The Impact of Cognitive Reserve and Emotional Affect on Working Memory Performance Among Younger and Older Adults: A Multiple Moderation and Neuroimaging Investigation

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Abstract

Canada’s population is aging rapidly, with the number of older adults 65+ expected to reach over one billion within the next ten years. Aging is often associated with cognitive decline and is something that many older adults fear. Thus, it is imperative to conduct aging-related research to determine if there is anything that can be done to postpone cognitive decline and improve the ability to age successfully. Within recent years, the discussion surrounding mental health and emotional wellbeing has been at the forefront of many news articles and research studies. Our emotions play a vital part in all aspects of our lives, including our cognitive abilities. Experiencing more positive emotions has been associated with greater brain activation which helps build up cognitive and psychological resources that may be useful later in life. In addition to our emotions, another protective factor such as cognitive reserve has been extensively studied within recent decades. Cognitive reserve cannot be studied directly as of yet, so various proxies of cognitive reserve such as education or occupation have been included in previous research studies. Cognitive reserve has been theorized as something that an individual can build up throughout their lifetime and could help preserve cognitive abilities later in life when age-related brain changes occur, or the effects of neurodegeneration are more prevalent.

Although previous research has noted the significant impact emotions and cognitive reserve have on memory, few studies have assessed how both could potentially moderate the association between age and working memory performance. Thus, the current study used multiple moderation to investigate this association using a sample of healthy young (n=50) and older (n=46) adults and a delayed match-to-sample letter task. Cognitive reserve was assessed using years of education as a proxy, and emotional affect was assessed using the positive and negative affect schedule questionnaire. Every participant was asked to complete this questionnaire at the start of each testing session to indicate how they were feeling at that moment. An average score for positive and negative affect was calculated, with higher scores reflecting greater positive/negative affect, and lower scores reflecting lower positive/negative affect.

Based on results from the first session, significant multiple moderation was found. The interaction between age and cognitive reserve was significant, as well as the interaction between age and positive affect. Specifically, these results indicated a strong age effect which demonstrated that younger adults with greater cognitive reserve and positive affect performed better on the working memory task compared to older adults (b=1.04, $p<0.001$). This effect was also noticeable when cognitive reserve was low and positive affect was high (b=0.41, $p=0.001$), suggesting that emotional wellbeing can aid in working memory performance even when cognitive reserve is lower. Additional analyses combined the response time and accuracy values together using the inverse efficiency score to better assess the differences or similarities between this combined score and response times alone. Results from these models also found significant multiple moderation, and the effects were even stronger. The impact of negative affect was assessed in separate multiple moderation models, but no significant effect of moderation was found regarding negative affect; however, cognitive reserve continued to remain a significant moderator in all models.

Results from the second session utilized data that was taken while participants completed the same working memory task in an MRI to assess brain-related changes between both age groups. A reduced sample of younger adults (n=41) and older adults (n=40) was used since some participants were not able to complete this portion of the study. No significant multiple moderation was found during the second session; however, the main effect of age remained significant across all models. Using SPM12, various brain regions were identified in which older adults recruited more brain activity in order to complete the working memory task. These regions included the left precentral gyrus, right lingual gyrus, and right postcentral gyrus, which are comparable to other studies that used a similar task.

Overall, the results from this study build off the previous literature surrounding emotions and cognitive reserve and highlights the importance of emotional wellbeing and cognitive reserve as we age. By clarifying the role these variables play, various changes could be made throughout an individual’s life to strengthen one’s emotional wellbeing and cognitive reserve, which may help later on in life when age-related brain changes or neurodegeneration may occur.

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ANS	Autonomic Nervous System
BIC	Brain Imaging Center
BOLD	Blood Oxygenation Level-dependent
CI	Confidence Interval
CR	Cognitive Reserve
DMS	Delayed Match-to-Sample
fMRI	Functional Magnetic Resonance Imaging
GLM	General Linear Model
GM	Grey Matter
HRF	Hemodynamic Response Function
IES	Inverse Efficiency Score
LPFC	Lateral Prefrontal Cortex
MNI	Montreal Neurological Institute
MoCA	Montreal Cognitive Assessment
MRI	Magnetic Resonance Imaging
PANAS	Positive and Negative Affect Schedule
PHAC	Public Health Agency of Canada
REB	Research Ethics Board
ROI	Region of Interest
ROMHC	Royal Ottawa Mental Health Center
RT	Response Time
SD	Standard Deviation

SE	Standard Error
SNR	Signal to Noise Ratio
SPM	Statistical Parametric Mapping
VBM	Voxel-based Morphometry
VSWM	Visual-spatial Working Memory
WHO	World Health Organization
WM	White Matter

Chapter 1: Introduction

1.1 The Aging Population

The global population of older adults aged 65+ is projected to reach 994 million by 2030 and 1.6 billion by 2050, with the largest increase likely to occur in Eastern and South-Eastern Asia (United Nations, 2022). In Canada specifically, the population of older adults aged 65+ has also been increasing quickly, reaching approximately 7 million in 2021, with over 860,000 older adults aged 85+ (Statistics Canada, 2022). Additionally, the number of centenarians in Canada exceeded 10,000 people in 2019, which is triple the number since 2001. Due to this significant increase in population aging in Canada and around the world, this will likely put more strain on an already overwhelmed healthcare system and may strongly impact families who are trying to support their loved ones as they potentially develop further health issues with age.

Indeed, with such a rise in the number of older adults, there also comes an increase in the prevalence of age-related diseases such as dementia and Alzheimer's. Dementia is an umbrella term used to describe diseases that negatively impact an individual's memory, language, or behaviour; Alzheimer's is the most common cause of dementia, accounting for 60-80% of all cases (Alzheimer's Association, 2020a). Globally, there are approximately 44 million people living with dementia (Alzheimer's Association, 2020b). In Canada, it is estimated that over 747,000 people have Alzheimer's or dementia, and this number is projected to rise to approximately 1.4 million by the year 2031 (Alzheimer's Association, 2020b; Alzheimer Society of Canada, 2020). In addition to the rise in the number of people with Alzheimer's or dementia, Canada has experienced an increase in total healthcare spending from approximately $6,448/per person in 2018 to an estimated $7,068/per person in 2019 (Canadian Institute for Health Information, 2020).

Given the projected rise in our aging population, and specifically in the number of people who have or may develop Alzheimer’s or dementia, it has become increasingly evident that age-related research be conducted. It is well known that one of the key aspects of Alzheimer’s or dementia is having impaired memory functioning (Baddeley et al., 1991). One of the reasons why this occurs is due to the neuropathological changes that take place, namely the development of neurofibrillary tangles and β-amyloid plaques (Basso et al., 2006). Additionally, with the advancement of neuroimaging, researchers have found that pathologic changes in the medial temporal lobe correlate strongly with the severity of memory impairment observable among people with Alzheimer’s or dementia (Basso et al., 2006; Rombouts et al., 2000).

Retaining our memory ability into old age is paramount to aging well, and may help individuals avoid or delay the onset of Alzheimer’s or dementia. Of the different types of memory, there has been a particular focus on the role of working memory and the differences noticed between healthy individuals and those with Alzheimer’s. Working memory involves the temporary storage and manipulation of information in order to perform cognitive tasks, and it is central to everyday life (Baddeley, 2002). Indeed, working memory is needed for learning, problem-solving, comprehension (e.g., reading and writing), or for navigation (e.g., driving). Researchers have found that people with Alzheimer’s or dementia tend to have impaired working memory compared to healthy controls (Belleville et al., 1996). This was most noticeable once task-load difficulty increased, which may indicate that some difficulties with working memory are hidden at low levels of demand and are only revealed once the task becomes more challenging.

A number of factors can contribute to working memory performance. For example, the age of an individual can impact working memory ability, such that older adults tend to have longer reaction times compared to younger adults (Mattay et al., 2006). Increased years of education also tends to be positively associated with working memory performance (Pliatsikas et al., 2019). Additionally, researchers have also studied the impact emotions may have on working memory. Indeed, findings reported throughout the literature indicate a complex bidirectional relationship between emotions and working memory, such that more positive feelings may help with working memory performance and more negative feelings may lead to worse performance (Ashby et al., 1999).

1.2 Emotions and Mental Health

Emotions, whether positive or negative, are fundamental to the human experience. Emotion and affect are terms often used interchangeably throughout the literature; however, there are clear distinctions between the two. Emotions are typically experienced when something personally meaningful happens, and they tend to be quite brief (Fredrickson, 2001). Conceptually, emotions can be categorized into families such as anger, fear, joy, and interest. On the other hand, affect tends to be longer lasting and is usually conceptualized as having two dimensions: valence and arousal. Valence refers to what is good/bad or positive/negative; the positive end could indicate feeling grateful, appreciative, or happy, while the negative end could reflect feeling irritable, contemptuous, or unhappy (Fredrickson & Losada, 2005). Arousal is associated with emotional states and is influenced by the sympathetic nervous system, the autonomic nervous system, and the endocrine system (Storbeck & Clore, 2008). Together, emotions and affect have been continuously studied in the literature, providing valuable information about their influence on the human body and mind. Overall, there is a complex bidirectional relationship between our emotions/affect and our cognitive and physical systems, which requires further exploration.

1.2.1 Cognitive Effects of Emotions

One of the key areas responsible for controlling emotions and memory is found within the forebrain and is known as the limbic system (Mesulam, 2000). Two of the main components of the limbic system are the amygdala, which processes emotions, and the hippocampus, which is the primary memory system of the brain (Phelps, 2004). Building upon the earlier research of Papez (1937), Yakovlev (1948), and Maclean (1949, 1952), researchers Catani, Dell'Acqua, and de Schotten (2013) identified three networks to help describe the limbic system. These networks include: the *hippocampal-diencephalic and parahippocampal-retrosplenial network*, which is focused on memory and spatial orientation; *the temporo-amygdala-orbitofrontal network*, which is responsible for integrating emotions with cognition and behaviour; and the *default-mode network*, which generally consists of the medial cortices which decrease during goal-directed tasks and increase during quiet resting states (Catani et al., 2013). Damage to these networks of the limbic system can have a profound impact on an individual's emotional processing and memory, which could include an inability to properly express emotions, and reduce attention and motivation (Catani et al., 2013). Thus, the limbic system is vital for understanding the interaction between emotions and memory and should be studied further so that its neural mechanisms can continue to be clarified.

Along with the limbic system, the cognitive effects of emotions have also been thoroughly explored by Fredrickson (1998) with her development of the broaden-and-build theory. Specifically, this theory is focused on understanding the psychological benefit of positive emotions, such as joy, interest, love, and contentment (Fredrickson, 2004). According to this theory, these discrete emotions help broaden one's momentary thought-action repertoires, which in turn helps build their physical, intellectual, social, and psychological resources (Fredrickson, 2001). In other words, the momentary thought-action repertoires are broadened through exploration and integration of new information, thereby building enduring personal resources which can be drawn upon to improve the odds of survival (Fredrickson, 2004). In contrast, negative emotions such as fear and anger, tend to narrow the thought-action repertoires, and do not aid in building our personal resources (e.g., physical and intellectual) (Fredrickson, 2001). Therefore, our emotions, whether positive or negative, will either help build-up our personal resources, or not help at all, which may later impact our cognitive health as we age.

Additionally, there is the concept of emotion regulation that also plays a role in the cognitive effects of emotions. Emotion regulation refers to how we influence our emotions by experiencing and expressing them in various ways in different situations (Gross, 2008). Our emotions strongly impact how we interact with the world and other people; emotion regulation helps to influence our emotions in a positive and helpful manner rather than in a negative and harmful way (Gross, 2015). This can be accomplished using two different techniques: *cognitive reappraisal* and *expressive suppression*.

Cognitive reappraisal tends to be more of an adaptive strategy that involves reinterpreting emotion-related situations so that we can modify the impact of our emotions; whereas expressive suppression tends to be less of an adaptive strategy that involves inhibiting our emotions during an emotionally arousing situation (Megias-Robles et al., 2019). As such, people who use more cognitive reappraisal strategies typically experience greater positive emotions and fewer negative emotions, have better psychological health, stronger relationships with people, less depressive symptoms, and better overall life satisfaction compared to people who tend to suppress their emotions. In terms of age differences, older adults have been found to prioritize their emotional well-being and use emotion regulation strategies to increase their level of positive affect and decrease their negative affect (Winecoff et al., 2011). Overall, the ability to regulate emotions is vital and may enhance our positive affect and general well-being both cognitively and physically.

1.2.2 Physical Effects of Emotions

The autonomic nervous system (ANS) plays a central role in describing the physical effects emotions may have on the body. The ANS is composed of three major subdivisions: the *sympathetic system*, which activates the fight-or-flight response; the *parasympathetic system*, which activates the “rest and digest” calming response; and lastly, the enteric system, which regulates food processing and secretory gland activation (Robertson et al., 2011).

In a review of the literature surrounding the impact of the ANS and emotions, Kreibig (2010) examined how positive and negative emotions influence the cardiovascular and respiratory systems. In particular, positive emotions such as amusement, happiness, joy, pride, and relief all tended to show an increase in heart rate, while affection and contentment showed a decrease. Moreover, an increase in respiratory rate was also noticed for the majority of positive emotions. In terms of negative emotions such as anger, anxiety, disgust, and fear, both heart rate and respiratory rate were shown to be elevated. Additionally, a number of studies focused primarily on positive affect and physical health have found that positive affect could modify our immune system and could also influence the behaviours people engage in to promote health, such as physical activity (Cameron et al., 2015; Pressman & Cohen, 2005). Indeed, interactions between the ANS and emotions strongly indicate that our emotions experienced throughout our life can affect our health and longevity (Danner et al., 2001). Therefore, based on the extensive review by Kreibig (2010) and the findings from other studies (e.g., Cameron et al., 2015; Danner et al., 2001; Pressman & Cohen, 2005), it is clear that the ANS plays a vital role in understanding the physical effects of emotions.

1.2.3 Mental Health

Since emotions appear to have a strong connection to our cognitive and physical health, maintaining positive mental health is vital for all individuals, including older adults so that they may retain their level of independence and dignity as they age (Montgomery et al., 2018; Orpana et al., 2002). According to the World Health Organization (WHO) (2022), mental health plays an important role in our overall state of health and wellbeing, and it is complex with states ranging from optimal wellbeing to debilitating suffering. Similarly, The Public Health Agency of Canada (2006, p. 2) defines mental health as "the capacity of each and all of us to feel, think, and act in ways that enhance our ability to enjoy life and deal with the challenges we face. It is a positive sense of emotional and spiritual wellbeing that respects the importance of culture, equity, social justice, interconnections and personal dignity." Thus, throughout our lives, mental health can fluctuate depending on our current situation (WHO, 2022). When circumstances are challenging, people may be at a higher risk of experiencing adverse mental health. Indeed, it is estimated that 1 in 5 Canadians will suffer from some form of mental health issue during their lifetime (McDonald et al., 2017). However, there are a number of protective factors that may help strengthen our mental health resilience such as social and emotional skills, level of education, or living conditions (WHO, 2022).

1.2.4 Resiliency

In general, resiliency helps individuals adapt to life's challenges in various ways such as developing proper coping strategies within ourselves or seeking support from friends or family (Kobau et al., 2011). The field of positive psychology also highlights the beneficial changes that may occur when learning more optimistic ways of thinking to improve resiliency. Overall, our mental health is strongly connected to how we think and feel, and it affects how we cope and manage ourselves during challenging times (Bhugra et al., 2013). As we age, more of life's challenges may arise that affect our overall health and wellbeing. For example, decline in memory function over the lifespan is considered one of the greatest worries older adults have about aging (Read et al., 2020). Thus, it is vital to understand how memory is affected by age, especially given the forthcoming increase of older adults over the next few decades.

1.3 Working Memory

1.3.1 Evolution and Components of Working Memory

One of the ways to assess the effects of possible memory decline with age includes studying working memory performance. The term 'working memory', generally defined as the ability to temporarily store and manipulate information in order to successfully perform complex tasks, has been used throughout the literature for many decades, with earliest accounts being mentioned in the book titled *Plans and the Structure of Behavior* by Miller, Galanter, and Pribram in 1960 (Baddeley, 2002; Baddeley, 2010). In an influential paper, Atkinson and Shiffrin (1968) also used the term working memory, referring to it as an individual's short-term store. However, this unitary model did not sufficiently explain how the working memory short-term store feeds into long-term memory (Baddeley, 2010). To overcome this issue, working memory was studied in more detail in the well-known paper by Baddeley and Hitch in 1974. These researchers built upon the unitary model developed by Atkinson and Shiffrin (1968), and proposed a new model involving three separate, but interacting, components: the *phonological loop*, the *visuospatial sketchpad*, and the *central executive* (Baddeley, 2010).

The first component, the *phonological loop,* is focused on auditory phenomena, which attempts to maintain and rehearse auditory information (Wynn & Coolidge, 2011). This system is assumed to have a temporary storage system whereby auditory information can be formed as memory traces, which spontaneously fade away after 2-3 seconds (Baddeley, 1996). If the information is repeated, the memory trace is likely to be remembered, and could then be maintained after continuous rehearsal.

The second component, the *visuospatial sketchpad*, involves processing visual information (i.e., shapes and locations) (Wynn & Coolidge, 2011). It is assumed that this system can temporarily maintain and manipulate visuospatial information, and can be accessed through our sensory systems or from long-term memory (Baddeley, 2002). Neuropsychological studies have also helped confirm the visuospatial sketchpad as a multicomponent system involving the occipital lobe for visual patterns, the parietal lobe for spatial aspects, and the frontal lobe to help coordinate and control the information (Baddeley, 2002; Smith & Jonides, 1996).

The third component, the *central executive*, is perhaps the most important, but least understood component of working memory (Baddeley, 2003). Primarily, it is assumed to be responsible for the attentional control aspect of working memory (Baddeley, 1996). In other words, it is involved in processing attentional stimuli, decision making, planning, and updating the information between the phonological loop and visuospatial sketchpad (Wynn & Coolidge, 2011).

An additional fourth component, the *episodic buffer*, was also added to Baddeley and Hitch’s 1974 model to help address the interaction between working memory and long-term memory (Baddeley, 2003). This component holds together the information provided by the phonological loop and visuospatial sketchpad and is attentionally controlled and processed by the central executive (Baddeley, 2003; Wynn & Coolidge, 2011). In other words, the episodic buffer is episodic in the sense that it integrates information from the visual and auditory systems, as well as long-term memory, into episodes; it acts as a buffer by temporarily storing this information and is accessed by the central executive through conscious awareness (Baddeley, 2010).

Given the aforementioned information, working memory could be defined as a multicomponent model whereby incoming information becomes temporarily stored and manipulated (Baddeley, 2002). In other words, working memory involves a number of necessary systems required for retaining information while performing complex tasks, such as reasoning, comprehension, and learning (Baddeley, 2010). These systems have been studied thoroughly over the past decades, using many forms of working memory tasks to elucidate its neural mechanisms. Indeed, working memory has become one of the most well-researched topics in neuropsychology and cognitive neuroscience, providing a greater understanding of the functions of the human mind (Wynn & Coolidge, 2011).

1.3.2 Examples of Working Memory

One of the most widely used procedures for studying verbal working memory involves using a delayed match-to-sample (DMS) task (Daniel et al., 2016; Sternberg, 1966). The DMS task involves three steps: 1) a presentation of stimuli on the screen (e.g., letters), which participants attempt to memorize; 2) a delay where no stimuli are presented, and participants must try and maintain the information shown in the first step; and 3) participants are shown an additional stimulus (e.g., letter) and must make a choice as to whether or not it is the same stimulus seen in step one (Daniel et al., 2016). As this task is quite simple and allows task-load difficulty to be parametrically manipulated, it has become an ideal working memory task to employ in functional magnetic resonance imaging (fMRI) studies.

Such studies have found a few common and consistent areas of brain activation (Daniel et al., 2016). Using a DMS task with letters and fMRI, Habeck and colleagues (2005) found significant increasing activation in the lateral prefrontal cortex (LPFC), parietal lobe, anterior cingulate, and cerebellum; decreasing activation was also noted in the occipital-temporal lobe and medial prefrontal cortex. Of these areas, the LPFC has been of particular interest when studying the neural mechanisms of working memory (Habeck et al., 2005). In a separate fMRI study using a DMS task with letters, researchers found decreasing activation in the ventral LPFC and increasing activation in the dorsal LPFC while the task increased in difficulty (Rypma et al., 2002). It has been noted in the literature that the ventral and dorsal LPFC play different roles. Specifically, the dorsal LPFC tends to become activated when the information to be remembered exceeds the working memory capacity of 4±1 items; the ventral LPFC is presumed to decrease in activation once this occurs (Cowan, 2001; Habeck et al., 2005).

In addition to the verbal domain, another aspect of working memory is the visual-spatial domain (VSWM). In general, tasks testing this domain require participants to retain visual and/or spatial information for a limited amount of time and manipulate it (McAfoose & Baune, 2009; Voyer et al., 2017). For example, participants may be asked to study the location of an image (e.g., dot) on a screen, attempt to remember this location, and then indicate if a probe stimulus is in the same location as the original stimulus. Additionally, the Corsi Blocks task is another measure of a VSWM task that is commonly used (Voyer et al., 2017). This task places nine blocks in front of a participant and the researcher taps on a number of the blocks per trial; the participants then must try and reproduce the order in which each block was tapped.

Much like the aforementioned studies used to assess the neural mechanisms of working memory for the DMS task (using letters as stimuli), many studies have also been conducted to understand the neural correlates of VSWM. In their study, researchers Diwadkar, Carpentar, and Just (2000) asked participants to remember the most recent location of either 1 vs. 3 objects (i.e., circle, triangle, or cross) on the screen as they were presented using a 2D or 3D array. Similar to the aforementioned DMS task findings, results indicated significant activation in the dorsal LPFC and the parietal lobe as the task difficulty increased. Indeed, a number of studies have found significant activation in the frontal and parietal areas of the brain during VSWM tasks (Klingberg, 2006).

Lastly, one final experiment commonly used to study working memory is the n-back task. During the n-back, participants are asked to respond to a given stimulus (e.g., letter) whenever it is the same as *n* trials before; *n* is specified beforehand as 1, 2, or 3, etc. (Veltman et al., 2003). Attempts to clarify the areas of brain activation while completing the n-back have also been conducted, with a comprehensive meta-analysis reporting the main findings (Owen et al., 2005). Regions of the brain most highly activated during the n-back were similar to the areas previously mentioned for the DMS and VSWM, namely the dorsal and ventral LPFC and the medial and lateral posterior parietal lobe.

Although there are many similarities regarding the three aforementioned working memory tasks, there are also some differences. For instance, the n-back requires both maintenance (e.g., remembering one previous letter during the 1-back) and manipulation (e.g., increasing task difficulty from 0-back to 2-back); whereas, the DMS task focuses mainly on recognition memory and the ability to maintain the stimuli (e.g., letters) so that proper recognition can take place once the probe stimuli is presented (Veltman et al., 2003). However, the DMS task can also include a form of manipulation, either explicitly (e.g., alphabetizing the letters after retrieval), or implicitly (e.g., increasing the memory load from 1 letter to 9 letters) (Rypma, 2006). Similarly, the VSWM includes a maintenance period whereby the image (e.g., dot) is maintained in memory (utilizing spatial memory for location), as well as manipulation (e.g., the number of the dots on the screen is increased). Thus, each task can provide valuable information regarding an individual’s working memory ability, while using slightly different approaches.

Given these examples of working memory, it is clear that the dorsal and ventral LPFC and parietal lobe play an important role in understanding the neural mechanisms of working memory. It is also worth noting that several factors (e.g., age, education, emotions) may influence an individual’s working memory ability, and thus should also be considered in future age-related research focused on cognitive health (Ashby et al., 1999; Koch et al., 2007; Linnenbrink et al., 1999; Ziaei et al., 2017).

1.4 Cognitive Reserve

Even though memory-related challenges likely occur with age, there are some factors that may provide a protective effect (Zarantonello et al., 2019). For example, having more years of education tends to reflect better working memory performance compared to those with fewer years of education. This protective effect of education can also be described as a proxy for cognitive reserve (Stern, 2002; Zarantonello, 2019). The concept of cognitive reserve has been discussed extensively throughout the academic literature. Essentially, cognitive reserve refers to adaptability of cognitive processes such as efficiency, capacity, or flexibility, which helps the brain to cope with age-related changes or pathology without compromising cognitive function (Song et al., 2022; Stern et al., 2020; Stern, 2021). Thus, cognitive reserve can be considered as an active process, thereby allowing certain individuals the ability to cope with more brain pathology but still retain their cognitive abilities (Stern, 2021). This demonstrates that various brain networks may be more efficient or adaptable to age-related changes or pathology, representing a discrepancy between these brain-related changes and observed cognitive deficits that are expected based on that pathology (Barulli & Stern, 2013; Stern et al., 2005). Two potential neural mechanisms have been identified to support the theory of cognitive reserve: *neural reserve* and *neural compensation* (Stern, 2009).

1.4.1 Neural Mechanisms of Cognitive Reserve

Neural reserve refers to the inter-individual variability in brain networks, which can differ based on the capacity or efficiency of these networks (Steffener et al., 2012; Stern, 2009). Thus, healthy individuals may be able to use these networks as task demands increase in difficulty, or these networks may also be activated to help individuals complete cognitively demanding tasks despite brain pathology (Stern, 2009). As such, individuals who have brain networks which are more efficient or flexible (i.e., high cognitive reserve) might be more capable of coping with the negative effects imposed by brain pathology (Steffener et al., 2012; Stern, 2009). Indeed, those with more efficient brain networks would require less activation compared to those with less efficient brain networks in order to complete the same task at a similar level of performance (Barulli & Stern, 2013). These individuals may also demonstrate higher capacity, such that they are able to increase their capacity level as tasks become more challenging.

Neural compensation refers to changes in cognitive processing that may occur when there is brain pathology (Stern et al., 2005; Stern, 2009). Thus, neural compensation may be present when individuals are using brain networks that are not normally used by others who have intact brains in order to compensate for brain pathology. In other words, neural compensation requires the use of compensatory brain networks to accomplish cognitive tasks when pathology or age-related changes are present (Barulli & Stern, 2013). Additionally, individuals with higher cognitive reserve may be able to activate additional brain networks more effectively even when brain pathology is present in order to maintain their cognitive function. These additional brain networks might be used in different ways, or additional brain areas may be recruited to compensate for the inability to use a healthy brain response when tasks increase in difficulty (Stern et al., 2005). Indeed, further evidence suggests that those with higher cognitive reserve have more efficient brain networks, allowing them to more effectively manage neuropathology using compensatory mechanisms (Porricelli, 2024).

1.4.2 Measures of Cognitive Reserve

Cognitive reserve has often been estimated using various proxy variables such as years of education, which has been used most frequently in the literature (Song et al., 2022). Additional common proxies have included IQ, occupational complexity, leisure activities, vocabulary or literacy level, and socioeconomic status (Barulli & Stern, 2013; Harrison et al., 2015; Song et al., 2022; Steffener et al., 2012). These proxies of cognitive reserve have been associated with a decreased risk of developing dementia, as well as better successful aging (Barulli & Stern, 2013). Specifically, among older adults who have higher levels of education, studies have shown that they have slower rates of cognitive declines and a decreased risk of neurodegeneration (Harrison et al., 2015). Additional research by Richards and Sacker (2003) found that life experience such as educational attainment by early adulthood, childhood IQ, and occupation in middle age, all contributed to cognitive performance in later life, suggesting that cognitive reserve can be built up throughout the lifespan. Indeed, numerous studies have also shown that cognitive reserve proxies can moderate the association between brain pathology and clinical outcomes such as dementia (Song, et al., 2022).

1.4.3 Neuroimaging and Cognitive Reserve

Since cognitive reserve is a theoretical construct, it is challenging to determine ways to measure it directly (Stern et al., 2020). The use of cognitive reserve proxies offers one way to assess the possible development of cognitive reserve; however, these should not be treated as directed measures of cognitive reserve. As such, various functional imaging approaches have also been used to get a better understanding of the neural mechanisms underlining cognitive reserve. If different resting states or functional states of brain networks can be identified and validated, it may indicate a more direct measure of cognitive reserve compared to proxies. According to research by Steffener et al. (2012), individuals with low cognitive reserve required the use of more brain networks to perform at a similar level on a cognitive task compared to those with high cognitive reserve. Additionally, it has been reported that younger adults are more likely to utilize neural reserve as they tend to have more intact neural capacity; whereas older adults or those with neurodegeneration are more likely to utilize neural compensation, recruiting additional brain areas to complete similar cognitive tasks (Anthony & Lin, 2018; Stern, 2002).

In a separate fMRI study, 40 younger adults were asked to complete a letter Sternberg task which increased in difficulty from 1 to 6 letters (Habeck et al., 2005; Stern, 2009). It was expected that those with more efficient brain networks would show less activation as the task became more difficult. Several brain regions were identified during the task, including the lateral PFC, parietal lobe, cerebellum, and anterior cingulate. Individuals with greater activation in these areas also showed longer response times, which suggests a link between processing efficiency and response times. Indeed, those with greater efficiency required less brain activation in those areas as the task increased in difficulty. This finding demonstrates the concept of neural reserve and indicates that cognitive reserve might be associated with greater neural efficiency. Lastly, it was hypothesized that the individuals with higher cognitive reserve and greater neural efficiency might be better able to cope with age-related brain changes.

A follow-up study also used fMRI and the letter Sternberg task but included a sample of 18 older adults and 40 younger adults to examine the differences between the age groups (Stern, 2009; Zarahn et al., 2007). The imaging results identified similar spatial patterns for younger and older adults during the stimulus and probe phases of the task, which allowed the researchers to assess the age-related differences in neural efficiency. By doing this, the researchers found that older adults required greater brain activation compared to younger adults but did not benefit from this increase in terms of their task performance, suggesting that age-related brain changes can limit the efficiency of a brain network. Both age groups showed brain activation in common working memory areas such as the cerebellum, frontal lobe, and parietal lobe. A secondary brain network of the right parahippocampal gyrus was used only by the older adults, indicating neural compensation; however, the authors noted that this additional activation did not help the older adults perform better, but simply allowed them to maintain their functional ability in order to complete the task.

1.5 Neuroimaging

1.5.1 Structural Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is typically divided into structural MRI and functional MRI (fMRI). Structural MRI is used to assess the neuroanatomical structures of the brain, which include measures of grey matter (GM) and white matter (WM) (Anatürk et al., 2018). One method to analyze structural MRI data is voxel-based morphometry (VBM) (Fasano et al., 2018); voxels are described as cubes of brain tissue (Gerber & Peterson, 2015). This technique allows researchers to conduct a voxel-wise comparison of local GM concentrations between two groups of participants (Ashburner & Friston, 2000). To achieve this, all structural MRIs are spatially normalized to a common stereotactic space, segmented into GM and WM, and smoothed before performing a statistical test to observe any significant differences between two groups of participants (Mechelli et al., 2005).

Structural MRIs are commonly referred to as a T1 or T2-weighted image, which is high in resolution and low in noise (Gennatas et al., 2017). The quality of the structural brain image is strongly influenced by two characteristics: spatial resolution and signal to noise ratio (SNR) (Symms et al., 2004). Slice thickness, frequency and phase encoding, and scan time are some of the ways in which spatial resolution and SNR are impacted. Therefore, it is important for all participants to remain still while the structural images are being acquired. Once processed, the structural MRI can then be used to attain GM/WM volumes and cortical thickness from various regions of the brain.

A number of studies have explored how the size and shape of structural components of the brain are influenced by age. For example, brain atrophy tends to be common with aging, with GM loss often noticed in the prefrontal cortex, as well as in subcortical structures which include the hippocampus (Allen et al., 2005; Anatürk et al., 2018). Indeed, GM volume reduction typically begins in early adulthood and continues to decrease linearly throughout adulthood (Giorgio et al., 2010). WM volume loss has also been noticed globally and in region-specific areas of the brain (Allen et al., 2005; Anatürk et al., 2018). Changes in total WM volume tend to be nonlinear in terms of aging, increasing until approximately fifty years old, and decreasing thereafter (Giorgio et al., 2010). Overall, structural brain changes, such as GM and WM volume loss, can strongly influence an individual’s life and may lead to cognitive decline in late adulthood (Anatürk et al., 2018).

1.5.2 Functional Magnetic Resonance Imaging

Along with structural MRI, functional MRI (fMRI) is an important tool for researchers, with thousands of studies reported annually (Kim & Ogawa, 2012). Indeed, fMRI research allows researchers to evaluate changes in brain aging among healthy individuals and those with diseases (e.g., Alzheimer’s), conduct animal research studies, and perform clinical evaluations before surgery (Chow et al., 2017; Glover, 2011). Additionally, fMRI is non-invasive, relatively inexpensive, and provides good spatial resolution of brain images, which can be analyzed afterwards (Glover, 2011). The brain images acquired from fMRI scans were first reported in 1990 by Ogawa and colleagues when they determined that functional brain mapping was possible by using an MRI contrast they termed as ‘blood oxygenation level-dependent’ (BOLD) (Kim & Ogawa, 2012).

The BOLD contrast is typically used in fMRI research studies and occurs because of changes in the amount of oxygen found within the hemoglobin (Glover, 2011). Specifically, the BOLD signal indirectly measures brain activity, reflecting changes in cerebral blood flow, volume, and oxygenation level (Soares et al., 2016). Thus, the BOLD contrast is dependent on changes in deoxyhemoglobin, whereby increases in local deoxyhemoglobin concentrations lead to changes in MRI signal intensity (Kim & Ogawa, 2012). Among researchers who conduct fMRI studies, there is general consensus regarding the fact that an increase in brain activity is stimulated by increased blood flow and greater consumption of energy; however, the relationship between brain activity and the BOLD response continues to be studied as there is still more that can be learned about this complex relationship (Ciuciu et al., 2003; Soares et al., 2016). In particular, the hemodynamic response that accompanies the increases in brain activation is an intensive area of research.

As brain activity increases, there is a short delay before the vascular system responds and blood flow begins to increase; this mechanism is referred to as the hemodynamic response function (HRF) (Ciuciu et al., 2003; Soares et al., 2016). Consequently, the hemodynamic response has a time scale of several seconds, whereas neuronal activity occurs within milliseconds (Ciuciu et al., 2003). Despite the differences in time, the BOLD signal tends to follow the shape of the HRF and is usually modelled by imaging software (Soares et al., 2016). Typically, the software creates a canonical model of the HRF which begins as a gradual rise, peaks around five seconds (following a stimulus), and then gradually returns to baseline after approximately twelve seconds (Soares et al., 2016).

In terms of actually conducting an fMRI experiment, two approaches can be used: i) a block-based design, or ii) an event-related design (Glover, 2011). Using a block-based design, trials alternate between an experimental condition (stimuli presented) and a control condition (typically with no stimuli presented); each block typically lasts for a few tens of seconds. In contrast, the event-related design is set up so that all the trials are relatively brief in time, occurring at random inter-trial intervals and tend to have a longer control time which allows the hemodynamic response to properly return to baseline. Regardless of the approach, 3D volumes of the brain are continuously acquired over a period of time (typically called a ‘run’ lasting approximately 10 minutes), and the T2*-weighted signal from the fMRI is measured in each voxel, which changes as a function of the BOLD response (Ciuciu et al., 2003). The overall goal is to test whether the signals from the experimental condition are significantly different from the signals of the control condition, thereby indicating that significant brain activation was required while performing the administered task (Glover, 2011). Before reaching this final analytical step to determine significance, a number of quality checks and pre-processing steps are required.

The following pre-processing steps are typically used to make sure the imaging data are constructed properly before conducting first-level or secondary-level statistical analyses. The steps include: i) *slice-time correction*: involves adjusting how the imaging slices were acquired so that the voxel data from each slice is matched to the timing of a reference slice, which helps eliminate the acquisition time differences for each slice – as images are acquired one slice at a time, there is a delay between the first and last slice, which is adjusted by interpolating the time-course voxel information from each slice and matching the timing to a reference slice; ii) *motion correction*: involves correcting for head motion, which typically involves realigning/transforming each volume to a reference volume (e.g., first or last volume); iii) *spatial transformations*: the images from an individual are aligned to their structural T1 image (co-registration) and normalized to a common standard space (e.g., Montreal Neurological Institute (MNI) templates) – this step is crucial, as it aligns the brain images for each individual to a common space, allowing researchers to perform group-level analyses and identify specific locations in the brain where activation occurs; and lastly, iv) *spatial smoothing and filtering*: used to improve the signal to noise ratio (SNR) by averaging the data points together, creating a blurring effect which helps enhance lower frequency signals and suppresses higher frequency ones; low and/or high pass filtering may also be applied during this step to help control for additional noise such as slow scanner drifts, and physiological noises from breathing and heart beating (Glover, 2011; Soares et al., 2016). Once these pre-processing steps have been completed, the data is statistically analyzed. The most common method is to use statistical parametric mapping (SPM), which is based on the general linear model (GLM) since it is usually the most straightforward and easy to compute and interpret (Soares et al., 2016). First-level statistics are completed first, and are performed separately for each individual. This step creates a parametric map of the brain by generating a test statistic for each voxel. Once these maps are created, second-level statistics may be used to assess participants as a group. (Soares et al., 2016). For example, the brain scans from a group of older adults could be compared to a group of younger adults to determine if older adults recruit additional areas of the brain to successfully perform a complex task. Overall, fMRI research has helped uncover some of the mysteries of the brain and will continue to evolve as technology improves.

1.6 Summary: Aging, Emotions, Cognition, & Cognitive Reserve

Aging is often associated with a decline in physical abilities and cognition, with specific declines in memory and processing speed (Mohindru et al., 2023). These changes may occur due to declines in grey and white matter volume, which can affect overall functioning on a daily basis and may have a big impact on the overall psychological wellbeing of an individual. However, it is worth noting that although cognitive decline occurs with age, emotional wellbeing tends to remain stable (Kunzmann & Wrosch, 2015). Specifically, emotional-motivational development is often adaptable and shifts in terms of one's emotional goals across adulthood, showing a positive trajectory with age. Indeed, emotional affect and cognition interact together by altering attentional mechanisms, memory, and may also influence the development of cognitive reserve across the lifespan (Mather & Cartstensen, 2005; Mohindru et al., 2023).

Along with cognitive aging, individuals may also experience emotional aging, which refers to pursuing emotionally meaningful goals while placing more emphasis on positive emotions compared to negative emotions (Mohindru et al., 2023). Being able to shift from negative to positive emotional goals helps improve overall competency and the ability to properly regulate emotions. Emotional regulation is centered on the goal of achieving emotional wellbeing and tends to be relatively unaffected by aging and may even improve with age as other cognitive abilities decline (Scheibe & Carstensen, 2010). With regards to the brain, emotional regulation is dependent on the prefrontal and cingulate cortex, which activate emotion-related subcortical systems such as the amygdala and insula (Ochsner & Gross, 2005).

Various theories regarding emotional aging have also been developed to help understand the role emotions have on overall wellbeing. For example, the socioemotional selectivity theory purports that older adults are more motivated to prioritize positive information over negative information compared to younger adults (Löckenhoff & Carstensen, 2004). One reason why this occurs is due to the remaining time they have left and the desire to focus more on positive aspects and less on negative aspects. As a result of placing more emphasis on emotional aspects of situations, greater emotional wellbeing may be experienced; however, it is worth noting that always focusing on the positive may be detrimental. Selecting choices that may be beneficial in the present moment may jeopardize future wellbeing; thus, it is important to take into consideration both positive and negative emotional states even though unpleasant or anxious feelings may occur.

The selective optimization with compensation model by Baltes and Baltes (1990) also helps explain the role of emotional aging and wellbeing. This model explains how older adults select goals while keeping in mind the restrictions of time and energy as we age, optimize resources to achieve these goals, and compensate by using alternative means to achieve the same goals. Thus, these changes with age may affect an individual’s independence and overall wellbeing, and highlights the importance of accumulating resources (e.g., cognitive reserve) in the earlier stages of life so that they can be utilized in later stages of life.

Of these theories, the socioemotional selectivity theory (Carstensen, 1992) has been the most successful in explaining the role of emotional health with aging (Mohindru et al., 2023). It highlights the motivational shift that makes older adults orient themselves more towards positive information and less towards negative information (Carstensen, 1992, Carstensen et al., 1999). For example, when time is viewed as something limited, people tend to focus more on positive affective states. This is also known as positive affect bias or the ‘positivity effect’ which is ultimately used to maximize overall wellbeing and achieve emotionally satisfying goals by having more of a preference for positive information compared to negative information (Larsen, 2000). Therefore, the motivational shift older adults use may help improve their emotional wellbeing and optimizes the limited time they have left to enjoy their life.

As previously mentioned, cognitive reserve may act as a valuable resource later in life when the effects of age become more apparent. Cognitive reserve may be built up throughout an individual’s lifetime regarding their educational attainment, occupation, and leisure activities (Stern, 2009). These variables all represent proxies of cognitive reserve since there is no single direct measure of cognitive reserve (Stern et al., 2020). Having higher cognitive reserve may help reduce cognitive decline and the risk of neurodegeneration. Overall, cognitive reserve is something that continues to evolve over the lifespan and is not fixed.

Emotional aging factors such as emotional regulation and emotional motivation might serve as protective factors when it comes to maintaining cognitive abilities with aging (Mohindru et al., 2023). Indeed, the beneficial effects of emotional wellbeing may enhance cognition by building resilience. Most of the previous studies have highlighted the relationship between cognitive reserve and emotion regulation using emotion-related stimuli. For example, Guerrini et al. (2022) found that proxies of cognitive reserve (i.e., Cognitive Reserve Index Questionnaire, National Adult Reading Test) did not predict performance on emotion recognition tasks but did predict performance on cognitive tasks. In contrast, a separate study did find a significant association between cognitive reserve (i.e., years of education) and emotion recognition among older adults (Demenescu et al., 2014), reflecting a discrepancy in the literature. Therefore, it is important to clarify how cognitive reserve and emotional affect interact to better understand their role in cognitive and emotional aging. Taken together, it is possible that factors of cognitive reserve (e.g., education, occupation) and emotional affect (particularity positive emotions) may moderate the effect between aging and an individual's cognitive abilities (Mohindru et al., 2023).

1.7 The Current Study

Although previous research has indicated strong relationships between cognitive reserve and working memory performance, as well as the effect emotions have on task performance, there remains a gap in the literature regarding the combined effect of both variables. Thus, given the aforementioned research and literature regarding aging, cognitive reserve, emotions, and working memory, the present study aimed to examine the moderating effects of cognitive reserve and emotional affect on the relationship between age (younger vs. older adults) and working memory. The use of multiple moderation offers a nuanced way of exploring this relationship and helps to better understand the influence of cognitive reserve and emotional affect when both are included in the same model.

The first session assessed the working memory of all participants using a delayed match-to-sample letter task, yielding a cognitive capacity score, which was used during a block-based version of the task. This value was also used during the second session when all participants performed the same working memory task in an MRI to observe brain-related differences between the age groups. It was expected that cognitive reserve would moderate the relationship between age (younger vs. older) and working memory such that greater cognitive reserve would help participants perform better on the task. Additionally, it was expected that positive affect would moderate the relationship between age (younger vs. older) and working memory such that greater positive affect would lead to enhanced working memory performance; greater negative affect was expected to decrease working memory performance. Lastly, it was expected that older adults would recruit additional brain regions to complete the working memory task compared to younger adults, namely, frontal and parietal regions.

Chapter 2: Methods

2.1 Participants

One hundred participants between the ages of 18-30 or 60+ were recruited from Ottawa, Ontario for this study. Inclusion criteria required all participants to be proficient in the English language, right-handed, have normal or corrected-to-normal vision, in good self-reported health, and score at least 24/30 on the Montreal Cognitive Assessment (MoCA) (Malek-Ahmadi et al., 2015). Participants were excluded if they had any substantial head injuries, had previously tested positive for COVID-19 with severe symptoms, had been severely ill or hospitalized within the past six months, had a stroke or more than one risk factor for a stroke, had any neurological disorders, or if they did not satisfy the safety requirements for the MRI. Of the one hundred participants, four were excluded due to scheduling conflicts, leaving a final sample of ninety-six for full analysis for session one. A reduced sample of eighty-one participants from session two was used for additional analyses because fifteen participants were not able to complete the MRI portion of this study. A G*Power analysis was completed to determine the minimum sample size required for the current study. The parameters included: F-test (linear multiple regression: fixed model, R^2 increase), effect size 0.15, alpha 0.05, power 0.80, two tested predictors (interactions [age and cognitive reserve; age and emotional affect]), and five total number of predictors (i.e., age, cognitive reserve, emotional affect, and both interactions). Based on these values, a minimum sample size of sixty-eight was needed; thus, this value was satisfied for the current study. This study was approved by the Research Ethics Board (REB) at the University of Ottawa, and all participants signed consent forms and were compensated $60.00 for their time.

2.2 Assessments

2.2.1 Emotional Affect

The Positive and Negative Affect Scale (PANAS) questionnaire (Watson et al., 1988) was administered at the start of both sessions. This scale includes a list of twenty emotion-related words (e.g., interested, excited, scared, nervous) that are scored from 1 (very slightly or not at all) to 5 (extremely). Participants were asked to score each word based on how they were feeling in the current moment. Separate positive and negative affect averages are then calculated, which can range between 10-50, with higher scores reflecting greater positive/negative affect and lower scores reflecting lower positive/negative affect. High positive affect may indicate that an individual feels energized, motivated, or focused, whereas low positive affect may be indicative of sadness or lethargy. In contrast, an individual experiencing high negative affect may indicate greater feelings of anger, disgust, or nervousness, whereas low levels of negative affect may reflect calmness or serenity.

2.2.2 Cognitive Reserve and Working Memory

Cognitive reserve was assessed using years of education as a proxy, which has often been used in similar studies (Nogueira et al., 2022). Participants were asked for the total number of years they were in school, including any post-secondary education. Total years of education ranged from 12-20(±1.40) for younger adults and 11-27(±3.16) for older adults.

The delayed match-to-sample (DMS) task used letter stimuli to assess working memory (Fig. 1) (Rympa et al., 1999; Sternberg, 1966). A grid of 3x3 letters was presented on the screen for 2.5 seconds, which the participant had to study and remember. The letters then disappeared, and a green crosshair appeared on the screen for 3.5 seconds, during which the participants had to retain the previous letter(s) in their mind. A single probe letter then appeared on the screen for

2.5 seconds, during which time the participant would use the keypad to indicate if the probe letter was one of the letters they previously had to remember.

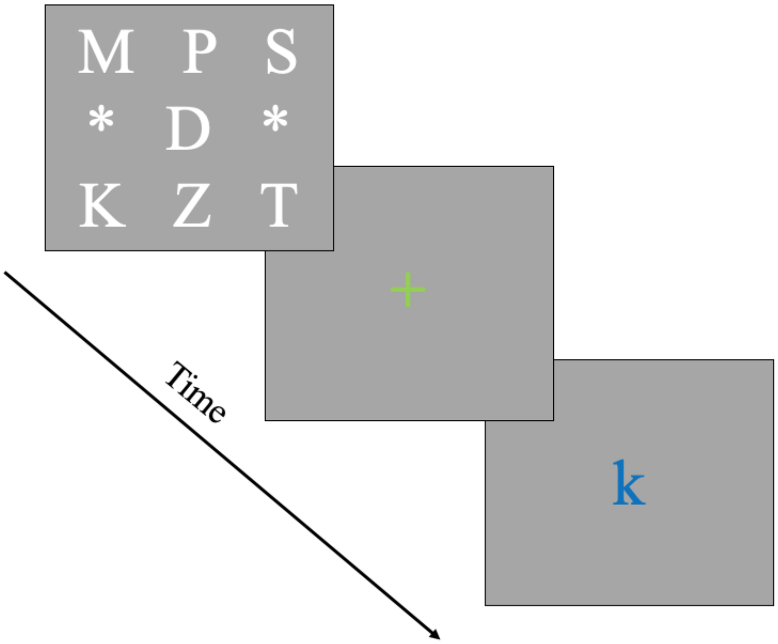

Figure 1. Example of a single trial of the delayed match-to-sample letter task.

During the encoding phase, stimulus letters were white and capitalized; asterisks were used in places where letters did not appear. The probe letter was in blue and lowercased to help avoid matching based on potential visual features of the letters. The trials included all letters from the alphabet except for vowels and ‘W’ to minimize word-forming. Each trial contained a new set of letters that were different from the previous trial, and the letters were not in alphabetical order.

Participants completed a short practice run of the task before starting the actual task to ensure they understood the instructions. The actual task used a three-up, one-down, staircase design throughout the trials. An incorrect response would decrease the number of letters in the grid by one, and three correct responses in row were needed to increase the difficulty by one letter again. This procedure yields approximately 80% accuracy and provided a measure of cognitive capacity which was needed for the final part of this task (described below). This task lasted for 7 minutes or 20 reversals (Karmali et al., 2016).

After the staircase design of the task was complete, participants started the block-based version. Five 56 second blocks with six trials each were presented on the screen. The first block started with only one letter, and load four included a specific number of letters related to their cognitive capacity score. Load five included one additional letter above their cognitive capacity score. Thus, each participant completed the block-based version of this task based on their cognitive capacity score and not based on a standardized set of letters.

Participants completed the practice, staircase design, and block-based design in session one, and two runs of the block-based design during session two while in the MRI, which used their cognitive capacity score from the first session. Both runs during the second session in the MRI were identical and used the same five 56 second blocks of six trials procedure as in the first session. A three-second countdown was shown on the screen before each block started, with 24 seconds of fixation on a red crosshair after each block. Individual variability of the hemodynamic response is better controlled by using this block-based technique of the task (Maus et al., 2010).

2.3 Procedure

People who were interested in our study contacted us through email or by phone. A short phone-screen was delivered to determine if they were eligible to complete the study. The individuals who met the inclusion and exclusion criteria were scheduled for their first session which took place at Lees campus, building E, room 250A at the University of Ottawa, and lasted approximately two hours.

Session 1: Once participants arrived at the lab, we went through the consent form and answered any questions they had before proceeding; a virtual signature using SurveyMonkey was needed. After accepting to be part of the study, participants were asked to complete the MoCA, where a score of 24 or greater was required (Malek-Ahmadi et al., 2015). A short demographic questionnaire was then given to the participants, followed by the PANAS questionnaire. Once these tasks were finished, all participants completed an extensive neuropsychological battery composed of various tasks focused on working memory, executive function, verbal ability, processing speed, and fluid ability (Appendix A) using PsychoPy3 (Peirce, 2019) on a MacBook Air computer. After all the tasks were completed, the participants were paid $20.00 (plus parking and transportation fees if applicable), and a date was selected for their second session. Participants were also sent a longer lifestyle/behaviour questionnaire (Appendix B) to complete at home before coming in for their next session and were paid $10.00.

Session 2: The second session took place at the Brain Imaging Center (BIC) at the Royal Ottawa Mental Health Center (ROMHC) within one month after the first session. Participants met the researcher at the main doors of the Center and were escorted to the BIC. Once there, the participants changed into an MR-safe gown, and were asked to remove all metal from their body; an MR safety checklist was filled out and given to the MR technologist. Participants also completed the PANAS questionnaire for a second time, indicating how they are feeling at that moment. Once the scanner was ready, the MR technologist had a quick discussion with the participant about their safety form, and the researcher set up the equipment in the control room. The participants were then escorted to the MRI room where they are asked to lay down on the bed and were positioned by the MR technologist; proper ear protection was worn. A button pad with two buttons was given to the participant so that they were able to complete three working memory tasks (i.e., DMS, VSWM, and n-back) while in the machine. A squeeze ball was placed in their left hand in case they were in distress and needed to stop for any reason. A structural T1 scan was acquired first and took approximately six minutes; the participant was told to relax and not push any buttons during this time. The participants were then given instructions for completing the first working memory task (i.e., DMS letter), and performed two runs which were block-based (i.e., included five loads of increasing difficulty). The VSWM dot task was completed secondly, followed by the n-back, with two runs each. Functional scans were taken during each of these tasks using a TR of 1.11 seconds, 56 slices, 358 measurements for the DMS letter, 365 measurements for the VSWM dot, and 398 measurements for the n-back. After the functional scans were complete, additional scans were taken, which included: arterial spin-labelling (ASL), diffusion tensor imaging (DTI), and a neuromelanin scan. Total scanning time took approximately 1 hour and 45 minutes, after which the participants were paid $30.00 (plus parking and transportation fees if applicable). A copy of the T1 structural image was also given to the participants as a thank you for completing our study. For the purpose of this thesis, only the T1 structural scan and functional data from the DMS letter task were analyzed.

Incidental Findings: During the second session, there was the possibility of an incidental finding while reviewing the scans. When this occurred, the MR technologist notified the researcher, and the scans were sent to a qualified radiologist at the Ottawa Civic Hospital to be read. A formal report was then sent back to the MR technologist at the Royal and we were notified if the case was significant. If no significant abnormality was found, the participant was not notified; however, if a significant abnormality existed, the PI contacted the participant, and they were asked to follow-up with their primary physician. If they did not have a primary physician, they were sent a referral to the University of Ottawa health clinic.

2.4 MRI Data Collection Parameters

All neuroimaging used the 3T Siemens Biograph mMR MR-PET scanner at the Brain Imaging Centre (BIC) at the ROMHC. Participants were required to wear protective earplugs with a headset during the scans and held a squeeze ball in their left hand which could be activated if they were in distress and wished to terminate the scan. A button pad with two buttons was held in their right hand to complete the working memory tasks.

2.4.1 Structural MRI

A T1-weighted multi-echo magnetization prepared rapid acquisition gradient echo (MEMPRAGE) image was acquired sagittally (TR = 2530ms; TE 1/2/3/4 = 1.69/3.55/5.41/7.27ms; flip angle = 7°; 1mm isotropic resolution; 192 slices; 256mm field of view, ipat (acceleration) = 2, with 32 ref lines and a non-selective inversion time of 1150ms and 650 Hz/Px BW. Duration: 6:03min (van der Kouwe et al., 2008).

2.4.2 Functional MRI

The following acquisition parameters were used for all task-based data collection. A multi-band accelerated EPI sequence (Moeller et al., 2010) using an acceleration factor of 6, TR = 1110ms, TE = 16.6ms, 52-degree flip angle, phase partial Fourier 6/8, 56 slices collected in an alternating increasing slice order, 2.5×2.5mm in-plane resolution, slice thickness = 2.75mm, field of view: 220×200mm. Each run was 6:38min.

2.4.3 Pre-processing

All image pre-processing and statistical analyses used SPM12. For each participant's EPI dataset, images were temporally shifted to correct for slice acquisition order using the middle slice acquired in the TR as the reference. All EPI images were corrected for motion by realigning to the first volume of the first session. The T1-weighted (structural) image was coregistered to the first EPI volume using mutual information. This coregistered high-resolution image was used to determine the transformation into a standard space defined by the Montreal Neurological Institute (MNI) template brain supplied with SPM12 using the new segment tool (Ashburner & Friston, 2005). This transformation was applied to the EPI data and re-sliced using 4th degree B-spline interpolation to 2×2×2mm. Finally, an 8mm FWHM kernel smoothed each image.

2.4.4 Participant Level Time-series Analysis

The time series modeling for each participant had five regressors of interest, one for each level of memory load. Each block was modeled as a rectangular epoch of 56s in duration. All regressors of the time series models were convolved with a standard double-Gamma model of the hemodynamic response function (Glover, 2011, 1999). Masking was explicitly applied using all spatially normalized voxels identified as belonging to the brain. The two sessions were modeled together at the first level statistical modeling phase and combined via contrasts. Five contrasts modeled each level of task demand across the two sessions.

2.5 Statistical Analyses

All statistical analyses were completed using the IBM Statistical Package for Social Sciences (SPSS) version 29. An additional software package, PROCESS Hayes, was installed on SPSS to perform the moderation analyses (Hayes, 2018). SPM12 was used for all neuroimaging analyses.

Descriptive statistics included means and standard deviations. Independent samples t-tests and chi-square tests were used to assess significance. If Levene’s test was significant, then the results for equal variances not assumed was reported. Checks for normality and outliers were also completed and no changes were made to the data.

Multivariate statistics included multiple moderation using the PROCESS Hayes package (Hayes, 2018). The PROCESS macro uses regression to analyze all main effects and interactions and includes additional features such as bootstrapping and probing of moderating effects. Multiple moderation allows for testing two moderators in the model at the same time to observe their possible interaction effects with the independent variable (See Fig. 2). Age (younger vs. older) was entered as the independent variable, and response time (seconds) for the DMS letter task at load level four (i.e., at their cognitive capacity level) as the dependent variable. An adjusted Inverse Efficiency Score (IES) was also calculated using response times and accuracy values for each participant at load level four (response time ÷ proportion of correct responses) (Bruyer & Brysbaert, 2011; Townsend & Ashby, 1978, 1983), and was included as a dependent variable in separate models. This variable was used to provide additional information regarding possible significant effects when response times and accuracy values are combined; thus, it supplements the analyses involving just the use of response times alone. Moderators included years of education as a proxy of cognitive reserve and emotional affect (positive and negative tested in separate models). All continuous variables (i.e., education, positive affect, negative affect) were mean centered. Bootstrapping was used as a robust technique to aid with any imperfections with the data and included 95% bootstrap percentile confidence intervals (Jung et al., 2019; Tibbe & Montoya, 2022). Graphs of the data were created using the PROCESS Hayes code within SPSS (Hayes, 2018).

As such, the following models (Appendix C) were analyzed using data from the first session: Model 1: Age (younger vs. older) (independent variable), DMS Load 4 RT (seconds) (dependent variable), Cognitive Reserve (i.e., years of education) (moderator one), and Positive Affect (moderator two); Model 2: Age (younger vs. older) (independent variable), DMS Load 4 RT (seconds) (dependent variable), Cognitive Reserve (i.e., years of education) (moderator one), and Negative Affect (moderator two); Model 3: Age (younger vs. older) (independent variable), IES

Load 4 RT (seconds) (dependent variable), Cognitive Reserve (i.e., years of education) (moderator one), and Positive Affect (moderator two); Model 4: Age (younger vs. older) (independent variable), IES Load 4 RT (seconds) (dependent variable), Cognitive Reserve (i.e., years of education) (moderator one), and Negative Affect (moderator two). Models 5-8 used the same format as models 1-4 but included data from the second session.

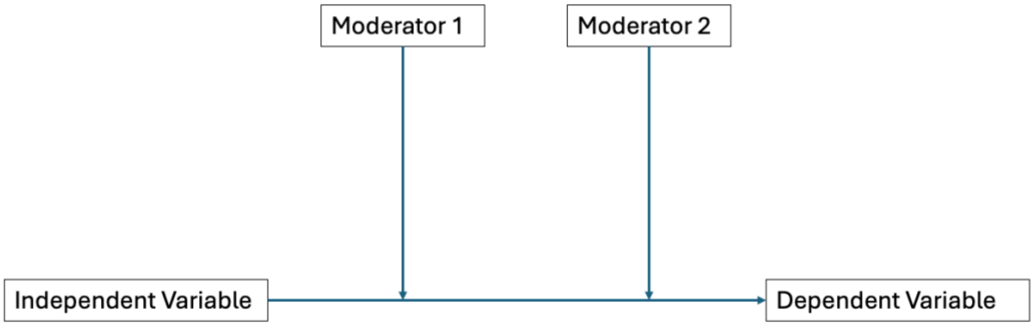

Figure 2. Multiple Moderation Model.

Regarding the fMRI analysis, specific regions of interest (ROIs) included typical working memory areas as previously mentioned. Based on the activation maps of various meta-analyses, these included the dorsal LPFC, ventral LPFC, fusiform gyrus, posterior parietal cortex, and cerebellum (e.g., Daniel et al., 2016; Emch et al., 2019; Rottschy et al., 2012). Differences between verbal vs non-verbal stimuli have also revealed different activation patterns such that DMS tasks using non-verbal stimuli had greater engagement in the right middle frontal gyrus and precuneus compared to DMS tasks using verbal stimuli (Daniel et al., 2016). A separate meta-analysis further revealed that certain regions (e.g., Broca’s region) was activated more during verbal working memory tasks, and the PFC (dorsal and ventral) was activated more during visual-spatial tasks (Rottschy et al., 2012). Lastly, a final meta-analysis found significant bilateral activation in the frontal cortex, left-lateralization in parietal regions, and right-lateralization in the cerebellum (Emch et al., 2019). Additionally, they determined significant differences in brain activation in terms of age, reaction time and task-load difficulty. Specifically, mean reaction time was positively associated with activation in the left medial frontal gyrus and left precentral gyrus; whereas task-load difficulty was associated with mainly bilateral activation in the PFC, fusiform gyrus, parietal cortex, and cerebellum; the impact of age mainly influenced the degree of activation in the left hemisphere.

2.6 Ethics

This thesis research project falls under the scope of a larger project approved by the Research Ethics Board at the University of Ottawa (REB #H-04-18-447). To ensure confidentiality, each participant was assigned a personal ID number instead of using their name. All electronic data are stored on password-protected computers, with additional passwords required for accessing the personal data files for each participant. All data are stored on Google Drive, which allows shared access between members of the lab. Additional backups are also saved on a separate hard drive which is encrypted, password-protected, and locked in the PIs office at the University of Ottawa. Any paper copies used for paying participants are locked inside a safe at Lees, building E, room 250A, which also requires a four-digit code to enter. A unique ID number was also used for all neuroimaging data and was processed on password-protected computers. All data will be stored for 15 years and then destroyed.

Chapter 3: Results

3.1 Participants

Session One results (Table 1): The mean age for younger adults was 23.10(±2.80) with 15.36(±1.40) years of education, and older adults had a mean age of 74.43(±6.43) with 16.65(±3.16) years of education. The means for positive and negative affect for younger adults were 29.36(±9.16) and 15.72(±2.98), and 36.22(±7.70) and 15.04(±1.93) for older adults. Regarding the DMS letter task, younger adults had a mean of 7.26(±0.96) for their cognitive capacity, 0.82(±0.15) for accuracy, 1.15s(±0.35) for response time, and 1.51s(0.79) for their adjusted inverse efficiency score (IES). For the same task, older adults had a mean of 7.02(±0.99) for their cognitive capacity, 0.80(±0.16) for accuracy, 1.66s(±0.31) for response time, and 2.16s(±0.59) for their IES.

Session Two results (Table 1) did not reassess age or education level, but the positive and negative affect scores were taken for a second time shortly before the MRI scan, and working memory performance was also reassessed while participants were in the MRI machine. Similarly to session one, the mean age for younger adults was 23.37(±2.81) with 15.54(±1.38) years of education, and older adults had a mean age of 73.50(±6.63) with 16.30(±2.83) years of education. The means for positive and negative affect for younger adults were 29.41(±8.50) and 16.02(±4.03), and 33.60(±8.45) and 15.03(±2.34) for older adults. Regarding the DMS letter task, younger adults had a mean of 7.22(±0.95) for their cognitive capacity, 0.84(±0.11) for accuracy, 1.07s(±0.27) for response time, and 1.31s(0.43) for their IES. For the same task, older adults had a mean of 7.07(±1.03) for their cognitive capacity, 0.81(±0.13) for accuracy, 1.55s(±0.23) for response time, and 1.96s(±0.50) for their IES.

Correlations between positive and negative affect were also analyzed for each session. For Session One, there was a non-significant positive relationship between positive and negative affect, $r(96) = 0.080$, $p = 0.436$. Similarly, there was a non-significant positive relationship between positive and negative affect during Session Two, $r(81) = 0.110$, $p = 0.330$.

Additional correlations were also assessed between the DMS Load 4 response times during Sessions One and Two, as well as the correlation between both runs of the DMS task while participants were performing the MRI component of this study. Significant positive correlations were found in both cases, $r(81) = 0.702$, $p < 0.001$ (between sessions – see Figure 3); and $r(81) = 0.791$, $p < 0.001$ (between both runs – see Figure 4). Separate correlations were also assessed within each age group. Younger adults (Session One and Two): $r(41) = 0.594$, $p < 0.001$; older adults (Session One and Two): $r(40) = 0.297$, $p = 0.063$; younger adults (Session Two – both DMS runs): $r(41) = 0.757$, $p <0.001$; and older adults (Session Two – both DMS runs): $r(40) = 0.483$, $p < 0.002$.

Table 1. Participant characteristics.

Session 1	**Younger Adults (n=50)**	**Older Adults (n=46)**	**Statistics**
Age, Mean Years (SD)	23.10 (2.80)	73.43 (6.43)	$t(60)= -49.00$, $p<0.001$*
Sex (M/F)	23/27	18/28	$\chi^2=0.46$, p=0.50
Education, Mean Years (SD)	15.36 (1.40)	16.65 (3.16)	$t(61)= -2.55$, $p=0.013$*
Emotional Affect			
Positive, Mean (SD)	29.36 (9.16)	36.22 (7.70)	$t(94)= -3.95$, $p=<0.001$
Negative, Mean (SD)	15.72 (2.98)	15.04 (1.93)	$t(85)= 1.33$, $p=0.187$*
DMS Letter Task			
Capacity, Mean (SD)	7.26 (0.96)	7.02 (0.99)	$t(94)= 1.24$, $p=0.218$

Load 4 Accuracy, Mean (SD)	0.82 (0.15)	0.80 (0.16)	$t(94)= 0.72$, $p=0.474$
Load 4 RT, Mean (SD)	1.15 (0.35)	1.66 (0.31)	$t(94)= -7.44$, $p=<0.001$
IES (SD)	1.51 (0.79)	2.16 (0.59)	$t(94)= -4.56$, $p=<0.001$

Session 2	**Younger Adults (n=41)**	**Older Adults (n=40)**	**Statistics**
Age, Mean Years (SD)	23.37 (2.81)	73.50 (6.63)	$t(52)= -44.48$, $p=<0.001$*
Sex (M/F)	17/24	15/25	$\chi^2=0.13$, $p=0.72$
Education, Mean Years (SD)	15.54 (1.38)	16.30 (2.83)	$t(56)= -1.54$, $p=0.130$*
Emotional Affect			
Positive, Mean (SD)	29.41 (8.50)	33.60 (8.45)	$t(79)= -2.22$, $p=0.029$
Negative, Mean (SD)	16.02 (4.03)	15.03 (2.34)	$t(64)= 1.37$, $p=0.176$*
DMS Letter Task			
Capacity, Mean (SD)	7.22 (0.95)	7.07 (1.03)	$t(79)= 0.69$, $p=0.490$
Load 4 Accuracy, Mean (SD)	0.84 (0.11)	0.81 (0.13)	$t(79)= 0.94$, $p=0.351$
Load 4 RT, Mean (SD)	1.07 (0.27)	1.55 (0.23)	$t(79)= -8.58$, $p=<0.001$
IES (SD)	1.31 (0.43)	1.96 (0.50)	$t(79)= -6.33$, $p=<0.001$

Abbreviations: DMS = delayed match-to-sample; IES = inverse efficiency score; RT= response time; SD = standard deviation

*Indicates Levene's Test was significant and the results for equal variances not assumed were reported

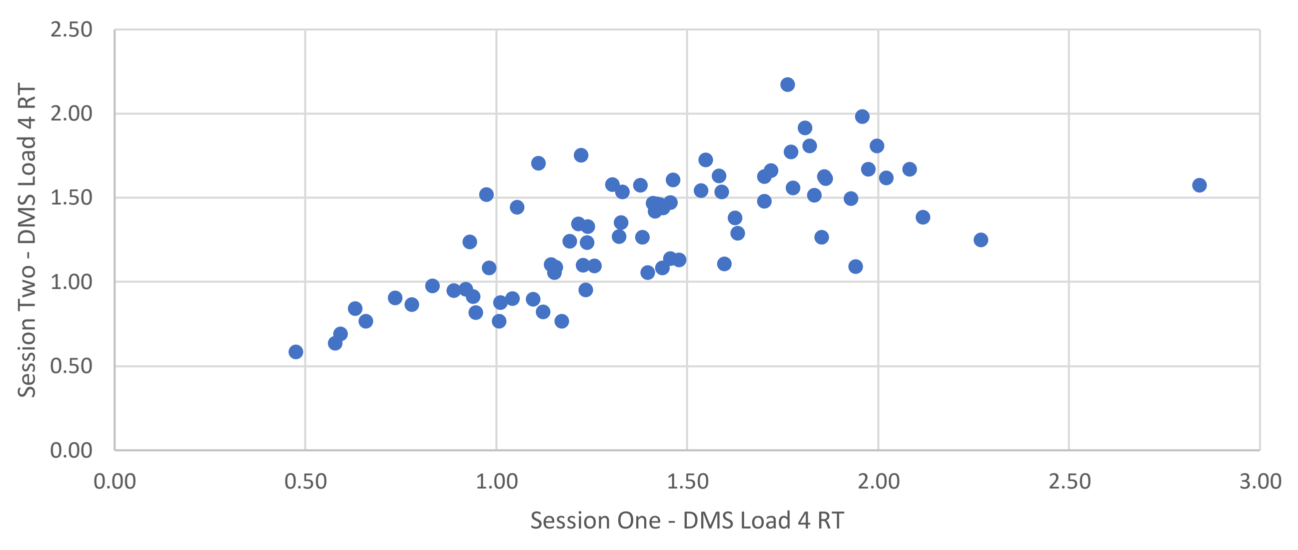

Figure 3. Scatterplot between DMS Load 4 RT during Sessions One and Two.

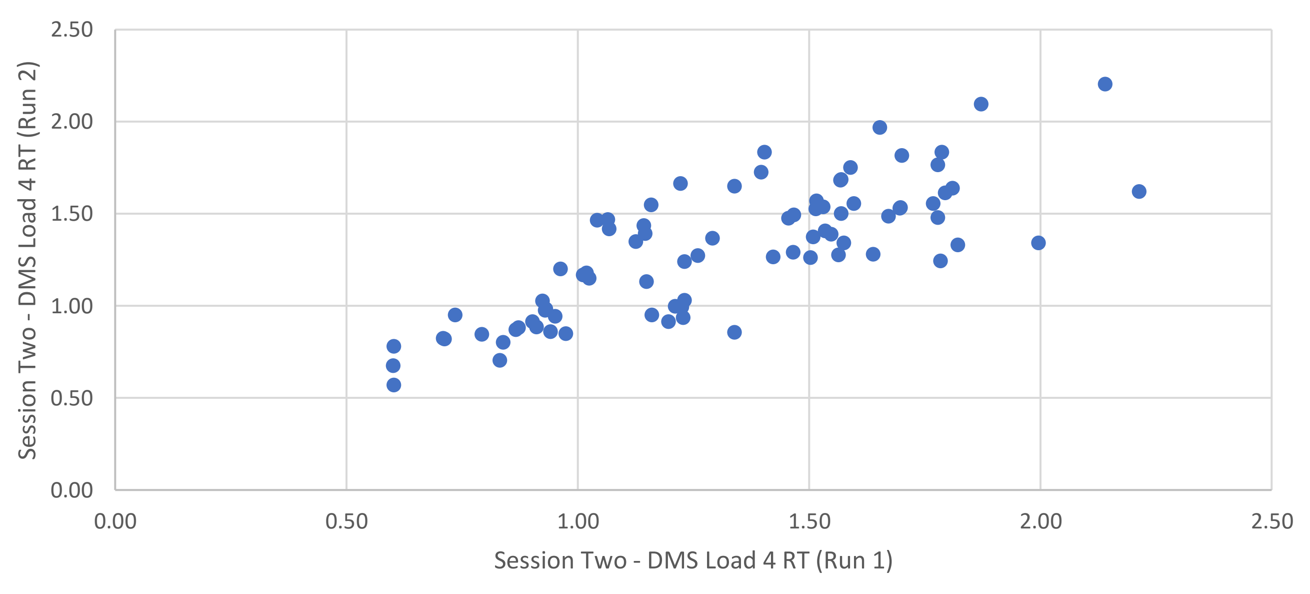

Figure 4. Scatterplot between DMS Load 4 RT of both runs during Session Two.

3.2 Multiple Moderation Analyses – Session One

In model 1 (Table 2), the independent variable was age (younger vs. older), the dependent variable was DMS Load 4 RT, moderator one was cognitive reserve (i.e., years of education), and moderator two was positive affect. The overall model was significant, $F(5,90) = 15.03$, $p < 0.001$, $R^2 = 0.47$. The main effects of age and education were significant, $b = 0.59$, $t(90) = 17.59$, $p < 0.001$, and $b = -0.13$, $t(90) = -2.64$, $p = 0.010$, respectively. The main effect of positive affect was not significant, $b = -0.01$, $t(90) = -1.77$, $p = 0.081$. The interaction of age x education was significant, $b = 0.13$, $t(90) = 2.54$, $p = 0.013$, as well as the interaction age x positive affect, $b = 0.02$, $t(90) = 2.08$, $p = 0.041$.

In model 2 (Table 2), all variables remained the same except for the positive affect moderator, which was replaced with the negative affect moderator. The overall model was significant, $F(5,90) = 14.87$, $p < 0.001$, $R^2 = 0.45$. The main effects of age and education were significant, $b = 0.60$, $t(90) = 8.32$, $p < 0.001$, and $b = -0.13$, $t(90) = -2.62$, $p = 0.010$, respectively. The main effect of negative affect was not significant, $b = 0.01$, $t(90) = 0.67$, $p = 0.506$. The interaction age x education was significant, $b = 0.13$, $t(90) = 2.53$, $p = 0.013$, and the interaction age x negative affect was not significant, $b = -0.02$, $t(90) = -0.70$, $p = 0.487$.

Similarly to model 1, model 3 (Table 2) included all the same variables but used the calculated IES value as the dependent variable. Overall, this model was significant, $F(5,90) = 7.51$, $p < 0.001$, $R^2 = 0.36$. The main effect of age, $b = 0.78$, $t(90) = 4.59$, $p <0.001$, and education, $b = -0.31$, $t(90) = -2.14$, $p = 0.035$, were significant, and the main effect of positive affect was not significant, $b = -0.01$, $t(90) = -1.34$, $p = 0.183$. Both interactions were significant: age x education, $b = 0.30$, $t(90) = 2.05$, $p = 0.043$, and age x positive affect, $b = 0.04$, $t(90) = 3.33$, $p = 0.001$.

Lastly, model 4 (Table 2) was similar to model 2 but used the calculated IES value as the dependent variable. The overall model was significant, $F(5,90) = 6.55$, $p < 0.001$, $R^2 = 0.31$. The main effects of age and education were significant, $b = 0.86$, $t(90) = 5.16$, $p < 0.001$, and $b = -0.29$, $t(90) = -2.04$, $p = 0.044$, respectively. The main effect of negative affect was not significant, $b = 0.003$, $t(90) = 0.93$, $p = 0.926$. The interaction age x education was significant, $b = 0.29$, $t(90) = 0.05$, $p = 0.051$, and the interaction age x negative affect was not significant, $b = 0.03$, $t(90) = 0.58$, $p = 0.579$.

Graphs from all four models were created to visualize the significant interaction effects (Figures 3-6). For the conditional effects of age at varying values of the two moderators, refer to Table 3. When cognitive reserve was low (i.e., fewer years of education) and positive (or negative) affect was low, younger adults had response times of 1.43s (model 1), 1.34s (model 2), 2.11s (model 3), and 2.00s (model 4). When cognitive reserve was low and positive (or negative) affect was high, younger adults had response times of 1.29s (model 1), 1.40s (model 2), 1.89s (model 3), and 2.02s (model 4). When cognitive reserve was high and positive (or negative) affect was low, the response times for younger adults were 0.81s (model 1), 0.75s (model 2), 0.70s (model 3), and 0.66s (model 4). Lastly, when cognitive reserve and positive (or negative) affect were both high, younger adults had the following response times, 0.67s (model 1), 0.81s (model 2), 0.48s (model 3), and 0.68s (model 4).

Regarding older adults, when cognitive reserve was low (i.e., fewer years of education) and positive (or negative) affect was low, older adults had response times of 1.56s (model 1), 1.67s (model 2), 1.78s (model 3), 2.09s (model 4). When cognitive reserve was low and positive (or negative) affect was high, older adults had response times of 1.70s (model 1), 1.64s (model 2), 2.36s (model 3), and 2.29s (model 4). When cognitive reserve was high and positive (or negative) affect was low, the response times for older adults were 1.56s (model 1), 1.68s (model 2), 1.75s (model 3), and 2.07s (model 4). Lastly, when cognitive reserve and positive (or negative) affect were both high, older adults had the following response times: 1.70 (model 1), 1.64s (model 2), 2.33s (model 3), and 2.27s (model 4).

Table 2. Association between age and working memory with cognitive reserve (i.e., years of education) and emotional affect as moderators (Session 1 (n=96)).

	b **(BP 95% CI)**	***SE B***	***t***	***p***
Model 1				
DMS RT (Load 4)				
Constant	1.04 (0.93, 1.15)	0.055	17.59	<0.001
Age	0.59 (0.44, 0.74)	0.072	7.36	<0.001
Education	-0.13 (-0.23, -0.06)	0.043	-2.64	0.010
Positive Affect	-0.01 (-0.02, 0.00)	0.004	-1.77	0.081
Age x Education	0.13 (0.06, 0.24)	0.046	2.54	0.013
Age x Positive Affect	0.02 (0.00, 0.03)	0.007	2.08	0.041
Model 2				
DMS RT (Load 4)				
Constant	1.06 (0.95, 1.16)	0.054	19.48	<0.001
Age	0.60 (0.47, 0.74)	0.068	8.32	<0.001
Education	-0.13 (-0.22, -0.06)	0.042	-2.62	0.010
Negative Affect	0.01 (-0.02, 0.04)	0.016	0.67	0.506
Age x Education	0.13 (0.05, 0.23)	0.044	2.53	0.013
Age x Negative Affect	-0.02 (-0.07, 0.04)	0.026	-0.70	0.487
Model 3				
DMS IES (Load 4)				
Constant	1.27 (0.99, 1.52)	0.133	9.22	<0.001
Age	0.78 (0.47, 1.11)	0.161	4.59	<0.001
Education	-0.31 (-0.59, -0.11)	0.123	-2.14	0.035
Positive Affect	-0.01 (-0.03, 0.01)	0.009	-1.34	0.183
Age x Education	0.30 (0.10, 0.59)	0.124	2.05	0.043
Age x Positive Affect	0.04 (0.02, 0.07)	0.013	3.33	0.001
Model 4				
DMS IES (Load 4)				
Constant	1.32 (1.07, 1.53)	0.114	10.49	<0.001
Age	0.86 (0.59, 1.17)	0.150	5.16	<0.001
Education	-0.29 (-0.56, -0.09)	0.119	-2.04	0.044
Negative Affect	0.003 (-0.05, 0.06)	0.029	0.93	0.926
Age x Education	0.29 (0.08, 0.57)	0.120	0.05	0.051
Age x Negative Affect	0.03 (-0.08, 0.14)	0.057	0.58	0.579

Abbreviations: BP = bootstrap percentile; CI = confidence interval; DMS = delayed match-to-sample; IES = inverse efficiency score; RT = response time

Table 3. Conditional effects of age at varying values of cognitive reserve (i.e., years of education) and emotional affect.

DMS RT (Load 4)

Cognitive Reserve	**Positive Affect**	**Negative Affect**	***b* (95% CI)**	***SE B***	***t***	***p***
Low	Low		0.13 (-0.13, 0.39)	0.133	0.97	0.334
Low	High		0.41 (0.16, 0.66)	0.125	3.28	0.001
High	Low		0.76 (0.37, 1.15)	0.196	3.86	<0.001
High	High		1.04 (0.68, 1.40)	0.182	5.71	<0.001
Low		Low	0.33 (0.06, 0.60)	0.137	2.42	0.018
Low		High	0.23 (-0.01, 0.48)	0.123	1.90	0.061
High		Low	0.93 (0.59, 1.27)	0.171	5.45	<0.001
High		High	0.83 (0.47, 1.19)	0.182	4.58	<0.001

DMS IES (Load 4)

Cognitive Reserve	**Positive Affect**	**Negative Affect**	***b* (95% CI)**	***SE B***	***t***	***p***
Low	Low		-0.33 (-0.97, 0.31)	0.323	-1.02	0.311
Low	High		0.47 (-0.16, 1.09)	0.313	1.49	0.140
High	Low		1.05 (0.18, 1.93)	0.440	2.39	0.019
High	High		1.85 (0.91, 2.79)	0.472	3.91	<0.001
Low		Low	0.09 (-0.64, 0.81)	0.367	0.24	0.815
Low		High	0.27 (-0.38, 0.91)	0.325	0.82	0.414
High		Low	1.41 (0.63, 2.19)	0.392	3.60	<0.001
High		High	1.59 (0.57, 2.61)	0.515	3.08	0.003

Abbreviations: CI = confidence interval; DMS = delayed match-to-sample; IES = inverse efficiency score

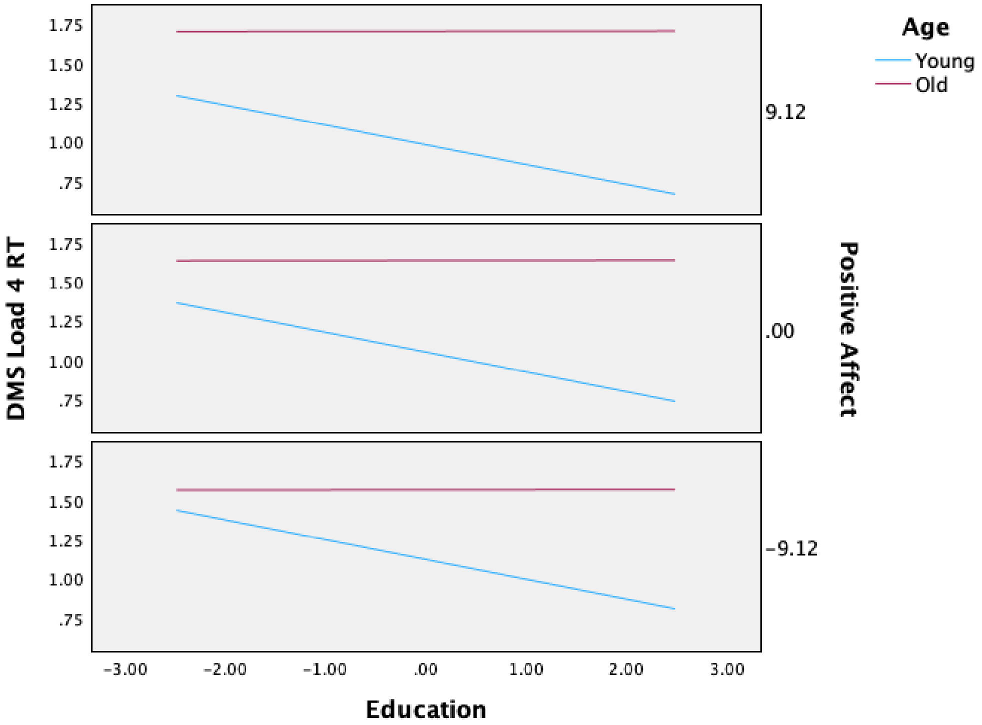

Figure 5. Multiple moderation of education (CR proxy) and positive affect on the relationship between age and DMS load 4 RT.

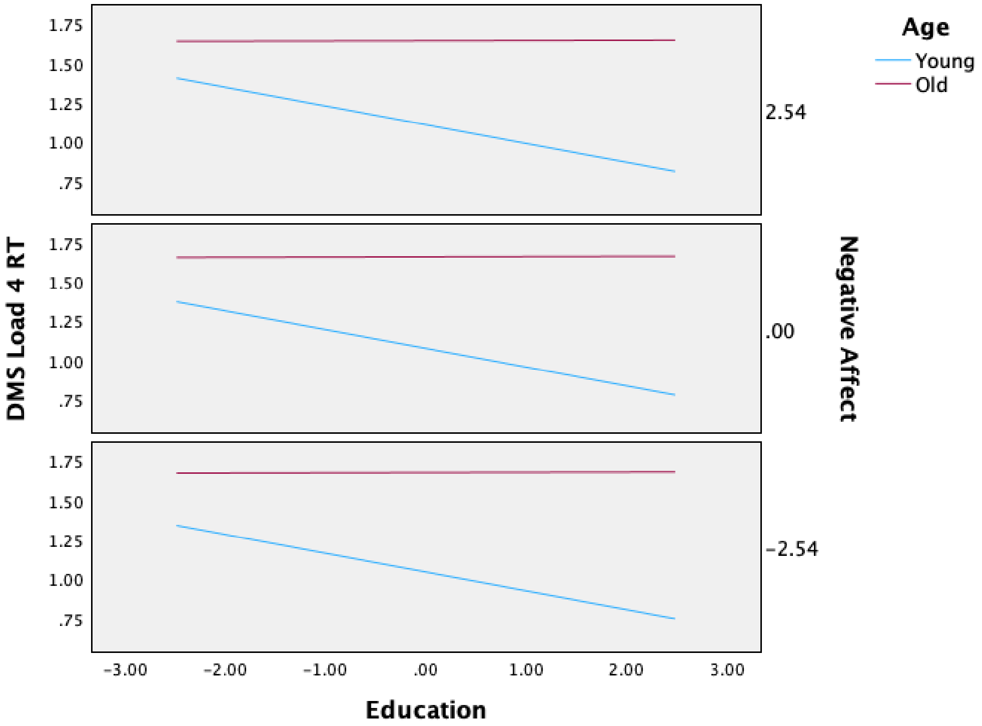

Figure 6. Multiple moderation of education (CR proxy) and negative affect on the relationship between age and DMS load 4 RT.

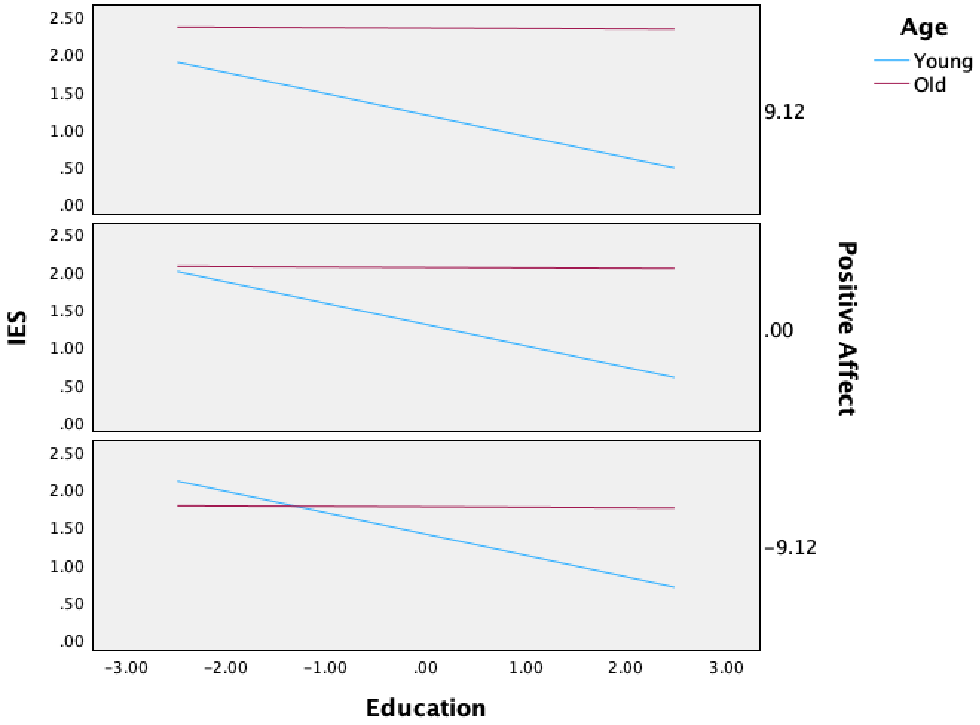

Figure 7. Multiple moderation of education (CR proxy) and positive affect on the relationship between age and IES.

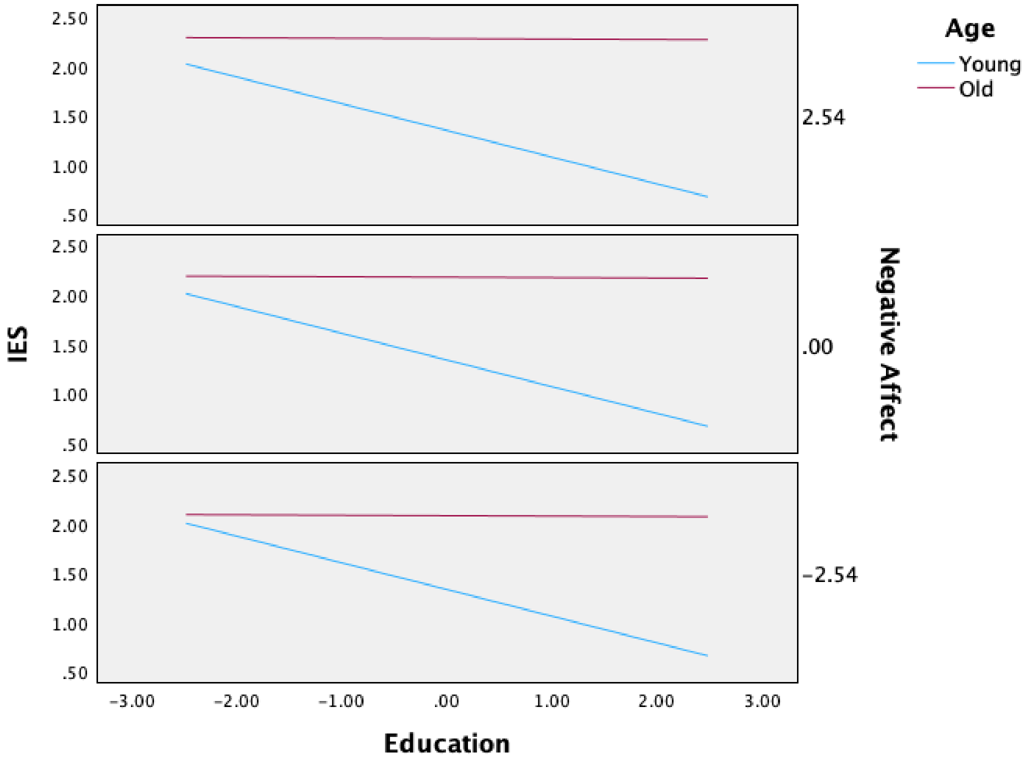

Figure 8. Multiple moderation of education (CR proxy) and negative affect on the relationship between age and IES.

3.3 Multiple Moderation Analyses – Session Two

All models from Session One were re-run using the data collected from Session Two (Table 3). From these results, most main effects and interactions were not significant: age x education, $F(1,75) = 0.007$, $p = 0.935$, $R^2 = <0.001$ (model 5); $F(1,75) = 0.0002$, $p = 0.989$, $R^2 = <0.001$ (model 6); $F(1,75) = 0.209$, $p = 0.649$, $R^2 = 0.005$ (model 7); $F(1,75) = 0.136$, $p = 0.713$, $R^2 = 0.003$ (model 8); and, age x positive/negative affect, $F(1,75) = 0.839$, $p = 0.363$, $R^2 = 0.006$ (model 5); $F(1,75) = 0.100$, $p =0.753$, $R^2 = <0.001$ (model 6); $F(1,75) = 1.236$, $p = 0.270$, $R^2 = 0.015$ (model 7); $F(1,75) = 2.084$, $p = 0.153$, $R^2 = 0.022$ (model 8). The main effect of age was the only variable that remained significant for each model: $b = 0.48$, $t(75) = 6.27$, $p < 0.001$ (model 5), $b = 0.48$, $t(75) = 6.43$, $p < 0.001$ (model 6), $b = 0.65$, $t(75) = 4.95$, $p < 0.001$ (model 7), and $b = 0.71$, $t(75) = 5.30$, $p < 0.001$ (model 8). No graphs of these models could be created since no significant interactions were found.

Table 4. Association between age and working memory with cognitive reserve (i.e., years of education) and emotional affect as moderators (Session 2 (n=81)).

	b **(BP 95% CI)**	***SE B***	***t***	***p***
Model 5 **DMS RT (Load 4 fMRI)**				
Constant	1.06 (0.95, 1.17)	0.055	16.77	<0.001
Age	0.48 (0.35, 0.60)	0.065	6.27	<0.001
Education	-0.01 (-0.11, 0.09)	0.053	-0.02	0.988
Positive Affect	-0.00 (-0.01, 0.01)	0.005	-0.24	0.808
Age x Education	0.00 (-0.10, 0.10)	0.054	-0.08	0.935
Age x Positive Affect	0.01 (-0.01, 0.02)	0.007	0.92	0.363
Model 6 **DMS RT (Load 4 fMRI)**				
Constant	1.06 (0.95, 1.18)	0.056	16.73	<0.001
Age	0.48 (0.35, 0.61)	0.067	6.43	<0.001
Education	-0.01 (-0.10, 0.09)	0.052	-0.02	0.982
Negative Affect	-0.00 (-0.03, 0.01)	0.010	-0.37	0.716
Age x Education	0.01 (-0.09, 0.11)	0.054	-0.01	0.989
Age x Negative Affect	0.01 (-0.03, 0.04)	0.017	0.32	0.753
Model 7 **DMS IES (Load 4 fMRI)**				
Constant	1.30 (1.14, 1.45)	0.080	13.82	<0.001
Age	0.65 (0.43, 0.89)	0.115	4.95	<0.001
Education	0.01 (-0.14, 0.16)	0.080	0.15	0.883
Positive Affect	-0.00 (-0.02, 0.01)	0.008	-0.58	0.562
Age x Education	-0.04 (-0.20, 0.12)	0.084	-0.46	0.649
Age x Positive Affect	0.02 (-0.01, 0.05)	0.014	1.11	0.270
Model 8 **DMS IES (Load 4 fMRI)**				
Constant	1.30 (1.13, 1.46)	0.084	13.70	<0.001
Age	0.71 (0.48, 0.97)	0.125	5.30	<0.001
Education	0.01 (-0.15, 0.15)	0.080	0.13	0.893
Negative Affect	0.01 (-0.02, 0.05)	0.018	0.58	0.562
Age x Education	-0.03 (-0.18, 0.14)	0.084	-0.37	0.713
Age x Negative Affect	0.06 (-0.02, 0.17)	0.046	1.44	0.153

Abbreviations: BP = bootstrap percentile; CI = confidence interval; DMS = delayed match-to-sample; fMRI = functional magnetic resonance imaging; IES = inverse efficiency score; RT = response time

3.4 Group Level fMRI Analyses

A contrast of Older adults > Younger adults (two-sample t-test) was used to assess the significant brain regions older adults used during the DMS letter working memory task compared to younger adults. A corrected p-value FWE 0.05 was used to assess significance and no masking was applied. A height threshold of T = 4.97 was reported, with three key areas of activation in the frontal, parietal, and occipital brain regions (Table 5). Specifically, there was significant activity in the left precentral gyrus (Fig. 7), right lingual gyrus (Fig. 8), and right postcentral gyrus (Fig. 9).

Table 5. Group Level imaging results.

Region	**Lat**	**BA**	**Xmm**	**Ymm**	**Zmm**	**Z**	**k**
Precentral	L	4	-34	-14	52	5.37	12
Lingual	R	19	18	-68	-6	4.96	50
Postcentral	R	2	60	-24	44	4.80	11

Abbreviations: BA = Brodmans area; Lat = laterality; k = cluster size

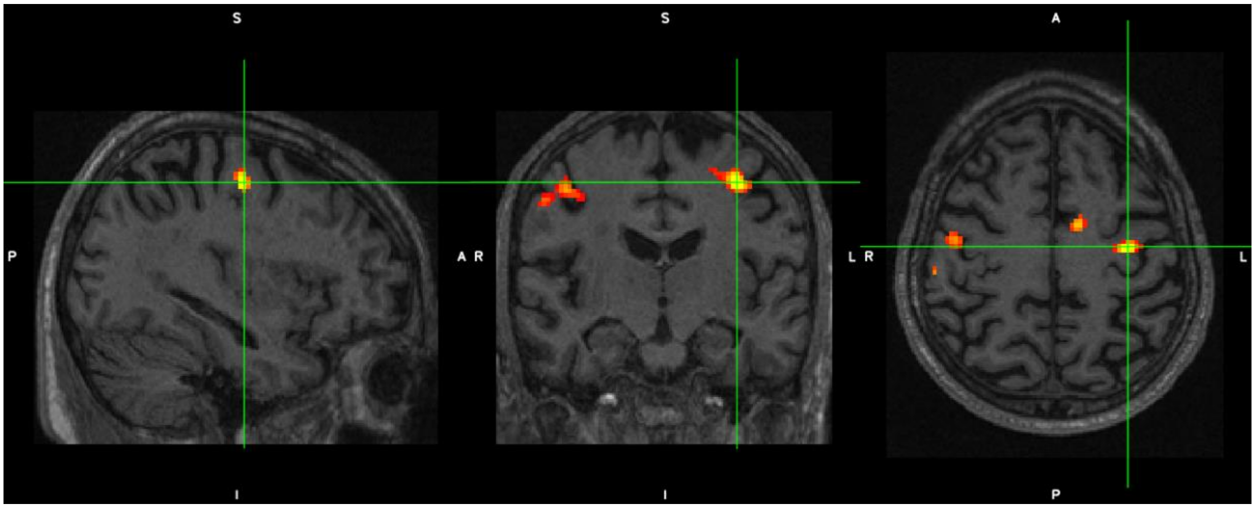

Figure 9. DMS Load 4 fMRI Older > Younger, Left Precentral Gyrus.

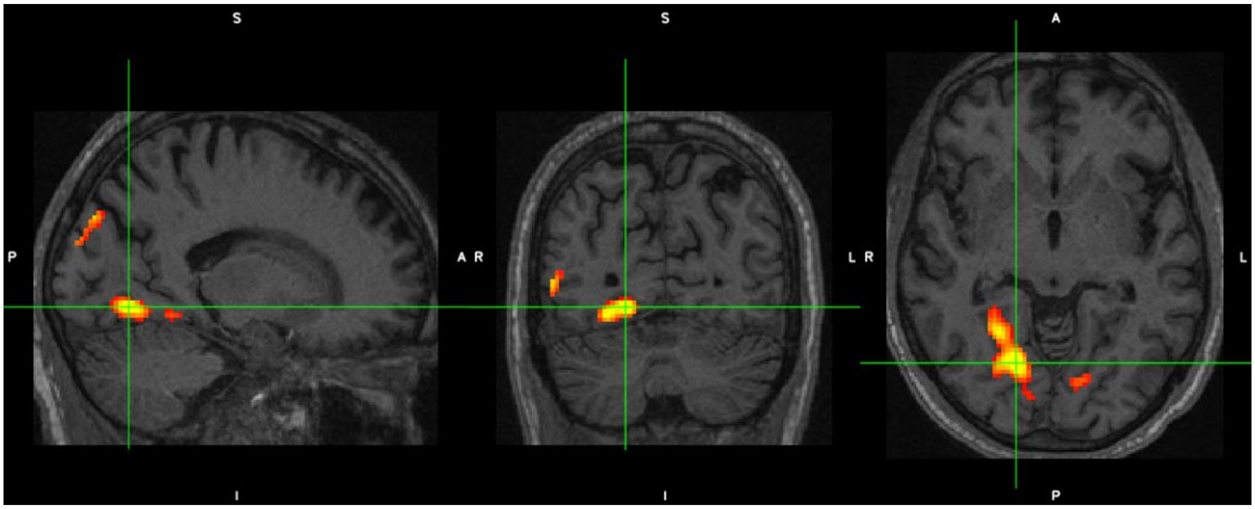

Figure 10. DMS Load 4 fMRI Older > Younger, Right Lingual Gyrus.

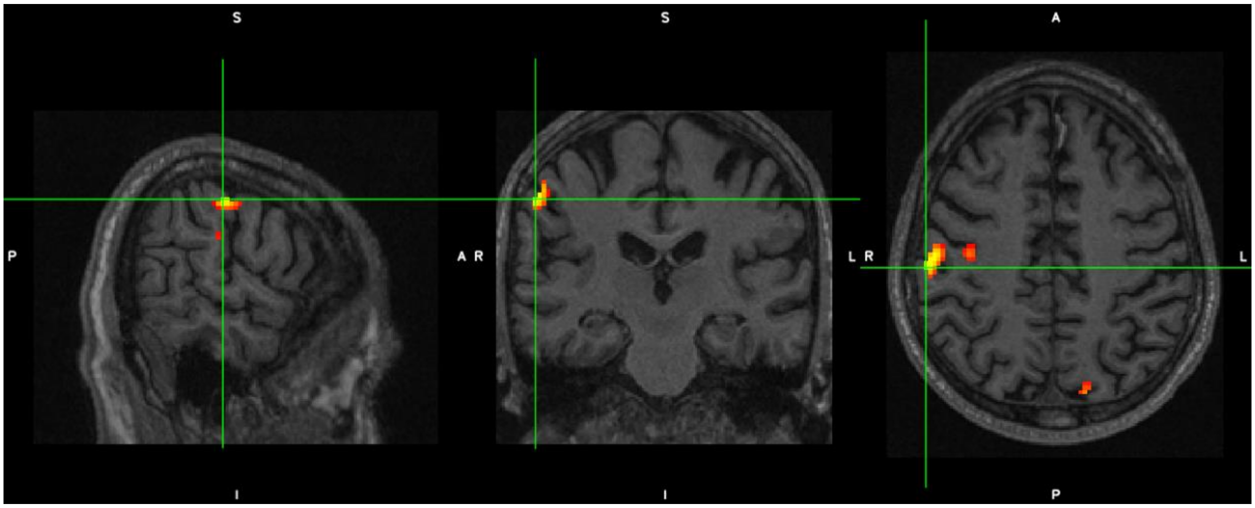

Figure 11. DMS Load 4 fMRI Older > Younger, Right Postcentral Gyrus.

Chapter 4: Discussion

The overall aim of this study was to investigate the potential moderating effects of cognitive reserve and emotional affect on the association between age and working memory performance. In terms of the literature regarding aging, emotions, cognition, and cognitive reserve, previous studies have largely focused on the moderating effects of cognitive reserve proxies (e.g., years of education, occupational attainment, leisure activities) regarding the relationship between age and cognition. For example, various fMRI studies found that higher cognitive reserve (e.g., more years of education) is associated with better working memory performance (Steffener et al., 2012; Stern, 2009). These studies have also reported a number of brain regions that are activated during the task, which varies between younger and older adults, highlighting the different mechanisms of cognitive reserve (i.e., neural reserve and neural compensation).

Along with cognitive reserve, emotions have also been found to have a powerful impact on cognition. Frederickson’s (1998) broaden-and-build theory helps elucidate how our positive and negative emotions affect our cognitive health and wellbeing. Positive emotions (e.g., joy, love, interest) provide a psychological benefit which helps broaden our thought-action repertoires and builds up our physical, intellectual, social, and psychological resources (Fredrickson, 2001, 2004). These resources can then be called upon when needed as we age. In contrast, negative emotions (e.g., fear, anger) tend to narrow our thought-action repertoires and do not aid in building personal resources.

Given the powerful influence positive and negative emotions have, emotional regulation and motivation may serve as protective factors regarding the maintenance of cognitive abilities as we age, and the beneficial effects of emotional wellbeing may enhance cognition by building brain resilience (Mohindru et al., 2023). Previous studies have highlighted the relationship between cognitive reserve and emotion recognition tasks (e.g., Demenescu et al., 2014; Guerrini et al., 2022), but the relationship between cognitive reserve and emotional wellbeing is less known. Therefore, these research studies as well as others previously mentioned provided the rationale for the current study.

Using multiple moderation, cognitive reserve (i.e., years of education) and emotional affect (positive and negative) were entered as potential moderators in various models exploring the association between age (younger vs. older) and working memory performance using a delayed match-to-sample letter task. It was hypothesized that there would be a significant interaction between age and cognitive reserve, such that greater cognitive reserve (i.e., more years of education) would be associated with better working memory performance. It was also hypothesized that there would be a significant interaction between age and positive affect, such that greater positive affect would yield better working memory performance. In contrast, it was hypothesized that greater negative affect would hinder performance on the working memory task. Lastly, it was hypothesized that older adults would require additional brain activation in frontal and parietal regions when performing the cognitive task while in the MRI.

4.1 Descriptive Analyses Findings

The initial descriptive analyses identified a significant difference in terms of years of education among younger and older adults, such that older adults had more years of education. This is understandable given that most of the younger adults included in the study were still completing their undergraduate or graduate degrees. As years of education was used as a proxy for cognitive reserve, this also highlights that the older adults had slightly higher cognitive reserve compared to the younger adults. Additionally, there was a significant difference regarding level of positive affect between both age groups. Older adults reported much higher positive affect compared to younger adults, which may be partially explained by the socioemotional selectivity theory (Carstensen, 1992). According to this theory, older adults tend to focus more on positive information and less on negative information due to their limited time they have left to live. In contrast, there was no significant difference between the age groups regarding negative affect, and both averages were low. Thus, having high positive affect indicates that participants may have been feeling energized, motivated, or focused, whereas the low levels of negative affect may have attributed to feelings of calmness or serenity (Watson et al., 1988). Lastly, participants also significantly differed in terms of their response times on the working memory task, with older adults requiring more time compared to younger adults, which has also been demonstrated in previous literature (Mohindru et al., 2023).

When taking into consideration response times and accuracy scores for both age groups using the inverse efficiency score (IES), older adults also had higher scores compared to the younger adults. This additional score was included in order to get a better sense of the age effect when response times and accuracy values are combined together and supplements the findings of only analyzing response times. For the purpose of the current study, accuracy values between groups were matched based on an approximate 80% accuracy rate; thus, the IES score predominately reflects the response time differences between both age groups.

When analyzing the results from the second session, a reduced sample was used due to fifteen participants being unable to complete the MRI portion of this study. As such, the significant difference based on years of education mentioned previously was no longer present in this reduced sample. However, there was still a significant difference in terms of positive affect, with older adults reflecting higher positive affect compared to younger adults; no significant difference was found regarding negative affect. Older adults also significantly differed in terms of their response time and IES, with higher scores compared to the younger adults.

There were significant positive correlations between the DMS Load 4 response times across both sessions, as well as across both runs during the MRI portion of this study. This highlights that participants performed similarly in terms of their response times between both session time points, and they also maintained similar performance levels when completing the DMS letter task for a second time while in the MRI.

Lastly, non-significant positive correlations between positive and negative affect were found across both sessions. This finding is supported in the literature (Watson et al., 1988; Watson & Clark, 1997), which has shown that these correlations tend to be very low. Indeed, a further study also found that positive and negative affect are independent of each other when assessed as trait affect (e.g., how someone is feeling on average) and state affect (e.g., how someone is feeling in the current moment) (Schmukle et al., 2002). Thus, the current study supports the findings that positive and negative affect are independent of each other with a specific focus on the state of the individual in the present moment when they completed the questionnaires during both sessions.

4.2 Multiple Moderation Findings – Session One

Significant multiple moderation was found when analyzing the data from the first session. Specifically, in model 1 the relationship between age (younger vs. older) and working memory performance on the DMS letter task at load level 4 (response time in seconds) was assessed using cognitive reserve (i.e., years of education) as moderator one, and positive affect as moderator two. Based on this model, there was a significant interaction between age (younger vs. older) and cognitive reserve (i.e., years of education) as well as a significant interaction between age (younger vs. older) and positive affect. These results are comparable to other studies which observed significant moderating effects of cognitive reserve (e.g., Steffener et al., 2012; Stern, 2009), as well as the literature surrounding the strong influence of positive emotions (e.g., Frederickson, 1998, 2001, 2004). However, to our knowledge, this is one of the first studies that used multiple moderation to get a better sense of how both cognitive reserve and emotional affect alter the relationship between age and working memory performance.

In model 2, which was based on the same format as model 1 but included negative affect as the second moderator instead of positive affect, there was a significant interaction between age (younger vs. older) and cognitive reserve (i.e., years of education), but no significant interaction between age (younger vs. older) and negative affect. The lack of a significant interaction with negative affect was expected based on the initial descriptive analyses which indicated low levels for both age groups.

Model 3 used the adjusted inverse efficiency score (IES) (Bruyer & Brysbaert, 2011; Townsend & Ashby, 1978, 1983) as the dependent variable, which combined the response time and accuracy values of the DMS load 4. Similarly to model 1, significant multiple moderation was found between age (younger vs. older) and cognitive reserve (i.e., years of education), as well as age (younger vs. older) and positive affect. These effects were larger in comparison to model 1 which only included response times as the dependent variable, highlighting the importance of exploring these relationships using combined response time and accuracy values. Model 4 also used IES as the dependent variable and a significant interaction between age (younger vs. older) and cognitive reserve (i.e., years of education) was found, but there was no significant interaction between age (younger vs. older) and negative affect, which was comparable to the findings from model 2.

Based on the significant interactions from the first session, graphs of the data were created using the PROCESS Hayes code generated in SPSS (Hayes, 2018) to get a better sense of how these moderators impacted the data. Regarding the interaction of age (younger vs. older) with cognitive reserve (i.e., years of education), and age (younger vs. older) with positive affect, there was a significant positive effect when i) cognitive reserve was low and positive affect was high, ii) cognitive reserve was high and positive affect was low, and iii) cognitive reserve was high and positive affect was high; no significant effect was found when cognitive reserve and positive affect were both low. These effects were strongest when cognitive reserve and positive affect were both high. When looking at the graphs, it appears that these significant effects were driven by the younger adults. Older adults maintained a similar response time regardless of their level of cognitive reserve or positive affect. These response times were consistently longer than the younger adults, highlighting a strong age effect.

These results differed slightly when assessing the models with IES as the dependent variable. Specifically, the significant effect found when cognitive reserve was low and positive affect was high was no longer significant when IES was included as the dependent variable. Significant positive effects were only found when cognitive reserve was high and positive affect was high or low, with the strongest effects noticeable when both cognitive reserve and positive affect were high. Similarly to the previous models using just response time as the dependent variable, these results were strongly driven by the younger adults, again highlighting an age effect.

It is also worth noting that in the models with negative affect as a second moderator, cognitive reserve (i.e., years of education) continued to significantly moderate the association between age (younger vs. older) and working memory performance (based on response time, or a combination of response time and accuracy). Indeed, higher cognitive reserve was associated with better working memory performance, and this effect was mainly noticeable among the younger adults.

4.3 Multiple Moderation Findings – Session Two

Models 5-8 analyzed the data from the second session where all participants performed the DMS letter task while in the MRI scanner. It was expected that significant multiple moderation would also be found during this session; however, only the main effect of age remained significant across all models. The lack of significant multiple moderation may be due the reduced sample that was used, which also lowered the effect size across all models.

4.4 Group Level fMRI Findings

Lastly, although no significant moderation was found during the second session, we still analyzed the brain activity pattern during the DMS letter task at load level 4 to identify any brain regions that older adults were using significantly more than younger adults. Significant brain activation was found in the left frontal precentral gyrus, right parietal lingual gyrus, and right occipital postcentral gyrus. These areas of activation are comparable to similar studies which found significant activation in frontal, parietal, and cerebellum regions (Stern, 2009; Zarahn et al., 2007). It is worth noting that these authors also found significant brain activity in the parahippocampal gyrus which older adults used as the letter Sternberg task increased in difficulty, but this was not observed with the current study. Thus, further research is needed in order to identify the reasons for this discrepancy.

4.5 Limitations

This study had several limitations that need to be discussed. Firstly, this study used a cross-sectional design, so no causal inferences can be made. Using a longitudinal design would be beneficial to observe the changes in cognitive reserve, emotional wellbeing and working memory performance over time. This study may also lack generalizability as most younger adults were acquired from universities in Ottawa, which may have yielded a sample with more years of education compared to the general population. To reduce possible selection bias, flyers were posted at recreation centers and other broader areas in Ottawa; participants were also recruited on a first come, first served basis. Additionally, this study is limited with regards to possible practice and order effects. In order to complete the study, it was necessary that participants fully understood the cognitive tasks by practicing them, and the behavioural portion of session one had to be completed before the neuroimaging portion of session two because information from the first session was used in the second session.

Additionally, cognitive reserve was only assessed using a proxy of years of education. Although this method is commonly used, a more efficient way of assessing cognitive reserve is by incorporating indicators of life experiences such as education, occupation and leisure activities as a composite measure, which provides a more reliable, accurate and complex representation of cognitive reserve (Porricelli et al., 2024).

It is also possible that participant fatigue may have occurred while completing the tasks during either session; however, this was mitigated to the best of our ability by taking breaks when needed. While in the MRI, participants may have experienced heightened levels of stress and anxiety. Indeed, past research has indicated that participants have greater anxiety when they see the narrowness of the bore, the claustrophobic and restrictive sensation once inside, and the loud noises during the scans (van Minde et al., 2014). To help prevent any excessive feelings of stress or anxiety, participants were asked how they were doing after each task was completed; if participants were in distress, they had the option of pressing a squeeze ball to stop the task.

As such, a number of participants were not able to complete the MRI session due to their body size, nervousness, or inability to properly see the screen during the working memory task. Despite satisfying the height and weight recommendations for the scanner, some participants were not able to get in a comfortable position regardless of our efforts. Once in the scanner, some participants became too nervous, and it had to be stopped. Although all participants confirmed that they would be able to do the scan, for many of them this was their first time, so future studies may want to use an available mock scanner to simulate the noise and size of the MRI machine prior to performing the actual scan. Unfortunately, some of the older adult participants were not able to clearly see the screen while in the MRI despite giving them MRI-safe glasses. While these lenses can help, they are not specific to everyone's prescription, so images on the screen appeared blurry. Increasing the size of the letters on the screen helped in some cases, but those with poorer eyesight were not able to complete the tasks.

Additionally, participants were asked to complete the DMS letter task as quickly and accurately as possible. This may have caused a speed-accuracy trade-off, whereby some participants may have attributed more attention to going quickly to have faster reaction times, or they may have gone more slowly to aid with accuracy. The current study matched participants based on 80% accuracy during Load 4 of the DMS letter task. This suggests that older adults still had longer reaction times despite achieving similar accuracy scores compared to younger adults. At Load 5 of the DMS letter task, older adults had slightly lower accuracy, but there was no significant difference between the age groups. Future studies may wish to assess physical limitations of participants (e.g., arthritis in the hands) prior to performing cognitive tasks which require speed and accuracy.

Lastly, the majority of our participants were excited to participate in this study, so their level of negative affect was quite low, and we were unable to determine any significant effects negative affect might have had in the models.

4.6 Conclusions and Future Directions

There was significant multiple moderation of cognitive reserve and positive affect on the relationship between age and working memory performance. Having higher cognitive reserve and greater positive affect led to the strongest positive effect. This effect was also noticeable when cognitive reserve was low and positive affect was high, indicating the beneficial role that emotional wellbeing has on working memory performance. These results were strongly driven by age, with younger adults performing faster than older adults. Regardless of the level of cognitive reserve or positive affect, older adults maintained consistently longer response times, highlighting the strong effect that age has on working memory performance. Lastly, despite older adults not performing as well as younger adults, they still recruited key areas of the brain to complete the task, namely, regions of the frontal, parietal, and occipital cortices.

Future studies would benefit from having a larger sample size and using a longitudinal study design to observe changes in cognitive reserve and emotional wellbeing as people age and how these changes may affect working memory performance. Additionally, having a larger sample size would also allow future researchers to use moderated moderation techniques to observe the potential moderating effects that positive and negative emotions have on cognitive reserve, which could then moderate the relationship between age and working memory.

Emotional wellbeing and mental health encompass many aspects, so it would also be advisable to use updated emotion-related and mental health questionnaires to better assess this variable. Similarly, cognitive reserve could be analyzed using a composite measure that combines education, occupation, and leisure activities, as this better reflects this measure than just education alone. Overall, having a clearer understanding of the roles that cognitive reserve and emotions having on working memory performance as we age may help individuals better adapt to age-related changes. Placing more emphasis on mental health at an earlier age by incorporating techniques such as meditation, mindfulness, or yoga, may help individuals age better and also potentially increase their level of cognitive reserve, which may help delay cognitive decline.

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Appendix

Appendix A: Neuropsychological Battery

1. Buschke Selective Reminding Test
    - Immediate Recall
    - Delayed Recall
    - Recognition
2. Progressive Matrices
3. Delayed match-to-sample Letter Task
    - Practice
    - Staircase Design
    - Block Design
4. Stroop
    - Colour
    - Word
    - Colour and Word
5. Wisconsin Card Sorting Test
6. Visual-spatial Working Memory Dot Task
    - Practice
    - Staircase Design
    - Block Design
7. Vocabulary
    - Antonyms
    - American National Adult Reading Test
8. N-back
    - Practice
    - 0, 1, and 2-back
9. Digit Span
    - Forward
    - Backward
10. Pattern Comparison Speed Task

Appendix B: Lifestyle/Behaviour Questionnaire List

1. Sleep Pattern Survey (Bastien, Vallières, & Morin, 2001; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989)
2. Instrumental Activities of Daily Living Survey (Fillenbaum & Smyer, 1981)
3. Loneliness Survey (De Jong Gierveld & Van Tilburg, 2006)
4. Subjective Cognitive Decline Survey (Rami et al., 2014)
5. Social Participation Survey (Derived from the Canadian Longitudinal Study on Aging protocol)
6. Social Networks Survey (Sherbourne & Stewart, 1991)
7. Depression Scale Survey (Beck, Steer, & Brown, 1996; Yesavage et al., 1982)
8. Nutrition Survey (Shatenstein, Nadon, Godin, & Ferland, 2002)
9. Language Test Survey (Anderson, Mak, Keyvani Chahi, & Bialystok, 2018; Birdsong, Gertken, & Amengual, 2012; Marian, Blumenfeld, & Kaushanskaya, 2007)
10. Health Survey (Steffener et al., 2016; Washburn, Smith, Jette, & Janney, 1993)

Appendix C: Multiple Moderation Models

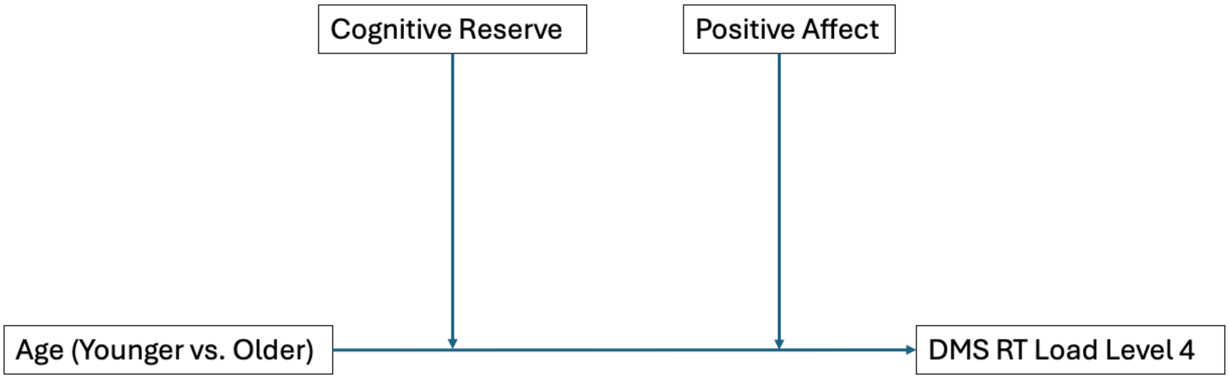

Figure 12. Multiple moderation model exploring the association between age and DMS response time with cognitive reserve and positive affect as moderators.

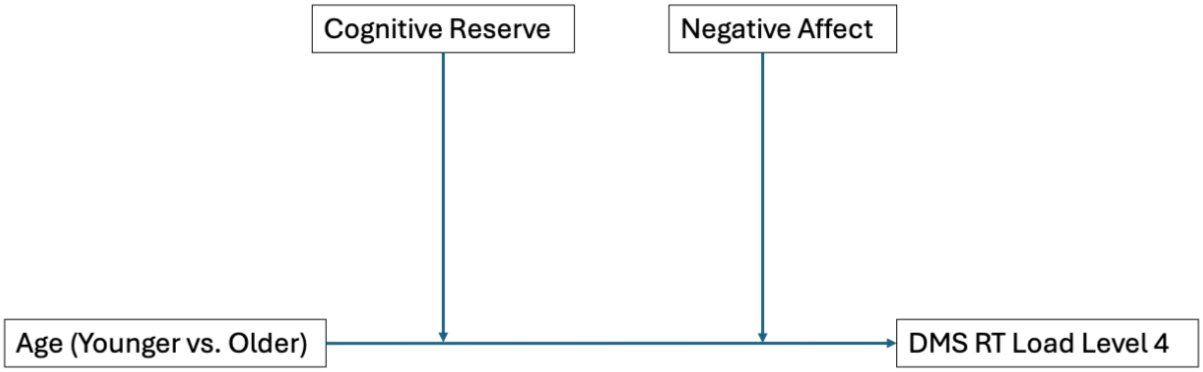

Figure 13. Multiple moderation model exploring the association between age and DMS response time with cognitive reserve and negative affect as moderators.

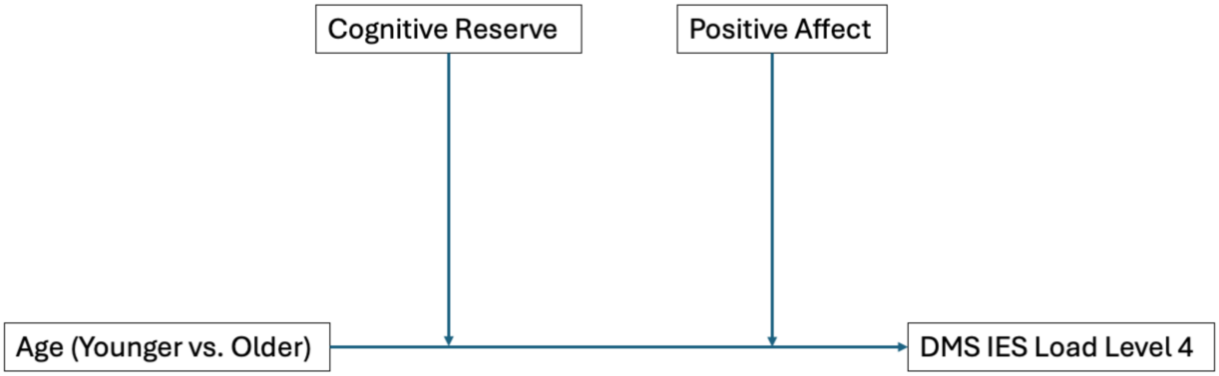

Figure 14. Multiple moderation model exploring the association between age and DMS IES with cognitive reserve and positive affect as moderators.

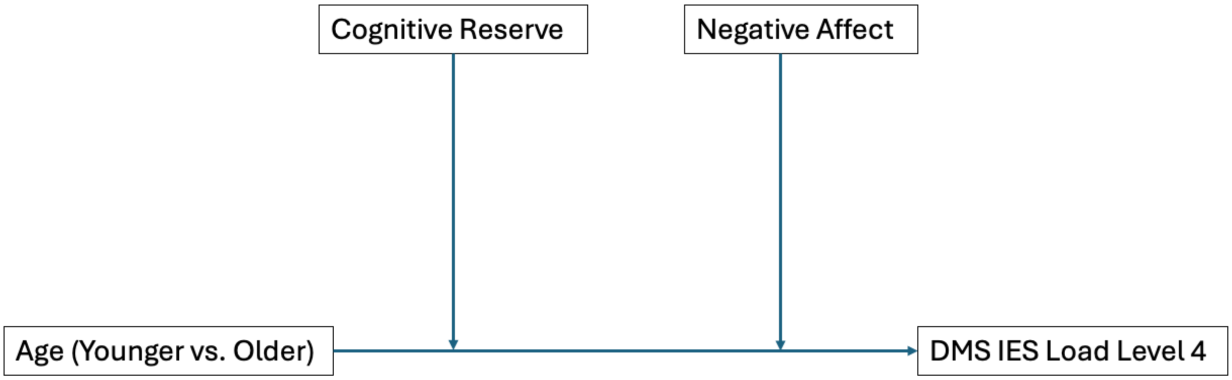

Figure 15. Multiple moderation model exploring the association between age and DMS IES with cognitive reserve and negative affect as moderators.