Top-Down Modulation and Memory Deficits: Neural Enhancement in the Context of Aging

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Top-down modulation from a broader perspective suggests that some effortful control over posterior brain regions occurs. This study examined the extent to which age-related differences in top-down modulation could explain age-related memory decline. The theory of top-down modulation suggests that neural transmission during encoding requires the enhancement of relevant information and suppression of irrelevant information for efficacious neural function. Enhancement of attention to stimuli should be greater under higher task demands. In this study, we compared cortical modulation in a less effortful facial encoding task to cortical modulation in a more effortful facial encoding task. One-hundred-thirty older adults (mean age = 66.43 yrs) and 30 younger adults (mean age = 24.13 yrs) completed 2 tasks of facial encoding using functional magnetic resonance imaging (fMRI), a structural magnetic resonance imaging (MRI) scan, and a computer administered test of facial recognition outside the scanning environment. Activity in the fusiform face area was extracted when participants were told to *view faces* in the first encoding task and *remember faces* in the second encoding task. An enhancement index reflected the change in neural activity in the fusiform face area moving from the *view faces* task to the *remember faces* task. As predicted, levels of neural enhancement in the fusiform face area significantly predicted older and younger adult participants' ability to correctly discriminate between faces they had and had not previously seen. Against predictions, the level of fusiform face area enhancement did not differ between younger and older adults. Thus, differences in enhancement levels are not driving age-related differences in facial recognition discrimination ability. In functional connectivity analysis, the idea that connections between the "top" and "bottom" components of the memory encoding network were examined. Consistent with predictions, the functional connection between right ventrolateral prefrontal cortex and the fusiform face area related with recognition. Taken together these data suggest that sensory enhancement is a critical component of efficacious memory encoding processes, but top-down enhancement of sensory activity does not adequately explain age-related decrement in memory performance.

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PREFACE

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1.0   INTRODUCTION

Due to innovations in medical treatment and the aging of the baby-boomer generation, older adults are quickly becoming the largest portion of the US population. Projections show that over the next decade a 36% increase is expected in the number of adults over age 65 ("A Profile of Older Americans: 2009," 2009) and there is a linear trend in this increase expected over the next 50 years (Werner, 2010; Wimo & Prince, 2010). Unfortunately, with the rise in the aging population's numbers comes an increased prevalence of health problems and aging-related cognitive decline and diseases. The costs associated with treating and caring for age-related cognitive decline are high (Batsch, 2012; Wimo & Prince, 2010); dementia care costs totaled $172 billion in 2010 ("Alzheimer's Disease Facts and Figures," 2010). The cost of treating Alzheimer's Disease alone is projected to be $20 trillion over the next 40 years ("Changing the Trajectory of Alzheimer's Disease: A National Imperative," 2010), an amount that will bankrupt the healthcare system. Given the importance of understanding age-related cognitive decline, there is a need for more research to uncover the mechanisms contributing to decline as well as methods of reducing it.

It is with this global aim in mind that I have constructed this dissertation. As an outline for this dissertation, the first three chapters of this document lay out the theoretical background. They cover aging and cognition generally, memory decline, and a theoretical framework for examining age-related differences in memory performance for younger and older adults. Formal hypotheses appear in chapter 3, after establishing more rudimentary concepts and reviewing the relevant and rich literature in cognitive aging.

1.1   AGING

There is an immediate need for current science and public health initiatives to better understand the influence of age on cognition. Widespread loss of cognitive function occurs with age. Yet, there remains considerable variability in the rate and extent of decline (Deary et al., 2009)

Cognitive decline is affected by a number of factors. Typical cognitive decline trajectories vary within aging brackets. If we examine adults in the sixth or seventh decade of life, then the answer is that

most cognitive abilities decline (Christensen, 2001; Salthouse, 2010, 2011; K. Schaie, Hofer, SM, 1996; K. W. Schaie, 1996).The time frame of cognitive decline varies by domain. Some abilities remain intact for a longer period of time, and others have an onset at younger ages; for example, memory loss and cognitive speed decline in the third decade of life, and sometimes sooner (Salthouse, 2002). A brief, but not exhaustive review of cognitive aging follows to provide context for the study's investigation in memory deficits.

1.1.1   Cognitive Aging

Rates and trajectories of typical cognitive decline differ by cognitive domains. Some cognitive functions, such as verbal abilities and general knowledge (i.e., crystallized intelligence), show very little age-related decline (Hedden & Gabrieli, 2004; Park et al., 2004; Park & Reuter-Lorenz, 2009). In fact, vocabulary knowledge has been shown to increase starting at age 20 and does not show signs of slowing until around age 60 and declines much later in life.(Salthouse, 2009) On the other hand, 'fluid' processes show a declining pattern with aging. Fluid processes include executive functions, processing speed, reasoning, and some aspects of memory[1] (Deary et al., 2009). When one fluid process declines, the other fluid processes tend to follow suit (Wilson et al., 2002). This may be because of the inter-related nature of these functions; some of these processes depend heavily upon one other as is the case for memory upon executive function.

There is a still-noted discrepancy regarding the trajectory of age-related decline between cross-sectional findings of cognitive aging and longitudinal findings. Longitudinal studies offer greater insight into the individual cognitive decline rates and risk factors but are subject to practice effects. Both types of studies show decline across most cognitive domains with age (Schaie et al., 1996; Salthouse, 2010). Though the trajectories and onsets of decline may differ, the overall decreasing trend across domains of function is similar across cross-sectional and longitudinal studies. The more accepted trajectory for the timecourse of cognitive decline is the slight hyperbolic function shown in longitudinal approaches. These data show that most cognitive functions improve through early adulthood and then begin to decline after midlife. One notable exception is that perceptual speed begins declining during early adulthood through late adulthood in a linear fashion.

In 'fluid' domains, the trend for cognitive decline is nearly linear, and the decline can begin at age 20 through the lifespan; this pattern has been longitudinally demonstrated in tests reflecting

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[1] This is a simplified view of the division of cognitive domains; Salthouse (2009a) convincingly argues that memory and processing speed are distinguishable from fluid mental ability.

reasoning, spatial visualization, memory, and processing speed (Salthouse, 2010). A longitudinal study of the same individuals from 20 to 60 years of age found that processing speed was the most affected and precedes deficits in working memory (Salthouse, 2010, 2011). Working memory and short-term recall also show significant age-related decline (Hebert et al., 2003). The changes in processing speed and memory function co-vary and may explain why normal-aging adults take longer to learn new information. The largest and most robust cognitive deficits occur in speed of processing, attention, executive function, and some types of memory (Drag & Bieliauskas, 2009).

In sum, cognitive function declines with age. Generally, with increasing age there are few changes in general knowledge or vocabulary, but steep and linear declines in cognitive domains that rely more upon processing speed or the transformation or manipulation of information. Thus, memory, executive function, and complex cognitive processing suffer most and earliest. Though cognitive aging is relatively well catalogued, the causes and mechanisms of cognitive aging are still hotbeds of scientific research.

It should be noted that cognitive aging is not caused by any one mechanism and many theories are still being tested to explain how cognitive aging occurs. Many systemic factors in the periphery and central nervous system interact to underlie cognitive decline. Epidemiological evidence suggests that genetic factors, which can act as modifiers; medical factors (e.g., hypertension or diabetes, metabolic syndrome); and behavioral factors (e.g., diet and exercise) all play some role in the cognitive aging story. Of these, one of the notable related systemic processes that influence aging is cardiovascular disease (CVD) (Jefferson et al., 2011; Larson, 2011; Zeki Al Hazzouri et al., 2013) as older adults are at high risk for developing CVD. The role of CVD on cognitive aging is explained through the "vascular hypothesis" of aging that explains that vascular diseases (and their risk factors) affect the brain as well as the heart (Casserly & Topol, 2004; Raz & Rodrigue, 2006). And through those effects on the brain, cognitive functions change. Several pathophysiological mechanisms can also explain vascular changes and aging changes on the brain and within cognition including lipid metabolism, inflammation, and changes in oxidative stress. Notwithstanding the role of the periphery in cognitive aging, few would dispute that changes in the aging brain (whether related or independent of peripheral factors) cause cognitive changes.

1.1.3   The Aging Brain

As adults age, brain structures generally show signs of deterioration, though not at uniform rates across the brain. Some observed signs of deterioration include losses in both gray and white matter (Raz, 2005; Piguet et al., 2009, Walhovd, 2005), increases in white matter hyperintensities (Yoshita et al., 2006), and more amyloid and tau plaques (Yankner, Lu, & Loerch, 2008). In terms of volume loss, the frontal cortex is most affected, though the temporal, parietal, and occipital cortices also show gray matter tissue loss (Huag & Eggers, 1991; Raz, 2005; Ziegler et al., 2010). In at least one study, white matter deterioration has been linked more with losses in cognitive function than gray matter, (Ziegler et al., 2010). Cortical thinning could be a case of pruning unhealthy or unused tissue or a case of degradation of healthy tissue. The brain volume losses are not linear; as adults age, the rate of age-related volume decline accelerates; for example, annual ventricular atrophy in young adults is 0.43%, and at age 70 increases to 4.25% (Raz et al., 2005). Although some losses in brain integrity are observed, neuronal health may not be affected.

Neuroanatomical studies reveal an inconsistent picture regarding neuronal health in aging. Some studies have shown subtle age-related reductions in neuronal count, dendritic branching, or spine count (i.e., signs of neuronal growth and integrity) (B. Anderson & Rutledge, 1996; de Brabander, Kramers, & Uylings, 1998) and others have shown either no change or preservation in neuronal count (A. H. Gazzaley, Thakker, Hof, & Morrison, 1997; Peters, 2002; West, Coleman, Flood, & Troncoso, 1994). It remains unclear whether structural alterations are driving cognitive deficits, though studies continue to report neuroanatomical change (Chao & Knight, 1997; Fischer, Nyberg, & Backman, 2010; Raz et al., 2003). Animal research has shown that changes in neurotransmitter signaling among neurons may drive some age-related cognitive deficits (A. H. Gazzaley, Siegel, Kordower, Mufson, & Morrison, 1996; Pedigo, 1994). This may explain why some human adults with structural volume loss still manage to maintain cognitive health by using their remaining brain capital more effectively than their peers. This principle suggests that changes in neural signaling between neurons or between brain regions may account for age-related cognitive deficits.

In addition to changes at the cellular level, there are also significant age-related changes happening in brain function that can be detected using *in vivo* neuroimaging tools. For example, age-related reductions in posterior cortical activity are coupled with increases in anterior cortical activity. Specifically, age-related reductions in occipitotemporal activity have been paired with increases in frontal activity during many cognitive tasks, such as attention, visuospatial, and memory tasks (see Davis et al., 2008 for a review). This has been termed the posterior-anterior shift in aging (PASA) model.

Some recent work suggests that PASA patterns may be particularly prevalent under more taxing cognitive demands (Ansado et al., 2012).

Some functional compensation theories attempt to account for age-related changes in functional activity. First, the cognitive reserve hypothesis proposes that the brain attempts to combat age-related changes by using pre-existing networks (i.e., neural reserve) or enlisting the help of other processes (i.e., neural compensation) (Stern et al., 2009). A theory of functional compensation has been offered to explain how the aging brain engages additional brain areas to generate the same functional result as their younger peers (Cabeza et al., 2002; Cabeza et al., 2004). Extending the functional compensation theory, scaffolding theory proposes that increases in functional brain activity, especially in the frontal cortex, demonstrate recruitment of additional circuitry that "shores" up aging structures (i.e., structures that have become noisy, inefficient, or both) (Park & Reuter-Lorenz, 2009).

Cortical activity in older age has a tendency to become noisy and some theories attempt to account for this finding. Noise in brain function can refer to, but is not limited to, reduced specialization (i.e., less differentiation) of cortical activity, erroneous supplemental cortical activity, and complementary supplemental cortical activity. Two common concepts, bilateral compensation and diffusion of neural signal have been observed with cognitive aging models.

One finding is that older adults show less hemispheric lateralization, especially in the prefrontal cortex, compared to their younger peers. These findings have been shown in simple motor tasks (i.e., button pressing; Mattay et al., 2002) and more complex tasks like working memory and memory retrieval (Bäckman et al., 1997; Cabeza et al., 1997; Reuter-Lorenz et al., 2000). These findings led to the development of the hemispheric asymmetry reduction in older adults (HAROLD) model; this model posits that bilateral prefrontal activity is correlated with better task performance in older adults, where the neural pattern is lateralized in younger adults (Cabeza et al., 2002). This model helped characterize age-related differences in observed laterality, but failed to explain how the additional regions were active. Theoretically, these supplemental bilateral regions are recruited in a bilateral fashion to aid in task performance. While a great addition to our understanding of cognitive age, the mechanism through which other regions are recruited remains unclear. This model is more descriptive than mechanistic.

Older adults often demonstrate a larger network of neural regions involved in cognition than do younger adults. For example, studies have shown that older adults show less neural specialization in the visual cortex than younger adults when processing visuospatial information (Grady et al., 1992: Park et al 2004); more regions in visual cortex are active for older adults than younger adults. One cognitive aging theory, the theory of dedifferentiation, suggests that declines in neuromodulation (i.e., direction and maintenance of information) lead to less accurate transmission of information. This less accurate transmission causes less distinct mental representation of the information involved in that transmission,

that lack of specificity causing less distinct neural activity, or more regions of visual cortex involved in its processing (Li & Lindenberger, 1999; Li, Lindenberger & Sikström, 2001). More cortical regions involved in processing or neural firing to a wider range of targets are examples of dedifferentiation. In this case, neuromodulation refers to the behavior of the prefrontal cortex, which provides top-down modulation of goal-based information to various posterior brain regions. The prefrontal cortex is thought to enhance the processing of relevant information and to suppress the processing of irrelevant information. Age-related declines in neuromodulation could lead to increased neural noise from failures of both enhancement and suppression. Threshold for neuronal network activation could become less sensitive and noisier with age (from Drag & Bieliauskas, 2009).

In a similar vein, a top-down modulation hypothesis of aging has been tested in the context of attention and memory processes (see Gazzaley et al., 2007 for a review). Stemming from this work, a deficit in the ability to suppress irrelevant information has been posited for age-related differences in memory and attention performance (Gazzaley et al., 2007). Top-down modulatory hypotheses of aging are still emerging, and data testing these theories still needs to be conducted.

The aging process takes its toll both physically and mentally. In this first chapter, an illustration has been offered to suggest that physiological changes impact the brain; cardiovascular diseases obstruct blood flow and reduce the amount of blood to the brain. The brain itself endures an onslaught of deleterious changes in structure and function. The functional output of these changes differs by domain, with some of the greatest detriments observed in memory and executive function. The progress toward a unifying theory of aging to explain changes in cognitive function is still underway; theories in top-down modulation as an explanation for functional changes in the aging process are emerging. An ideal place to examine these emerging theories is in one of the domains of cognition that show the earliest and most robust decline, memory.

1.2   AGING AND MEMORY

Many older adults report that their memories do not function as they once did (Reid & Maclullich, 2006; Vestergren, 2011). Despite this, subjective assessment of memory ability often differs from objective measurements of memory decline. Not all types of human memory have the same age-related trajectories. Cross-sectional and longitudinal studies have shown increases in some forms of memory, such as verbal memory that linearly increases almost throughout the entire lifespan or procedural memory that shows little age-related decline (Ronnlund, Nyberg, Backman, & Nilsson, 2005). These

same studies show that some forms of memory, such as short-term memory, have more rapidly declining trajectories than other types of memory (Cowan, 2008; Ronnlund et al., 2005; Salthouse, 1996; K. W. Schaie, 1996).

1.2.1 Memory

Broadly, memory can be defined as the retention of something, a stimulus, over an extended period of time beyond its presence (Balota, 2000). Briefly, there are five major memory systems that create and retreive memories (Tulving, 1983): episodic memory, semantic memory, working memory, sensory memory, and procedural memory. Episodic memory and semantic memory together create explicit memory (i.e., declarative memory), a more intentional system; we intentionally attempt to form memories and retrieve them in this type of memory system. Its counterpart is implicit memory, which includes procedural memory (i.e., how to ride a bike), which once learned, often becomes more automatized, or implicit. The creation of memories involves several memory processes called sensory memory, short-term memory, working memory, and long-term memory (Cowan, 2008). Sensory memory is the first memory system in which the information received (e.g., sensory input) is stored just long enough to be transferred to short-term memory (Coltheart, 1980). Short-term memory is one of the first memory processes involved, it temporarily stores sensory infromation that is easily accessible (i.e., for retrieval). Working memory temporarily maintains that sensory information, stores it, and updates that information and is not an entirely dissociable process from short-term memory. In this study, I conceptualize working memory as including short-term memory (Cowan, 2008), though some researchers would argue that working memory is an attention-only mechanism of memory (Engle, 2002). Long-term memory results from the successful transfer of information from temporary storage to long-term storage through consolidation of the material. Storage in long-term memory is thought to be relatively stable, have a long-duration, and a much larger capactity than the more transient short-term and working memory systems.

Long-term declarative memory is most often broken down into two types: semantic and episodic memory. As adults get older, their semantic memory performance improves, even into late life; semantic memory refers to concept-based knowledge (e.g., Kennedy was assassinated by a sniper in a motorcade) (Nyberg et al., 2003). On the other hand, episodic memory declines in late adulthood and at a steeper rate (Ronnlund et al., 2005); episodic memory is knowledge of personally experienced events (e.g., you were sitting in your 4th grade classroom drawing a puppy when you heard that Kennedy was assassinated). Semantic and episodic memory failure rates differ such that concept-based knowledge

remains more preserved, and losses occur on a smaller gradient. The difference in trajectories becomes clearer after adjusting for participants' education levels or practice effects.

Three stages of memory function describe how memory systems operate to form and retrieve information. These stages are encoding, storage, and retrieval. Encoding is the process of moving information from working memory to long-term memory, storage refers to the physiological or structural changes in the nervous system resulting from successful encoding, and retrieval refers to recalling or recognizing information that has been stored (F. I. Craik & Rose, 2012). Another important point is that encoding and retrieval can be visualized only using neuroimaging techniques; there is no visual representation of storage (F. I. Craik & Rose, 2012). This study focuses on the processes of encoding, but explanations of the other two stages of memory processing are still helpful. Of these three stages, one of the paramount points to understand is that *some specific measure of retrieval is required to objectively test the efficacy of encoding.* An example of how encoding is often measured occurs in a standard college classroom. Students in a classroom listening to a lecture are ostensibly attempting to encode, or memorize, the information. However, some objective measure (i.e., test or quiz) is required to assess whether encoding was successful. The most common measures of encoding's effectiveness include tests of recall and recognition. Recognition (i.e., identification of current stimulus to items stored in memory) is often compared to recall (i.e., the retrieval of information without prompts or assistance), though recall requires more cognitive effort than does recognition.

Tests of recall and recognition do not reflect only encoding efficacy. Deficits in the retrieval of information would appear identical to deficits of encoding through tests of recall and recognition alone. Methods to dissociate encoding from retrieval have been applied. Some best practices include isolating encoding and retrieval components in the task design. Approaches like these have illuminated some dissociable contributions of each to memory formation. However, a clear separation between these two related processes is difficult. In the present study, encoding and retrieval stages have been temporally isolated to enable a scientifically valid exploration of encoding effects on recognition.

Understanding the physiological changes that contribute to age-related memory decline remains a central issue in aging research. *The present study aims to explore the idea that encoding depends upon changes in executive function, or the ability to direct and maintain sensory input as well as distribute attentional resources.* An example of how executive function and memory work together follows. Consider you are at a party and having a conversation with the host when you decide to set down your keys. In order to remember where you intend to leave your keys, your brain must act in a coordinated fashion to attend to the location you place your keys, maintain that visual or semantic information, and transfer that information into long-term memory (i.e., successfully encode the location of your keys). This process will require that the brain take resources away from other processes (e.g., processes

reflecting your current conversation) and redirect those resources (i.e., attention) to the memory network. A detailed exploration into aging and memory follows to highlight memory function in the context of aging.

1.2.2   Age-Related Memory Decline

Memorizing phone numbers, shopping lists, and where you last left your keys are daily activities that depend upon the ability to effectively encode. Failures of memory include more than instances of forgetting; they include distortions of information, intrusive memories, and retrieval failures (Schacter, 1999). A failure to take daily medication or to turn off the stove after cooking can be dangerous for anyone. For older adults, memory failures occur more frequently. Further, older adults often lead more isolated lifestyles, this makes the event of a serious memory failure potentially more hazardous, and they have more serious medical conditions, compounding the consequences of memory failures, such as failing to take daily medications.

Generally, the scientific community agrees that memory performance declines as adults get older. However, losses are smaller in some areas of performance than others. And some losses do not occur until adults reach the years near the end of their lives. Of course, some older adults "successfully" age, showing little to no loss in memory function during their lives (Gutchess et al., 2005). For most adults, some memory loss is typical of aging, but varies by type of memory. For example, age-related losses in implicit memory performance (e.g., driving a car, priming effects) are typically small or non-existent (Light, LaVoie, Valencia-Laver, Owens, & Mead, 1992). Age-related implicit memory failures are smaller than explicit memory failures; older adults that passively view stimuli are able to encode them at similar rates to their younger peers. Short-term memory span deficits are also slight in the aging population; older adults retain the ability to repeat or recall information they have recently encountered. Conversely, age-related memory loss is large when adults attempt to recollect the original context in which an event occurred (Dennis et al., 2008), in prospective memory (i.e., remembering to complete a task at a later time) (G. Smith, Della Sala, Logie, & Maylor, 2000), and in working memory and episodic memory (F. I. Craik, 2008; F. I. Craik & Rose, 2012; F. I. Craik & Schloerscheidt, 2011). Age-related memory failures do occur, and most robustly, in tasks involving working and episodic memory (Cansino, 2009; Friedman, Nessler, & Johnson, 2007; Nyberg, Lovden, Riklund, Lindenberger, & Backman, 2012). Thus, the current study examines memory failures in the context of episodic encoding of faces given that episodic memory shows robust and early decline.

1.2.2.1 Moderators of Age-Related Memory Decline

We can consider memory loss a universal characteristic of aging; all humans will sooner or later experience some degree of memory decline. However, some factors moderate the relationship between aging and memory decline. These moderators can be global and affect age-related memory decline more broadly while others are more task-specific (Cabeza et al., 2004). For example, broadly, the same health, psychological, and physiological factors that affect cognitive aging generally also impact memory decline. Factors such as cognitive reserve, brain reserve, and brain maintenance have been specifically linked with individual differences in memory decline (Habib, Nyberg, & Nilsson, 2007; Nyberg et al., 2012); these refer to a structural and functional surplus gained through life experiences, genetic factors, and healthy lifestyles. Factors such as task complexity or form of assessed memory can impact the rate or magnitude of age-related decline.

Many memory-task-related factors affect the relationship between aging and memory loss. Increases in task complexity exacerbate age-related differences in memory performance (Verhaeghen, Marcoen, & Goossens, 1993; Verhaeghen & Salthouse, 1997). A similar pattern is observed in reference to the load, or intensity of the cognitive demand, a given task requires; increases in cognitive load are associated with greater age-related differences in performance (Druzgal & D'Esposito, 2001). A meta-analysis found age-related differences in memory performance to be *greater* when memory was assessed through recall rather than recognition (F. I. M. Craik, Jennings, J.M., 1992; Naveh-Benjamin, 2000; Spencer & Raz, 1995). Age effects are also greater under incidental rather than intentional efforts (Spencer & Raz, 1995; van der Veen, Nijhuis, Tisserand, Backes, & Jolles, 2006); thus, when older and younger adults are not engaging in a goal-directed effort to encode, age-related differences in memory performance are larger (Spencer & Raz, 1995). More familiar objects are more easily recollected; for example, older adults outperform the young in recognition of famous (i.e., familiar) faces (Wright et al., 2008; Yonelinas, 2002). Thus, greater age-related differences in memory have been observed under higher levels of task complexity (i.e., processing demands), during passive or unintentional encoding conditions, and when the measure is recall rather than recognition.

The memory task in the current study capitalizes on findings in the memory literature to maximize comparisons between older and younger adults' memory function. The task is a facial memory task. Facial memory performance typically shows age-related impairment, particularly for unfamiliar faces (e.g., Bartlett et al, 1989; Crook & Larabee, 1992). This facial recognition task involves two levels of complexity and is assessed through recognition. In this way, we are assessing the encoding of the facial information using the test of encoding that shows the smallest age-related difference as opposed to recall, which may place older adults at risk of performance floor effects. The two levels of complexity include a passive view condition, where incidental encoding would occur, and an intentional or effortful

condition, where individuals would be required to engage in more effortful processing. Because more familiar objects are more easily recollected and an age-difference exists for familiar faces, novel faces were selected as the photographs to be encoded in the present study.

1.2.3 Aging and Facial Memory

Memory for people's faces is an ability that is required on a daily basis. In the absence of syndromes, such as prosopagnosia, recognition of faces usually requires little effort, yet, as we age, this becomes more difficult. The ability to learn novel, or unfamiliar, faces peaks after age 30 (Germine, Duchaine, & Nakayama, 2011). In this study, we are concerned with the encoding and recognition of unfamiliar faces. Unfortunately, older adults consistently struggle with learning unfamiliar faces (Bartlett & Leslie, 1986; Bartlett, Leslie, Tubbs, & Fulton, 1989; Crook & Larrabee, 1992; Haxby et al., 1996; Hills & Lewis, 2011). This is not simply a reflection of task complexity; albeit faces are complex visual stimuli. Other complex visual pictures, such as objects or scenes, are more easily remembered, and thus encoded, and age-related recognition differences are smaller (F. I. M. Craik, Jennings, J.M., 1992; Grady, McIntosh, Rajah, Beig, & Craik, 1999; A. D. Smith, Park, Cherry, & Berkovsky, 1990). A number of factors are responsible for older adults' poorer ability to encode novel-faces.

Two factors that affect memory encoding in older adults are the quality of the sensory information presented to the cognitive system (F. I. Craik & Rose, 2012) and the length in which it remains available for processing (Walsh & Thompson, 1978). For example, the age-related declines in visual acuity could directly impact memory decline by providing less sensory input into the neural encoding network (Baltes & Lindenberger, 1997; Lindenberger & Baltes, 1994). Thus, the amount of sensory information available to memory systems would decline directly from sensory loss, in Figure 5 evidence of vision loss by age is demonstrated. Second, age difference in visual sensory memory have long been established showing that older adults show a shorter duration of maintenance of information in visual sensory memory (Walsh & Thompson, 1978) . Changes in vision are to some extent immutable, however, prevention and treatment options are available. However, restoration of age-related vision loss to younger levels of visual acuity is not realistic. In fact, it is these losses of vision that may set forth a cascade of age-related changes in memory function, possibly to compensate for this lower sensory input.

Another factor that influences long-term memory of facial information is disruptions of the memory system. Two distinct factors are commonly cited as cause of memory decline: the disruption of executive functions (e.g., working memory) and decline in long-term (declarative) memory (Buckner, 2004; Hedden & Gabrieli, 2004). Ostensibly underlying these causes are changes in brain structures (i.e.,

cortical tissue loss and reduced cerebral blood flow) and functions (e.g., increased bilateral neural activity), which contribute to memory loss and memory disruption (F. I. Craik, 2008; F. I. Craik & Rose, 2012; Grady, 1996; Raz et al., 2003). These neuroanatomical and neurophysiological changes limit both the resources available for memory encoding as well as the ability to control those resources (F. I. Craik, 2008; F. I. Craik & Rose, 2012). It is here in the neurological changes in the memory system that the current study explores aging and encoding. Unlike changes in visual acuity, less is known regarding how aging impacts encoding related changes in memory processes. A brief explanation of the critical regions involved in encoding at the crux of the current study follows.

1.2.3.1 Facial Encoding in the Brain

More detailed information regarding encoding networks and neural regions is useful as a primer to a discussion regarding age-related differences in facial encoding. Encoding networks are very large, relying on many regions in the brain. The involvement of cortical regions during encoding is task specific and stimulus specific. Under higher task demand, more cortical activity is evident. Encoding faces occurs primarily in different regions than encoding landscapes, though both are visual processes. Involvement in the encoding network also varies by sensory type. Visual sensory information is *primarily* processed in visual cortex and auditory information in temporal cortex. Generally, for the purposes of this study, the memory encoding network will be narrowed to a few critical components. Three regions involved in memory encoding are sensory regions, the frontal cortex, and medial temporal areas (Blumenfeld & Ranganath, 2006; Cabeza, 2001; Chao & Knight, 1997; Cohen et al., 2000; F. I. Craik, 2008; F. I. Craik & Rose, 2012).

Sensory regions are responsible for the processing of the stimuli into the cognitive system and are relatively specific to certain types of information. Visual information is primarily processed in the visual cortex moving from area "V1," primary visual cortex, through deeper and more complex processing regions in the extrastriate cortex, along two streams that process the location and identification of the visual information. Neuroimaging evidence has established that a particular region in the brain called the fusiform gyrus is sensitive, yet not exclusive, to the processing of facial information (Andreasen et al., 1996; Corbetta, Miezin, Shulman, & Petersen, 1991; Courtney, Ungerleider, Keil, & Haxby, 1996; Druzgal & D'Esposito, 2001; A. Gazzaley, Rissman, & D'Esposito, 2004a; Grady, 1996; Grady et al., 1996; Grady, McIntosh, Horwitz, & Rapoport, 2000; Grady et al., 2013; Haxby et al., 1994; Kanwisher, McDermott, & Chun, 1997; Kuskowski & Pardo, 1999; Tarr & Gauthier, 2000); it is also conceptualized as a cortical area that reflects processing of information for which there is substantial expertise (Gauthier & Tarr, 2002; Gauthier, Tarr, Anderson, Skudlarski, & Gore, 1999; Tarr & Gauthier, 2000). This is a simplified description of a complex visual perception

system. Evidence continues to link visual cortex activity with multi-directional loops to the frontal cortex.

The frontal cortex is an area involved with directing and maintaining stimuli and allocating attention in a goal-directed fashion (Blumenfeld, Parks, Yonelinas, & Ranganath, 2011; Blumenfeld & Ranganath, 2006). Ventral regions of the prefrontal cortex seem to contribute to the selection of goal-relevant information (Blumenfeld et al., 2011; Blumenfeld & Ranganath, 2006, 2007); goal-relevant information would be attending to features of the face in a facial-memory task. Dorsal regions of the prefrontal cortex assist in organizing multiple pieces of information into working memory (Blumenfeld & Ranganath, 2007). Medial-temporal areas are involved in the consolidation and storage of information (Persson et al., 2012). Thus, several regions of the frontal cortex are involved with the maintenance and manipulation of the information being processed in visual cortex and in the secondary processing in extrastriate visual cortex. After inputs enter sensory memory and are maintained, organized, and manipulated, successful encoding requires storage. This storage primarily occurs in medial temporal regions.

Just as for the other areas of memory encoding, medial temporal cortical activity is not isolated to one brain structure. The medial temporal regions most associated with storage and consolidation of information is the hippocampus (Alvarez & Squire, 1994). The medial temporal network includes not only the hippocampus, but also adjacent cortical areas (e.g., entorhinal, perirhinal, and parahippocampal cortex) as well as the dentate gyrus and subiculum (Alvarez & Squire, 1994; Leveroni et al., 2000; Mencl et al., 2000). Processing of sensory information outside the medial temporal regions can be conceptualized as occurring in streams, namely the "what" and "where" streams in the temporal and parietal lobe, respectively (Burwell, 2000; Witter, Groenewegen, Lopes da Silva, & Lohman, 1989; Witter, Van Hoesen, & Amaral, 1989). Processing in the perirhinal cortex forms associations. The parahippocampal cortex deals mostly with spatial and contextual feature processing of sensory information. In the hippocampus, these streams of processing merge and information is consolidated into long-term memory.

Many other regions are involved in the encoding of information as well but remain outside the scope of the current study aims. In the present study, focus will be given to frontal regions and sensory regions as the relationship between the two is explored. Specifically, age-related comparisons of cortical activity during encoding will be made. General patterns in the literature provide the basis for two aims that will frame the hypotheses presented in the next chapter.

Some general neural patterns highlighting age-related differences in the cortical processes of facial encoding have been observed. First, perceptual mechanisms are largely intact. Equivalent brain activity between older and younger adults has been reported in the fusiform gyrus (Fischer et al., 2010;

Grady, 1996) when encoding faces. This seems at odds with other research showing a drop in visual acuity among older adults. Thus, some mechanisms may be compensating at the neural level for the decreased amount of sensory information reaching visual cortex. The present study seeks to test a theory that may explain how older and younger adults tap-into a neural process to encode new information. That theory is called top-down modulation and will be outlined in detail in the next chapter.

Performance is an important factor to be considered when interpreting age-related differences in cortical activity during encoding. When older adults perform similarly to their younger peers, their patterns of cortical activity can also appear similar in terms of regional recruitment (Fischer et al., 2010; Grady, 1996). However the magnitude and other features can differ. When older adults performed similar to their younger peers, the older adults showed increased prefrontal activity and greater feedback from the prefrontal when encoding faces (McIntosh, Grady, Haxby, Ungerleider, & Horwitz, 1996; Morcom, Good, Frackowiak, & Rugg, 2003). Older adults have also shown more bilateral activity in cortical recruitment (Grady et al., 1995). Thus, older adults' cortical activity seems most like their younger peers under equivalent performance, or successful encoding, conditions. Without examining cortical activity through the lens of performance, there is a risk of confounding brain activations by performance. This highlights the importance of considering performance when examining neural age-related differences in encoding to explore what neural activity characterizes successful encoding among the old. These explorations will show how older adults may be able to overcome challenges to memory encoding that accompany the aging process. In the present study, performance is a critical factor considered when exploring top-down modulation in the context of neural aging and memory deficits. The next chapter begins with a brief history of theoretical explanations of neural aging and then provides a theoretical foundation for the present study.

2.0   TOP-DOWN MODULATION

Few would argue that age-related changes in cognition manifest in changes in cortical processing. In terms of memory function, age-related differences in memory encoding at the neural level are well documented. Studies of older adults with successful encoding abilities and well as age-related comparison studies show that some compensatory mechanisms come online to assist the aging brain. Several studies of encoding have found compensatory patterns described for facial encoding with various stimuli; lower sensory input is coupled with bilateral prefrontal activity for older adults relative to their younger peers (N. D. Anderson et al., 2000; Cabeza et al., 2004; Davis, Dennis, Daselaar, Fleck, & Cabeza, 2008; Gutchess et al., 2005; Morcom et al., 2003). Though differences are observed, a unifying and systematic theory to explain cognitive decline remains beyond our grasp. Some of the more widely cited and well-known theories have laid groundwork for newer mechanistic explanations. Some earlier theories were selected for brief discussion, as they are some of the most commonly cited and explored theories in relation to aging.

Some of the most cited models of cognitive aging include two models that are more descriptive than mechanistic. The HAROLD (hemispheric asymmetry reduction in older adults model) was proposed to explain age-related cognitive change via a large reduction in prefrontal cortex symmetry (Cabeza, Anderson, Locantore, & McIntosh, 2002). Cabeza and colleagues have argued this bilaterality, and greater frontal recruitment, reflects older adults' compensatory response to age-related encoding impairment stemming from reduced sensory activity. This model explains a common finding in the literature that older adults show more bilateral recruitment in prefrontal cortex where younger adults show lateralized activity (N. D. Anderson et al., 2000; Cabeza et al., 2004; Davis et al., 2008; Gutchess et al., 2005; Morcom et al., 2003). This model is falling out of favor in lieu of more mechanistic explanations. For example, one extension of the HAROLD model suggests that older adults compensate for age-related neural disruption by recruiting additional neural circuitry that do not necessarily belong to the contralateral hemisphere as would be expected in HAROLD (Berlingeri, Danelli, Bottini, Sberna, & Paulesu, 2013). Another commonly explored theory of neural aging is the PASA model (posterior anterior shift of aging), that posits functional shifts of activity from posterior brain regions to anterior brain regions accounting for cognitive performance differences (Davis et al., 2008). In this model,

differences in older and younger adults memory performance and visual perception have been linked with increases in prefrontal activity that correlate with decreases in sensory activity (Davis et al., 2008). Both of these models describe commonly observed patterns in memory function, but do not offer an explanation as to why these changes occur.

Many theories account for a pairing between increased frontal activity with reduced sensory processing. Most of these are descriptive in nature. One theory mechanistically explores how older adults might overcome age-related deficits in sensory deficits through greater prefrontal activity linked with sensory maintenance through the process of top-down modulation. This theory will be explained in detail in the next chapter; particular focus will be given to top-down modulation in the context of facial encoding.

To test a systematic explanation of aging and encoding deficits, a relatively recent theory is explored. The theory of top-down modulation explains that prefrontal circuitry selects to what we attend and what we ignore. In the aging process, a top-down modulatory hypothesis of aging suggests a disruption in the top-down selection and maintenance of information in working memory. What we remember depends critically upon what we attend, as that information becomes available for storage into memory. The selection of that information is a crucial process that can affect memory. A large body of literature shows how changes in attention can affect what is maintained (i.e., sensory representations in working memory) and eventually stored, into long-term memory. How this system functions is outlined using animal and human research in the next section. More recent research shows how this process occurs at a neural level in humans and relates to later recognition, a reflection of successful encoding. The first step in understanding the theory of top-down modulation as it applies to encoding requires a review of visual processing.

2.1   BIASED COMPETITION IN VISION

The cortical process during visual encoding is rather well known and established through links between single-cell physiology, EEG, and fMRI literatures, Visual information, like any sensory information, enters the brain and then undergoes cognitive processing. The visual environment is very complex, perhaps more complex than any other sensory environments. Biased competition theory states

that each object in the visual field competes for cortical representation and cognitive processing (Desimone & Duncan, 1995). Thus at all times, competition exists for cognitive resources. To what in your visual field will your brain attend?

The purpose of biased competition is to prioritize task relevant information to make visual processing more efficient (Desimone & Duncan, 1995). At any given point, a large amount of visual information is taken in; but some of that information is relevant and some is irrelevant. As the amount of information increases or cognitive load increases (i.e., task complexity), the competition for cortical resources increases. Thus, selective-attention mechanisms are required to operate in a goal-directed manner to selectively attend to objects that are considered relevant. At any given moment, relevance can shift. The competition for cortical resources, especially in visual processing, is high.

Imagine your first date with a romantic partner. During that date, there was a moment when you glanced at your date and wanted to obtain as much information about his or her face as possible, to memorize his or her face. In this scenario, your eyes and brain are searching for visual stimuli from an array of information in your visual field. Of course, at this moment you see more than your date's face. Also in your visual field are restaurant walls, a server, trees outside the restaurant, and various other items. At this point, everything except your date's face is irrelevant and only his or her face is relevant. This is because your goal is to memorize your date's face. This goal makes only his or her facial features relevant. If you changed goals and then decided to memorize the trees, the trees would become relevant, and your visual processing within the visual field would change.

Biased competition directs our attention toward relevant information and away from irrelevant information (Desimone & Duncan, 1995). The direction of attention relies upon both "bottom-up" processes and "top-down" processes. The bottom-up processes are termed such not because they do not involve feedback from other cortical areas in visual cortex, but because these processes tend to be largely automatic (Desimone & Duncan, 1995). Top-down processes, then are those that are dependent on higher-level cognition or task demands and do not operate "automatically" in the same manner as bottom-up visual processing (Desimone & Duncan, 1995). Top-down processes are purposeful, goal-directed, and involve more cognitive effort from the individual.

2.1.1   Top-Down Modulation of Visual Processing

The competition for extremely limited cortical resources is biased by top-down and bottom-up processes (Desimone & Duncan, 1995). The top-down mechanisms are responsible for the selection and maintenance of sensory representations in working memory during visual processing in a goal directed

fashion. The top-down attention stream is goal-directed (Bar, 2003). Top-down modulation is the process by which individuals enhance and suppress neural activity to relevant and irrelevant stimuli, respectively (A. Gazzaley & D'Esposito, 2007).

Bottom-up processing would involve the fine distinctions between faces and receive inputs from the visual association cortex (Barcelo, Suwazono, & Knight, 2000) and visual regions specific to facial processing (A. Gazzaley, Cooney, McEvoy, Knight, & D'Esposito, 2005a), among other inputs. The bottom-up mechanisms operate rather automatically upon stimulus characteristics (i.e., shape, location, brightness) and 2) and shift accordingly through changes in selective attention (i.e., top-down processes). A large animal and human literature shows how this process occurs in the context of visual processing. The earliest literature first explains what visual processing looks like in visual cortex, the bottom-up portion of visual processing, and how that process varies by changes in attention (i.e., top-down influences).

Top-down modulation involves maintenance of stimuli representations in working memory. Stimuli representations are a neural reflection of incoming information that we may want to process or in this case, remember. The integration of these "bottom-up" and "top-down" streams occurs in temporal cortices before moving further in the stream of processing (Bar, 2003). Some neural regions are involved in general aspects of encoding (e.g., maintenance of stimuli, consolidation, categorization) while other regions are stimulus-specific (Nyberg et al., 1996), especially regions involved in bottom-up processing. Most importantly, the signals that bias attentional selection occur outside the visual cortex (i.e., the bottom) (Beck & Kastner, 2009).

2.1.2   Finding the bottom in "bottom-up" processing

The animal literature in visual attention has shown that attention affects brain activity in regions responsible for processing stimulus features. A large monkey, single-cell recording literature was key in elucidating connections between receptive fields in single-cells and deliberate changes in attention. The single-cell recording literature in non-human primates has shown that neurons fire faster under attended conditions compared to unattended conditions (Motter, 1993; Reynolds, Pasternak, & Desimone, 2000). In the monkey, changes in attention have been linked with increased magnitude of single-cell recordings in extrastriate regions of visual cortex (i.e., V3,V4, V5/MT) This literature has shown that shifts of attention result in preferentially responding in stimulus-specific regions of visual cortex, especially in regards to location.

Single-cell recording studies in monkeys have also shown that directing attention within a visual field can modulate visual cortex activity. For example, recordings in V2 and V4 increase in magnitude, as would be expected, when monkeys attended to different objects within the same visual field (Reynolds, Chelazzi, & Desimone, 1999; Spitzer, Desimone, & Moran, 1988). The patterns of visual cortex modulation are similar in humans.

In humans, objects in the visual field are processed in a large network of cortical regions including the primary visual and extrastriate cortices (Desimone & Duncan, 1995). In one study, young adults were asked to attend to either moving or stationary dots in an fMRI task (O'Craven, Rosen, Kwong, Treisman, & Savoy, 1997). Stimuli were identical across trials and contained both stationary and moving dots. Thus, in the 'attend to moving dots" condition; attention should be paid to moving dots and not to static dots. Activity in motion-sensitive regions should increase more when attending to moving dots than attending to static dots, and vice versa. The results supported this idea in both primary and extrastriate visual cortex (i.e., V1 and V2).

Moving from primary through extrastriate cortices, neurons respond more and more selectively and with greater complexity (Desimone & Duncan, 1995). The ventral stream projects into the inferior temporal cortex and is important for object recognition (i.e., the "what" pathway), while the dorsal stream is important for spatial perception and visuomotor performance (i.e., the "where" pathway) (Ungerleider & Haxby, 1994). According to Desimone and Duncan (1995), the ventral stream underlies object recognition (i.e., visual processing regions) and should show evidence of increased and maintained cortical activity directed from top-down mechanisms or through more automatic bottom-up processes (i.e., stimulus attributes: size, luminescence, pop-out). Evidence of top-down modulation has also been shown in the dorsal stream in areas like visual area 3 (Hopfinger, Buonocore, & Mangun, 2000).

The early neuroimaging literature in humans has shown how attention to stimulus features relates to changes in visual cortex activity. An early positron emission tomography (PET) study showed how deliberate increases in attention to stimulus features (e.g., shape, color, and speed) resulted in increased activity in distinct extrastriate cortex regions responsible for processing those visual features (Corbetta et al., 1991). A large literature across neuroimaging modalities (e.g., PET, EEG, fMRI) has shown modulation of stimulus-specific extrastriate visual cortex through shifts in attention or focus.

In sum, we know that visual cortex is modulated by changes in attention. We also know that visual cortex activity is extremely specific to stimulus components. Thus, in selecting where to look for the "bottom" in a top-down modulatory framework, we must look in regions sensitive to particular stimuli. The ventral visual stream, rather than the dorsal stream, seems critical for recognition. Thus,

when looking for the bottom when processing faces, we would look for regions in extrastriate cortex shown to be sensitive to facial processing, like the fusiform face area.

In the proposed study, encoding will be examined in the context of a visually-presented task. Subjects intentionally or passively remembered faces, thus sensory regions that will be examined here should be restricted to areas sensitive to processing the raw inputs of faces. *The fusiform face area (FFA) is highly sensitive to facial processing and extremely active during facial encoding and processing of faces* (Dennis et al., 2008; Kuskowski & Pardo, 1999) as well as other complex stimuli (Tarr & Gauthier, 2000). The visual word form area is a region involved in the processing of words (Cohen et al., 2000)[2]. Thus, following the literature on biased competition and top-down modulation in monkeys and humans, we would expect that if adults were asked to attend to faces we would expect increased activity in the FFA. However, when attending to faces, increases in areas responsible for processing other stimuli, such as VWFA, would not be expected.

Thus, a relatively solid understanding of where the "bottom" exists in top-down modulation. Research shows that changes in attention results in changes in extrastriate visual cortex activity. But what is the source of these attentional effects? Otherwise asked, where is the "top" in top-down control?

2.1.3 Finding the top in "top-down" control

In the attempt to try to find the "top" in top-down control, recent neuroimaging studies have moved beyond single-cell studies to identify brain regions that appear to control attention. The story within the top-down processes are less clear, making the identification of the "top" more challenging than the identification of the bottom.

Research implicates a wide variety of regions in the parietal and frontal cortices involved in top-down modulation. Neural activity in regions outside of visual cortex in basic attention studies has been thought to be indicative of regions that support attentional control (Pessoa, Kastner, & Ungerleider, 2003) From single-cell recordings in monkeys, the parietal cortex would be implicated in attentional control (Goldberg, Bisley, Powell, Gottlieb, & Kusunoki, 2002). Frontal and parietal regions have been consistently implicated in visual attention, including the superior parietal lobule (SPL), the intraparietal sulcus (IPS), and the frontal eye field (FEF) (Corbetta, Miezin, Shulman, & Petersen, 1993; Hopfinger et al., 2000; Nobre et al., 1997). Other frontoparietal regions with this network have been shown to be

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[2] Processing of faces and words rely on many sensory regions; the selected regions are not active solely in the processing of these two types of stimuli. For example, FFA activity has been linked with processing of stimuli that require expertise (complex scenes and figures as well as faces). However, these regions are reliably active when processing faces and words.

involved in visual processing: superior frontal gyrus, middle frontal gyrus (Hopfinger et al., 2000). Each of these regions is currently being elucidated for their respective roles in top-down control. For example, shifting the location of attention has been shown to produce consistent, robust neural activity in SPL (Yantis et al., 2002).

Even if objects, such as faces are represented and adequate attention is given, those objects must be maintained long enough to form memories and manipulated in some manner to aid in encoding. Results from neuroimaging studies have repeatedly shown the lateral prefrontal cortex to be involved in working memory. Specifically, ventrolateral prefrontal cortex (VLPFC) activity has been associated with maintaining items in working memory (Blumenfeld & Ranganath, 2006; D'Esposito, Postle, Ballard, & Lease, 1999; Petrides, 2000) and with aiding in the maintenance of internal representations of sensory stimuli (Curtis & D'Esposito, 2003). But activity in the right VLPFC (RVLPFC) seems to be more sensitive for facial stimuli, while the left VLPFC seems more sensitive to verbal stimuli (Braver et al., 2001) or at least the degree to which stimuli can be verbalized. However, recent studies have found activity in both hemispheres of VLPFC when encoding faces, the amount of left PFC activity seems dependent upon the extent to which the object being encoding can be verbalized. Further, white matter tractography has shown links between visual cortex and prefrontal regions, suggesting a structural connection. Specifically, the occipital blade, which includes fibers in the anterior fusiform face area, receives projecting fiber bundles from the inferior and superior frontal regions (Oishi et al., 2008). We would want to examine whether top-down processes can adequately maintain sensory information in working memory, thus the VLPFC would be the area to be explored as a contributor in the network of top-down modulation.

Although many regions with the frontoparietal network have been implicated for their role in top-down control, one will be explored in the present study. *The role of the right VLPFC will be explored for its role in maintaining sensory stimuli in working memory.* Importantly, links between activity in "top" regions and activity in "bottom" regions will be explored. Links between functional regions are often explored using functional connectivity analysis. In such analyses, previous research has used the fusiform face area (FFA) as a seed voxel in functional connectivity analyses and found the facial encoding network included dorsolateral and ventrolateral PFC, the premotor cortex, the intraparietal sulcus, the caudate nucleus, the thalamus, the hippocampus, occipitotemporal regions, and FFA (i.e., the "seed")(A. Gazzaley, Rissman, & D'Esposito, 2004b). Thus, the selection of the right VLPFC seems in line with recent functional connectivity analyses of facial encoding.

2.2   TOP-DOWN MODULATION AND ENCODING

The key hypothesis of this proposal is that regions involved in the control of attentional top-down signals will bias processing under conditions of higher task demand. The literature on top-down modulation and encoding supports this idea. However, little work has been done to examine the modulation of specific sensory areas (e.g., V1, V2, sensorimotor regions, fusiform face area, parahippocampal place area) when linked with behavioral performance. Modulation of sensory activity has been established mostly in rodent models and in visual processing studies with humans. The current work now beings to examine the attention-related changes observed typically observed in sensory activity in light of behavioral performance. Essentially, this study seeks to explore the degree to which top-down modulation matters in terms of task performance. And then this study will explore how the relationship between top-down modulation and performance compares between younger and older adults.

In the encoding literature, top-down modulation can be conceptualized in many ways. Most commonly, top-modulation is measured as a change in some outcome measure compared across different conditions of attention. At the behavioral level, these could be changes in recognition (i.e., accuracy or response time). At the neural level, these outcome measures could be event-related potential latencies or fMRI bold magnitudes. In the functional connectivity literature, differences in functional connectivity between regions that support top-down processing and sensory activity can be examined. And changes in these measures that vary with changes in attention are considered evidence of top-down modulation.

In a series of studies, a team of researchers has examined top-down modulation using EEG and fMRI. Gazzaley colleagues (2005a) examined top-down modulation in 18 younger adults. In a face and place working memory task, they asked subjects to attend to different objects that appeared within the same. In different blocks, they were asked to: 1) remember faces and ignore scenes, 2) remember scenes and ignore faces, 3) remember faces and scenes, and 4) passively view images (pay no greater attention to faces than scenes). If top-down modulation were to exist, greater scene-selective sensory activity would be highest in block 2 when individuals were asked to remember scenes but ignore faces. In this approach, each block requires a different focus. In this way, attention can be shifted in a goal-directed manner because individuals are asked to attend to one stimulus but ignore the others in an event-related design. Thus, successful modulation would occur in block 2 if sensory activity in cortical regions responsible for scene processing (e.g., parahippocampal place area) are more active here than in the other 3 blocks *and* that upregulation of cortical activity relates to encoding performance (e.g., recognition). They were able to show that (for scenes) 82% of their younger subjects enhanced activity in the PPA above the passive view baseline and suppressed activity in PPA below passive view (A.

Gazzaley et al., 2005a). Younger adults activity was also enhanced in the fusiform faces area (FFA) in condition 1 (i.e., remember faces and ignore scenes), but no suppression was evident in the FFA. The relationship between cortical enhancement and later memory performance was not examined.

Evidence from EEG and fMRI in this study suggested that, younger adults could modulate scene and face specific sensory regions through deliberate shifts in attention. In the FFA, activity was greater when they attempted to remember faces and ignore scenes compared to ignoring faces and remembering scenes. The same pattern was observed in the parahippocampal place area (PPA), a visual region selective for scenes. Participants also showed a shorter (i.e., faster) event-related potential (ERP) latency for N170 learning response when remembering faces versus ignoring faces, suggesting they processed and learned faces faster when they were instructed to do so. And the degree of modulation (i.e., magnitude and speed) mapped on to later recognition.

In a recent study, evidence of top-down modulation is hinted at though not directly explored. In a classic neuropsychological working memory task, the *n*-back, participants must maintain and compare presented stimuli to those that appeared before. They compare the presented stimulus to the image present *n* stimuli before. In this manner, as *n* increases so do the task demands and the corresponding cognitive load. Using this paradigm in a face n-back, higher correlations among brain regions involved in facial working memory occurred as task demands (i.e., *n*) increased (Kim et al., 2012).

Of particular interest in these studies is how researchers have conceptualized and provided data to support top-down modulation. Enhancement and suppression measures that reflect top-down modulation were operationalized in seminal studies by the Gazzaley team. Other researchers have adopted that same comparison between levels of task demand as the approach to studying top-down modulation, as Kim and colleagues did (2012). Enhancement is one measure of top-down modulation. In the present study, two levels of encoding exist, a passive view condition and an intentional remember condition where participants are asked to attempt to remember the faces presented. I conceptualize these two conditions as difference of load or demand. In this manner, the difference in cortical activity in a particular region between the lower level of task demand, the passive view condition, and the higher level of task demand, becomes a reflection of enhancement.

Enhancement is the neural ability to upregulate attention in a goal directed manner as a comparison between two conditions. In the Gazzaley studies, enhancement is the magnitude of cortical signal difference that exists between a higher level of attention, the 'attended' stimuli of each block and the lower level of attention and the 'not attended' stimuli of each block in the same cortical region. Essentially, enhancement is a measure of an increased cortical signal change when moving from conditions of lower attention to higher attention. Other cortical measures can also reflect enhancement

and top-down modulatory processes. Changes in functional interactions between cortical regions also lend nicely to explorations in top-down modulation.

Functional interactions occur when signal in two or more neural regions covary. In a top-down modulatory framework, as described in this study, increased activity in prefrontal regions responsible for executing maintenance and manipulation should be related with increases in the maintenance of that information in sensory cortex. One example might be the observations of increased signal in the right dorsolateral prefrontal cortex coupled with increases of sensory activity in the fusiform face area. Functional connectivity analyses allow research to investigate the relationship between brain regions and can shed light into the prefrontal cortex's contribution to posterior brain regions during encoding.

Studies show that functional interactions between visual cortex and prefrontal regions do change with changes in attention (A. Gazzaley et al., 2007). In one study, a region of 7-contiguous voxels in each participant's left PPA was used to create functional connectivity maps for 3 encoding conditions (i.e., remember scenes and ignore faces, passive view, and ignore scenes but remember faces). Correlated functional activity was calculated using the beta series correlation analysis method (Rissman, Gazzaley, & D'Esposito, 2004). Correlated activity between PPA and prefrontal regions (e.g., middle frontal gyrus) was stronger when younger adults were intentionally trying to remember scenes compared to conditions in which they were instructed to ignore scenes. This difference in functional connectivity between the more attentive and least attentive conditions does suggest top-down modulation for the encoding of scenes.

Neuroimaging findings show consistent magnitude increases and speed increases that accompany increases in effort or attention by task-condition. In early studies, top-down modulation was explored by comparing cortical signal in sensory regions between conditions of high and low task demand. In these studies, data showed that decreased fusiform activity was associated with increased length of delay in a delay-match-to-sample task, suggesting that decreases in fusiform activity varied as a function of perceptual demands (Grady et al., 1998; J.V. Haxby, 1995). In one study, load increases in a facial n-back task were associated with increases in prefrontal activity and increases in FFA activity (Druzgal & D'Esposito, 2001), such that signal in both regions was higher under the 2-back for faces (i.e., the most effortful condition), than the 1-back for faces, or the 0-back (i.e., the easier conditions). Thus, data suggest that FFA would be modulated by changes in attention. Both previous studies highlight changes in cortical magnitude. The next neuroimaging study is an illustration of attention-dependent slowing of cortical processing. In one EEG study, participants were asked to direct their attention to 1 of 2 superimposed images. The degree to which participants modulated the early P100 (ERP) latency related with later recognition (Rutman, Clapp, Chadick, & Gazzaley, 2010), faster waves forms were associated with better performance. Shorter ERP latencies indicate faster cognitive

processing. Faster cognitive processing accompanied increases in attention. These data showed that effortful increases in attention can speed up encoding and relate with better performance. In this manner, top-down modulatory processes can affect cognitive speed. Taken together, mounting evidence shows that increases in attention can increase cortical activity and cognitive speed in regions heavily involved in the task at hand.

The encoding literature, in the context of top-down modulation is smaller than the top-down modulation of visual attention literature. Yet, examining top-down modulation (TDM) in the context of encoding is an improvement upon its examination in basic visual processing. Linking the observed pattern in top-down modulation with behavioral performance can help explain the neural substrates underlying this process. Though some rather compelling evidence suggests top-down modulation may change as adults age, clear links to performance have yet to be made. Without the confirmation of this pattern of modulation affecting performance, these could be interpreted as attention-driven effects independent of task performance, or simply increased effort without increased results.

One criticism with much of the literature that directly examines TDM and encoding is that much of it focused one sensory region. Replication of this phenomenon on other sensory regions is needed. Gazzaley (2005a), Grady (1998, 1995), Haxby (1995), and Druzgal and D'Esposito (2001) have all observed some evidence for modulation in FFA by changes in task demands. Yet some questions still remain. For example, what role do regions of the frontoparietal top-down network play in this modulation? Does top-down modulation apply to younger and older adults? And how does this modulation relate with behavioral performance? I will attempt to address some of these questions.

I predict that greater sensory enhancement in FFA will relate with better behavioral performance (i.e., facial recognition) when moving from lower to greater attentional demand when encoding faces. I predict that this relationship would hold for younger and older adults. If this does turn out to be the case, then changes in top-down modulatory function could explain some of the reductions observed in memory encoding among older adults. Specifically, this would explain age-related differences only if poor performing older adults exhibit difficulty in modulating sensory activity. Support for this hypothesis would suggest that the enhancement component of top-down modulation contributes similarly to effective encoding across age. If disruptions in top-down modulation can explain deficits in encoding, it should be able to do so for younger and older adults.

I will also explore the behavioral component of top-down modulation. *I predict that higher functional correlated activity between FFA right VLPFC will relate with better performance*, *regardless of age.* We know that increases and decreases of functional activity within regions involved in the encoding network can impact memory performance (A. Gazzaley et al., 2008; Grady, McIntosh, &

Craik, 2005), but further replication is warranted. These contributions will shed light on the contributions of these regions and their interaction to better memory formation.

This dissertation builds upon the existing literature by expanding our understanding of top-down modulation in the context of aging. Very few studies examine neural encoding deficits, specifically enhancement deficits, in the context of aging. Even fewer adopt the top-down modulatory approach. However, the top-down modulation hypothesis offers a parsimonious explanation for aging-related changes in memory function that improves upon other theories. This study predicts that deficits in top-down modulation occur among older adults, evidence by lower visual sensory enhancement when trying to memorize faces. This study also predicts that disruptions in the functional connectivity between the "top" and "bottom" of the memory encoding network can explain age-related deficits in memory performance.

2.3   ENCODING AND AGING IN THE CONTEXT OF TOP-DOWN MODULATION

Most of the research in encoding is conducted either in rather young or rather old adults (i.e., both human and non-human animals). In these developmental explorations of encoding, the younger adult is often treated as the reference group for comparison. This makes sense given that younger adults usually encode with much higher accuracy; thus, are treated as the paragon of optimal function.

Aging significantly reduces memory encoding ability, function, and performance (N. D. Anderson et al., 2000; Cabeza et al., 1997; Dennis, Daselaar, & Cabeza, 2007; Dennis et al., 2008; Grady et al., 1995; Grady et al., 1999; Gutchess et al., 2005). Encoding failures have been explained by deficits or disruptions in upstream executive function, including failures in selective attention (Chao & Knight, 1997, 1998; A. Gazzaley & Nobre, 2012; Zanto, Rubens, Thangavel, & Gazzaley, 2011), dampened inhibition (Stevens, Hasher, Chiew, & Grady, 2008), or simply weakened cortical activity (Grady et al., 2005). The mechanisms that explain this change in memory encoding are not completely clear. Changes in functional connectivity between critical encoding regions, such as prefrontal cortex and hippocampus (Della-Maggiore et al., 2000; Grady, McIntosh, & Craik, 2003), changes in function of regions that support encoding (Dennis et al., 2007; Dennis et al., 2008), reductions in cortical structural size and reductions in cortical activity and behavioral function (Raz et al., 2003), and reductions in vasculature or blood flow (Grady, 1996) impact memory encoding. As adults age, encoding-related cortical activity patterns, magnitude, and regional recruitment also change (Gutchess et al., 2005; McIntosh et al., 1996; Tisserand, McIntosh, van der Veen, Backes, & Jolles, 2005{McIntosh, 1996

#112). In the proposed study, age-related differences in patterns of top-down modulatory activity will be explored.

Specifically, if top-down modulation explains age-related encoding deficits, certain criteria would need to be met. Evidence of encoding would need to be established in younger and older adults; this will be provided by the hypotheses laid out in the above section. First, links between sensory enhancement (i.e., or suppression) and performance must be established (Hypothesis 1). Functional connections between the "top" regions and "bottom" regions in top-down control of encoding must relate with performance (Hypothesis 2). Then, if this theory is to explain the deficits in older adults encoding function, age-related changes in enhancement (i.e., or suppression) need to be shown and linked with changes in behavioral performance. Exploring this notion is the final aim of the proposed dissertation. Previous work has laid a working structure from with which to continue.

In a seminal study of top-down modulation and aging, older and younger adults were shown to differ in their ability to modulate sensory activity in different encoding conditions (A. Gazzaley, Cooney, Rissman, & D'Esposito, 2005b). The same methodology was adopted as above. Older and younger adults were asked to 1) remember faces and ignore scenes, 2) remember scenes and ignore faces, 3) remember faces and scenes, and 4) passively view images (pay no greater attention to faces than scenes). In the previous study, they found that 82% of younger subjects could both enhance PPA signal and suppress PPA signal, under the appropriate task demands. A total of 88% of the older adults were able to enhance information and only 44% were able to suppress information. Older and younger adults differed in their abilities to suppress, but not enhance information.

In terms of enhancement, both younger and older adults showed evidence of enhancement. In fact the magnitude of difference for older adults between the passive view and remember scenes condition was larger for older than younger adults, this difference was not significant. But the difference in suppression abilities significantly differed between groups. These findings are not entirely consistent with their earlier work (A. Gazzaley et al., 2005a). In both studies, younger adults adequately enhanced signal in PPA when viewing faces. However, in the earlier study with only younger subjects, younger subjects were *not* able to suppress face-related sensory signal when requested; the inconsistencies between PPA and FFA data were abandoned in later studies.

When encoding faces, the age-related differences in suppression continued, and mapped on to performance. A small sample of six older adults were unable to recognize the faces they attempted to encode (i.e., average accuracy was approximately 70%), those same adults were also unable to effectively suppress faces in the ignore condition. Higher performing older adults demonstrated suppression ability similar to younger peers.

In this seminal study, the role of enhancement on performance was not examined (A. Gazzaley et al., 2005b). During encoding, older adults showed a similar ability to enhance as their younger peers. Because the role of enhancement in facial recognition was ignored by age, we cannot yet conclude that enhancement plays an insignificant role compared to suppression in predicting performance, as the authors argue (A. Gazzaley & D'Esposito, 2007).

Other researchers have shown that changes in brain regions thought to support top-down modulation vary with age during facial encoding tasks (Grady, 1996, 2002; Grady, Bernstein, Beig, & Siegenthaler, 2002; Grady et al., 1998; Grady et al., 2003, 2005; Haxby et al., 1996). Involvement of different critical regions of the prefrontal cortex especially had been shown to differentially increase with task demands and conditions by age (Morcom et al., 2003). Findings even show that prefrontal activity increases under task demands and compensates for decreased medial temporal activity thought to contribute to lower recognition in older adults (Gutchess et al., 2005). The evidence for age-related variations in regional activity known to contribute to top-down attentional control have been shown.

Summary. The missing link for a top-down modulatory explanation for age-related deficits remains in the "bottom" of top-down modulation. *Direct examinations of modulation of sensory activity by effort and age are rare.* Some evidence suggests that FFA responds less selectively as adults age, this could be interpreted as a reduction in enhancement and suppression (Lee, Grady, Habak, Wilson, & Moscovitch, 2011). To date, Gazzaley (2005b) remains the most promising investigation in age-related changes in top-down modulation. To expand this work and continue the argument for top-down modulation, I will explore the follow age-related question: To what extent do younger and older adults differ in their ability to enhance sensory signal alongside increases in effortful attention? *I predict that younger adults will show significantly greater sensory enhancement in FFA than older adults.*

This will be explored by comparing younger and older adults' enhancement in the FFA during the encoding of faces (i.e., Enhancement = Intentional Encoding – Passive Encoding). If younger adults enhance better than older adults, deficits in the enhancement component of top-down modulation may be a feasible explanation for older adults failing encoding abilities, assuming enhancement and performance do not vary by age. Though older adults are expected to enhance less than their younger peers, that enhancement should still relate similarly with task performance. If not, if age and sensory enhancement interact to predict task-performance (i.e., accuracy), considerations need to be made when arguing for enhancement modulation effects as a cause for decreases in memory encoding for older adults.

The following hypotheses were examined in this study.

1. *Hypothesis 1. Greater sensory enhancement in FFA will relate with better behavioral performance (i.e., facial recognition) when moving from lower to greater attentional demand when encoding faces.*

2. *Hypothesis 2. Higher functional correlated activity between FFA and right VLPFC will relate with better performance, regardless of age.*

3. *Hypothesis 3. Younger adults will show significantly greater sensory enhancement in FFA than older adults.*

3.0   RESEARCH DESIGN AND METHODS

3.1   PARTICIPANTS

Data for this study was gathered from a sample of 200 participants enrolled in the Healthy Active Lifestyle Trails (HALT) at the University of Illinois between 2005 and 2009. The HALT project was a 1-yr randomized, controlled trial (RCT) researching the links between aerobic exercise, brain health, and cognition in younger and older adults. Data from this project includes demographic information, cognitive testing, and neuroimaging measures, specifically structural and functional MRI data. Although the HALT project includes data from multiple time points, all data in the present study were collected at the baseline sessions occurring at entry to the RCT. At this baseline MRI session, younger and older adults provided structural and functional magnetic resonance (fMRI) images and completed memory recognition tests. A total of 43 young and 183 older adults completed MRI scans.

At the time of testing, HALT participants were between the ages of 18 and 81. Older adults' ages ranged from 59 yrs to 81 yrs ($M = 66.43$, $S=5.72$). Younger adults' ages ranged from 18 yrs to 35 yrs ($M = 24.13$, $S=4.62$). Inclusion criteria for the HALT study for *older* adults included: age greater than 59, absence of cognitive impairment, capability to perform exercise, absence of clinical depression, normal or corrected vision, completion of a cardiorespiratory fitness test, and a sedentary lifestyle. All older participants were screened for dementia by the revised and modified Mini-Mental Status Examination (Stern, Sano, Paulson, & Mayeaux, 1987) and were excluded from participation if they did not reach the required cut-off of 51 (i.e., high score of 57). All younger and older adults also had to have no previous head trauma, no previous head or neck surgery, no diagnosis of diabetes, no neuropsychiatric or neurological condition including brain tumors, and no metallic implants that could interfere with or cause injury due to the magnetic field. All participants had to demonstrate strong right handedness (e.g., 75% or above on the Edinburgh Handedness Questionnaire; (Oldfield, 1971). Participants signed an informed consent approved by the University of Illinois.

A total of 56 older participants and 12 younger participants were excluded from all the analyses due to poor data quality, specifically inadequate coverage of the visual cortex; another 3 older

participants and 1 younger participant were removed for incomplete behavioral measures; one additional older participant was removed due to limited cortical activity suggesting that he or she fell asleep within moments of beginning the study task. The remaining sample in the present study included 153 participants (123 older adults and 30 younger adults).

3.2   ASSESSMENTS

Participants first completed an MRI session including a task to localize faces and a separate task involving memory for faces. Recognition of the to-be-remembered items presented in the scanner was conducted immediately following the MRI session. Images were collected on a 3T Siemens Allegra scanner. Stimuli were presented via a MRI-safe fiber-optic goggle system (Resonance Technologies, Inc).

3.2.1   Structural magnetic resonance imaging

All participants completed structural MRI scanning. High resolution (1.3 3 x 1.3 3 x 1.3 mm) T1-weighted brain images were acquired using a 3D MPRAGE (Magnetization Prepared Rapid Gradient Echo Imaging) protocol with 144 contiguous slices collected in an ascending fashion (see Erickson et al., 2009 for further scanning details). For MR images, parameters were: echo time (TE) 3.87 ms, repetition time (TR) 1000 ms, field of view (FOV) 256 mm, an acquisition matrix of 192 x 192 mm, and a flip angle of 8 degrees.

3.2.2   Echo Planar Images (EPI)

A face localizer sequence was run prior to running the Facial Encoding Task. Each functional set of images used a fast echo-planar imaging (EPI) sequence with blood oxygenation level dependent (BOLD) contrast. For each set of localizer images, T2*-weighted images (TR=1.5 s; TE= 24 ms; flip angle = 90 degrees) were collected. Twenty-eight slices (4mm thickness; 3.4 mm in plane resolution; 0 gap) were collected in a sequential ascending fashion parallel to the anterior and posterior commissures.

Cortical activity in these sequences isolated visual cortex activity sensitive to facial and word encoding. Images used in the localizer and face-word encoding task were normed for attractiveness, familiarity, emotional expression, and luminescence. All images in the face encoding task appeared in color and were images of attractive, Caucasian, young women.

3.2.2.1 Face-House Localizer

Faces and houses (places) were presented in alternating blocks to localize stimuli-specific regional activity in the cortex. Participants were instructed to "*Look at the Images on the Screen*". A total of 180 T2*-weighted images were collected. Over 270 s, 3 separate 20-s blocks of faces and buildings were alternated with three 20-s blocks of scrambled images. Scrambled images were created from randomizing the pixels in the face and house images. The fixed-order of blocks was FACE then PLACE, repeated 4 times (See Figure 1). Each block contained 20 unique black-and-white images controlled for luminance and dimension. A total of 80 unfamiliar, female faces were presented. Within each block, images appeared for 1-s without inter-trial fixations. This is treated as data for *passive encoding of faces, or the lower attentional demand condition.*

Figure 1. View Faces Task Design
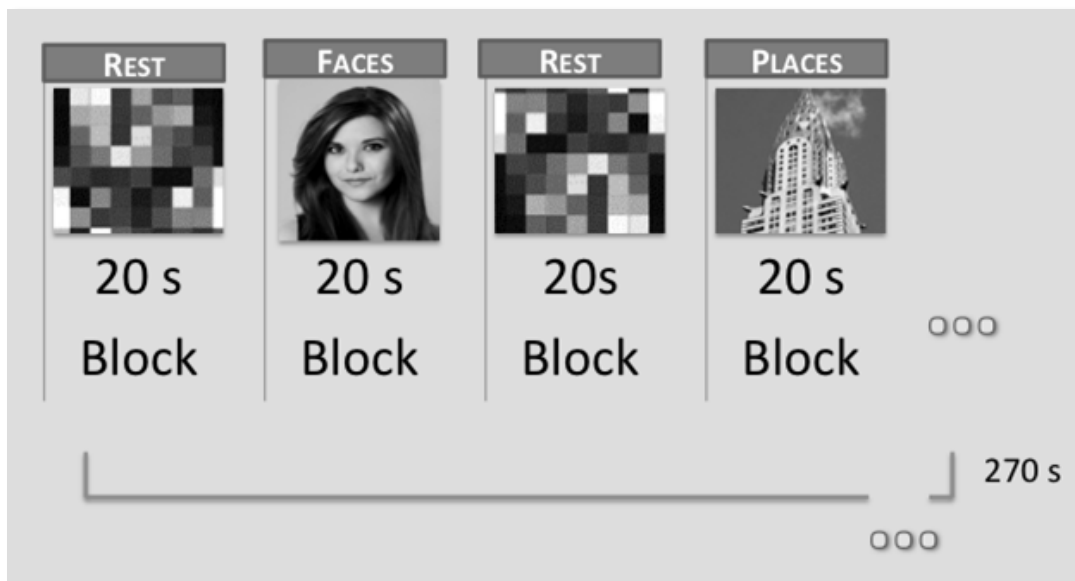
Above is the *view faces* encoding task design, this task is also known as the localizer. Alternating 20-s blocks of Faces and Places occurred after 20-s rest periods for a total of 270 s. A total of 80 unfamiliar faces were viewed in this task. Average neural activity while viewing faces in this task was used to determine the sample-specific fusiform face area.

3.2.2.2 Face-encoding Task: Remember Faces

Intentional encoding was tested using alternating blocks of faces and words. Participants were instructed to *"Remember these Faces and Words"*. 180 T2*-weighted images were collected for this sequence. After an initial crosshair was presented on the screen for 9 s, 4 sets of alternating blocks of faces and words appeared in a fixed order (i.e., starting with a block of encoding words). The faces were matched for attractiveness and luminescence, but unlike the localizer, these faces were presented in color. Within each of the 8, 36-s blocks, each stimulus appeared on the screen for 3 s, with a 1.5 s interstimulus interval. Between blocks, a fixation crosshair was presented on the screen for 21 s (i.e, a total of 7 fixations appeared between blocks). After the last face block, a fixation crosshair appeared on the screen for 16 s. Total task duration was 7 m, 40-s (see Figure 2). Cortical activity from this task was considered the *intentional encoding* condition. For this analysis, activity associated with word-encoding and viewing the fixation crosshair is conceptualized as comparison conditions to isolate activity specific to encoding of faces.

Figure 2. Remember Faces Task Design

Above is the intentional encoding or remember faces task design. The top panel (a) shows the block design of the entire task. Alternating blocks of words and faces were presented on the screen for 36 s. following block of fixation crosshiar. The lower panel (b) shows the design within each 26-s face-encoding block. A total of 48 unfamiliar faces were viewed in this task.

3.2.2.3 Behavioral Measures of Task Performance

Recognition memory of the faces was tested using a computerized recognition task approximately 10 minutes after the end of the encoding task, and immediately after exiting the MRI machine. Hence, MRI data is only captured for encoding and not recognition results. Of 64 faces presented used in the recognition paradigm, 32 of them were previously seen faces (i.e., possible hits) and the other 32 were faces not seen during encoding (i.e., possible false alarms). For each face presented during the recognition test, participants were asked whether or not they had previously seen the image. Hits and misses were calculated for face recognition. Hit rate was used to reflect overall accuracy in the present study and selected because its distribution was most normally distributed and had similar variance for younger and older adults. Response time for recognition was also recorded for faces and words. The other outcome variable used in this study was d', or the measure of accuracy accounting for response bias. The d' distribution was positively skewed enough among older adults to limit its use as the sole outcome measure.

3.3   PROCEDURE

Participants were recruited through physician referrals and local advertisement. Potential participants were screened over the phone for inclusion and exclusion criteria. If participants passed the phone screen, they were invited to a group orientation to receive more information regarding the study. At orientation, participants completed a battery of questionnaires to return at the following visit. Demographic information collected at this orientation session was used in the present study. After this orientation session, participants completed four baseline sessions. Sessions 1 to 3 included a blood draw, neuropsychological testing, a mock MRI session, and a cardiovascular fitness assessment. No data from these sessions is included in the present study. Session 4 included the MRI scan for which the data and analysis were used in the present study. This session lasted approximately 2 hours and included the collection of structural and functional MRI data for each subject.

3.4   STATISTICAL ANALYSES

3.4.1   Performance Calculations

The percentage of total hits and false alarms were calculated. Hits reflect correct identification of previously viewed faces. False alarms occurred when participants reported having seen a face they had not previously seen. The difference between false alarms and hit rates was calculated to reflect participant's discrimination index (d') that displays accuracy accounting for response bias. Facial recognition hit rate was used for the dependent measure in the present study. D-prime was calculated by converting hit and misses for each subject to z-scores and subtracting the difference, in this way d' reflects and index of accuracy accounting for a responding bias (Best, Morrongiello, & Robson, 1981) and has been cited as an accurate measure of working memory performance (Haatveit et al., 2010). For all discrimination analyses, one outlier with a d' score beyond three standard deviations from the mean was removed and the four participants with missing scores on hit or false alarm rates were excluded from analyses.

3.4.2   Neuroimaging Data

MR and fMRI data was processed using tools in the FMRIB Software Library version 5.98 (Image Analysis Group, FMRIB, Oxford, UK; http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/; (S. M. Smith et al., 2004). Structural and functional processing occurred in two separate streams. Structural images were processed to 1) remove non-brain matter that would influence statistical analysis and registration, and 2) normalize each participant's brain into the common Montreal Neurological Institute (MNI) template. All raw blood oxygen level dependent (BOLD) functional images were processed to 1) linearly correct for motion using a rigid body transformation and an intra-modal correction tool based on optimization and registration techniques, 2) temporally filter to remove frequencies outside the range of the time series and signal frequency in question, 3) spatially smooth functional maps with a 6.0 mm isotropic Gaussian smoothing kernel to improve signal to noise ratio, 4) restrict the false positive rates by setting the cluster-wise threshold at $p = .05$ and the voxel-wise threshold at $z = 2.3$. All functional data were modeled with a single gamma response due to the block design of the tasks. The full set of processing and acquisition parameters applied to each participant's structural and functional data appear in Appendix A. Analyses were first conducted independently of age group, and then secondary analyses stratified by age group.

Images presented for display purposes are presented in the standard neurological convention with the right side of the brain appearing on the right side images, unless otherwise stated.

### 3.4.2.1 Region of Interest Development

The fusiform face area (FFA) has been reliably found to be active when processing faces and is the main region investigated in the present study. We were also interested in the connection between the FFA and the prefrontal cortex, specifically the right dorsolateral prefrontal cortex (RDLPFC) and right ventrolateral prefrontal cortex (RVLPFC). To reduce potential Type I error, a number of steps were taken when defining these regions. 1) First, the regions of interest were selected for exploration *a priori*. To define the FFA, the Harvard subcortical structural atlas was used to highlight the occipital and temporal fusiform cortex, regions known to support processing of faces. The benefit of a priori selection of this nature reduces that requirement of correction of multiple tests as would be necessary if exploring a large number of regions or large number of voxels in the brain (Poldrack, 2007). 2) Second, the functional localizer task was used to identify the face-selective fusiform face area similar to Bollinger et al. (2011). In this analysis, the group statistical maps were used to define the FFA from the contrast of viewing faces compared to viewing a fixation crosshair. This type of approach is prevalent in FMRI studies of visual processing. Though common, one drawback is the possibility of incorrectly ascribing functions to region based solely on fMRI data (Podrack, 2007). Thus, to overcome this limitation, the functionally defined maps were overlaid with structural maps. 3) The overlap between the anatomical area derived from the Harvard Atlas and the functional localization of face processing (thresholded at $z =$ 2.3) were combined into a specific region-of-interest.

Finally, once this region was defined, average signal change from baseline during the presentation of faces was extracted for each participant. The coordinates for the peak activity for each subject in this space were averaged to create the FFA region of interest. A 10 mm sphere surrounding this anatomically and functionally derived region was created and used for all subsequent analyses of the FFA. A similar approach was used to define the RDLPFC and RVLPFC. The defined regions and coordinates appear in Table 1 and pictures of these regions can be found in Figure 3. The RDLPFC was chosen as a control region for comparison purposes. The defined regions and coordinates appear in Table 1 and pictures of these regions can be found in Figure 3.

Table 1. Coordinates for Study Specific Regions of Interest

Name	MNI Coordinates			Diameter (in mm)	No. Voxels
FFA (fusiform face area)	46	-72	10	10	33
RDLPFC (right dorsolateral prefrontal cortex)	40	39	21	10	33
RVLPFC (right ventrolateral prefrontal cortex)	46	24	15	10	33

Figure 3. Regions of interest (ROIs) chosen from a conjunction of structural and functional searches.
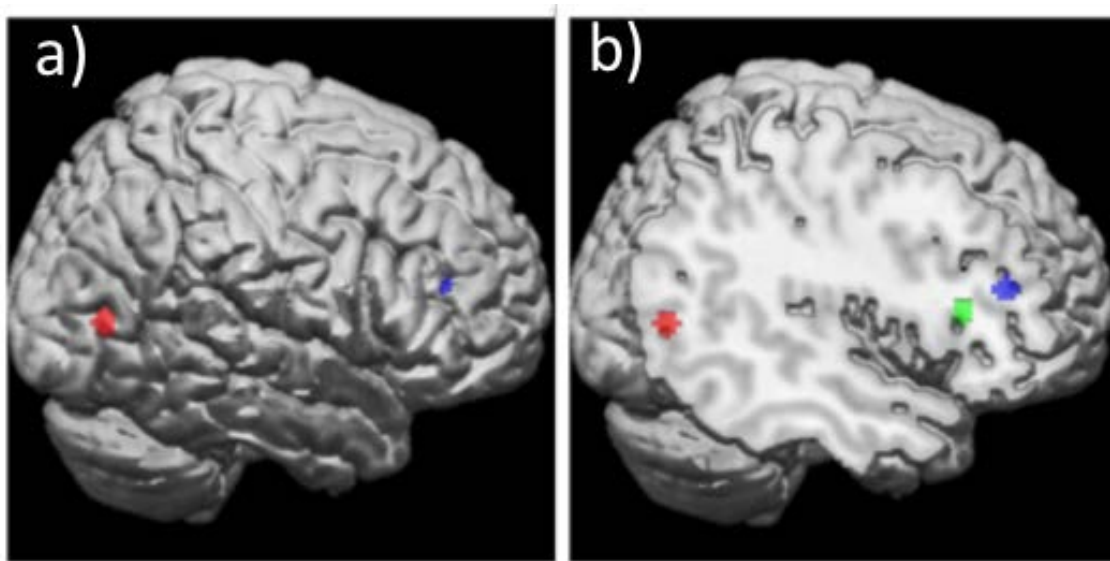
Panel a shows the FFA (red) and RDLPFC (blue) on a whole brain. Panel b shows the FFA (red), RDLPFC (blue) and RVLPFC (green) with tissue from the right dorsal hemisphere removed for better visualization of the RVLPFC.

3.4.2.2 Whole Brain Analysis

The primary aim of this study was to examine age-related differences in top-down influences on sensory activity. To characterize the data set, whole-brain analyses were conducted to compare older and younger adults' facial encoding activity. Task-dependent changes in BOLD signal were modeled with independent task regressors modeling the time course for each condition. Separate mixed effects General

Linear Models (GLMs) were used to separate neural activity within tasks blocks for each participant. Two task-blocks were modeled relative to the fixation crosshair baseline in both the face localizer task (*view faces*) and in the encoding task (*remember faces*). These statistical tests produce a z-statistic at each voxel representing the difference between neural activity for faces versus baseline. Since a z-statistic is presented at each voxel, this produces a statistical "map", commonly referred to as a z-statistic map. Activity in the first set of z-statistic maps reflects cortical activity where the fixation is treated as baseline, thus neural activity present when viewing the fixation crosshair is subtracted from neural activity when viewing or remembering faces.

These statistical maps can be compared in a GLM approach to make contrasts. Differences between individual maps or even averages between maps can be calculated. For this study, differences between maps produced for separate blocks of neural activity were created. In the *view faces* task, maps were *contrasted* to examine the portion of cortical activity sensitive to facial processing above and beyond other visual processing. Thus, in a GLM approach, on a voxel-by-voxel basis, cortical activity was contrasted to show which voxels showed significantly greater activity when viewing faces compared to viewing houses. The resulting z-statistic map reflects cortical activity that is unique to facial processing above and beyond shared visual processing with houses. The same procedure was adopted to create a contrast of facial activity greater than word activity in the *remember faces* task.

In the next stage of analyses, these individual results were used to explore group differences. This is commonly referred to as group analysis. In this process, individual statistical maps were aggregated to collect group averages reflecting the difference in neural activity for faces greater than baseline for older and younger adults, separately. Each individual z-statistic map was registered to a common space (e.g., the MNI T152 template). Statistical tests produced age group-level maps for 1) face >baseline (fixation crosshair) and 2) face > other visual stimuli (houses or words, respectively for view faces and remember faces tasks).

All whole brain analyses produced z-statistic images that were conservatively thresholded at $z = 2.3$ with a clusterwise threshold of $p = .05$. Average motion was covaried for each subject. All maps are presented in neurological convention (right to right and left to left).

3.4.2.3 Fusiform Face Area Analysis

First, percent signal change was extracted from the FFA region in the localizer and intentional encoding task on a subject-by-subject basis. Then subtracting FFA activity when participants *view faces* from

activity when participants are instructed to *remember the faces* created an enhancement index. In this way, the enhancement index (Enhance) shows how much individuals demonstrated increased activity when viewing faces during the localizer to intentional efforts to encode during the face-encoding task. Then a linear regression analysis tested whether greater FFA enhancement would be related to better facial recognition performance. If percent signal change from baseline in the FFA predicts accuracy, this suggests top-down modulation explains variation in task performance. If the age-differences in enhancement were significant, this would suggest that sensory signal in the FFA may differentially influence accuracy. This would suggest that top-down enhancement effects explain accuracy better for one age group than another. Testing the following model provides the data to assess Hypothesis 1 that greater sensory enhancement in FFA impacts behavioral performance

$$Performance = AgeGroup + EnhanceFFA + AgeGroup * EnhanceFFA$$

We predicted that younger adults would show more FFA Enhancement than older adults. To test this, a t-test was calculated comparing FFA Enhancement by Age Group. This formally tests Hypothesis 3, that younger adults show greater sensory enhancement than their older peers.

3.4.2.4 Functional Connectivity Analysis

Functional connectivity network (FCN) maps were created for each participant as described in Zanto et al., 2011. FCN maps were created by constructing a GLM design matrix in FEAT, part of the FMRIB Software Library. Only task activity during intentional encoding was used for functional connectivity analysis. The first regressor task design modeled faces over baseline and words, in this manner the variance from task-related activity is removed from the produced connectivity maps. This controls for the onset and offsite of faces according to the task design. The second regressor was the time series that was extracted from the FFA for each subject. This enters the main variable interest (after accounting for task design). This main variable of interest reflects the signal change in the FFA from baseline and produces one measurement per volume of time for the entire time series. These regressors are used to predict voxel-by-voxel Beta correlations with that FFA time series throughout the entire brain. Because the Betas exist at every voxel, the statistical map of cortical connectivity that is created is referred to as Beta map. Modeled in this manner, the FCN maps reflect the correlations in the entire brain with the time series in the FFA for each subject. Beta values averaged from within the FFA were correlated across trials (i.e., the task time course) with every brain voxel. This created a condition-specific correlation map of brain activity correlated with the FFA time course for each subject. This was

done at an individual level on a subject-by-subject basis and then carried up into age-related group analysis similar to method describe above for univariate group analysis.

Then, in an ROI based approached, functional correlations were extracted. Functional correlations were then calculated for older and younger adults in the view faces task and in the remember faces task. For each subject functional correlations between the right FFA and RVLPFC were extracted by applying a binary map of the RVLPC (defined above) to the Beta map for each subject in each task. Beta values within this RVLPFC region were averaged to reflect average signal connectivity in the RVLPFC with the FFA time series. These functional correlations were then used to assess correlations with task performance (similar to Bollinger et al., 2011). Then functional correlations were compared from the view faces task and the remember faces task.

If functional correlations between RVLPFC and FFA and performance significantly and positively relate to one another across ages, this would suggest that connectivity between these regions impacts performance. This analysis directly tests Hypothesis 2 *that higher correlated activity between FFA and RVLPFC will relate with better facial recognition.*We would also expect correlations between these brain regions and performance to be stronger during the remember faces task than in the view faces task because of the top-down modulatory increase of network of memory encoding to which these regions belong. This would suggest that activity in the RVLPFC covaries with FFA activity, such that increases in functional connectivity occur when viewing faces and not when viewing words or a fixation crosshair. To explore age-related differences in functional correlations, younger and older adult's group-average Beta were compared using the Fischer's *r*-to-*z* transformation method. A similar method was applied to comparing correlations between tasks. Functional correlations reflect associations and are not causal.

This essential functional connectivity has been selected because it allows the comparison between tasks. If our tasks, and hence levels of attention, were combined into a single unit, this would afforded a psychophysiological interaction (PPI) approach. The method applied in the current study models other work of a similar nature where expectation-driven changes in functional connectivity were explored (Bollinger et al., 2010). Using this approach, they found connections between FFA and 1) Right IFJ, and Right MFG, Right IFG, Right IPS, and the cingulate cortex all related with recognition performance. They also found signal changes in FFA between task conditions. However, they did not explore functional connectivity differences between the conditions. In a similar vein, the present study links the functional correlations between FFA and RVLPFC and examines that relationship in both the lower level of task demand and higher level of task demand. Greater functional connectivity in the remember faces task compared with the view faces task would suggest task-related top-down modulation of the FFA. If both task conditions, view faces and remember faces were present in the same task, a PPI

approach may have better informed investigations of top-down modulation. However, PPI analysis, especially in this study, faces many challenges. In the present study, the task design does not include all levels of attention. All psychological and physiological confounds should be entered as covariates in an attempt to bolster the main variable of interest, this greatly affects power. PPI also requires approximately a 2% neural change from baseline to detect an effect. Given the power requirements of PPI, it is less likely to detect change within each of the separate task in the present study than through use of an essential functional connectivity approach.

3.4.2.5 Power Analysis

Power analyses indicate sufficient power to detect results in the current study. Previous work by Gazzaley and colleagues (2005b) found evidence for top-down modulation of the fusiform face area. Estimates from this data provide an illustration of how well the current dataset would be powered to determine effects (i.e., estimates are calculated from figures). Gazzaley examined the ability of older and younger adults to suppress irrelevant information during encoding and found that older adults (change in $B = 0.55$; $S= 2.06$) failed to suppress activity in the FFA compared to younger adults (change in $B =2.35$, $S = 1.20$), arguing for top-down modulation of sensory activity. This results in a moderate-to-large effect size of the effect of top-down modulation on sensory processing, Cohen's $d = 1.07$, effect size= .47. Given an effect size of .47, approximately 35 younger subjects and 16 older subjects, the current study would be powered at 1.00 using an alpha rate of .05 to detect age-related changes in the top-down modulation of sensory activity, that younger adults would show greater enhancement than would older adults.

4.0   RESULTS

4.1   DESCRIPTIVES

4.1.1   Participant Characteristics and Performance

Characteristics of the 153 participants are summarized in Table 2. The variance of age across the whole sample is rather large and the data are bimodal. This violation of normality is large enough to warrant a categorical rather than continuous treatment of age in the present study. Consistent with previous work, younger adults' unfamiliar facial recognition was similar to that of older adults, with both groups on average achieving approximately a 60% hit rate, $t(151) = 0.92$, $p = .40$[3]. Older adults tended to respond that they had previously seen faces when they had not, explained by a 35% false alarm rate compared to the 20% false alarm rate of their younger peers, $t(151) = -5.26$, $p = .000$. This bias negatively influenced older adults discrimination index, such that older adults showed a strong bias toward responding that they had seen *all* faces before, whether they were indeed presented or not, $t(151) = 4.31$, $p = .000$. On average, younger adults demonstrated a higher discrimination index ($M = 1.24$, $S = 0.13$) than did older adults ($M = 0.71$, $S = 0.71$), $t(146) = 4.31$, $p = .000$. The present study was concerned with components of neural function linked with performance. Both accuracy and discrimination indices were explored as performance measures.

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[3] For all *t*-tests, when Levene's test for equality of variances is significant (meaning variances difference between groups) then unequal variance adjustment are incorporated into *t*-test calculations.

Table 2. Participant characteristics

Characteristic	Whole Sample N = 153 M (S)	Older Adults n= 123 M (S)	Younger Adults n = 30 M (S)
Age (years)	58.14 (17.73)	66.43 (5.72)	24.13 (4.62)
Sex (% female)	72	70	83
Hit Rate	.58 (.17)	.58 (.17)	.61 (.19)
False Alarm Rate	.32 (.16)	.35 (.15)	.20 (.11)
d'(discrimination index)	.74 (.75)	.62 (.71)	1.24 (.70)

4.1.2 Univariate fMRI Activity

Consistent with other research, older adults showed robust activity in the occipital regions and as well as other areas implicated in memory processing. Examining the most robust localizer derived contrast possible, cortical activity that was greater when participants viewed faces compared to a fixation crosshair. This is the localizer "Face > Baseline" contrast. Here younger and older adults passively viewed faces and places with no goal-directed efforts to remember these images. Younger and older adults activated similar cortical regions when told to *view faces*. In this manner, the data show which cortical regions become active more than what is active during viewing a fixation crosshair. Thus, some activity common to both viewing the fixation crosshair and viewing faces has been removed. Data show that in the passive encoding condition, both age groups rely primarily on primary visual and extrastriate cortices when viewing faces. Other regions reliably active include the left and right dorsal prefrontal cortices, the middle frontal gyrus, and medial temporal areas, including the hippocampus. Generally speaking, activity is bilateral for both age groups. The right fusiform face area used as the region of interest in the current study is shown circled in white in Figure 4. This area was created using a combination of this functional contrast with the cortical atlases to restrict the search space within the brain (refer to Methods). Functional activity in this contrast was used to create the ROI, but is not used in further analysis.

Figure 4. Younger and Older Adults' Cortical Activity for the Faces Greater than Baseline Contrast in the Passive, View Faces Task.
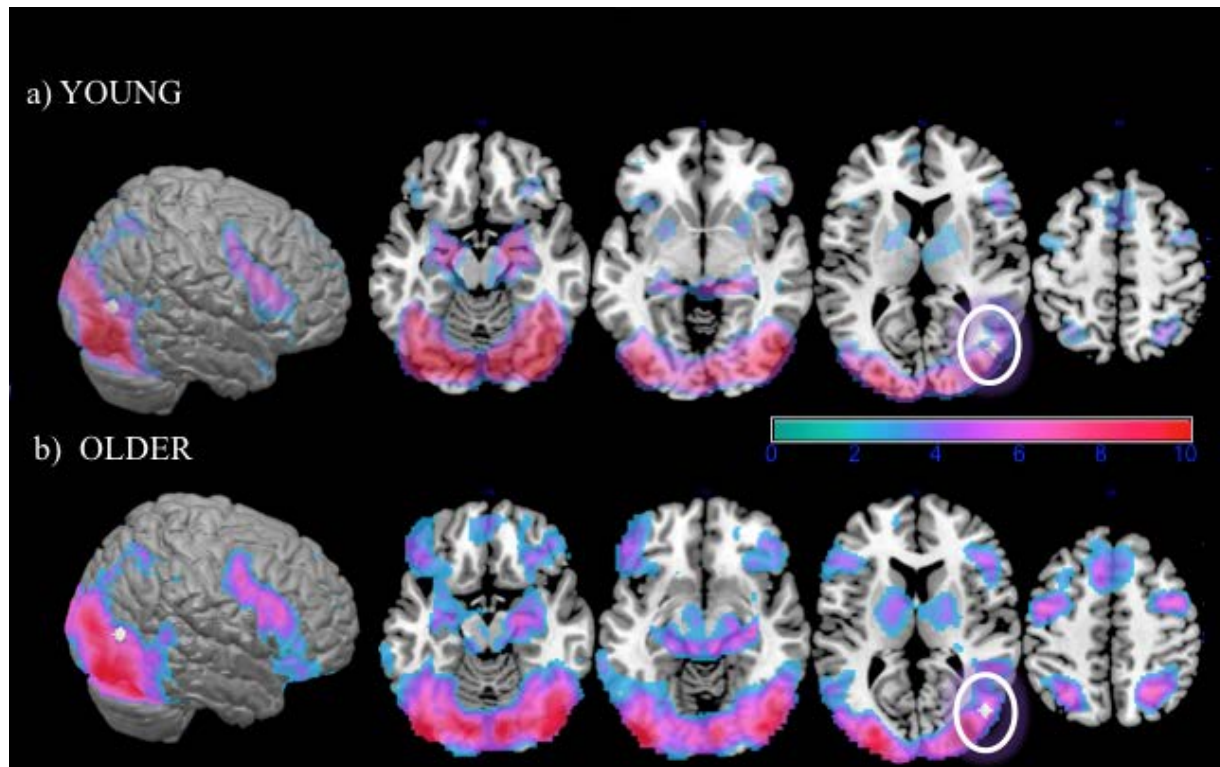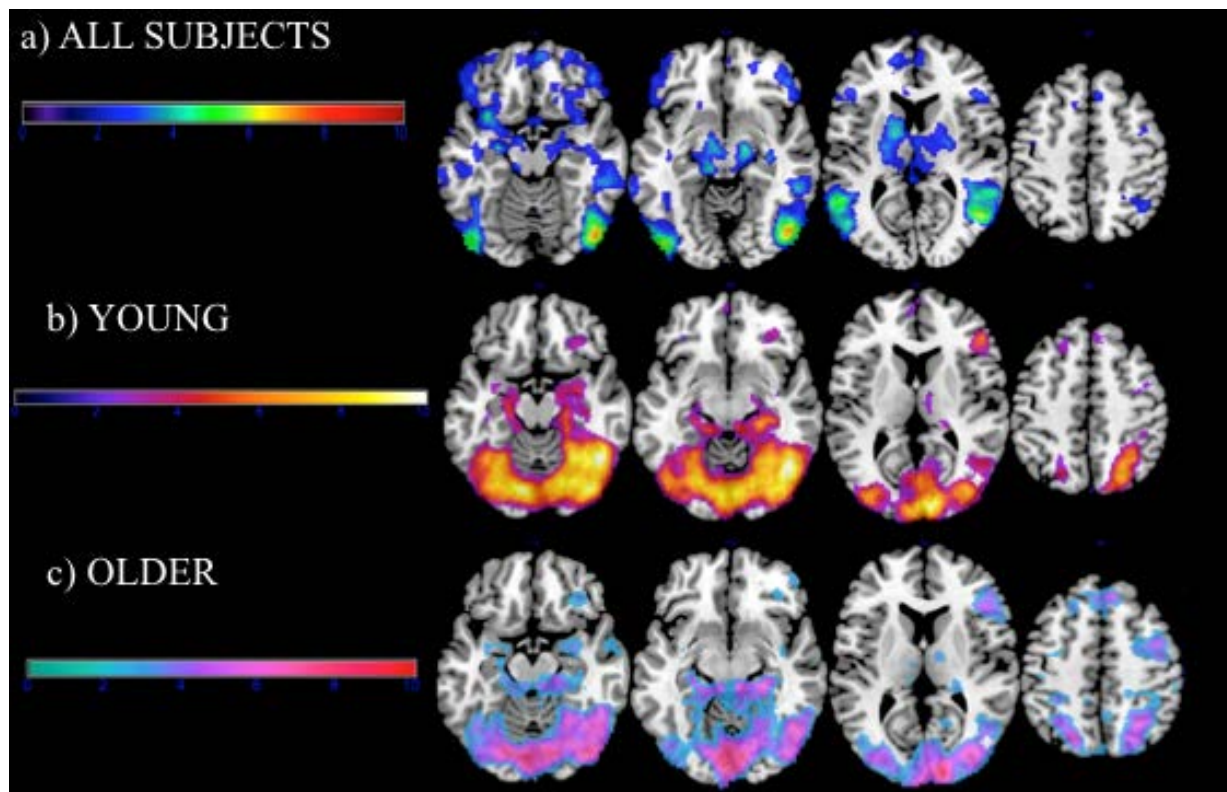

The figure above shows cortical activity for the faces greater than baseline contrast. Images are presented in neurological convention. These functional activity maps were calculated using a *z*-score threshold of $z = 2.3$ and a clusterwise threshold of $p = .05$. Panel a shows cortical activity for younger adults and panel b shows cortical activity for older adults. In each panel a key for interpreting the color range for the z-statistic maps appears.

In the view faces task, the contrast of interest examines cortical activity resulting from activity resulting from viewing faces being greater than neural activity when viewing places. In the remember faces task, the contrast examined neural activity where viewing faces was larger in magnitude than the neural activity from view words. A brief description of the resulting whole-brain z-stats maps provides context for the creation of a neural enhancement index derived from the difference between these contrasts. The neural enhancement index will be presented in the next section.

When told to view faces, a similar visual processing network is active for older and younger adults. However, younger adults show activity in the middle frontal gyrus that older adults do not exhibit. The localization of activity in right prefrontal areas differs by age as well. In Figure 5 data show that younger and older adults showed some similar and some dissociable patterns in face-selective visual activity.

Figure 5. Younger and Older Adults' Cortical Activity for the Faces Greater than Places Contrast in the Passive, View Faces Task

The figure shows cortical activity for the faces greater than places contrast in the view faces task. Images are presented in neurological convention. These functional activity maps were calculated using a z-score threshold of $z = 2.3$ and a clusterwise threshold of $p = .05$. Panel a shows cortical activity for younger adults and panel b shows cortical activity for older adults. In each panel a key for interpreting the color range for the z-statistic maps appears. The FFA ROI appears in white.

When told to remember faces, a similar visual encoding network is active for older and younger adults. In this contrast, activity is restricted to regions where facial encoding activity is greater than processing of words in the remember words block in the same task. Data show that left and right lateral occipital cortices reliably show activity. Younger adults show a network with fewer regions involved in encoding, overall. However, in shared regions of encoding activity, the magnitude of neural activity is similar between groups. Thus, intentional face-selective activity during facial encoding involves a network with similar neural substrates for older and younger adults. In Figure 6 data show that younger and older adults showed some different patterns of face-selective visual activity during the *remember* faces task.

Figure 6. Face-selective neural activity overall and by age during the remember task
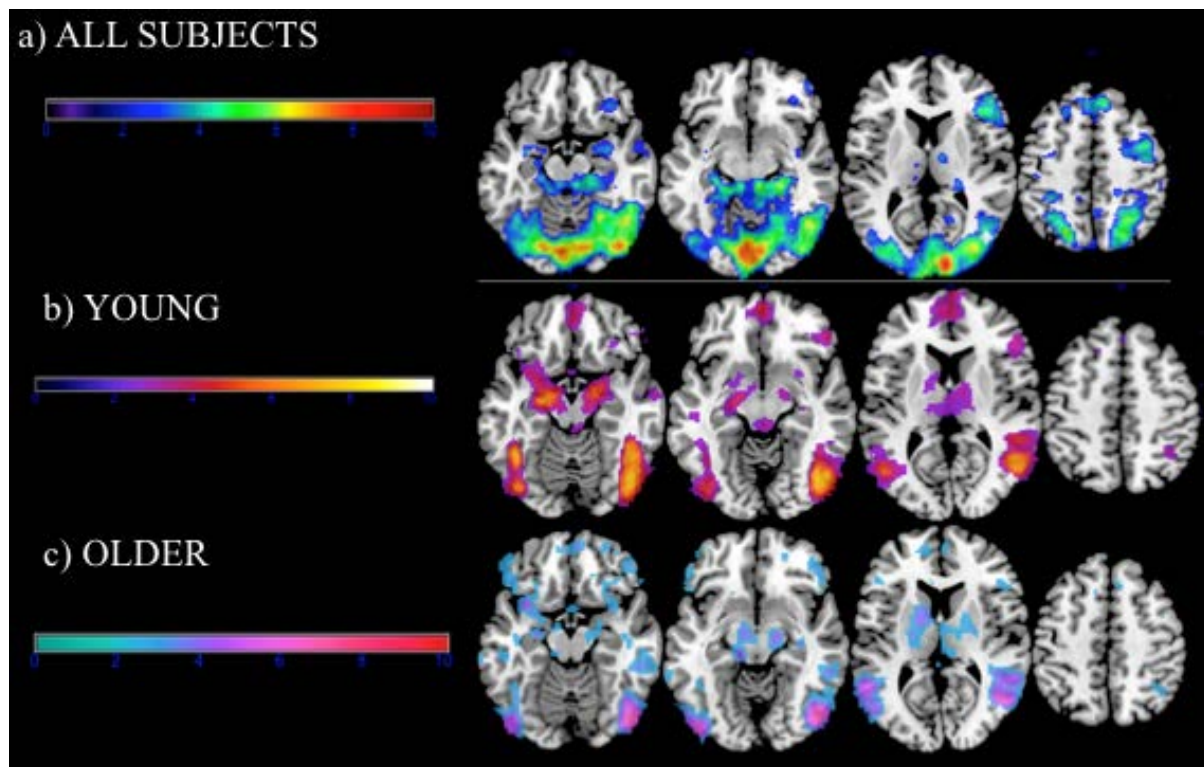
The figure shows cortical activity for the faces greater than words contrast in the remember faces task. Images are presented in neurological convention. These functional activity maps were calculated using a z-score threshold of $z = 2.3$ and a clusterwise threshold of $p = .05$. Panel a shows cortical activity for younger adults and panel b shows cortical activity for older adults. In each panel a key for interpreting the color range for the z-statistic maps appears. The FFA ROI appears in white.

The next sections explore how activity in the fusiform face area manifests through a variety of methods. In that section, activity will be explored by age and in relation to task performance. Though

patterns of cortical activity appear similar, they may still contribute to performance in unique ways by age. The next two sections test this idea. The first section examines the magnitude of activity in the fusiform face area and the following section explores functional connectivity in the brain with the timeseries activity in the fusiform face area.

4.1.3   Fusiform Face Area Cortical Activity

Next, I examined whether FFA neural activity was enhanced during the remember faces task relative to the view faces task (for the face-selective face>words and face>place contrasts). The view faces task used in this experiment provide the perceptual, bottom-up baseline from which activity in the remember faces task could be compared. In the fusiform face area, most of the younger and older adults showed greater face-selective neural activity when instructed to *remember* faces than when told to *view* faces. The present data explored the faces greater than other visual stimuli contrast. When subjects were told to view faces, the contrast explored neural activity for faces after subtracting neural activity for places, leaving the neural activity specific to facial processing not shared with other complex imagery such as houses. When told to remember faces (i.e., the encoding task), the contrast explored neural activity for faces after subtracting neural activity for words. Comparing activity for *face-specific contrasts*, data showed that 60% of the younger adults (18 out of 30) show greater percent signal change from baseline in the FFA when trying to remember faces than when passively viewing faces. Similarly 62% of older adults showed the same pattern. This shows that in the fusiform face area, roughly 60% of the participants showed *face-selective visual cortical enhancement* in the FFA during intentional encoding, seen in Figure 7. In the general facial activity contrasts (faces greater than fixation baseline) less enhancement was observed when subtracting cortical activity in the *view faces* condition from the cortical activity in the *remember faces* condition. Without removing shared cortical activity due to visual processing of houses and words, only 37% of younger participants and 34% of older participants showed greater activity in the *remember faces* task than in the *view faces* task.

Figure 7. Percent signal change from baseline for viewing faces by encoding task and age
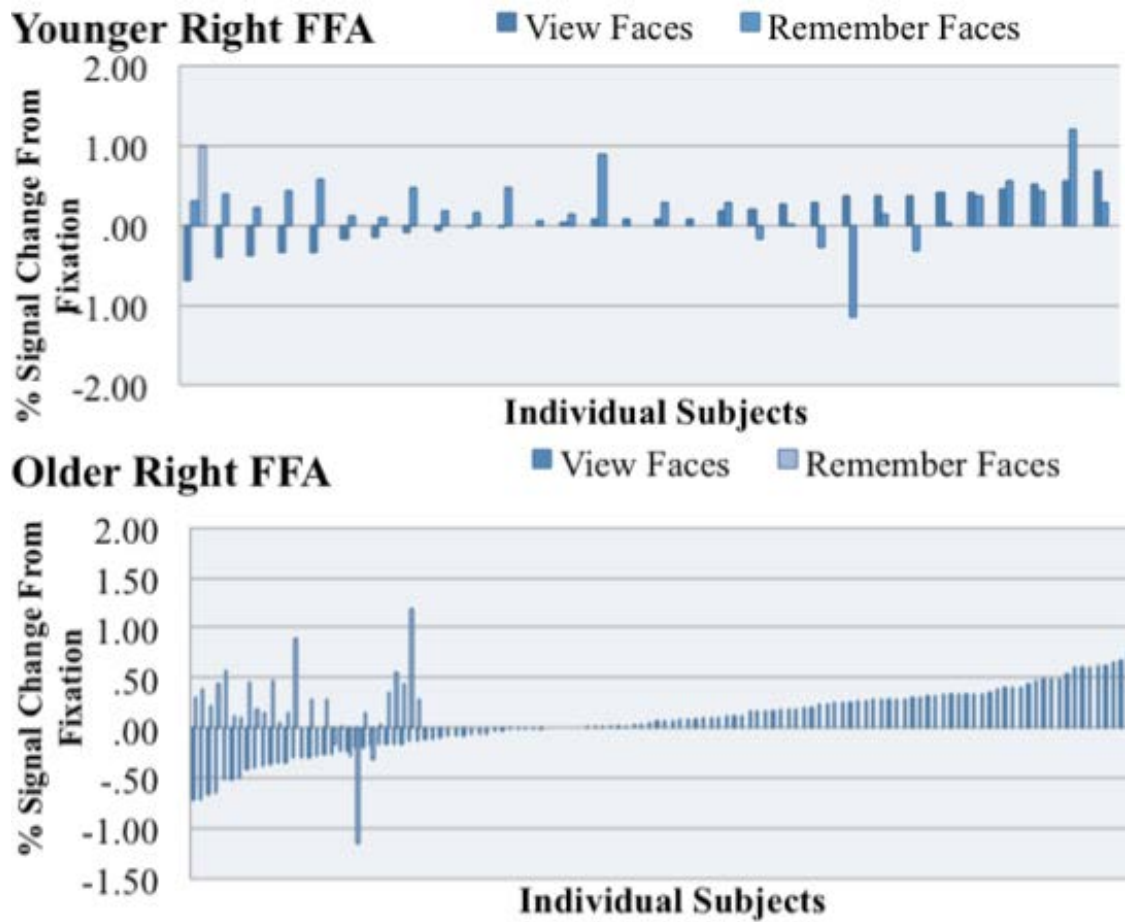
Individual subject signal change from baseline (fixation) data for *View* and *Remember* conditions by age group. The top panel shows that of the 30 younger adults, 60% showed more cortical activity in the FFA for the face selective contrasts (faces greater than houses or words). For the same contrast, 65% of the 132 older adults showed similar enhancement comparing view faces to remember faces.

## 4.2   INFERENTIALS

The following subsections provide data that directly test the study hypotheses. Each study hypotheses are laid out within each subsection. Following these analyses, exploratory questions are explored. A summary concludes the section.

4.2.1 Fusiform Face Area Regression Model

The enhancement portion of the top-down modulation is bolstered by providing evidence that greater FFA enhancement relates to better facial recognition performance (Hypothesis 1). To describe this relationship, scatterplots of FFA enhancement by age were produced (see Figure 8). First, the explorations for hit rate were explored followed by explorations of recognition discrimination.

Figure 8. Scatterplots showing the relationship between FFA enhancement and facial hit rate by age group
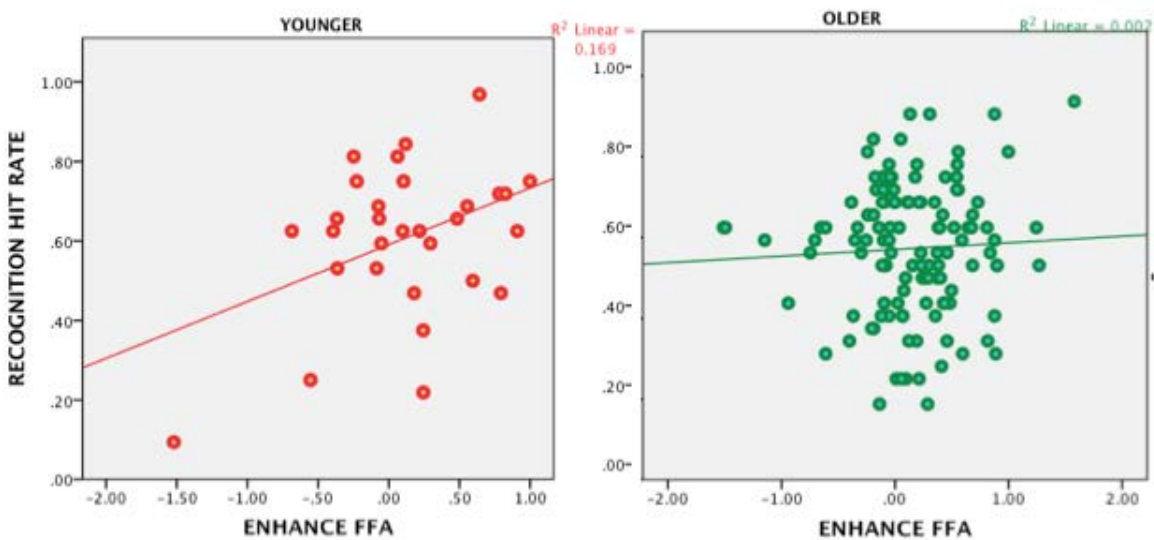
A linear regression explored the following proposed model using *face-selective* enhancement activity to predict facial recognition hit rate. Predictors were centered and dichotomized where appropriate before entering the model.

$$Accuracy = AgeGroup + EnhanceFFA + AgeGroup * EnhanceFFA$$

As expected, results showed that face-selective enhancement in the fusiform face area (EnhanceFFA) significantly predicted facial recognition hit rate across all subjects (see Table 3). Neither age group nor the interaction between FFA enhancement and age group significantly predicted facial recognition hit rate. However, the interaction term was marginally significant and the third model including the interaction terms was marginally significant. Betas and significance levels for the tested and final model appear in Table 3. In line with predictions, a one standard deviation increase from the mean of percent signal change for face-selective cortical enhancement in the FFA was marginally associated with a .43 standard deviation increase in facial recognition. These suggest a trend in line with

Hypothesis 1 and the role of enhancement on accuracy. However, it appears that the relationship between age and face-selective enhancement might vary as a function of age. This means that for younger adults, increasing age does not seem to impact enhancement, but as older adults age, their enhancement seems to decrease.

Table 3. FFA Enhancement and Facial Recognition (Hit Rate) Model Testing

Model	β (p)			
	Age Group	Enhancement FFA	Age Group * Enhancement FFA	Model F (p)
1	-.08 (.33)	--	--	0.98 (.33)
2	-.08 (.30)	.13 (.055)	--	1.85 (.16)
3	-.09 (.26)	.43 (.007)	-.33 (.05)	2.54 (.06)

Note. ps for Enhancement FFA are 1-tailed given the directional hypothesis for this term, all other ps are 2-tailed. Bootstrapping for coefficients was conducted based on 1000 age group stratified samples. The only coefficient to reach significance was Enhancement FFA in model 3 with the inclusion of the interaction term in the model.

These marginal age-related enhancement interactions suggest that stratifying regression models by age group may better elucidate the relationship between enhancement and facial recognition. Thus models were then tested separately for older and younger adults. For younger adults, a one standard deviation increase from the mean of percent signal change in the face-selective activity in the FFA was significantly associated with a .41 standard deviation unit increase in facial recognition and explains 17% of the variance in facial recognition, $F(1,29) = 5.71$, $p = .02$. For older adults, this relationship did not hold.

Thus, although older adults showed similar levels of enhancement in the FFA, this data suggest that only younger adults capitalize on the greater sensory signal in a manner than improves task performance. However, restricting older adults to only those that were able to perform the task with proficiency showed that these older adults were able to capitalize on FFA enhancement in a manner that contributes to performance. Among the 63 older adults with 58.1% accuracy or better (i.e., higher than the group mean), a one standard deviation increase from the mean of percent signal change in the face-selective activity in the FFA was significantly associated with a .31 standard deviation unit increase in facial recognition and explained 10% of the variance in facial recognition, $F(1,62) = 6.76$, $p = .01$. Among the 58 older adults with facial recognition performance below the group mean (i.e., < 58%), enhancement did not predict facial recognition accuracy ($F(1,52) = 0.88$, $p = .35$, Enhance FFA β = .13).

Next, face-selective enhancement in the fusiform face area was used to predict discrimination (d'). Consistent with the results for accuracy, enhancement in the FFA significantly relates with discrimination for younger but not older adults (see Figure 9). Unlike the results for hit rate, and in line with the hypothesis, the interaction of age group and enhancement in the fusiform face area did not approach significance, suggesting two separate main effects for age group and FFA enhancement (see Table 4). The final model using standardized Betas that explains the relationship between FFA enhancement and discrimination, accounting for age differences in discrimination follows.

$$Discrimination = -.38\ AgeGroup + .15\ EnhanceFFA$$

Figure 9. Scatterplots showing the relationship between FFA enhancement and facial discrimination rate by age group
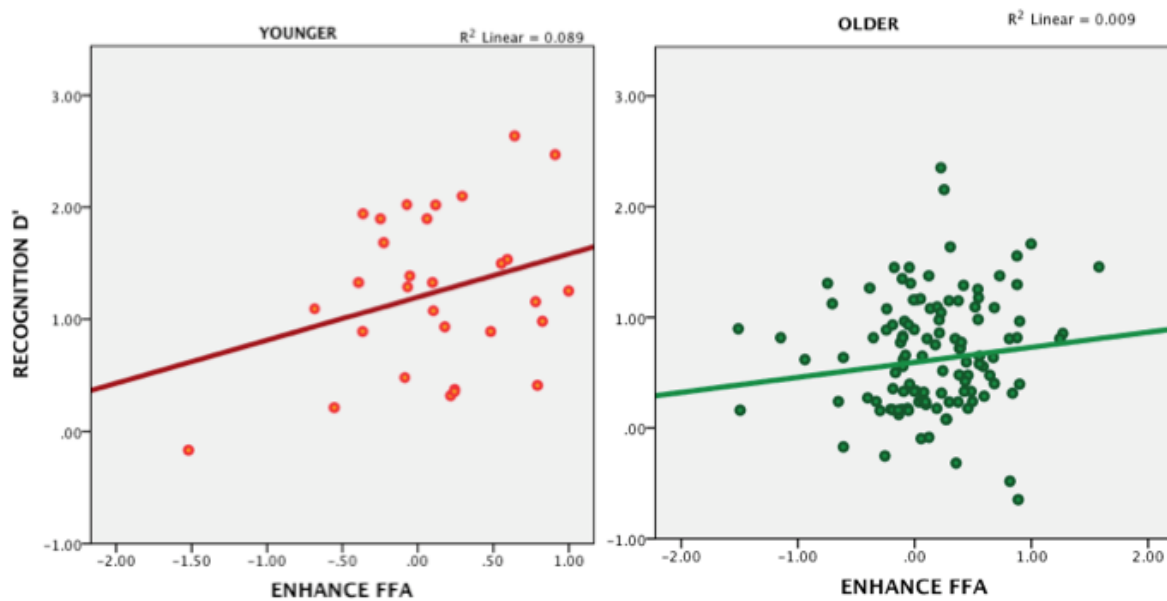
The figure displays the correlations (Pearson's r) between the enhancement index in the fusiform face area (FFA) and the discrimination index for younger adults (left) and older adults (right).

Examining neural enhancement in the FFA by discrimination produces a different picture than exploring recognition through hit rate. Here, evidence suggests an age-related difference in task performance. It seems enhancement in the FFA relates with facial discrimination for younger, but not older adults. However, the data do not show evidence of this dissociation of the relationship between FFA enhancement and facial discrimination by age. Overall, that FFA enhancement predicts facial

discrimination supports Hypothesis 1. Enhancement in the FFA predicts task performance (discrimination) and this effect was not moderated by age.
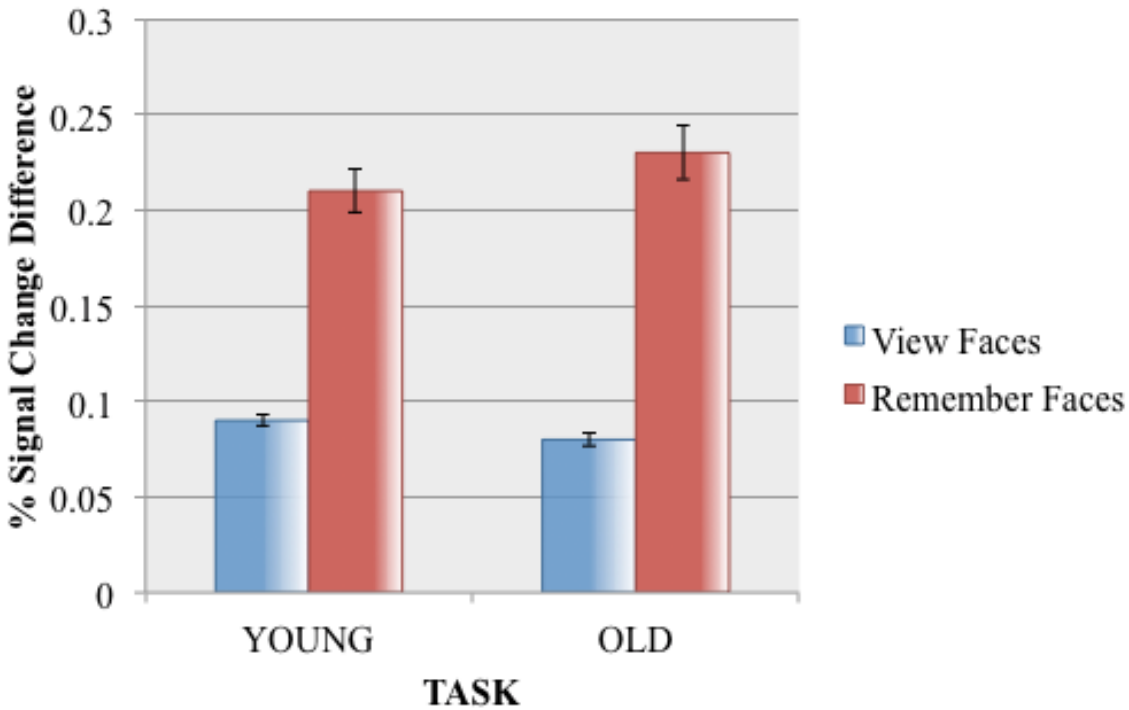
Table 4. FFA Enhancement and Facial Recognition (Discrimination) Model Testing

| Model | β (p) | | | |
	Age Group	Enhancement FFA	Age Group * Enhancement FFA	Model F (p)
1	-.38 (.000)	--	--	24.35 (.000)
2	-.39 (.000)	.15 (.03)	--	14.28 (.000)
3	-.39 (.000)	.15 (.03)	-.048 (.541)	9.81 (.000)

Note. Final retained model is boxed. *p*s for Enhancement FFA are 1-tailed given the directional hypothesis for this term, all other *p*s are 2-tailed. Bootstrapping for coefficients was conducted based on 1000 age group stratified samples. The final model shows that age and enhancement in the FFA impact discrimination.

To further illustrate this point and formally test Hypothesis 3, levels of enhancement in the FFA in the facial selective contrast were compared. In contrast with our predictions, younger adults demonstrated a similar FFA enhancement to their older peers. One average, younger adults showed a .12 (S = .09) percent signal change increase in FFA activity in the *remember faces* task compared to FFA activity in the *view faces* task. Older adults showed similar levels of FFA enhancement. Older adults showed a .15 (S = .05) percent signal change increase in FFA activity in the *remember faces* task compared to FFA activity in the *view faces* task. However, against predictions, younger adults did not enhance FFA activity more than their older peers, t (150) = -0.35, $p_{1\text{-tailed}}$ = .27 (see Figure 10). However, age group significantly predicted a difference in discrimination among older and younger adults. A mechanistic exploration of functional connectivity may better explain how enhancement and performance relate. The next section takes a different approach to exploring enhancement effects of top-down modulation and their age-related impact on facial recognition.

Figure 10. Changes in cortical activity between view and remember faces task by age group

It is likely that the relationship between facial recognition memory and enhancement is modulated by some factor that affects performance ability. Those adults able to remember faces during the encoding task may show different patterns of neural activity than those that do not remember faces as well. Thus, facial recognition performance was used to group participants into high performers (80% accuracy and above), average (51%-79% accuracy) performance, and low performers (<51 % accuracy) in a manner similar to Gazzaley and D'Esposito (2007). FFA face-specific enhancement did not differ for high and low performers (using accuracy) (see Figure 11). Then enhancement levels in the FFA were compared for older and younger adults in the hit rate performance subgroups. Comparison of the performance subgroup contrasts of enhancement show that high and low performing older and younger adults enhance cortical activity to a similar degree. This shows that sensory enhancement does not explain facial recognition hit rate.

Figure 11. Facial Recognition Hit Rate and Enhancement Index Contrasts

a) FACE RECOGNITION FOR INDIVIDUAL OLDER SUBJECTS

b) ENHANCEMENT INDEX PERFORMANCE CONTRAST

c) ENHANCEMENT INDEX SUBGROUP CONTRASTS BY AGE GROUP
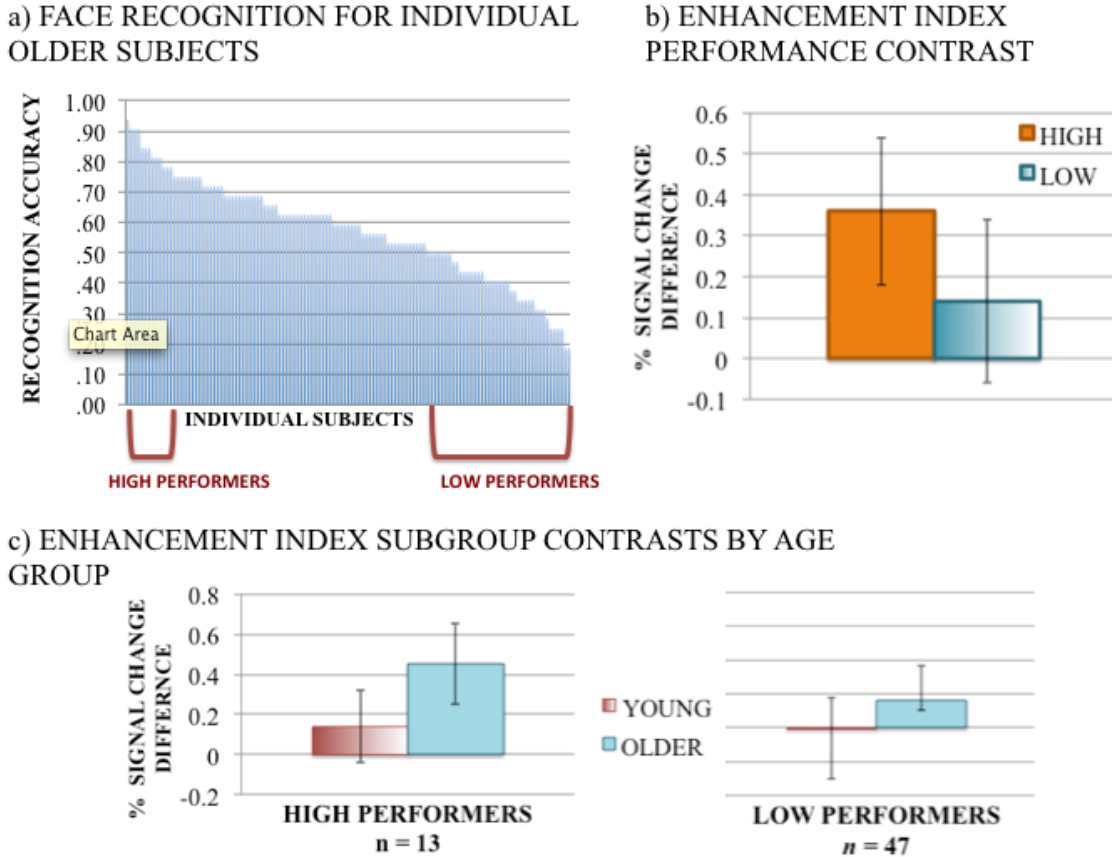
In panel a) older adults' individual facial recognition hit rate are displayed and grouped with brackets to indicate high and low performers. Many older adults performed poorly rather than well. Panel b) shows the FFA percent signal change from baseline compared for high and low performers. No significant difference emerged. Panel c) displays an enhancement index contrast for high performers and low performers by subgroup. No differences by hit rate subgroup were evident.

To examine whether or not sensory enhancement alone could explain facial discrimination, similar analyses to those above were conducted. As shown in Figure 12, no clearer explanation was elucidated by examining discrimination in lieu of accuracy. Subgroup calculations were not conducted as only 2 older adults had d' scores greater than 1.75.
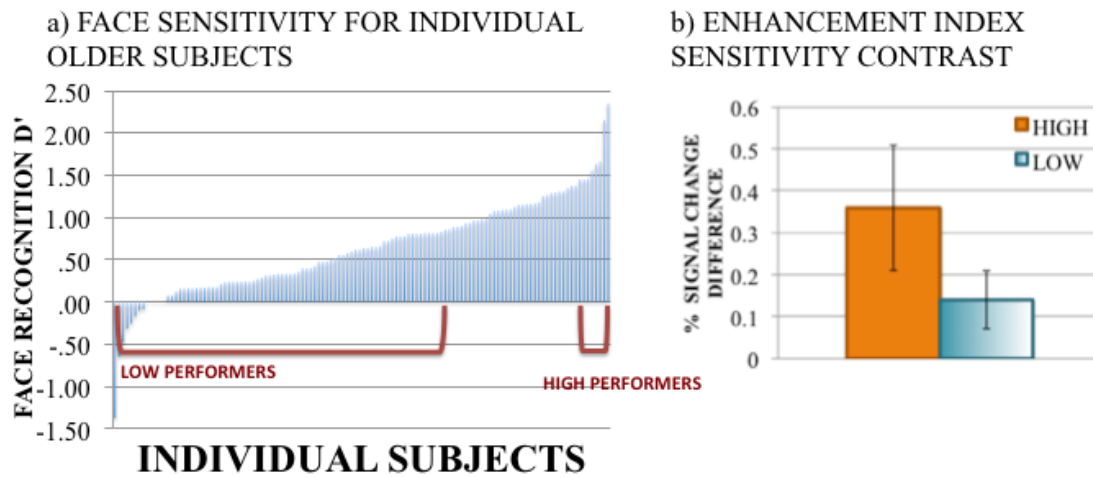
Figure 12. Facial Recognition Discrimination and Enhancement Index Contrasts


In panel a) older adults' individual facial discrimination rate are displayed and grouped with brackets to indicate high and low performers. Many older were unable to discriminate. Panel b) shows the FFA percent signal change from baseline compared for older high and older low discriminators, where no significant difference in enhancement was found between high and low performers.

4.2.2   Functional Connectivity Analyses

To evaluate interactions between regions in the encoding network, correlation analysis was performed on the face encoding period data for each participant using the right fusiform face area as a seed. The time series was correlated with activity in the rest of the brain. Qualitative analysis of the group connectivity maps for the two tasks (View Faces and Remember Faces) separately by age showed strikingly similar functional connections between the FFA time series data and the rest of the brain. Areas that showed high connectivity in the view faces and remember faces tasks included primary visual cortex through the extrastriate visual cortex, regions near the functionally defined FFA, hippocampus, and left and right prefrontal regions, precentral gyrus, precuneous regions, superior frontal gyrus. The *a priori* selected RVLPFC was also functionally connected with the FFA time series data. Differences between the view faces and remember faces connectivity maps suggest more bilateral connectivity under the high task demands in the remember faces task, possibly implicating an enhancement of the memory encoding network (see Figure 13). A repeated measures ANOVA revealed that functional connectivity between RVLPFC and FFA actually decreased with increased task demand when moving from the *view faces* task (Mean B = .78, S = .31) to the *remember faces task* (Mean B = .25, S = .17) , $F(1, 152) = 342.59$, $p =$

.000. These maps illustrate promise for hypothesis 3, that functional connectivity between FFA and RVLPFC reflects an important component of memory encoding that relates to performance. However, the great difference between functional connectivity in the *view faces* task and *remember faces* task warrant exploration into each task separately. An enhancement index of functional connectivity cannot be calculated given that as task demand increases (as it was conceptualized in this study), functional connectivity decreases.

Figure 13. Functional connectivity beta maps for all participants for the view faces and remember faces encoding task using the FFA time series seed
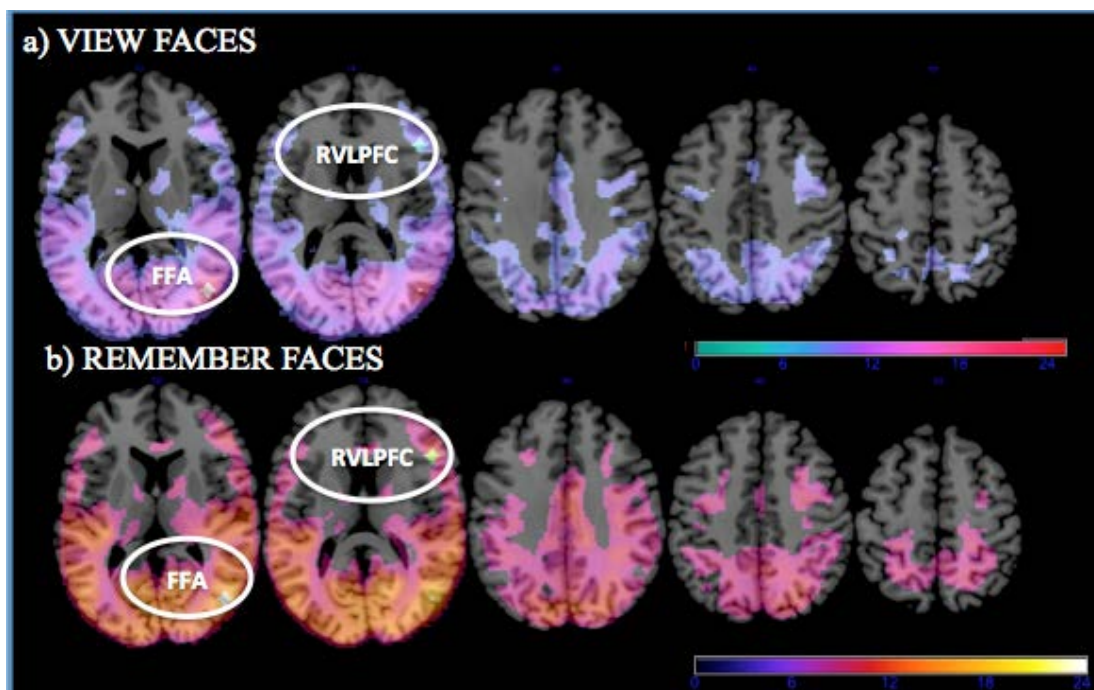
Time series data from FFA seed (circled) provided estimates of mean cortical activity in this region on a volume-by-volume basis. These data were correlated with all regions' time series in the brain on a voxel by voxel basis. The resulting Beta maps above reflect functional connectivity between the FFA and the rest of the cortex. RVLPFC is also circled. Beta maps were thresholded at $z = 8$ to aid visualization.

To directly test Hypothesis 3, functional correlations were used to predict performance and age was included in these models. Testing of these models for the *remember faces* task revealed that neither age, nor functionally connectivity between RVLPCC and FFA, nor their interaction term, predicted recognition hit rate (see Table 5). Consistent with previous results, only age impacted recognition discrimination. Hence, these results were inconsistent with predictions.

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Table 5. Tested models examining link between functional connectivity and remember faces task performance

Model	Age Group	Correlation between FFA and RVLPC (RVLPFC Corr)	Age Group * RVLPFC Corr	Model F (p)
		β (p) for Recognition Hit Rate		
1	.035 (.35)	--	--	.85 (.36)
2	.035 (.48)	.09 (.37)	--	.82 (.44)
3	.039 (.52)	-.08 (.75)	.001 (.997)	.54 (.65)
		β (p) for Recognition Discrimination		
1	-.34 (.000)	--	--	18.60 (.000)
2	-.31(.000)	-.02 (.78)	--	9.28 (.000)
3	-.32(.000)	-.09 (.71)	.07(.76)	6.18 (.001)

Note. Bootstrapping for coefficients was conducted based on 1000 age group stratified samples. The only coefficient to reach significance was Age in model 1 predicting recognition discrimination.

4.2.3   Exploratory Analyses

4.2.3.1 Functional Connectivity Analyses

To evaluate whether functional connectivity could mechanistically explain how top-down modulation differs between older and younger adults, functional correlations between the RVLPFC and FFA were then examined by age. Older adults showed greater connectivity between FFA and RVLPFC

(*M Beta* = .27, *S* = .02) compared to their younger peers in the *remember faces* task (*M Beta* = .18, *S* = .24), *t* (151) = -2.63, *p* = .009. Figure 14 shows the *remember faces* functional connectivity maps for the remember faces condition in the bottom panel, restricting the *z* scores of the connectivity maps to a z-score of 8 (i.e. also a reasonable correction for multiple comparisons) shows that older adults' magnitude of connectivity outweighed their younger peers. This suggests that older adults may be engaging the entire memory encoding network in a more effortful fashion following the time course of activity in the FFA during the *remember faces* task. During the *view faces* task, older adults showed a higher level of functional connectivity between FFA and RVLPFC (*M Beta* = .27, *S* = .02) than did their younger peers (*M Beta* = .20, *S* = .04). However, this difference by age group was not significant, *t* (146) = -1.54, *p* = .10.

Age-related differences in functional connectivity are not evident for either group. On a group level, older adults show equivalent levels of functional connectivity when told to view faces and when told to remember faces. Younger adults, however, do show a slight upregulation in functional connectivity with increasing task demand (i.e. moving from view faces to remember faces, the difference in mean connectivity is .02 Beta. This suggests not age-related difference in the coupling of the memory encoding network.

Figure 14. Age related comparison of functional connectivity for encoding tasks
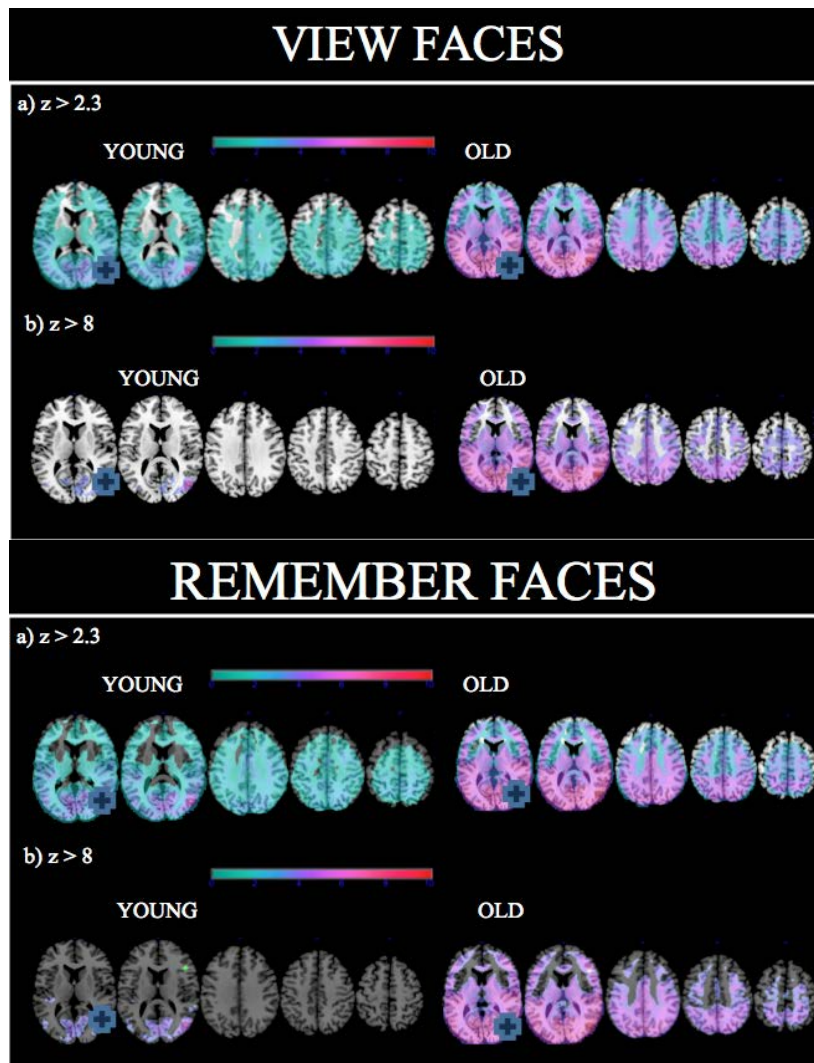
The figure shows functional correlations between the whole brain and the FFA seed. Images are presented in neurological convention. These functional activity maps were calculated using a z-score threshold of $z = 2.3$ and a clusterwise threshold of $p = .05$. The top half of the figure shows functional connectivity in the view faces task for young and old adults a) thresholded at $z = 2.3$ and b) thresholded at $z = 2.8$. The bottom half of the figure shows functional connectivity in the remember faces task for young and old adults a) thresholded at $z = 2.3$ and b) thresholded at $z = 2.8$. The FFA seed is marked with a blue cross.

In whole-brain analyses, older adults showed greater functional connectivity throughout the brain. An age-related contrast compared older and younger adults cortical activity in both encoding tasks. Older adults exhibited a larger functionally connected memory encoding network both when *viewing faces* and *remembering faces*. Functionally connectivity is stronger among older adults than younger adults in medial temporal areas, in extrastriate visual cortex, in the superior frontal gyrus

(supplementary motor cortex), inferior frontal gyrus, precentral gyrus, superior parietal lobule, and precuneous cortex. Patterns are similar in both tasks (see Figure 15).

Figure 15. Older adults' greater functional connectivity during encoding tasks
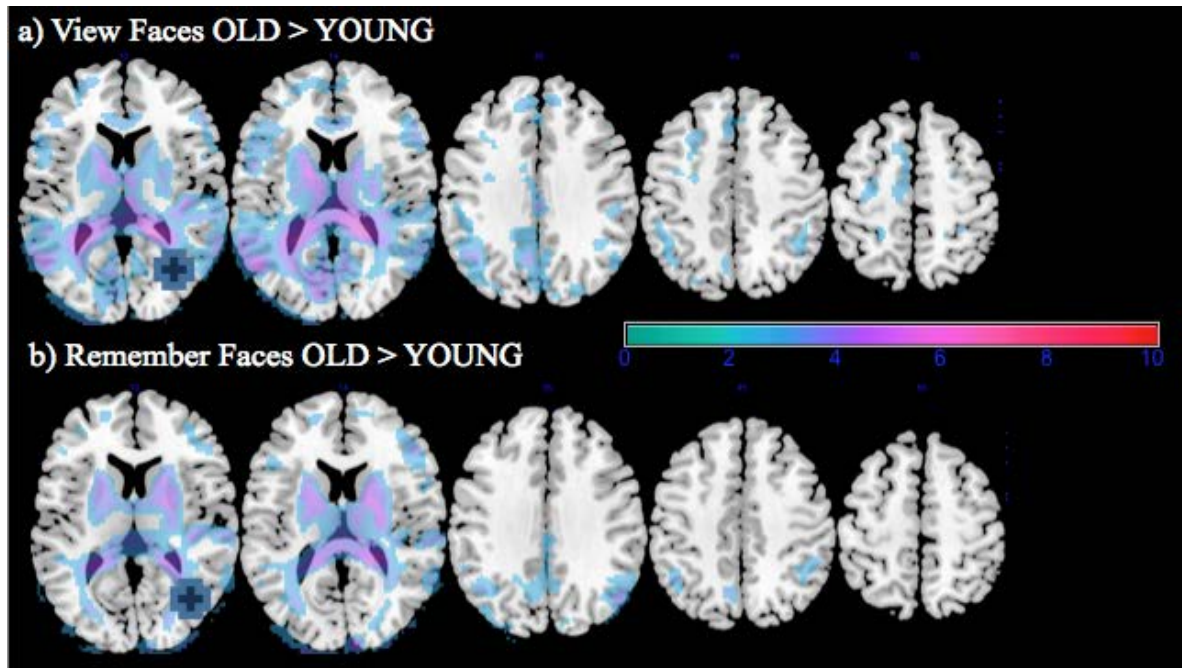
The figure shows age-related contrasts (older connectivity greater than younger connectivity) of the functional correlations between the whole brain and the FFA seed. Images reflect the differences in mean Beta values for the older greater than younger contrast for the view faces task (Panel a) and the remember faces task (Panel b). Images are presented in neurological convention. All images are thresholded at $z = 2.3$. The FFA seed is marked with a blue cross.

4.2.3.2 Performance Analysis

It is possible that functional connectivity between RVLPFC and FFA in the encoding task varies as a function of performance. Perhaps functional correlations only impact performance among those able to perform the task. First, the functional activity for high ($> 80\%$ hit rate, $n = 14$) and low performers ($<50\%$ hit rate, $n = 39$) was compared across age. A functional connection in the *remember faces* task between RVLPFC and FFA emerged between these regions for the 14 high performers ($r = .75$, $p = .002$) but not the 39 low performers ($r = .14$, $p = .39$). A Fisher's *r*-to-*z* transformation and test of correlations then showed that this difference was significant, $z = 2.42$, $p_{2\text{-tailed}} = .02$. This effect could be greatly influenced by younger adults driving up the connection between RVLPFC and FFA with accuracy. Collapsing across age, the same pattern emerged for discrimination. High discriminators ($n = 7$, d' > 2) showed better functional connectivity ($r = .45$, $p = .31$) than did low discriminators ($r = -.02$, $p = .87$, $n = 99$. d' < 1). However, neither of these correlations reached significance.

If functional connectivity relates with performance for high performers but not low performers, this suggest that the top-down modulatory network is disrupted for low performers. Among older high performers ($n = 10$), the relationship between functional connectivity and hit rate is strong and positive, $r = .65$, $p = .04$. Among the older low performers ($n = 40$), this relationship disappears, $r = .24$, $p = .14$. However, a Fisher's transformation of *r*-to-*z* and correlation difference test showed that these two relationship do not statistically differ, $z = 1.29$, $p_{\text{two-tailed}} = .20$. However, the small sample size of 10 high performing older adults could be affecting this relationship.

Thus, to fully examine the above relationship partial correlations between accuracy and the functional connectivity in the *remember faces* task, partial correlations were calculated. Among high performers, the relationship between accuracy and functional connectivity between the FFA and RVLPC was strong and significant when controlling for age group, $r_{AB.AgeGroup} = .77$, $p = .001$. Among low performers, the relationship between accuracy and functional connectivity between the FFA and RVLPC disappears when controlling for age group $r_{AB.AgeGroup} = .14$, $p = .20$. The relationship between functional connectivity and hit rate for high performers versus low performers differed, $z = 2.56$, $p_{1\text{-tailed}} = .01$. These data suggest that higher functional correlations may contribute to better task performance among those able to do the task.

In the *remember* faces task, the relationship between connectivity (between RVLPFC and FFA) and performance is stronger for high performers than low performers, when controlling for age. It is possible that the correlation between RVLPFC and FFA is stronger for high performers than low performers because of co-occurring age-differences in magnitude of the functional correlation. A t-test revealed this is not the case, high performers (*M Beta* $= .24$, *S* $= .03$) and low performers (*M Beta* $= .28$,

$S = .03$) show similar levels of functional connectivity, $t(59) = .85$, $p = .40$. To explore whether or not this is a network wide phenomenon or specific finding, functional connectivity with FFA and RDLPFC was also tested among high performers and low performers. Partial correlations were calculated accounting for age and compared by performance category. Among high performers, no relationship between accuracy and functional connectivity between the FFA and RDLPC emerged when controlling for age group, $r_{AB.AgeGroup} = -.27$, $p = .36$. RDLPFC functional connectivity also does not relate with performance for low performers, $r_{AB.AgeGroup} = .09$, $p = .54$. These data suggest that functional correlations in the *remember faces* task between FFA and RDLPFC do not contribute to performance in the same manner than do the functional connections between FFA and RVLPFC. Functional connectivity was also explored in the *view faces* task. High performers and low performers were compared controlling for functional connections between the FFA seed and RDLPC, controlling for age. The functional correlation between FFA and RDLPC was not related with performance, $r_{AB.AgeGroup} = .09$, $p = .78$. Among low performers, functional connectivity between RDLPFC and FFA marginally related with recognition $r_{AB.AgeGroup} = .28$, $p = .07$. Figure 16 shows these ROIs with the FFA seed and functional connectivity maps for both encoding tasks.

Figure 16. Functional connectivity dissociation between RVLPFC and RDLPFC
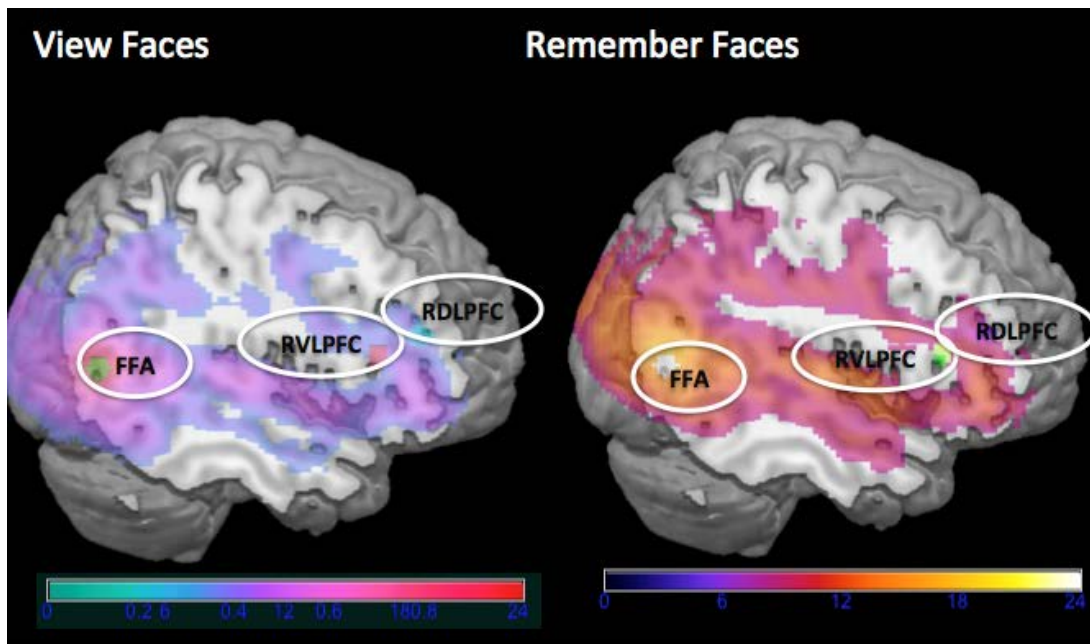
The above images reflect the functional connectivity z-stat maps (thresholded at $z = 8$) for the view faces task (right) and remember faces task (left). The FFA seed and investigated ROIs, RVLPFC and RDPFC.

The following analysis explores the idea of top-down modulation in the context of performance by age. To explore whether the expected upregulation of functional connectivity occurs according to an increase in task demand, functional connections between FFA and RVLPFC were compared in a repeated-measures ANOVA. Data did not show any main effect of an increase in functional connectivity coinciding with increased attention to faces $F(1, 151) = 2.24$, $p = .14$. However, a significant age by condition (or task difficulty) interaction occurred, such that the slope of the functional correlation's change from the view faces task to the remember faces was different for younger and older adults, $F(1, 151) = 6.05$, $p = .02$. When moving from the less attentive to more attention facial encoding tasks, older adults show the expected pattern of functional connectivity increase. Conversely, younger adults show a decreases in functional connectivity between FFA and RVLPC (see Figure 17). At first glance, this suggest that younger adults do not rely on the connection between RVLPFC and FFA to encode in the same manner as older adults. This suggests that older and younger adults are tapping into either two distinct face-selective regions within FFA or are possibly recruiting from different memory encoding networks and processes.

Figure 17. Functional connectivity by task difficulty and age
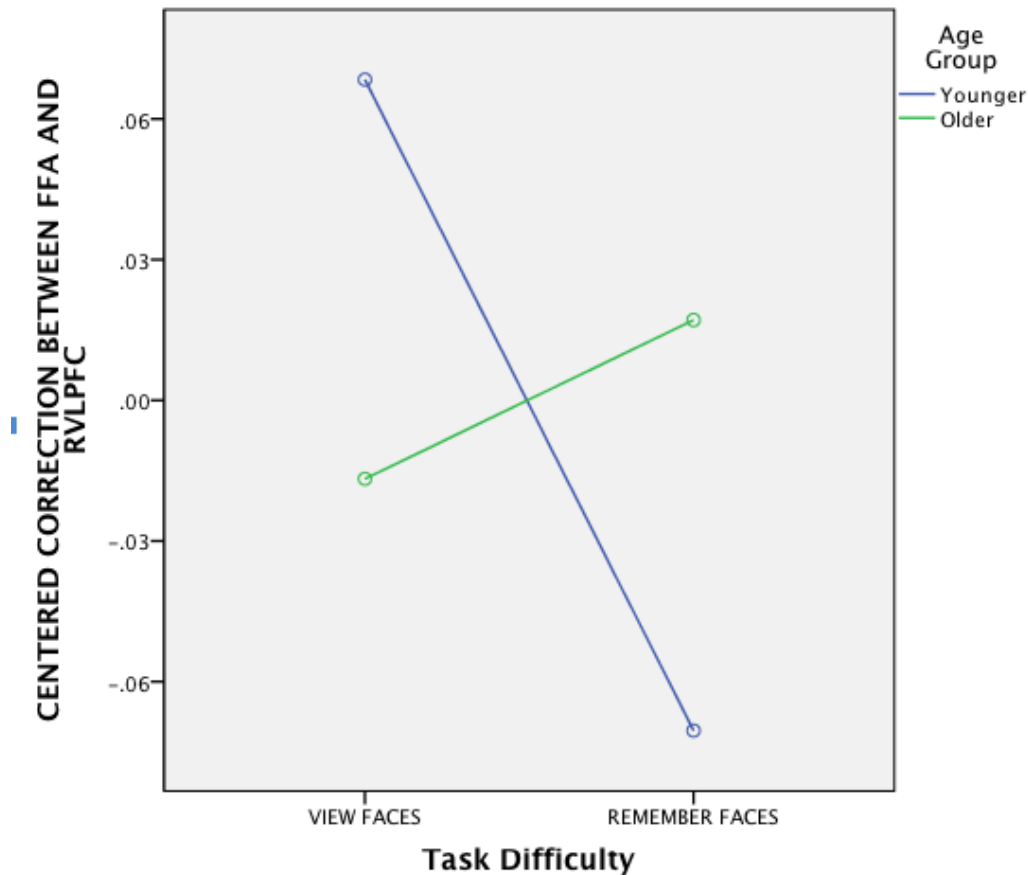
This figure shows that younger and older adults show different patterns of changes in functional connectivity between RVLPFC and FFA when moving from the view faces task to the remember faces task. Older adults show a modest increase of functional connectivity and younger adults show a steep decrease.

In another set of exploratory analysis, the association between performance and neural activity was explored. To do this, facial recognition hit rate was used to predict functional activity in a GLM approach. Each individual's hit rate was used to predict his or her whole brain activity. The resulting cortical activity maps reflected neural activity that was associated with task performance. Performance based (hit rate) activity maps were generated to examine 1) the relationships between performance and neural activity in the *view faces* localizer and 2) the relationships between performance and neural activity in the *remember faces* encoding task. Then activity was grouped by age to highlight any age related differences in links between cortical activity and task performance.

Neural activity that is associated with task performance during the localizer can be interpreted in many ways, which will be discussed later. At this point, this activity can simply be interpreted as a visual processing network. In the figure below, accuracy was used to predict neural activity during the view

faces and shows that older adults and younger adults show very similar activation patterns that predict performance. Other regional activity includes the dorsolateral and ventrolateral prefrontal cortex, the middle frontal gyrus, and medial temporal regions, including the bilateral hippocampi. Patterns are strikingly similar for older and younger adults, yet more activity survived the 2.3 z-score threshold for older adults. This shows that older adults recruited from a greater number of distinct brain regions than regions than did younger adults in order to passively view faces.

Figure 18. Whole-brain association between facial recognition and face-selective neural activity for older and younger adults.
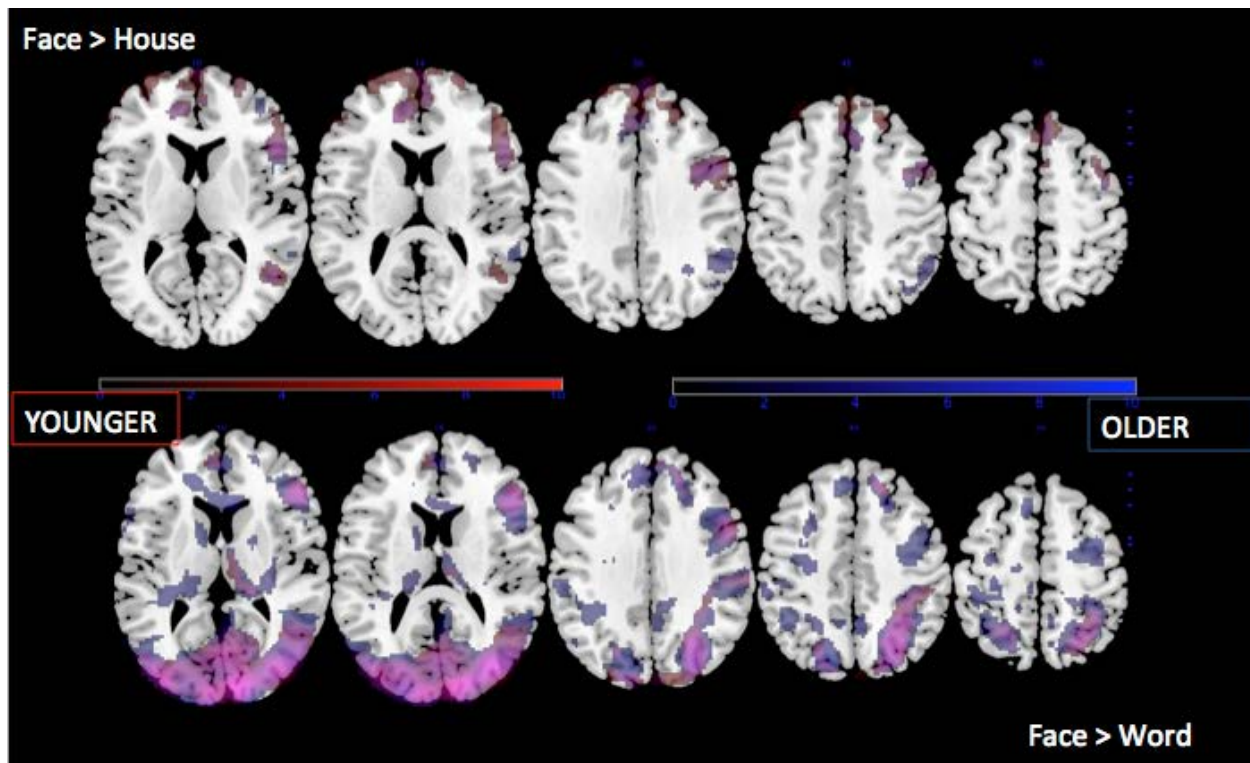
This figure shows regions in the brain associated with accuracy for the *view faces* task (top) and the *remember faces* task (bottom). Accuracy (hit rate) was used to predict cortical activity in the brain. Z-stat maps reflect regions in the brain positively associated with hit rate. Note that older adults (blue) show many regions of activity related performance absent for younger adults. Yet, younger adults' active regions of recruitment cover more cortical tissue within the right prefrontal and visual cortices.

5.0   DISCUSSION

Through a series of hypotheses this study sought to test whether differences in sensory enhancement via increasing task demands could explain memory deficits in older adults. Data analysis first explored whether there were performance deficits in older adults. Efforts were then made to link sensory activity in the fusiform face area to facial memory performance. Then sensory signals were compared among older and younger adults to test whether differences in sensory enhancement could drive changes in memory function. Finally, functional connectivity analyses were conducted to explore whether functional correlations between the "top" and "bottom" components of the top-down modulation model could predict memory performance. This study is concerned with explaining memory decline.

Older adults in the present study clearly showed evidence of an age-related memory deficit. Interestingly, there was no age-related difference in recognition hit rate, the most traditionally explored form of accuracy. However, older adults failed to discriminate faces they had seen from those they had not. Younger adults we better able to correctly say that a face they had never seen was in fact new and not part of a set of faces they had encountered during the encoding task. Thus, where older and younger adults differed in memory performance in the present study was in their discrimination index (see results on page 54), evidence of their discrimination ability. On average, younger adults demonstrated a higher discrimination index than older adults. The next sections attempt to address how this study explored this age-related memory performance deficit through a top-down enhancement deficit model of aging.

5.1   ENHANCEMENT AND MEMORY PERFORMANCE

Hypothesis 1 explored the role of sensory enhancement on memory performance. We predicted that greater sensory enhancement in FFA would relate with better behavioral performance (i.e., facial recognition) when moving from lower to greater attentional demand when encoding faces. This hypothesis was supported. We tested this hypothesis by extracting neural signal from the fusiform face area (FFA) during the *view faces* task and *remember faces* task. Remember that conceptually the

remember faces task is more demanding. Thus, more cortical activity was expected in the FFA during the *remember faces* task compared to *view faces.* A FFA enhancement index was calculated by subtracting *z*-scores of neural activity in the *view faces* task from *z*-scores of neural activity in the *remember faces* task. Approximately 60% of younger and older adults showed evidence of enhancement (see results on page 60). To support exploration of top-down enhancement deficit in aging, sensory enhancement in FFA had to predict some form of memory performance for older and younger adults. To test this idea, enhancement, age group, and the age group were used to predict memory performance.

As predicted, results showed that sensory enhancement in the fusiform face area predicted better memory performance, specifically discrimination ability, for older and younger adults. Results showed that age group and FFA enhancement were both significant predictors of facial discrimination (see results on page 63). This suggests that age group and sensory enhancement both directly impact discrimination ability. The interaction term was not significant showing that the relationship occurs in the same positive manner for both older and younger adults, such that better FFA enhancements are linked with better facial discrimination. Older adults had significantly lower discrimination scores than their younger peers.

Hypothesis 1 was supported. This is the main finding of the current study. No other studies directly examine the link between cortical enhancement and facial recognition discrimination. This is the first study to examine this relationship. Other work has link cortical enhancement to picture memory accuracy, but not discrimination. Consistent with that body of work (Gazzaley et al., 2005a; Gazzaley et al., 2005b), we found cortical enhancement to be critical factor contributing to facial discrimination for younger adults. This is the also the first study to critical examine visual cortical modulation in older adults and link it to task performance. Data show that both younger and older adults modulate signal in visual cortex in a manner that impacts task performance. These findings warranted the further exploration into the relationships between enhancement and facial discrimination in the context of top-down enhancement.

5.2   AGE-RELATED DIFFERENCES IN SENSORY ENHANCEMENT

The most parsimonious explanation for age-related deficits in facial discrimination would be offered by showing a difference in sensory enhancement by age. Thus, we tested the hypothesis that *younger adults would show significantly more FFA sensory enhancement than older adults.* If this were true, this could suggest that age-related decreases in sensory enhancement drive deficits in memory performance via

lower discrimination ability. The argument here would have simply been that older adults could not upregulate FFA activity as well as their younger peers in response to increasing task demand. To test this, FFA enhancement was compared between older and younger adults.

Against predictions, we found no age-related difference in the ability to enhance FFA neural activity when moving from the *view faces* task to the *remember faces* task. Younger and older adults showed about a .10% neural increase in the FFA regions moving from the *view faces* task to the *remember faces* task. These levels of enhancement did not differ by age (see results on page 65). These data did not provide support for an enhancement deficit in aging. We failed to reject the null hypothesis for Hypothesis 3.

These null findings are consistent with previous work in visual recognition and top-down modulation. Only one other study formally examines top-down modulation in the context of aging (Gazzaley et al., 2005b). In that study, researchers found that younger and older adults were able to equivalently enhance visual cortical activity in response to increasing attentional demands by condition. This extends the current literature by providing another point of evidence to suggest that an inability to upregulate cortical signal in visual cortex in response to increasing task demand or attentional focus *does not* sufficiently explain detriments in visual memory. Gazzaley and colleagues have explored another arm of the top-down modulation argument as one cause of older adults' poorer visual memory, deficits in suppression of irrelevant information. This may be a contributing factor to poorer memory function among older adults. Thus, while there is no evidence in the present study for age-related changes in top-down modulation via enhancement, age-related suppression deficits may indeed occur.

Yet, these findings are still promising. We have established that adults 30-60 older than younger adults can still equivalently upregulate cortical signal. The implications here for brain training remain to be explored. If were possible to isolate the weaker parts of the memory encoding network, strategic brain training to strengthen those areas in the functional network could prove helpful. Upregulation, in an of itself, it not beneficial unless it relates to some behavioral outcome. In this study, we did show that the degree of enhancement *does* impact facial discrimination, or memory performance.

To explore the possibility of top-down enhancement deficits through another lens, another set of analyses was conducted. In the next section, the functional connectivity analysis used to explore the last tested study aim is discussed. In these analyses, we explored the connection between the "top" and "bottom" components of the memory encoding network as they relate to task performance.

5.3   CONNECTIONS BETWEEN THE "TOP" AND "BOTTOM" AND FACIAL ENCODING PERFORMANCE

A set of functional connectivity analysis explored the hypothesis that higher functional correlations between FFA and right ventrolateral prefrontal cortex (RVLPFC) would relate with better performance, regardless of age (Hypothesis 2). The connectivity data presented in the current study suggested that a functional relationship between RVLPFC and FFA contributes to performance, when examined by performance subgroups. These data provide partial support for this hypothesis. Using partial correlations between FFA and RVLPFC connectivity and recognition hit rate, a difference in those correlations by age group emerged. A strong and positive correlation was found among high performers, or those able to complete the task with efficacy. Among those unable to remember faces, the relationship between accuracy and functional connectivity between the FFA and RVLPC disappeared. The relationship between functional connectivity and hit rate by performance group differed (see results on page 73). Despite these findings, we argue that Hypothesis 2 is only partially supported. Collapsing across all performance levels, no discernable relationship between functional connectivity of the "top" (RVLPFC) and "bottom" (FFA) with hit rate emerged. These data suggest that higher functional correlations may contribute to better task performance *only* among those able to do the task. Discrimination analyses divided into subgroups were less helpful due to small samples limiting generalizations and valid statistical analysis, thus were not conducted. There were only 7 adults meeting the criteria to be included in the high performing samples, only 2 of which were older adults.

A set of analyses that examined the change in functional strength according to task demand pointed to many possibilities. First, these data showed that younger adults showed evidence of a decoupling of the RVLPFC and FFA memory encoding network that related with increased attentional demand. These data could be reflective of an automaticity of the network requiring less and less attentional control of visual regions due to some practice effect or learning. However, the steep decline in the strength of the relationship (see Figure 23) more likely suggests that younger adults tap into a different set of distinct regions than the common ROIs used in the present study capture. As seen for older adults, increased task demands relate with better neuronal coupling. Future work, could define separate ROIs by age group within larger focal areas or define ROIs on a subject-by-subject basis.

5.4   CONCLUSION

5.4.1   General Conclusion

Three hypotheses had to receive support in order to make strong claims suggesting that enhancement deficits drive an aging deficit in memory performance. Current data do not provide a compelling argument to suggest this is the case. Some study data showed that older adults show more enhancement than younger adult (see Figure 22). These data point to alternative interpretations. Data suggest that older and younger adults' enhancement contributes to their ability to discriminate from hit and false alarms, showing enhancement and correct identification of faces are linked. Data from this study suggest that older and younger adults enhance FFA equivalently when moving from the *view faces* task to the *remember faces* task. Finally, among the "super performers" or those able to memorize faces, the degree of functional connectivity between RVLPFC and FFA may contribute to task performance. We know that the RVLPFC is an important component of working memory for its role of maintaining sensory representations. These data suggest that high performers may be able to tap into the encoding network in a manner that upregulate an advantageous connection between RVPFC and FFA. Although the results are less than compelling, some interesting findings have come to light throughout this study.

The first contribution of the current study is to reinforce the importance of continuing to explore the relevance of enhancement in models of age-related encoding disruption. Enhancement of sensory activity in the FFA occurred for approximately two-thirds of the sample. These enhancement findings are consistent with other studies showing sensory enhancement in visual cortex with increasing attention or task demand (A. Gazzaley & D'Esposito, 2007; Zanto, Rubens, Bollinger, & Gazzaley, 2010). We supported one hypothesis showing that enhancement is a significant predictor of facial discrimination ability. Future studies should explore the distinction between those able to enhance and those unable to enhance. Approximately 40% of the sample failed to show reliable enhancement in the fusiform face area when moving from one encoding task to a more demanding encoding task.

Nonetheless, sensory enhancement was associated with recognition memory performance. However, the driving force behind the age-related differences in discrimination was not simply due to differences in levels of sensory enhancement. If that were the case, then older and younger adults would have differed in levels of sensory enhancement. If we accept the null hypothesis that no differences in sensory enhancement occur by age group (H3), what then explains the age-related deficit in memory performance? We showed in this study that older adults fail to discriminate as well as their younger

peers. What other mechanisms could be driving this difference? One of the possibilities is a failure of the upregulation of the memory encoding network outside of the sensory cortex. It is also feasible that in this task sensory activity reached or approached a ceiling and that enhancement effects occurred in other neural areas of the memory encoding network. If that were the case, functional connectivity with the FFA seed could test this idea.

To that end, in another exploration of a top-down enhancement deficit theory of memory decline, functional connectivity was explored. Interestingly, functional connections between RVLPFC and FFA were singled out as possible contributors to memory encoding ability. Among high performers, a positive and significant relationship existed during *remember faces* task activity for FFA and RVLPC that did not exist for FFA and RDLPFC. Thus, functional connectivity between regions in the encoding network may to differentially contribute to memory encoding performance. This is rather interesting given findings that show functional bidirectional links between RVLPFC and RDLPFC (Jackson, Morgan, Shapiro, Mohr, & Linden, 2011). This suggests, that it may be the maintenance of information in working memory that shows decline and contributes to memory decline. The RDLPFC may not show evidence of functional correlations to the FFA seed that vary with task performance due to little disruption of its function as the bridge between extrastriate and parietal cortex.

Another contribution of the present study is the direct comparison of neural processes to behavioral outcomes in a top-down modulation exploration. Few studies have the statistical power to examine these relationships as well as the current data have characterized them. Even here, we found some floor effects on performance, which limited explorations. Here, we were able to explore memory encoding performance as hit rate and a discrimination index, which provided different patterns of results. Studies that simply use hit rate as their dependent measure could be influencing future investigations by failing to explore a more sensitive measure of memory performance.

The functional correlations outlined in the present study are associations that could reflect greater neuronal coupling. For that reason, the observed relationship between RVLPFC and FFA could be caused by a shared relationship to another region involved in the encoding network (e.g., feedforward and feedback loops with the hippocampus). Thus, at this point, it remains a tentative statement to claim that increased functional activity between RVLPFC and FFA is directly associated with better facial recognition. In light of more recent white matter tractography results, I would suggest that functional connectivity between RVLPFC and FFA reflects a spurious association. Since the start of this study, new findings have come to light that show two tracts in face-responsive regions of the brain (Gschwind et al., 2012). One tract connects FFA to occipital regions and in another, more dorsal tract, separate processing for faces occurs in frontoparietal areas and the superior temporal sulcus. These findings suggest that facial processing occurs in two segregated streams, one in the visual cortex, and the other in the frontal

regions. The present study shows a functional relationship between these regions, suggesting some coordinated effort between these streams. This does entirely exclude the idea of top-down modulation, but suggests that the model would need to incorporate an explanation for the coordination of these segregated processing streams.

However a top-down enhancement deficit model of cognitive aging cannot fully explain memory decline. Several alternative explanations are possible. Though enhancement contributes to performance, younger and older adults do not differ in FFA enhancement. One alternative explanation is that the FFA selection in the present study does not accurately capture face-specific sensory activity. A more likely explanation is that companion processes, like suppression of irrelevant information contribute to changes in memory encoding processes (A. Gazzaley et al., 2005b; A. Gazzaley & Nobre, 2012). The basic model of top-down model argues that *two* processes, enhancement and suppression of attention form the basis of selective attention. Promising evidence shows age-related deficits in suppression ability that relate with task performance (A. Gazzaley et al., 2005b; A. Gazzaley & Nobre, 2012). This suppression deficit may be at play in the present study, but remains beyond our ability to explore due to methodological limitations.

Compared to younger adults, older adults typically perform poorly on a variety of memory tasks. This study highlights how important the behavioral measure of performance can be. In this study, though discrimination varied by age group, overall accuracy rates did not vary between groups. This is due to older adults tending to report they had always seen faces whether they indeed had or had not. These results contradict previous findings showing a difference in facial memory hit rate (A. Gazzaley & D'Esposito, 2007).There was no evidence that increased signal in the fusiform face area predicted recognition hit rate. This is most likely due to the aforementioned response bias confounded the analysis. However, this also suggests that this facial working memory task in the present study is such that older and younger adults perform similarly in terms of accuracy rates. The lower rates of accuracy in this study compared to other tests of facial encoding also suggest this task may have been too difficult for both older and younger adults or that the 10 minute delay between completed of the task and recognition testing interfered with results.

The inconsistency between behavioral performance outcomes by age group is somewhat disconcerting. The majority of studies in memory encoding use accuracy as the sole outcome measure. Moving forward, future studies should include both accuracy and discrimination to better explain memory deficits. In the current study, had accuracy been the only measure explored, no age-related memory deficits would have been found. Further, no links between sensory enhancement and discrimination ability would have been made. More sensitive measures than hit rate should be adopted in

explorations of memory function. Advanced neuropsychological batteries now include relatively common measure of working memory tasks that include a range of performance measures.

In the present study, we found that cortical enhancement predicted facial discrimination but not hit rate. What is the conceptual difference between these two constructs? Response bias, or discrimination, might reflect something other than task performance. It might reflect a difference in strategy. In this manner, discrimination might reflect the use of a different neural network than hit rate. That may explain the pattern of findings in the present study, where enhancement contributes only to discrimination ability.

The results described in this study suggest that enhancement is important for memory performance but does not explain age related differences in memory function. First, encoding processes were temporally separated from the out of scanner recognition assessment. In this way, no neural signal from recognition bled into the encoding activity. Another strength includes the use of multiple conceptualizations of behavioral performance to explore neural activity in light of performance. Much of the previous work in facial encoding and top-down modulation has infrequently been associated with recognition or recall performance. In this way, the data can more concretely explore mechanistic explanations of memory decline. Another strength includes a large sample size, which allowed for sufficient power to test the main hypotheses of the study. Though subgroup analysis were often limited by a floor effect with respect to task performance.

5.4.2 Limitations and Future Considerations

Some limitations of the present study may limit its interpretability. One possibility is the aforementioned floor effect. Neither younger nor older adults performed particularly well on this task, both groups' accuracy rates were approximately 60%. Discrimination was also poor for both groups, though extremely poor for older adults. Restricting the sample to those able to perform the task could improve results. Future studies should use a behavioral practice that occurs outside the scanner and restrict participation to those able to achieve some facsimile of adequate facial recognition. Another option is to explore familiar faces were older adults tend to perform equivalently or better than their younger peers to allow for a more distributed outcome measure. That being said, both accuracy and discrimination in the present study were normally distributed, ranges were simply narrow.

Another limitation is the low rate of enhancement in the present study. This is somewhat limiting in that is skews the data in a manner that we are forced to examine what related with a lack of enhancement with many of the study's data point. One might ask why over a third of the sample fails to

enhance. If we conceptualized these tasks correctly, the incidental (view faces) encoding task should require less cognitive resources from the FFA than would the intentional (remember faces) encoding task. We see that is not the pattern of neural activity for a large enough portion of the sample to question this conceptualization. One possibility is that the instructional manipulation between these cues was not large enough to produce the enhancement effect. Other researchers using instructional manipulations based upon effort (try and try harder, for example) have seen stepwise increases in neural activity in response to effortful increases (Bastin & Van der Linden, 2005; Grady, 2002; Reber et al., 2002). Another possibility is that the tasks were correctly conceptualized in the present study, but the magnitude of difference between these steps was not large enough to show reliable enhancement. Yet another option is that the two tasks are conceptually different. For example, the view faces task may be tapping into an explicit memory system and the remember faces task tapping into a more explicit memory system.

Considering these limitations, future studies assessing enhancement should consider a synthesis of current best practices. First, several levels of manipulation should be examined. These levels should include a suppression condition, a baseline, and at least two levels of effortful encoding (e.g., try to remember and try harder to remember). In this way, the range of possible modulation may be best captured. A large number of trials in an event-related paradigm will allow for power to assess these relationships on a trial-by-trial basis and eliminate some of the washout effects of a block design. To eliminate fatigue effects, rests should be built into the design. Memory encoding tasks of a complex nature, such as that used in the present study should not occur at the end of the long MRI batteries in an attempt to avoid fatigue effects. Separating the encoding and recognition portions temporally will provide the clearest exploration of each. As seen in the present study, restricting the neural data to face-selective activity produced more information data that held relationship with performance when simple fusiform face activity did not. Thus, studies of sensory enhancement should include multiple stimuli of similar complexity to allow for isolation of stimuli-specific neural enhancement.

In this study, we compared cortical modulation in a less effortful facial encoding task to cortical modulation in a more effortful facial encoding task. This study may not have applied the best approach to test the theory of top-down modulation. Other approaches use more of a divided attention model (N. D. Anderson et al., 2000; A. Gazzaley et al., 2008; A. Gazzaley et al., 2005a; A. Gazzaley et al., 2005b; A. Gazzaley & D'Esposito, 2007; A. Gazzaley & Nobre, 2012; McDowd & Craik, 1988). Maximizing constraints on attention may better allow for examination of top-down modulation by providing competition for cortical resources. A few approaches to increasing competition for resources come to mind. One approach involves the presenting multiple stimuli in the visual field. Combining partially

transparent images and instructing participants to attend to one but ignore the other can do this. The other approach is to use a composition of opaque images, such as a landscape of mountains with a face appearing in front of those mountains. Another approach is to use a virtual environment task that involves completing one task while also trying to encode stimuli. An example would be completing a driving simulation while attempting to encode stimuli. Any of these approaches can place more rigid limits on attentional capacity. A word or caution should be applied here. It would be necessary to keep task simple enough that task demand could also be increased without maxing the threshold for cortical activity.

5.4.3   Summary

Overall, the results we report here do not support the theory that older adults memory deficits emerge from a deficit in top-down enhancement. This study shows that enhancement is a critical component for discrimination. These data suggest that older as well as younger adults may be relying on enhancement of sensory activity to bolster task performance. Also, age-related comparison of functional connectivity in the encoding tasks in the present study showed that older adults show larger recruitment of the encoding network and recruitment of that network at a higher magnitude. Finally, dissociation in the relationships between functional connectivity between the top and bottom components of the memory encoding network was shown. Data suggests that in some manner the connection between RVLPFC and FFA contributes to task performance in a way the connection between RDLPFC and FFA does not. This is most likely that the RVLPFC can upregulate maintenance of sensory information provided by the FFA, but rates of transmission through the RDLPFC remain unchanged with task demand in the present study. Future explorations into the nature of age-related differences in enhancement as contributing factor to encoding decrements are warranted.

The present study adds some evidence to the neuroimaging and aging literature. The two most descriptive and popular theories of cognitive aging describe function patterns consistent with data in this study. The increased coupling of the posterior FFA to the anterior RVLPFC evidence in older but not younger adults could be interpreted as evidence of the PASA model of aging. Also, throughout the whole brain analysis, z-stat maps produced consistent evidence of older adult's increased bilateral activity during memory encoding, suggesting evidence for compensatory models of the aging brain (e.g., HAROLD). The data show that enhancement components of top-modulatory processes remain intact as adults age and that older and younger adults may have dissimilar networks of memory encoding. In this vein, findings are consistent with Gazzaley and colleagues (2005a) who found no deficits in

enhancement during visual encoding.

Consistent with the prior research, we show that older adults suffer in their ability to learn novel, unfamiliar faces. The novel contribution of the current study is the examination of neural function and top-down modulation in the lens of behavioral performance. Also we demonstrate no age-related difference in the ability to upregulate visual cortex. We did however, show that only younger adults seem to capitalize on that upregulation in a manner that improves later facial recognition. For older adults, a relationship between fusiform cortical enhancement and later recognition was not evident. Despite this, we found an upregulation of the connection between the "top" and "down" components of the memory encoding network that varied according to increases for task demand for older but not younger adults. Taken together, these results move the field forward by showing that older adults seem to upregulate connections between the "top" and "bottom" of the memory encoding network without difficulty, but this upregulation does not impact performance. Thus, remaining mechanisms need to be elucidated to explain age-related deficits in memory encoding.

APPENDIX A

Table A1. Processing parameters for neuroimaging data

Parameter	Localizer	Encoding Task	Structural Image
Slice Time Correction	NO	NO	NA
Motion Correction	MCFLIRT Linear, Rigid Body	MCFLIRT Linear, Rigid Body	NA
Mean/Max Motion in mm *	0.255859 ; 0.625207	0.246632 ; 1.16567	NA
No. Spikes > ½ voxel size**	0	0	NA
Temporal Filters			
Low Pass	-1	-1	NA
High Pass (2 * Block A + Block B)	80	94	NA
Signal-to-Noise Ratio*	67.123219	68.827060	NA
Repetition Time (TR)	1.5 s	1.5 s	1.0 s
Echo Time (TE)	35	35	NA
No. Slices	28	28	144
No. Volumes (Images)	180	302	0
Dimensions [x y z]:	[EPI]: 3.44 x 3.44 x 4.00	[EPI]: 3.44 x 3.44 x 4.00	[MPRAGE]:1.33 x 1.33 x 1.30
EPI Matrix	64 x 64	64 x 64	160 x 192
Acquisition Direction	Inferior-to-Superior	Inferior-to-Superior	
Spatial Smooth	6.0mm	6.0mm	7.00 mm
Linear Registration	Registration to Main Structural using normal search,	Registration to Main Structural image using full search	Registration to MNI template using full search
Registration DOF	7	7	6
Voxel Threshold	(z): 2.3	(z): 2.3	(z): 2.3
Cluster Threshold	(p): 0.05	(p): 0.05	(p): 0.05

Note. *Reported data derived from participant 14. Processing parameters were identical for each participant. **Participants with more than 5 motion spikes were motion-corrected to control for the directions of significant motion above and beyond MCFLIRT.

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