Adults

Interestingly, the results also indicated that there was a significant difference in response rates for AC word pairs, *F(1,38) = 22.540, p < .001*, with young adults (*mean = .400, SE = .040*) leaving less responses blank than older adults (*mean = .707, SE = .053).* Memory measures regarding the study phase of the AB-DE (3x) and AC-FG (1x) word lists are reported in table 3 (see below).

Table 3. Memory Performance Measures in Young and Older Adults during Study

Measure	Young Adults	Older Adults	*F-stat*	p-value
AB (1x)	.545 (.044)	.349 (.044)	**9.878	<.005
DE (1x)	.402 (.322)	.299 (.040)	3.425	.072
AB No Response (1x)	.209 (.051)	.265 (.072)	.431	.516
DE No Response (1x)	.257 (.062)	.278 (.069)	.052	.820
AB (2x)	.844 (.033)	.583 (.061)	**15.122	<.001
DE (2x)	.749 (.040)	.556 (.051)	**9.005	.005
AB No Response (2x)	.095 (.028)	.111 (.044)	.097	.757
DE No Response (2x)	.116 (.040)	.176 (.049)	.887	.352
AB (3x)	.937 (.016)	.750 (.055)	**11.991	.001
DE (3x)	.870 (.031)	.716 (.051)	*7.015	.012
AB No Response (3x)	.021 (.009)	.040 (.017)	1.030	.317
DE No Response (3x)	.048 (.022)	.071 (.025)	.511	.479
S2 AC	.437 (.031)	.275 (.037)	**11.534	.002
S2 FG	.294 (.032)	.303 (.035)	.035	.852
S2 AC No Response	.193 (.044)	.272 (.070)	.958	.334
S2 FG No Response	.347 (.063)	.293 (.075)	.300	.587
S2 AB Intrusions on AC	.220 (.054)	.133 (.049)	1.363	.251

The results showed that there were significant differences in initial learning of the AB word pairs on the first study-test cycle, *F(1,38) = 9.878, p < .005,* such that the young adults (*mean AB = .545, SE = .044*) remembered more pairs than the older adults (*mean AB = .349, SE = .044).* Similarly, there were significant differences in the second repetition of the AB list learning, *F(1,38) = 15.122, p < .001,* with the young adults (*mean AB = .844, SE = .033*) remembering more pairs than the older adults (*mean AB = .583, SE = .061).* Results showed that the young adults (*mean AB = .937, SE = .016*) had learned the AB word pairs significantly better, *F(1,38) = 11.991, p = .001,* by the final repetition than the older adults (*mean AB = .750, SE = .055).* DE word pairs were also remembered at a significantly higher proportion in the final study repetition, *F(1,38) = 7.015, p = .012,* in the young adults (*mean DE = .870, SE = .031)* as compared with the older adults *(mean DE = .716, SE = .051).*

Regarding the AC-FG word pairs, there were significant differences in the AC word list learning, *F(1,38) = 11.534, p = .002,* such that the young adults (*mean AC = .437, SE = .031*) remembered more pairs than the older adults (*mean AC = .275, SE = .037)*; however, there were no significant differences in FG word pairs, *F(1,38) = .035, p = .852,* such that the young adults (*mean FG = .294, SE = .032*) remembered similar amounts of the FG pairs as compared with the older adults (*mean FG = .303, SE = .035).* Moreover, there was no significant difference between the amount of AB intrusions during the AC word pair learning, *F(1,38) = 1.363, p = .251,* such that the young adults (*mean intrusions = .220, SE = .054*) experienced similar amounts of intrusions compared to the older adults (*mean intrusions = .133, SE = .049).* It should also be noted that 7 of the young adults and 2 of the older adults didn't follow the instructions for the AC-FG word pairs and sometimes responded with two words for the AC

word pairs; however, the data was scored as correct if they identified the correct AC word pair because this was evidence for correct recall, regardless of whether they also supplied the AB word pair as well. Similarly, intrusions were only defined as AB word pairs intruding on the recall of AC word pairs such that only the AB word pair was recalled during the AC word list testing. Unfortunately, instructions for the final MMFR test did not explicitly advise participants to worry about the order in which they were initially studied, and thus intrusions on the MMFR could not be scored.

3.2 FAST ANALYSIS

FAST was used in order to show total tissue concentration differences between young and older adult brains; these results are reported in Table 4 (see Table 4 below).

Table 4. VBM FAST RESULTS

Measure	Young Adults	Older Adults	*F-stat*	p-value
CSF (% of TIV)	.221 (.002)	.264 (.005)	79.746	<.001
GM (% of TIV)	.426 (.003)	.375 (.005)	93.799	<.001
WM (% of TIV)	.354 (.003)	.361 (.004)	2.530	0.120

The results indicated that there was a significant difference in CSF percentage of total brain volume, $F(1, 38) = 79.746$, $p < .001$, with young adults (mean CSF% = .221, SE = .002) having less CSF than older adults (mean CSF% = .264, SE = .005). The results also showed that there was a significant age-related decrease in GM percentage of TBV, $F(1, 38) = 93.799$, $p < .001$, with young adults (mean GM% = .426, SE = .003) having more GM than older adults (mean GM% = .375, SE = .005). The results showed no significant difference in WM percentage in

regards to total TBV, *F(1, 38) = 2.530, p = .120,* between young adults (mean WM% = .354, SE = .003) and older adults (mean WM% = .361, SE = .004). A Pearson product-moment correlation coefficient was computed within each group to assess the relationship between global GM and proactive interference; however, results revealed no significant correlation between percent GM and PI for the young adult group *(r= .046, n = 21, p = .844)* or the older adult group *(r = -.132, n = 18, p = .602).* A scatterplot summarizes these results showing no significant correlation between the two variables (see figure 6 below).

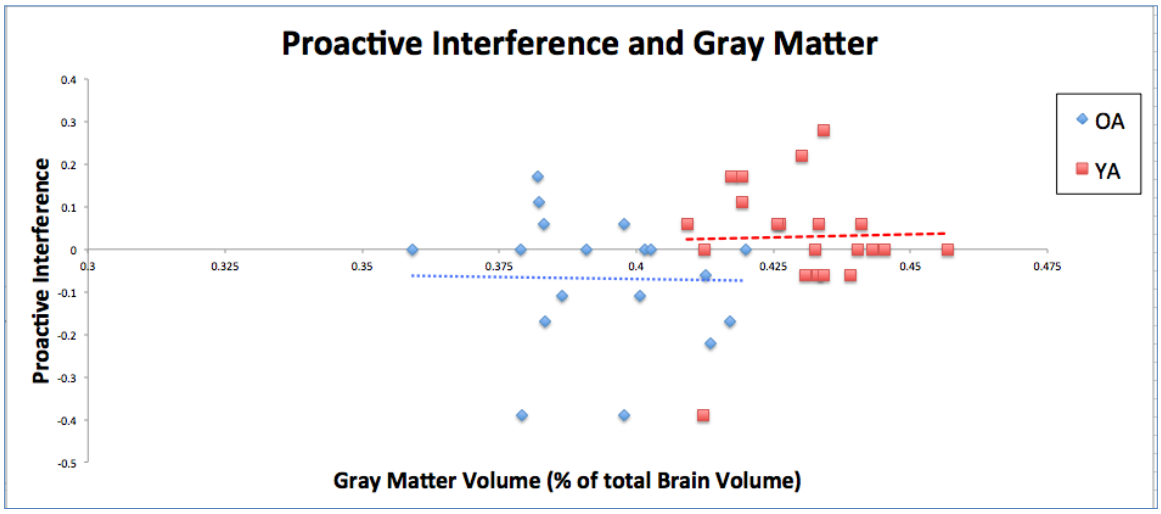

Figure 6. Proactive Interference and Gray Matter Volume

3.3 WHOLE-BRAIN VBM ANALYSIS

After identifying specific tissue differences between the two age groups using FAST, a whole-brain VBM analysis was conducted in order to produce statistical parametric maps for displaying the areas that show significant differences between older and young adults. The identification of which regions these areas belong to was defined using FSL's atlas tools, which use probability

maps derived from the Harvard-Oxford subcortical structural atlas. As evidenced by the VBM results, there were widespread significant differences showing greater volume of GM in YA as compared to OA (see figures 7, 8, & 9 below).

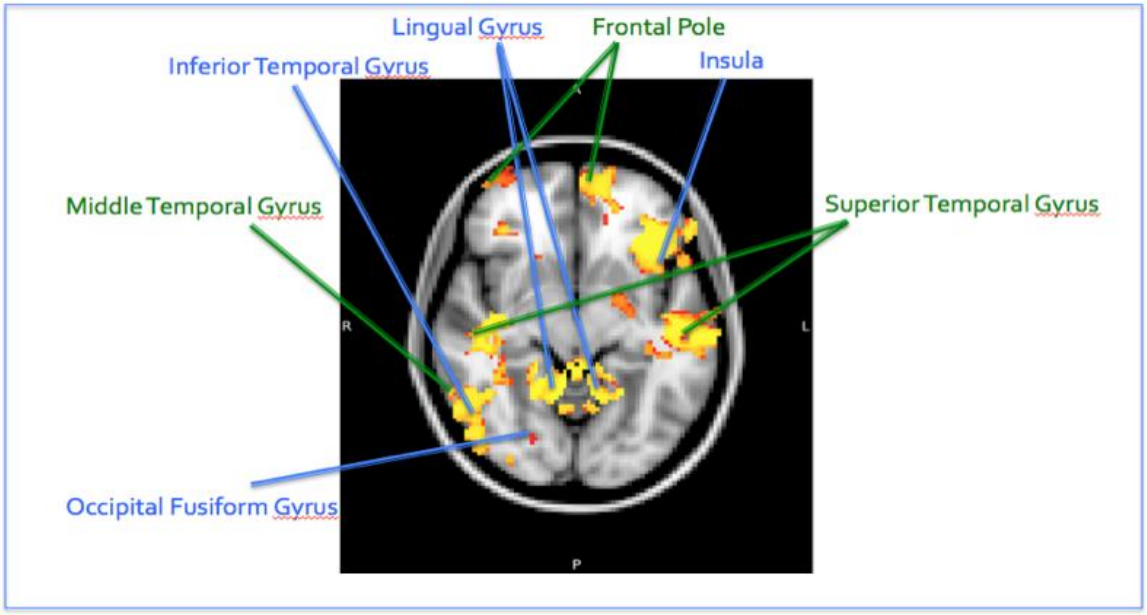

Figure 7. YA > OA Contrast

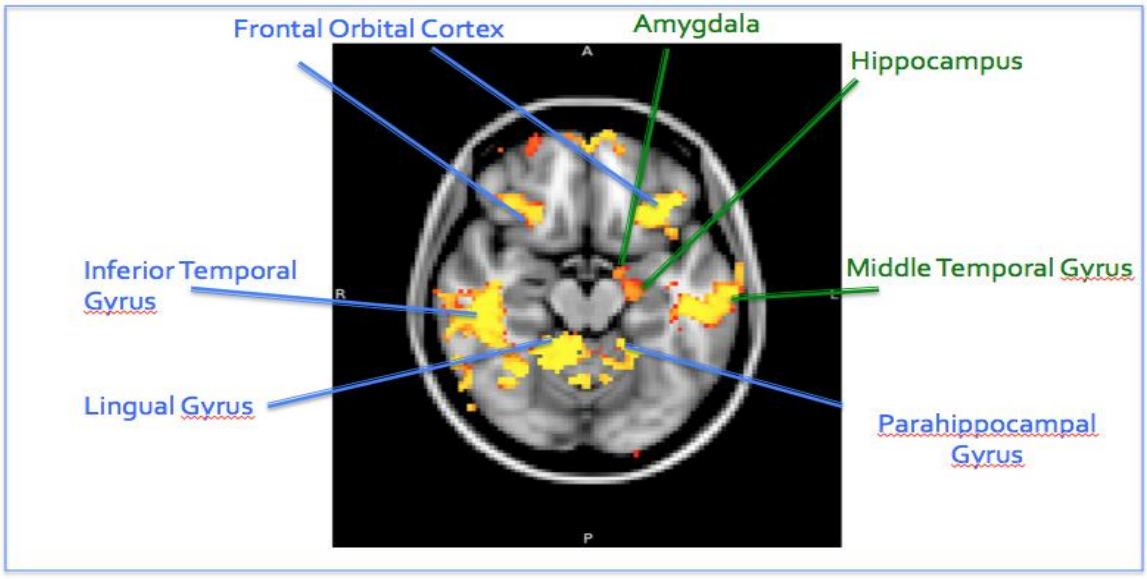

Figure 8. YA > OA Contrast (additional view)

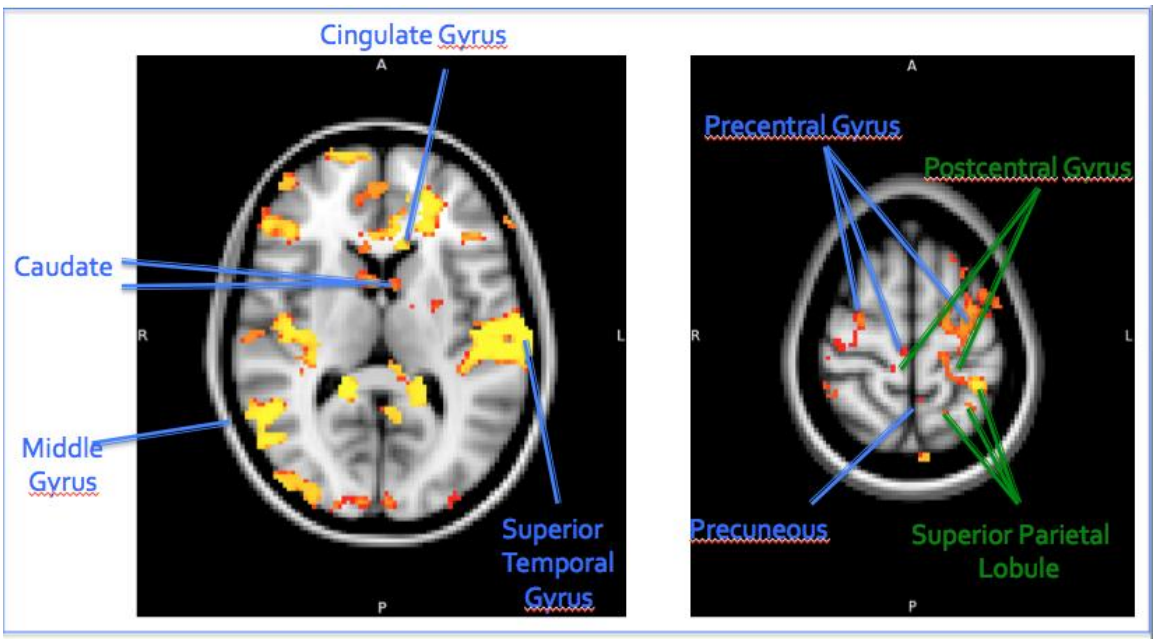

Figure 9. YA > OA Contrast (additional views)

All significant clusters containing contiguous voxels of 15 or more are reported in Table 5 (see below); the clusters with the highest significance and their coordinates for the center of gravity (COG) were found in the following regions: right lingual gyrus, right and left cingulate gyrus, left superior parietal lobule, left superior temporal gyrus, left amygdala, right occipital pole, right precentral gyrus, right precuneous, left juxtapositional cortex (supplemental motor cortex), and right occipital fusiform cortex.

Table 5. VBM RANDOMISE RESULTS: YA > OA

Cluster Index	Voxels	1-p	Z-COG X (vox)	Z-COG Y (vox)	Z-COG Z (vox)	Brain Region
29	13599	1	28.9	41	32.9	R Lingual Gyrus
28	8951	1	43.8	82	43.2	R Cingulate Gyrus
27	5635	1	63.1	41.2	59.9	L Superior Parietal Lobule
26	4598	1	71.5	51	33.6	L Superior Temporal Gyrus
25	553	0.985	54.1	58.4	28.1	L Amygdala
24	453	0.986	41.1	16	44.6	R Occipital Pole
23	359	0.978	31.7	56.6	67.8	R Precentral Gyrus
22	267	0.978	42.2	37.5	60.4	R Precuneous Cortex
21	192	0.979	43.4	51.9	72.5	R Precentral Gyrus
20	107	0.967	42.5	46.7	56	R Cingulate Gyrus
19	100	0.975	49.3	61.3	57.8	L Juxtapositional Cortex
18	98	0.96	44.8	55.9	51.4	L Cingulate Gyrus
17	80	0.965	43.6	30	57	R Precuneous Cortex
16	39	0.981	33.3	23.7	34.3	R Occipital Fusiform Cortex
15	31	0.957	37.3	47.2	66.1	R Precentral Gyrus
14	22	0.968	38	35.8	53	R Precuneous Cortex
13	21	0.966	39.2	10.7	37.8	R Occipital Pole

Correlational analyses between memory performance scores and brain volume was conducted on the two age groups independently, using FSL's built-in GLM. This was done to make sure that the influence of one specific age group was not driving the correlations. General linear modeling was used to identify which brain regions were correlated with the memory performance metric of interest, PI. The results of the VBM correlational analyses can be seen in figure 10 (see below).

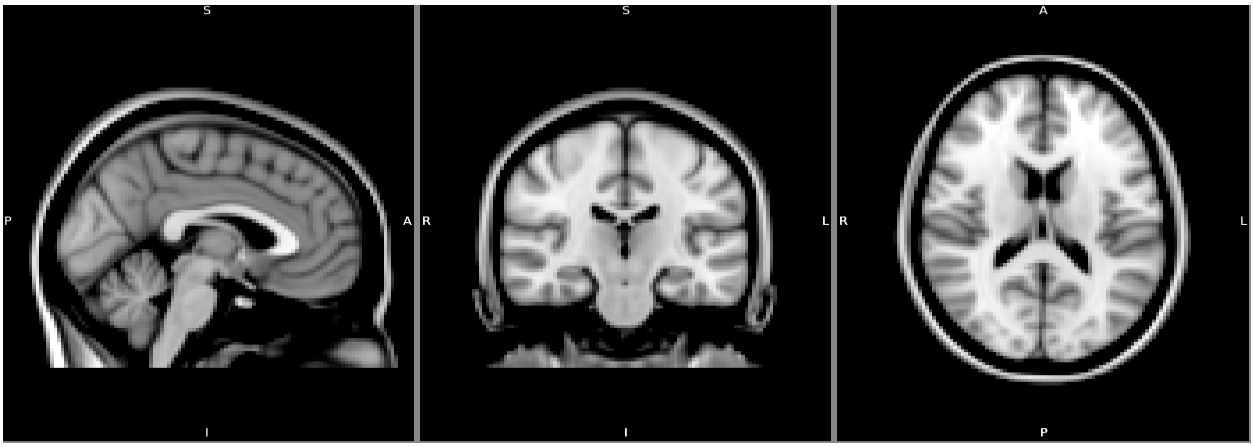

Figure 10. VBM Results for relationship between PI and GM (No significant regions found) in both OA & YA

As suggested by the images, there are no significant brain regions that correlate with scores of PI for older or young adults, as suggested by the lack of significant clusters/regions. In fact, the maximum p-value for any cluster in the OA group was .999 and .975, respectively for positive or negative relationships with PI. Similarly, the maximum p-value for any cluster in the YA group was .999 and .965, respectively for positive or negative relationships with PI.

4.0 CONCLUSION

This study replicated previous findings that showed older adults experience more proactive interference than young adults. Surprisingly, there were no significant age-related differences regarding retroactive interference. One cause for the lack of differences between the two groups could be due to the fact that the AC-FG list was only studied and tested 1 time, as compared to the AB-DE list, which was studied 3 times. It's possible that the additional study sessions strengthened the memory trace for the initial pairs so strongly that no differences could be seen regarding retroactive interference, which is supported by previous research on variable study-test cycles (Sheth et al., 2012). Interestingly, there were no differences in AB intrusions on AC pair learning. Similarly, there were no differences in the amount of no responses during the initial study phases; however, there were differences showing that older adults left more answers blank in the MMFR for the AC word pairs, which may reflect less recall as well as a propensity for less guessing. In regards to the age-related differences in brain volume, the current study replicated previous findings that CSF volume increases with age, which could be explained by the increased ventricles that are commonly seen in aging. Consistent with previous research, the current study shows that GM volume is reduced in older adults, which is likely due to neurodegeneration and atrophy, which is also common in aging. Surprisingly, there were no differences found between WM volume of young and older adults, which is somewhat

inconsistent with the literature; however, more recently, studies have been reporting less about WM volume and emphasizing the integrity of WM instead. As for the whole-brain VBM results, significant differences were found in the contrast between YA > OA, which demonstrates that YA have significantly more gray matter in the following regions: right lingual gyrus, right and left cingulate gyrus, left superior parietal lobule, left superior temporal gyrus, left amygdala, right occipital pole, right precentral gyrus, right precuneous, left juxtapositional cortex (supplemental motor cortex), and right occipital fusiform cortex. As expected, gray matter volume was significantly reduced in the OA group as compared with the YA group. Although COG coordinates and their corresponding brain regions were reported, there were many regions that were quite large in size and spanned across multiple brain regions. Some of these regions that were also implicated in the whole-brain VBM analysis, as seen in figures 6-8 (see above) were the left and right caudate, the left parahippocampal gyrus, the left hippocampus, both frontal poles, as well as the left and right frontal orbital cortex. Although no significant relationship between local GM and memory performance was found for any one specific brain region, there is a possibility that the current investigation was limited in its power to detect significant results due to the relatively small sample size, which may also limit the generalizability.

The findings of this study potentially have many implications for future investigations of memory interference, regarding behavioral and neural data. By failing to identify specific brain regions that are correlated with proactive memory interference in either young or older adults, it begs the question as to whether specific gray matter differences between the two populations are correlated at all to episodic memory abilities. Additional research with a larger sample size that also includes a wider range of memory performance measures could be helpful to improving the

understanding of age-related memory differences, specifically regarding memory interference and its underlying causes. In addition, the current study is the first to our knowledge to investigate age-related brain changes involved in memory interference. If specific brain regions that are highly correlated with memory interference measures could be identified, then perhaps an intervention approach that has been shown to modify GM volume, such as exercise, could be used to examine whether the differences in performance are directly related to brain volume.

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