

POTENTIAL RELATION BETWEEN VASCULAR DEPRESSION AND
AUTOBIOGRAPHICAL MEMORY SPECIFICITY
IN AN OLDER ADULT POPULATION ACCORDING TO THE CAR-FA-X MODEL

by

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B.A. Stanford University, 2013

A thesis submitted in partial fulfillment of the requirements
for the degree of Master of Science
in the Department of Psychology
in the College of Sciences
at the University of Central Florida
Orlando, FL

Spring Term
2018

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ABSTRACT

Vascular depression is a type of depression that has its onset later in life, and it has been associated with cardiovascular or metabolic diseases. Depression can be costly and associated with other health problems, which is why it becomes imperative to uncover the multiple mechanisms of action for depression symptomatology. A proposed mechanism of action for the emergence of depressive symptomatology is poor autobiographical memory specificity according to the CaR-FA-X model. However, it remains unclear whether this mechanism contributes somehow to the vascular depression specific type. The purpose of this research was to determine the potential relationship between the mechanisms proposed by the CaR-FA-X model and the presence of vascular depression, which has not been addressed by previous literature or research. Forty three older adults over the age of seventy from the Orlando area completed multiple measures including the Geriatric Depression Scale, Autobiographical Memory Test, and physiological measures. Results showed no support for a relationship between CaR-FA-X model elements and vascular depression; however, support was found for the relationship between cerebrovascular burden and depression as proposed by the vascular depression theory with rumination serving as a moderator. To our knowledge, this is the first time a study finds the moderating effect of rumination in the development of vascular depression. Further studies will need to address other potential mechanisms that increase risk for this specific type of depression as well as investigate the reasons under which, if any, autobiographical memory specificity might be related to vascular depression by using other measures that might be more sensitive to a non-clinical population.

To my mother Luisa whose far reaching candor and warmth
will continue to guide my work for as long as I live

ACKNOWLEDGMENTS

I would like to express my deepest appreciation to my committee chair, Dr. Daniel Paulson, for his feedback and guidance that were so important for the completion of this project.

I would also like to thank committee members Dr. Rapport and Dr. Sims for their valuable input and suggestions while conducting statistical analyses and during the writing process.

I would also like to recognize the team of colleagues and research assistants who helped during data collection for the Vascular Aging Study including David Brush, Rachel Bassett, Simone Camacho, Cory Walsh, and Sabrina Campodonico.

Finally, I am deeply thankful to my dear aunt, Clara Legon, whose constant support and encouragement helped me keep an optimistic attitude during challenging times.

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LIST OF ACCRONYMS (or) ABBREVIATIONS

AMS	Autobiographical Memory Specificity
AMT	Autobiographical Memory Test
CVB	Cerebrovascular Burden
CVRF	Cerebrovascular Risk Factors
ED	Executive Dysfunction
EF	Executive Functioning
FA	Functional Avoidance
GDS	Geriatric Depression Scale
IC	Interference Control
TICS	Telephone Interview for Cognitive Status
VD	Vascular Depression
WBSI	White Bear Suppression Inventory

CHAPTER ONE: INTRODUCTION

Because of numerous factors, including the increase in life expectancy, the American population is increasingly aging. As the Baby Boom generation reaches retirement age, the need for research on psychological and medical problems affecting the elderly is more pressing than it has ever been before. Even though depression is not a normal part of aging, and the majority of older adults experience satisfaction in their everyday lives, the National Institutes of Health still recognizes depression as a frequent problem in older adults. Depression might contribute in great part to suicide rates in adults 65 and older, which are higher than for the national population (National Institute of Mental Health, 2013). Depression in adults 65 and older was among the most common chronic conditions affecting Medicare beneficiaries. The prevalence rate for depression in the United States was 13.6% in 2014, which was higher than that of cancer, HIV, osteoporosis, chronic obstructive pulmonary disease and other conditions (Centers for Medicare and Medicaid Services, 2014).

Furthermore, several studies have shown that patients with one or more chronic conditions and comorbid depression incur more expenses than those without depressive symptoms. For example, in a study of more than fourteen thousand Medicare recipients with diabetes mellitus, congestive heart failure, or both, patients with depression incur almost twice the healthcare costs faced by patients who did not report any depressive symptoms (Unützer et al., 2009). In another study of more than five hundred thousand subjects, depressed patients incurred more non-mental healthcare costs across 11 chronic comorbid diseases studied compared with non-depressed patients, with values ranging from a \$1570 difference for obesity to a \$15,240 difference for congestive heart failure (Welch, Czerwinski, Ghimire, & Bertsimas, 2009). Similar findings about

the additive effects in healthcare costs of chronic conditions such as depression were found by Choi and colleagues in a study done with 1740 participants in the National Health Interview Survey (Choi, Hasche, & Nguyen, 2015). Late life depression is usually underdiagnosed and undertreated because its symptoms might not be apparent in the context of other medical disorders that are common in later life (Lebowitz et al., 1997). Furthermore, executive deficits, which usually accompany late-onset depression, are predictive of slow and poor response to antidepressant medication (Alexopoulos et al., 2011) affecting up to one third of older adults suffering from depression (Mulsant & Pollock, 1998), and poorer response to acute treatment has been associated with increased subcortical white matter hyperintensities found in older patients with major depression (Simpson, Baldwin, Jackson, & Burns, 1998). In addition, behavioral deficits associated with executive dysfunction (ED) worsen clinical presentation (Alexopoulos, Raue, Kanellopoulos, Mackin, & Arean, 2008); thus, they might deter effective outcome of commonly used psychotherapeutic interventions for depression, such as cognitive behavioral therapy.

Depression experienced by older adults is qualitatively different from depression in earlier life. Depression in older adults is frequently comorbid with other physical and mental illnesses that are distinctive to the process of aging such as cardiovascular disease, diabetes and Alzheimer (Blazer, 2003). It follows that some subtypes of depression and its associated symptoms are more common in older age, such as melancholia with its associated psychomotor retardation (Newmann, Engel, & Jensen, 1991; Parker, Roy, Hadzi-Pavlovic, Wilhelm, & Mitchell, 2001), the syndrome of depression without sadness (J. Gallo, Rabins, & Anthony, 1999), psychotic depression (Meyers, 1992) and vascular depression (VD) (Alexopoulos, Meyers, Young, Campbell, et al., 1997; J. R. Sneed, D. Rindskopf, D. C. Steffens, K. R. R. Krishnan, & S. P. Roose, 2008). For these reasons, distinctions such as the one between early and late onset depression have been made; we still need a better understanding of predictors and mechanisms of depression particularly among older adults,

which can result in useful information for healthcare practice and policy as well as the development of novel interventions.

Depressive symptomatology among older adults relates to a variety of medical and demographic risk factors. Specifically, these include loss of independence resulting from motor impairment and medical burden, chronic pain, cognitive decline, involuntary employment exit (Hyde, Hanson, Chungkham, Leineweber, & Westerlund, 2015) or retirement (Olesen, Rod, Madsen, Bonde, & Rugulies, 2015), bereavement after the loss of a significant other, family members or friends (Fried et al., 2015; Hashim, Eng, Tohit, & Wahab, 2013), and reduction in the number of social interactions (Dorfman et al., 1995; Nicholson, 2012; Teo et al., 2015). Other factors, such as socio-economic status, gender and ethnicity also play a role in rates of depression. Furthermore, medical comorbidity, cognitive impairment, disability, frailty, and infections can adversely direct the course of depression in older adults, and depression in turn can aggravate these medical and functional problems and confer additional impairment. Because of its unique presentation and prognosis, treatment for depression should take into consideration the age of the patient when evaluating the multiple factors that might contribute and exacerbate depressive symptomatology.

CHAPTER TWO: LITERATURE REVIEW

Vascular Depression Theory

Vascular depression is conceptualized as a subtype of depression that has a late onset usually in individuals who are 60 and older and has little to do with family history or psychosocial etiologies. Instead, the vascular depression hypothesis posits cerebrovascular lesions or damage to the brain - a consequence of vascular disease – precipitates and perpetuates the development of depressive symptoms among older adults (Alexopoulos, Meyers, Young, Kakuma, et al., 1997; K. R. R.; Krishnan & McDonald, 1995). The high comorbidity of depression with cardiovascular disease, stroke or white matter hyperintensities (Halaris, 2009; Kang et al., 2015; Soares & Mann, 1997; Whyte et al., 2002) is indicative of the relationship between cerebrovascular disease and depressive symptomatology and broadly supports the vascular depression theory. The basal ganglia, which is involved in functions of movement as well as emotion recognition and regulation (Adolphs, 2002; Kumfor et al., 2014), is connected to prefrontal structures responsible for executive functioning (EF); thus, damage to the basal ganglia and disruption to its connections with higher order brain structures in the prefrontal cortex is related to the development of depression, lack of insight and ED (Alexopoulos, Meyers, Young, Campbell, et al., 1997).

Neuroanatomical correlates of later-life depression are not limited to the prefrontal cortex. In a comparison study between elderly depressed patients and healthy controls, researchers found that 40 % of inpatients without neurologic history and 75% with a neurological history had more lesions in the thalamus and the basal ganglia compared to 5% of normal elderly patients (Alexopoulos, Bruce, Silbersweig, Kalayam, & Stern, 1999). In addition, not only are brain structures abnormalities found in patients suffering from depression, such as enlarged pituitary (K

Ranga Rama Krishnan et al., 1991) and enlarged adrenal gland (Nemeroff et al., 1992), but many of these brain areas with structural abnormalities also exhibit abnormal cerebral blood flow and irregular glucose metabolism (Drevets, Price, & Furey, 2008; Drevets et al., 1997). In addition, damage to the frontostriatal circuitry might result in dysregulation of neurotransmitters found in this area like acetylcholine, dopamine and opioids (Alexopoulos et al., 1999) with neurotransmitter imbalance having a possible influence in the development of depressive symptomatology.

Neuroimaging evidence supports the hypothesized relationship between cerebrovascular burden (CVB) and depression. For example, people who suffer from hypertension might exhibit volumetric reduction in brain tissue as well as increased white matter hyperintensities in the prefrontal cortex (Raz, Rodriguez, & Acker, 2003). Low systemic blood flow has also been associated with development of white matter hyperintensities adjacent to the subcortical nuclei (Jefferson et al., 2007). Other studies highlight differences in cerebral blood flow and metabolic activity as well as volumetric reduction of gray matter in the brains of subjects suffering from mood disorders (Drevets et al., 2008; Drevets et al., 1997). Subcortical hyperintensity burden has been positively correlated with risk factors for vascular disease while deep white matter hyperintensities and periventricular hyperintensities have been found to be more common in depressed patients than in controls (Coffey, Figiel, Djang, & Weiner, 1990; J. R. Sneed et al., 2008). In trying to isolate features that are unique to VD, Sneed and colleagues looked at older adults with late-life depression in two clinical samples. They identified a subgroup of patients with deep white matter hyperintensities, high subcortical gray matter hyperintensities, ED and late-onset depression. Their primary finding was that the presence of deep white matter damage alone was enough to include subjects in the subgroup of VD given its sensitivity and specificity values. Though Sneed et al. (2008) replicated past findings, they provide the most compelling evidence to date that VD presents with unique neuroanatomical features, suggesting it is distinguishable from

other depression presentations.

In addition to neuroimaging studies, further support for vascular depression theory examines the relationship between depressive symptomatology and clinical markers of cerebrovascular risk. Mast and colleagues (2004) evaluated one hundred patients six and eighteen months after discharge from a rehabilitation stay and found that those with two or three cerebrovascular risk factors (CVRF) were more likely to become depressed during follow up. Along a similar line of research, in a sample of women eighty years and older from the Health and Retirement Study, Paulson and colleagues (2013) found that higher CVB was predictive of a greater number of depressive symptoms. Interestingly, they also found that educational attainment appears to delay but not completely prevent the development of VD in older adults. This finding suggests that brain reserve effect applies to VD, and provides an additional parallel between VD and other geriatric syndromes of neurological origin (Stern, 2002). Further research should examine other factors that might delay or prevent the onset of VD in older adults. As it has been demonstrated by the numerous studies mentioned above spanning years of research, the effect of cerebrovascular disease in the development of depressive symptomatology is well established.

CaR-FA-X Model

The CaR-FA-X model as proposed by (Williams, 2006; 2007) articulates a model of affective control managed by three comprising factors, which are capture and rumination (*CaR*), functional avoidance (*FA*) and executive functioning (*X*). According to the CaR-FA-X model, overgeneral recollection of past events as opposed to recollection of specific memories constitutes a distinguishing feature of depression or emotional disturbance. That is, individuals suffering from depression have a harder time than controls trying to remember specific past events in their lives. To understand the logic behind the model's proposition, each of its

constituting components are discussed below in detail and separately.

Capture and rumination. According to Nolen-Hoeksema (1991), rumination is the tendency to engage in self-focused, repetitive thinking about one's emotive state and its implications. There are two subtypes of rumination, brooding, which involves anxious and melancholic thoughts, and reflection, which involves introspection and problem solving. From these two forms, the former subtype has been more associated with depression (Debeer, Hermans, & Raes, 2009). This difference between brooding and reflection can be traced at the neurobiological level. For example, in an fMRI study by Berman and colleagues, they evaluated behavioral rumination and looked at default network connectivity, specifically between the subgenual-cingulate cortex and the posterior-cingulate cortex. They found that MDD patients exhibited greater default-network activation than controls, and activation of the subgenual-cingulate correlated particularly with brooding rumination. Also, marked differences in activation during rest versus task periods suggested that MDD subjects did not ruminate when engaged in a task while ruminating in excess while at rest (Berman et al., 2011). The absence of ruminative processes in people with depression while engaged in a task might have important implications for treatment of the disorder.

Furthermore, inability of individuals suffering from depression to maintain balanced or homeostatic brain functioning during rest or task periods might allude to EF deficits. People with depression might have to exert greater effort in allocating limited cognitive resources for the completion of tasks that require external attention, which shows in reduced activation of the subgenual-cingulate when engaged in a task. However, when external engagement is no longer required, there is sufficient brain capacity for the subgenual-cingulate to become active once again. The cingulate cortex (Bijanki et al., 2015; Greicius et al., 2007; Wang, Ashley-Koch, Steffens, Krishnan, & Taylor, 2012), and the subgenual-cingulate have shown to be linked to depressive

symptomatology (Greicius et al., 2007), and the subgenual-cingulate might be a potential intervention target for treatment and remission of such symptoms (Johansen-Berg et al., 2008). Indeed, EF deficits are associated with an inability to inhibit ruminative processes as demonstrated in the study by von Hippel and colleagues (2008), in which they looked at rumination in particular as a potential mediator in the relationship between ED and depression. They found that rumination mediated the relationship between EF and depressive symptoms among subjects with late-onset depression at sixty years or older, but not among those with early-onset depression. This finding supports the argument for a relationship between ED, rumination, and late-onset depression in older adults (Von Hippel et al., 2008).

Functional Avoidance The FA or affect regulation hypothesis presents FA as an adaptive inhibitory mechanism used to suppress temporarily episodic representations or thoughts that might elicit negative affect (Williams et al., 2007). This hypothesis states that reduced autobiographical memory specificity (AMS) occurs because the memory search process is aborted at a general level before more specific memories can be retrieved (Dalgleish et al., 2007). This top-down regulatory process can be maladaptive when employed indiscriminately; avoidance as a functional strategy can then become a pervasive retrieval style in which memories are always summarized into categories impeding access to specific memories (Raes, Hermans, Williams, & Eelen, 2006). A suggestion has been made that memories are categorized and set together through a mnemonic interlock or ruminative thinking. A variety of avoidant coping behaviors, especially social behavioral, experiential, and that of thought suppression, have been shown to be negatively associated with AMS possibly as a mechanism to protect the individual from negative or painful memories (Hermans, Defranc, Raes, Williams, & Eelen, 2005). For instance, Debeer and colleagues (2013) measured reliance on cognitive avoidance in 41 participants and then assigned participants to either a priming avoidant or approach condition. Results for this study showed that participants who exhibited a high avoidance trait also showed higher reduction in AMS from pre- to post-priming period as well as AMS after priming compared to participants who did not exhibit such traits. These differences were present independently of the condition that participants were assigned to (Debeer et al., 2013). Furthermore, FA seems to be related to reduced AMS especially when affective cues (e. g., happy, sad, angry, lonely, safe) are used rather than cues that are incongruent with identified valuable personal traits. The later was found to elicit more ruminative reflection, thus supporting an argument for the particular relationship between FA and affect or emotion regulation. For example, Wessel and colleagues (2014) used an affective and a self-discrepant versions of the autobiographical memory test (AMT) in a sample of 64 women, and found that the relationship

between AMS and avoidance was greater for women in the affective condition. This further indicated that sensitivity of the AMT test to the CaR-FA-X mechanisms is dependent on the type of cue that is used. In sum, the expression of FA is dependent on individual traits as well as the nature of the stimulus. Other work by Dalgleish and colleagues (2007; 2008) suggests that FA and EF may moderate the relationship between emotional distress and memory specificity differently for dissimilar clinical populations. This effect can be summarized by comparing between samples of patients with and without a history of trauma, for whom the FA mechanism plays a greater role in affect regulation than ED, which is more influential in samples of patients with depressed mood whether they report posttraumatic symptoms or not. Furthermore, the effects of the mechanisms in the CaR-FA-X model might be additive in the sense that those individuals who suppress specific memories through the FA mechanism and have neurocognitive deficits might be less capable of retrieving specific memories than those with EF difficulties alone. For example, a study by Kuyken and Brewin (1995) found that women with a history of childhood physical or sexual abuse were less able to recall specific memories during the AMT than were non-victimized women with depression. In sum, while FA alone might be adaptive, it is the chronicity of an avoidant style maintained through rumination, and the interaction of FA with cognitive deficits that result in poorer AMS and the development of depressive symptomatology.

Executive control. Executive control refers to the mechanism involved in planning, monitoring and inhibition of irrelevant information. EF tasks are sensitive but not specific to frontal lobe dysfunction (Alvarez & Emory, 2006; Mast, Yochim, et al., 2004), and the executive system could be a fractioned rather than a unitary system that can be fragmented into three relatively independent operative types, which are updating, shifting and inhibition. Inhibition in particular refers to the ability of withholding inappropriate or intrusive prepotent responses (Fisk & Sharp, 2004), and it plays an important role in the recall process of specific autobiographical memories because failure to inhibit unnecessary categorical descriptors during the memory search process results in reduced AMS or overgeneralization (Dalgleish et al., 2007). Interference control (IC) is required to maintain the search in the autobiographical memory database as well as to reach event specific memories that are located deeper than categorical autobiographical summaries in a hypothetical hierarchy of the self-memory system as proposed by Conway and Pleydell (2000). Furthermore, it is well established that as we age, EF and cognitive functioning in general declines with some areas experiencing greater deterioration, such as processing speed and working memory while others are spared from this deterioration like verbal ability and procedural memory (Park et al., 2002; Park & McDonough, 2013). There are several theories as to why EF declines with age including a depletion of cognitive resources (Craik & Byrd, 1982), a slowing down of processing speed (Salthouse, 1996), or even a decline in sensory functioning that impacts cognitive functioning (Lindenberger & Baltes, 1994). Fisk and Sharp (2004) used factor analysis to examine the effect of age and other variables on scores in four different factors that were representative of cognitive functioning. They found that age differences accounted for statistically significant differences in performance in cognitive tasks. Thus, based on previous evidence, older adults in general should experience greater difficulty than younger populations to effectively complete the search process of relevant specific autobiographical memories that might override general categorical clusters.

Moreover, Von Hippel and colleagues (2008) state that ED seems to be especially associated with late onset depression through the mediating effect of rumination, that is because of age related reduced capacity to redirect attention from negative ideation or inability to inhibit ruminative responses in the face of negative events. Furthermore, they found that performance in EF tasks was poorer in older adults with late onset depression than in those with onset of depressive symptoms earlier in life, which offers a convincing argument for the relationship between the development of depressive symptomatology later in life and ED. Additionally, EF seems to be a moderator variable in the relationship between vascular risk and depressive symptomatology. That is, people with two or more CVRF and poorer EF are at greater risk of developing depression than those people who also have the same number of CVRF but do not exhibit impairment in central executive functions (Mast, Yochim, et al., 2004). In sum, CVB, EF, rumination, and depression seem to be interconnected in such a manner that once the pieces are in place, they form a synergistic elaborate loop. As discussed above, this insidious coalition of detrimental factors is especially likely to occur in older populations. The CaR-FA-X model defines EF as one of the key mechanisms associated with AMS, and this relationship has been found to be independent of mood state (Dalglish et al., 2007; J. A Sumner, 2012). Thus, depressive mood is neither a moderator nor a mediator variable in the effect of EF in AMS. Nonetheless, the effect of ED in AMS is not straightforward by any means. In a study by Sumner and colleagues (2014), it was found that EF affected AMS of patients with and without a history of major depressive disorder (MDD) depending on whether participants were high or low on brooding with mutually opposite combinations of MDD and brooding resulting in reduced AMS. Also, according to Williams and colleagues (2007), individuals who are experiencing depression will have increased access to generalized negative schemas that might be activated through ruminative thinking, which in turn is made possible because of insufficient control of executive functions. As such,

rumination might influence or explain the association between poor EF and lower AMS in individuals suffering from depression or in individuals who are in the remission stage of MDD, but only when ruminative processing paths are activated.

Autobiographical Memory Specificity. The CaR-FA-X model posits that rumination, FA, and EF, relate to AMS, which in turn is associated with depressive symptomatology. In accordance with previous findings, reduced AMS has been found to be present not only during depressed mood but also during the remission stage of a major depressive episode. By contrast to those who had never experienced a depressive episode, women in remission from a major depressive episode had comparably poor AMS; nevertheless, these differences were only significant in the presence of negative cues as opposed to positive ones (Mackinger, Pachinger, Leibetseder, & Fartacek, 2000). Based on those findings, it might seem that poor AMS is a consequence rather than a cause of depression. However, other studies have failed to find reduced AMS in individuals with remitted depression. Discussed in previous sections, poor AMS is not simply related to depression, but this relationship seems to happen under the effect of specific activating mechanisms that involve executive functions, avoidance and rumination to a certain extent. Also, poor AMS is largely specific to people suffering from depression, post-traumatic disorder or both more than to any other mental disorder or illness (Williams et al., 2007). Poor AMS is related to PTSD and seems to play a role in the maintenance of this disorder (McNally, Litz, Prassas, Shin, & Weathers, 1994). Poor memory specificity is also associated with a history of trauma (Hauer, Wessel, Geraerts, Merckelbach, & Dalgleish, 2008), impairment in problem solving (J. Evans, Williams, O'loughlin, & Howells, 1992; Goddard, Dritschel, & Burton, 1996, 1997) as well as with difficulty imagining specific future events (Williams et al., 1996).

Our recollection of events is biased by mood state in the moment that recollection occurs.

Individuals who are experiencing depression may tend to recollect negative events faster than positive ones (Clark & Teasdale, 1982; Lloyd & Lishman, 1975; Teasdale & Fogarty, 1979; Williams et al., 2007). When remembering past events, people suffering from depression will be prone to do so accompanied by comprehensive and negative mode rather than in a selective and positive manner. Also, people build on their past experiences to presently project their views about the future (Sansom-Daly, Bryant, Cohn, & Wakefield, 2014; Schacter, Addis, & Buckner, 2007; Williams et al., 1996). A general negative perception of our past life can result in catastrophic thinking, which in addition to ruminative cognitive propensity, might worsen the condition of already depressed people. Indeed, reduced AMS predicts a greater pervasiveness of depressive symptomatology over a time period (Hermans, Vandromme, et al., 2008; J. A. Sumner, Griffith, & Mineka, 2010, 2011) as well as higher levels of hopelessness in patients who report parasuicidal events (J. Evans et al., 1992). It remains to be seen if the risk factors for the VD subtype, specifically the combination of high CVB and executive impairment, in older adults are also associated with impairment in AMS. Older adults might have problems remembering daily events and tasks, which are more specific in nature and form part of our episodic memory. Poor memory specificity is already a sign of cognitive decline in older adults, but this symptom should present itself at its worst in those suffering from vascular depression. Little is known about how CVB relates to AMS among older adults. The present integration of vascular depression theory and the CaR-FA-X model suggests a clear theoretical link between vascular disease and impairment of cognitive mechanisms of emotional regulation described in the CaR-FA-X model. A clear relationship exists between CVB and ED among older adults, which may in turn adversely affect adaptive employment of both rumination and FA. For instance, disruption of adaptive memory search processes may result from the individual's inability to inhibit irrelevant thoughts or clusters of memories resulting in rumination, and more specifically brooding.

Alternatively, this pattern could happen through FA, which is described in terms of early disruption in the searching process. Past work demonstrates a robust relationship between reduced AMS and depressive symptomatology. Integration of vascular depression theory suggests that older adults with high CVB will be more vulnerable to this pattern of impairment.

CHAPTER THREE: PROPOSED RESEARCH

The primary goals of this thesis are: (1) to relate vascular depression theory with the CARFAX model and identify the specific mechanisms through which this relation might take place.

Hypothesis 1: Participants with cerebrovascular burden will exhibit impairment in interference control compared to those who do not have cerebrovascular burden.

Hypothesis 2a: Participants who exhibit greater impairment in interference control will exhibit higher depressive symptomatology compared to those participants who do not exhibit impairment in interference control.

Hypothesis 2b: Greater impairment in interference control will be associated with higher endorsement of ruminative thinking.

Hypothesis 3a: Greater impairment in interference control will be associated with diminished autobiographical memory specificity.

Hypothesis 3b: Higher ruminative thinking will be associated with diminished autobiographical memory specificity.

Hypothesis 3c: Higher functional avoidance will be associated with diminished autobiographical memory specificity.

Hypothesis 4: Participants with reduced autobiographical memory specificity will exhibit higher depressive symptomatology compared to those participants with higher autobiographical memory specificity.

Hypothesis 5: Rumination will mediate the relationship between interference control and depression.

Hypothesis 6: Autobiographical memory specificity will mediate the relationship between interference control and depression.

Finally, the intersection of the CaR-FA-X and vascular depression models will be examined in the following hypotheses:

Hypothesis 7a: The relationship between cerebrovascular burden and depressive symptomatology will be moderated by ruminative thinking whereby endorsement of depressive symptomatology will be predicted by the combination of high cerebrovascular burden and high rumination.

Hypothesis 7b: The relationship between cerebrovascular burden and depressive symptomatology will be moderated by functional avoidance whereby endorsement of depressive symptomatology will be predicted by the combination of high cerebrovascular burden and high functional avoidance.

CHAPTER FOUR: METHODOLOGY

Participants

Previous studies that are targets of replication for this research have been completed with sample sizes of 55 or fewer. Results of a power analysis conducted using G*Power suggested that a sample size of 40 would provide an 80% probability of identifying an effect of .35, which is similar in size to that reported by Von Hippel and colleagues (2008). Furthermore, empirical estimates of sample sizes needed for a power of .80 using path coefficients similar to those seen in the mediation model by Von Hippel et al. (2008) showed that a sample of at least 53 participants would be required (Fritz & MacKinnon, 2007). The study was approved by the Institutional Review Board at the University of Central Florida prior to data collection. All participants in the study were 70 years of age or older, and they were required to speak English fluently to participate. Recruitment was completed through flyer distribution in the University of Central Florida main campus, senior centers, and other locations of interest in the Orlando area; online advertising, and word of mouth were also other recruitment methods that were employed. Exclusion criteria for this study included having a language other than English as a first language, presence of moderate to severe dementia, severe mental illness, previous brain or head trauma with known cognitive impairments, or a history of cerebrovascular event such as an ischemic or hemorrhagic stroke. Presence of moderate to severe dementia was screened using the Telephone Interview for Cognitive Status (TICS); phone screenings were conducted by two graduate studies involved in the development of the study. All subjects were required to provide written consent before they participated in the study. Participants' information on demographic variables such as age, gender,

race, socio-economic status, and level of education was obtained through a screening survey given to participants before administration of a subsequent series of measures that assessed participants' performance across diverse areas that targeted depressive symptomatology, cognitive status, episodic memory, ruminative tendencies, FA and EF. Outcome variables were measured through instruments and assessment tools described below.

Measures

Neuropsychological functioning. The Halstead-Retain Neuropsychological Test Battery is designed to evaluate neuropsychological functioning and condition of the brain and the nervous system. The test is intended for individuals 15 years and older, and it is composed of eight assessment areas or subtests. Only the Trail Making Test Parts A and B from the Halstead-Retain Neuropsychological Test Battery were used in this study. The test-retest correlation for Parts A and B of the Trail Making Test are .79 and .89 respectively.

Cognitive Functioning and Ability. Cognitive functioning was assessed through a modified version of the Telephone Interview of Cognitive Status (TICS) measure (Brandt, Spencer, & Folstein, 1988). The TICS is a reliable test (test-retest reliability coefficient of .97 over a period of six weeks), a valid measure of cognitive functioning, and it also screens for dementia showing a sensitivity of 94% and a specificity of 100% (Brandt et al., 1988; Herzog & Wallace, 1997). The modified version has a sensitivity higher than 99% and specificity of 86% (Fong et al., 2009; J. J. Gallo & Breitner, 1995). The TICS includes questions assessing orientation, immediate and delayed word list memory, working memory, mathematical skills, and language (Herzog & Wallace, 1997). The maximum score is 35 with higher scores reflecting higher cognitive functioning, and it is administered verbally.

Executive Functioning. Executive functioning, and more specifically IC, was evaluated using a modified version of the Flanker Task (Eriksen & Eriksen, 1974). This task was completed using in a computer monitor. Instructions were presented to participants, and they were not time limited. After reading instructions, participants saw a fixation cross for 20,000 ms before practice trials began. The practice block consisted of 14 trials including 7 control and 7 experimental trials, and each of these appeared for 5,000 ms separated by a fixation cross that appeared for 1,000 ms. Feedback to participants, which followed all practice trials, consisted of correct, incorrect, or no response. Participants completed four control blocks and four experimental blocks, and each of them began with a 20,000 ms fixation cross. Each of the 12 trials in the block lasted 3,000 ms with a fixation cross between them that lasted 1,000 ms. Participants were presented a stimuli screen comprised by five arrows, and indicated the direction of the center arrow, which pointed left or right. Participants indicated direction by pressing corresponding keys on the keyboard. Peripheral arrows pointed in the same or different direction than that of the center arrow varying from trial to trial. These trials were alternated with control tasks in which only a single arrow pointing left, or right was shown on the screen. The Flanker Test measures participants' IC capacity. Both reaction time and accuracy were used as variables in this study.

A computerized version of the Stroop Test (Stroop, 1935) was another executive functioning task completed by participants. The dependent variable being measured in this task was IC. The Stroop was composed by four different subtasks. A fixation cross was shown between subtasks for 1,000 ms. Each of these four blocks began with non-timed instructions as well as related practice for that block. Practice sections lasted 5,000 ms each. A 20,000 ms fixation cross was shown between practice and experimental sections. The first three experimental blocks consisted of 24 trials each of which lasted for 3,000 ms while the last block had 36 trials. First,

participants needed to press the keyboard key that corresponded to the color of the stimulus shown in the screen, which was blue, green or red. No words were shown for the first condition. Second, participants saw the words “Red,” “Green,” or “Blue,” and they had to match the word with the corresponding colored key on the keyboard. As opposed to the first condition, no colors were shown this time, but words were presented as black text. The third condition presented the same three target words as the second condition, but this time the words had different colors that were consistent with the word being shown. For example, the text “Blue” was presented in blue color. Finally, in the fourth trial, target words “Red,” “Green,” or “Blue” were presented with colors that were incongruent with the color they described. For example, the word “Red” was shown in green color or blue color. The Stroop Test measures selective attention, processing speed and cognitive flexibility.

Rumination. The Ruminative Responses Scale (Nolen-Hoeksema, 1991) consisting of 22 items was used to evaluate ruminating thinking. The scale is meant to be a continuous measure rather than a categorical one, which means that instead of distinguishing between ruminators and non-ruminators, it allows for some degree of flexibility in identifying high ruminators versus low ruminators. This is useful in the sense that most people engage in ruminating thoughts every now and then. The Likert type scale ranges from 1 (almost never) to 4 (almost always), and it has a coefficient alpha of 0.90 as well as a test-retest correlation of 0.67 over a year period (Nolen-Hoeksema, Larson, & Grayson, 1999). Also, from two factors of rumination captured by the scale, our study was mostly concerned with brooding, which has been consistently related to depression (Debeer et al., 2009; Treynor, Gonzalez, & Nolen-Hoeksema, 2003).

Functional Avoidance. The White Bear Suppression Inventory (WBSI) is a self-report measure that consists of 15 items on a 5 point scale, with 1 being “Strongly Disagree” and 5 being “Strongly Agree.” It measures tendency to suppress unwanted thoughts as a maladaptive strategy, which can be happen through intrusive thoughts, suppression attempts and self-distraction. The scale’s alpha coefficient is 0.89 showing satisfactory internal consistency, and the test-retest reliability of this measure is .69 over a period of three months, and .92 over a period of one week (Wegner & Zanakos, 1994). Another measure that was used to evaluate FA is the Acceptance and Action Questionnaire-II. This is a 7-item questionnaire assessing degree of psychological inflexibility and experiential avoidance. The measure has a concurrent validity of .97 and improved internal consistency with respect to the first version. Its mean alpha coefficient is .84, and it has shown a test-retest reliability of .81 and .79 after three and twelve months respectively (Bond et al., 2011).

Autobiographical Memory. The AMT measures degree of specificity of autobiographical memory by using cue words or images. For the specific purposes of this study, researchers used the affective version of the AMT. Participants were prompted with fifteen words that described various emotional states (e.g., sad, happy, safe). Then, participants vocally described a past event in their lives that they could associate with each word. Meanwhile, the researcher manually recorded responses. The test evaluates how specific each recollection was as well as its vividness and elicited pleasantness on a Likert-type scale of 1 to 5. Each response is timed measuring both latency and completion time. The alpha coefficient for the AMT is 0.67 (Griffith, Kleim, Sumner, & Ehlers, 2012), and test-retest reliability ranging from 1 to 5 months were .53 and .68 respectively (Raes, Williams, & Hermans, 2009).

Depression. The Geriatric Depression Scale (GDS) originally developed by Yesavage and colleagues in 1982 was used to evaluate participants' level of depressive symptomatology. The GDS is a well-standardized and brief 30-item self-rating measure that is frequently used in research and clinical work with older adults. Several studies have suggested a cutoff score of 11 for the highest trade-off between specificity and sensitivity in identifying depression. The GDS has a Cronbach's alpha of 0.94, and test-retest reliability over a period of a week is .85 (Yesavage et al., 1982). Later studies have confirmed the validity and reliability of the GDS (Leshner, 1986; Montorio & Izal, 1996; Yesavage & Sheikh, 1986).

Cerebrovascular Burden. Several noninvasive measures including self-reporting and physiological instruments were used to gather biomarker data. Physiological data will be recorded by two graduate students involved in the development of this study. For example, an automatic sphygmomanometer placed on the right arm above the elbow was used to measure systolic and diastolic blood pressure while resting heart rate and blood oxygen saturation were measured using a pulse oximeter. Endorsement of diabetes, hypertension, cardiac disease in general, or history of cerebrovascular events, such as a stroke, was assessed through self-report data. Two variables were used for CVB including CVB as determined by self-reported health conditions only (CVB-SR), and overall CVB as (CVB-O).

In sum, collected data (described above) was indicative of mood and affective control, various facets of executive functioning and cognitive control, episodic memory, physiological functions, as well as demographic data. There will not be long-term follow up for any of the procedures or primary data collected in this study.

Statistical Methods

Hypotheses citing executive functioning made use of a composite variable representing

executive measures of IC and determined by two dimensions including accuracy and response time. Accuracy was calculated using percentage scores on the Flanker task, and the Stroop test. There were four easy trials and four hard trials in the Flanker task. Each trial had a corresponding accuracy percentage for each of the participants depending on the number of correct responses out of the total number of available options. The four percentages corresponding to hard trials were added and their average became the overall accuracy for each participant. Similarly, there were four trials in the Stroop test, and each trial had a corresponding accuracy percentage for each of the participants. The percentage for the incongruent trial became the overall accuracy in the Stroop test taking inhibitory processes into account. Finally, a total score for accuracy was obtained by averaging the summation of overall accuracy scores in the Flanker task and the Stroop test.

Response time included a summation of the differences in completion time between Trail Making Tests A and B (Bowie & Harvey, 2006), Flanker task hard and easy trials, and the Stroop test incongruent and congruent trials measured in seconds. In the case of the Flanker task an overall score for time in the hard trials was obtained by adding the time of four hard trials, and an overall score for time in the easy trials was obtained by adding the time of four easy trials. Then, overall time score in easy trials was subtracted from overall time score in hard trials to produce the inhibitory response time for the Flanker task. Similarly, in the Stroop test overall time score in the congruent trial was subtracted from overall time score in the incongruent trial and their difference became the inhibitory response time for the Stroop test. Finally, a total score for IC response time was obtained by adding the time in Trails, Flanker and Stroop tasks.

Because indicators of CVB were of varying scales, and arguably represented CVB in diverse ways, CVB was conceptualized using self-reported health conditions (maximum of four) based on previous literature, and objective measures (e.g., diastolic and systolic blood pressure,

heart rate, oxygen saturation). Thus, two main composite variables reflecting CVB were estimated. One of these variables encompassed self-reported health conditions exclusively ranging from 0 to 4. To obtain a second variable for CVB that included both self-reported health conditions and objective measures, the previously described variable reflecting self-reported health conditions was dichotomized where 0 to 1 health conditions reflected minimal risk for CVB and 2 or more health conditions were considered elevated risk as based on previous literature. This dichotomous self-reported CVB was then added to dichotomous variables of objective measures that were obtained using established clinical cut-offs explained below. As such, an overall CVB variable was obtained by adding dichotomized scores of five indices including self-reported health conditions and four physiological measures of diastolic and systolic blood pressure, heart rate, and oxygen saturation.

Based on the assumption of risk, scores for oxygen saturation were dichotomized in advance to safe and unsafe levels using a cutoff score of 94 following similar cutoff scores on previous literature (Roffe, 2002; Vold, Aasebø, Wilsgaard, & Melbye, 2015). Elevated heart rate in the sample was considered a heart rate of 90 and above, which was deemed appropriate based on research literature for a sample within the selected age range. On the other hand, recommended safe values for blood pressure in healthy older adults are lower than 140 for systolic blood pressure and 90 for diastolic blood pressure. As such, these values of 140 and 90 were used as cut-off values for safe versus unsafe levels.

Bootstrapping, first introduced by Bradley Efron (1979), was the principal statistical method of analysis, and for this study, researchers used the bias-corrected and accelerated (BCa) bootstrap developed by Efron in 1987 and available in SPSS through an observed variable path analysis modeling tool called *Process* created by Andrew Hayes (Hayes, 2012). Bootstrapping is a method that allows to describe how one variable depends on another while controlling for

confounding variables, and at the same time and because this method uses the same sample with replacement, it has the advantage it can be used with small samples, and it is not dependent on assumptions of normality or homogeneity of the sample to be accurate; thus, we can be confident of robust analysis through the use of bootstrapping even in the absence of the assumptions previously mentioned. Mediation effects were analyzed through bootstrapping in the context of rumination (Hypothesis 5) and AMS (Hypothesis 6) as potential mediators in the relationship between EF and depression. Moderating effects of rumination (Hypotheses 7a) and FA (Hypothesis 7b) on the relationship between CVB and vascular depression were examined using moderation models. Bootstrapping was performed with 5000 iterations using the bias corrected method and 95% confidence intervals.

CHAPTER FIVE: FINDINGS

Sample Demographics

The final sample included in statistical analysis consisted of 52 participants. Demographic characteristics of participants can be found in Table 1. Mean age of participants was 76.40 (4.60), and 63.46% of the sample was female. In addition, 90.39% identified themselves as White. Mean education of the sample was 16.46 (2.94) years, and interquartile range for reported income was \$42,500.00 while median income was \$62,500.00. The mean score for depressive symptoms in the sample was 6.23 ($SD = 4.10$). The cut-off score designated for the original measure by its creators was 11 with scores from 1 to 10 falling within the normal range (Wrobel & Farrag, 2006). In our sample, 6 participants, about 12% of the sample had scores that fell above the cut-off score in the GDS, and the highest reported score was 22.

Additionally, cardiovascular characteristics of the sample were identified using several measures described above. Participants self-reported numerous health conditions, but only four of them representing risk factors for cardiovascular or metabolic disease were included in the analysis (e.g. problems with high blood pressure, problems with heart and circulation, problems with chest, and problems with diabetes). Each condition was a dichotomized variable in which a score of 1 signified the presence of that condition and a score of 0 its absence. The mean score for self-reported conditions in our sample was 1.02 ($SD = 1.20$). Consistent with past research, participants who report no more than one risk factor (low CBV) can be grouped separately than those who report two or more risk factors (high CVB) (Mast, MacNeill, & Lichtenberg, 2004; Mast, Yochim, et al., 2004; Paulson et al., 2013). Fourteen participants, about 27% of the sample, reported scores

that fell above the cut-off score of 2 meaning that they were considered at high risk for CVB, and the highest number of self-reported conditions was 4.

An additional risk factor that was not self-reported was oxygen saturation. The mean value for oxygen saturation level was 95.02 (5.43). The cut-off value used in this study was 94%; those participants whose oxygen saturation level fell below this value were considered at high risk for CVB. Oxygen saturation data for one of our participants was missing. In total, 11 out of 51 participants from our sample, about 22%, fell below the safety cut-off score of 94 with the lowest score being 76. Regarding heart rate, the mean score in the sample was 71.67 ($SD = 13.71$) while for systolic and diastolic blood pressure the means were 134.77 ($SD = 16.63$) and 71.58 ($SD = 10.05$) respectively. Three out of 52 participants, or about 6% of the sample had heart rate levels above the cut-off of 90 with the highest value being 126, 21 participants, or about 40% of the sample, were above the cut-off value for systolic blood pressure of 140 with the highest value being 172, and 3 participants, or about 6% of the sample fell above the cut-off score for diastolic blood pressure with the highest value being 104.

Further analysis evaluated the executive functioning variable represented by total reaction time (seconds) and accuracy (percentage correct) separately. Executive functioning was evaluated in 41 participants who completed all three tasks measuring IC (Flanker, Stroop, and Trails); 11 participants were not included because there was no data available for them in one or more of these tasks. In the case of total reaction time, which was obtained by adding the total time in the Flanker task hard trials, total time in the Stroop task incongruent trial, and total time in Trails B, the cut-off score for impairment was defined at 1 standard deviation above the mean ($M = 5550.49$; $SD = 1000.17$) with those scores falling above this value meeting criteria for impairment, and an additional cut-off score was established for severe impairment for those participants who fell 2 standard deviation above the mean. In total, 7 participants, or about 14% of our sample, met criteria

for impairment, and 3 participants, or about 6% of the sample, met criteria for severe impairment using the criteria for reaction time mentioned above. Cut-off scores for impairment and severe impairment taking accuracy into account were established using the mean value of 95.88% and the median value of 99.17 as a reference. Scores lower than 95% were determined to be within the impairment range and scores lower than 90% correct were considered in the severe impairment range; both cut-off scores were chosen arbitrarily a priori. In total, 4 out of 45 participants, or about 9%, met criteria for impairment using the cut-off described above for accuracy, and 5 participants, or about 11%, met criteria for severe impairment. No participants in the study met criteria for impairment using both reaction time and accuracy-based cut-off scores.

Simple Regression Analyses: Main Effects

Simple main effects relating key variables of interest were assessed using regression analyses. As stated above CBV was conceptualized in two ways, that is CVB as determined by CVB-SR and CVB-O. The correlation between CBV-SR and CVB-O was .91 ($p < .001$). Results were that that CVB-O was not associated with IC of participants when considering accuracy ($\beta = -0.004$, $SE = 0.01$, $p = .73$) or response time ($\beta = 0.09$, $SE = 0.16$, $p = .58$). Similarly, CVB-SR was not associated with IC of participants when considering accuracy ($\beta = 0.002$, $SE = 0.02$, $p = .90$) or response time ($\beta = 0.17$, $SE = 0.21$, $p = .41$). Furthermore, depressive symptomatology was not associated with IC based on accuracy ($\beta = -0.91$, $SE = 5.42$, $p = .87$) nor response time ($\beta = -0.30$, $SE = 0.42$, $p = .49$). Interference control was not associated with ruminative tendencies based on accuracy ($\beta = 2.02$, $SE = 3.01$, $p = .51$) nor response time ($\beta = -0.20$, $SE = 0.23$, $p = .39$). In a similar manner, autobiographical memory specificity was not associated with depressive symptomatology ($\beta = -0.002$, $SE = 0.06$, $p = .98$), interference control as determined by response accuracy ($\beta = 0.08$, $SE = 11.20$, $p = .99$), interference control determined by response time ($\beta = 1.34$, $SE = 0.82$, $p = .11$), ruminative tendencies ($\beta = 0.18$, $SE = 0.58$, $p = .76$), or functional

avoidance ($\beta = -0.01, SE = 0.08, p = .92$).

A further bivariate correlation analysis was conducted to evaluate how multiple variables included in the simple regression analyses related to one another. Results showed that depression correlated positively with cerebrovascular burden as determined by self-reported health conditions ($r = .30, p = .03$), functional avoidance ($r = .51, p < .001$), and rumination ($r = .49, p < .001$); also, functional avoidance correlated positively with rumination ($r = .67, p < .001$). Neither interference control nor autobiographical memory specificity showed significant correlation with any of the other variables mentioned above. These results can be found in Table 2.

Mediation Analyses

Results of a mediation analysis using Model 4 in Process were conducted on data for 45 participants for reasons described above, and they showed that ruminative tendencies did not act as a mediator between IC and depressive symptomatology (*Hypothesis 5*). When considering accuracy, IC was not associated with ruminative tendencies ($\beta = 2.02, SE = 2.49, p = .42$), nor it was related to depression ($\beta = -3.02, SE = 4.72, p = .53$). However, ruminative tendencies were significantly related to depressive symptomatology ($\beta = 1.05, SE = 0.37, p = .01$) (Figure 1). Similarly, when considering response time, IC was not associated with ruminative tendencies ($\beta = -0.20, SE = 0.17, p = .23$), nor it was related to depression ($\beta = -0.08, SE = 0.39, p = .84$). However, rumination was significantly associated with depressive symptomatology ($\beta = 1.07, SE = 0.36, p = .01$) (Figure 2).

Similarly, autobiographical memory did not mediate the relationship between IC and depression (*Hypothesis 6*). When considering accuracy, autobiographical memory specificity was not associated with IC ($\beta = 0.08, SE = 11.87, p = .99$), nor it was associated with depressive symptomatology ($\beta = -0.02, SE = 0.06, p = .69$). In addition, IC was not significantly associated with depression either ($\beta = -0.91, SE = 5.42, p = .87$) (Figure 3). Similarly, when considering

response time, autobiographical memory specificity was not associated with IC ($\beta = 1.34$, $SE = 0.78$, $p = .09$), nor it was associated with depressive symptomatology ($\beta = -0.02$, $SE = 0.06$, $p = .79$). As in the prior analyses, IC again was not significantly associated with depression ($\beta = -0.27$, $SE = 0.32$, $p = .39$) (Figure 4).

Moderation Analyses

Process (Hayes, 2012) was used to conduct a moderation analysis using Model 1. The two variations of CVB (e.g. CVB-SR, CVB-O) were considered in moderation analysis. When using CVB-SR, results showed that, as proposed by *Hypothesis 7a*, rumination moderated the relationship between CVB and depressive symptomatology ($\beta = 0.47$, $SE = 0.20$, $p = .02$) (Figure 5). The interaction effect was positive. Further analysis of the significant interaction effect demonstrated that there is no relationship between CVB and depression at low levels of rumination ($\beta = -0.10$, $SE = 0.56$, $p = .85$). On the other hand, for average levels of rumination, one increase in CVB contributes .94 to depressive symptomatology ($\beta = 0.94$, $SE = 0.40$, $p = .02$). Similarly, at high levels of rumination, an increase in CVB contributes 2.04 to depression symptoms ($\beta = 2.04$, $SE = 0.65$, $p = .003$).

When using CVB-O, the moderation effect of rumination in the relationship between CVB and depressive symptomatology disappeared ($\beta = 0.24$, $SE = 0.17$, $p = .15$) (Figure 6). *Hypothesis 7b* was not supported in that FA was not a significant moderator in the relationship between CVB and depression when considering CVB-SR ($\beta = -0.002$, $SE = 0.02$, $p = .91$) (Figure 7) or CVB-O ($\beta = -0.01$, $SE = 0.02$, $p = .71$) (Figure 8).

CHAPTER SIX: CONCLUSION

In sum, results from simple regression, moderation and mediation analyses showed partial support for one of our initial hypotheses. The significant relationship between subjectively-reported cerebrovascular burden and depression was significantly moderated by rumination with a positive interaction effect; also, rumination was a consistent predictor of depressive symptomatology across analyses. By contrast, cerebrovascular burden calculated using objective measures (blood pressure, heart rate, oxygen saturation) was not significantly related to depressive symptomatology. This finding supports past work on clinically-defined vascular depression (Mast, Neufeld, MacNeill, & Lichtenberg, 2004; Mast, Yochim, et al., 2004; Paulson et al., 2013). The CaR-FA-X model rationale for the hypothesized relationship between autobiographical memory specificity and depressive symptomatology was not supported by analyses on available data.

There could be two reasons why autobiographical memory specificity did not relate to any of the other components in the CAR-FA-X model including rumination, functional avoidance, executive functioning, and depression. One of the reasons could be the advanced age of most participants in our sample; age range of our sample was 70 to 89 with a mean of 76.28 (4.48). The other studies that were found that used participants within our age range was one conducted by Ros, Latorre, and Serrano (2009) in which one of the two sample groups catalogued as “older adults” had ages ranging from 57 to 80 years old with a mean of 65.98 (5.54), and another study in which older adults’ age range was 60 to 86 years with a mean age of 73.70 (7.10) (Phillips & Williams, 1997). It is worth noting that the sample that resembles ours more closely in terms of age is the one in the latter study, and even in this sample only one out of the 22 participants was considered to exhibit normal aging (Phillips & Williams, 1997). In that sense, our sample is the

first one to use a non-clinical population of healthy participants who are 70 years or older to assess AMS. Most studies supporting the CaR-FA-X model have been conducted using younger samples (Dagleish et al., 2008; Debeer et al., 2012; Debeer et al., 2013; Hauer et al., 2008; Hermans, De Decker, et al., 2008; J. A. Sumner et al., 2011). A previous meta-analysis found age to be a significant moderator in the relationship between AMS and depression (J. A. Sumner et al., 2010) meaning that the AMT might exhibit ceiling effects for younger populations. In the same manner, floor effects could be present in a sample of very old individuals. There is a certain decline in executive functioning paired with aging (Salthouse, Atkinson, & Berish, 2003), which in turn might affect the ability of older adults at large to retrieve specific memories.

Another probable reason for which we did not find any relationship between AMS and any of the other components in the CAR-FA-X model could be attributed to the very nature of depressive symptomatology, and proposed differences between vascular depression and depression that has its onset earlier in life. Our sample of healthy older adults was screened for diagnosis of any psychological condition at any point in their lives. The rationale for this was to prevent participants who had been diagnosed with depression at a younger age to be included in the study and confound our results, which was more concerned with vascular depression specifically, which has a late onset. It could be that mechanisms causing and sustaining regular depression might in turn be related to poorer AMS whereas mechanisms of action in vascular depression do not necessarily relate to AMS in the same way. Alternatively, a great portion of studies in AMS have been conducted with clinical populations with major depressive disorder or a trauma history (Kuyken & Brewin, 1995; Mackinger et al., 2000; McNally et al., 1994), in which depressive symptomatology tends to be more pronounced. On the other hand, the mean depression score in our sample was 6.23 (4.10). A score between 0 and 9 is considered normal, a score between 10 and 19 is considered mild depression, and a score of 20 to 30 is considered severe depression (Yesavage et

al., 1982).. In our sample, six participants, or about 12% of the sample, had a score within the mild depression range, and one participant had a score within the severe depression range. Also, the mean for all depression scores was within the normal range. Previous literature has suggested that the AMT might lack sensitivity in non-clinical populations (De Beer, Hermans, & Raes, 2005; Raes & Hermans, 2002; Raes, Hermans, Williams, & Eelen, 2007), and that AMS is not related to depressive symptomatology or brooding in non-clinical populations (Raes, Pousset, & Hermans, 2004).

Results in this study, with respect to the AMT, were null effects. While further work is needed to understand this, one interpretation is suggested by the Self Memory System model. This model, proposed by Conway and Pleydell-Pearce (2000), authors suggest that autobiographical memory specificity is not only the result of mere access to the episodic memory system, which encompass sensory perceptual information about past events, but it is the product of three systems working together, one of which is the long term self, which includes life story schemas, personal scripts, self-guides and beliefs. Clinical populations seem to over rely on the long-term self when asked to recollect past events rather than integrating information from episodic memory system with information in the long term self-system (Conway, Singer, & Tagini, 2004; Crane, Barnhofer, & Williams, 2007). Following this model, some authors have found that autobiographical memory specificity as captured by the Autobiographical Memory Test relates to depression depending on the self-relevance of the cue word, and this relationship is only consistent in individuals who have suffered from depression previously. Regression analyses showed that depression history moderated the relationship between cue-self relevance and autobiographical memory specificity (Crane et al., 2007). One possible interpretation is that participants who have lived with depression for a longer time have established schemas for emotional content in the long term self-system, which become automatically activated with cue words in the AMT. These participants tend to

mitigate sensory details from past events in the episodic memory system. On the other hand, those participants with no history of depression prior to later-life may not have strong networks in the long term self-system. This may result in a better integration of information, thus mitigating the apparent relationship between AMT score and depressive symptomatology. In sum, the advanced age of all our participants might have resulted in floor effects, and that added to the non-clinical status of the sample might have resulted in null findings contrary to those hypothesized based on previous literature on AMS.

Implications

The vascular depression theory was partially supported, with ruminative tendencies serving as a moderator on the relationship between CVB and vascular depression. In addition, the interaction between these two variables seems to take place at average and high levels of rumination, but not low levels of rumination. Furthermore, the interaction was significant when CVB made use of self-reported health conditions but not when the same variable also included physiological measures administered to participants during the testing session. These inconsistent results could be justified in that most of our participants reported taking medication to control their respective health problems, which in fact could normalize physiological measures of cerebrovascular burden that were considered in this study. Also, it is important to consider that physiological measures are more state dependent (e.g. could be influenced by whether participants took their medications during testing day, caffeine or food intake, mood state, etc.), and they are subject to variability during a day, month, and a week. To make a state dependent variable a more stable representation of a certain condition, repeated measures of that same physiological variable would be necessary over an extended period, which were not performed during this study. Alternatively, clinical markers that reflect biological variance over a period, such as A1C, may be employed. Unfortunately, laboratory methods necessary for acquisition of A1C data were not

available for the present study. On the other hand, participants' self-reported health conditions may be a more stable representation of the construct in question (CVB) because the existence of these conditions are not constrained by time or situation, but participants have lived with these conditions for months or years. Therefore, CVB that makes use of self-reported health conditions, as conceptualized in previous research by Mast, Neufeld, et al. (2004); Mast, Yochim, et al. (2004) and Paulson et al. (2013), might be a better representation of CVB for results in this study than CVB that includes physiological measures obtained during the course of one testing session with each participant.

Moderation in this case indicates that the relationship between cerebrovascular burden and vascular depression varies by level of ruminative tendencies (Figure 9). A simple regression analysis of the CVB-SR variable on the depression variable showed that the relationship between CVB and depression was significant even without the presence of ruminative tendencies. Sneed and others have found relationships between neuropathological markers of CVB, namely WMH, and depressive symptomatology using MRI technology. This methodology provides a more direct assessment of CVB-mediated brain aging. Past work on clinically-defined vascular depression assumes a relationship between CVB and white matter integrity, though, like other studies employing the clinically-defined framework, that relationship was not directly examined in this study. It is likely that many older adults with cerebrovascular risk factors may not have developed WMH at the time of this study, and it is safe to assume that such hallmark neurological features have not developed in those without high CVB. One interpretation of the finding that rumination moderates the relationship between CVB and depressive symptomatology is that those with high CVB and corresponding brain changes may develop ruminative coping patterns, thus leading to depressive symptomatology, at higher rates than those with either high CVB but non-diseased

white matter, or those with low CVB. Mast, Yochim, et al. (2004) reported that executive deficits moderated the relationship between high CVB and depressive symptoms. Given the analytical model, this would be a parallel finding that is consistent with the above results. This empirical question may be addressed through future research using structural imaging methodologies.

Taken together these findings indicate that cerebrovascular burden along with other risk factors might precipitate the onset and development of vascular depression to different extents. Also, previous research has shown that ruminative tendencies also serve as a mediator in the relationship between executive functioning and depression (Von Hippel et al., 2008). The development of vascular depression could result from an intricate web of multiple mediating and moderating factors, which emerging research is starting to identify.

Further studies should work to identify other potential mediators and moderators in the relationship between CVB and vascular depression. In addition, longitudinal studies could evaluate the relationship between CVB and depression using repeated physiological measurements over a certain period and then evaluate how these results compare to CVB as obtained by self-reported health conditions only. By understanding the specific moderators and mechanisms of action, researchers may better identify novel therapeutic psychotherapeutic targets for late-life depression. Another possible avenue for future research involves selecting depression psychotherapies (life-review therapy, problem solving therapy, cognitive therapy, behavior activation) based on individual patients' cognitive presentations using variables such as rumination, executive impairment, or functional avoidance.

Limitations

One limitation of our study is that our findings might not generalize well to the older population at large. Our sample was a highly selected group of healthy, Caucasian, older adults in the Orlando area with high levels of education and physical activity on average, and who remain

largely involved in the community. In fact, many of our participants were recruited from the Learning Institute for Elders (LIFE) at the University of Central Florida, which is a group that provided learning experiences for adults who are fifty and older, and who continued to be interested in educational pursuits. Many LIFE members hold bachelor or graduate degrees and are retired professionals. Although our recruitment process was open to all members of the Orlando community, our sample might be considered a convenience sample. Furthermore, minorities remained underrepresented in this study as well as others of a similar nature. Additionally, because most of our participants remained physically active, they might be more health focused than the average older adult, and consequently they might exhibit less pathology and medical comorbidity. In fact, previous studies have suggested that exercise might reduce brain tissue loss (Colcombe et al., 2003), improve cardiovascular functioning (Mazzeo et al., 1998), and protect executive functioning in older adults (D. R. Evans & Segerstrom, 2015).

Another limitation is our sample size. Even though a power analysis suggested a sample size of 35 for an 80% probability of seeing hypothesized effects, our unique sample of 43 participants may not have been sufficient to identify the relationships among multiple variables in the simple regression analyses. It is worth noting that this limitation would not apply to moderation and mediation analyses in which this problem was eliminated using bootstrapping.

Future Directions

Results in this study evidences the need for future research on the areas of autobiographical memory specificity, vascular depression, and these two combined in the older adult population. It is clear that in spite of research findings over the span of three decades that support the vascular depression theory (Alexopoulos, 1990; K. R. R.; Krishnan & McDonald, 1995), and the relationship between autobiographical memory specificity and depression proposed by Williams

and Broadbent (1986), the knowledge on these areas remains in its infancy when compared to what remains to be discovered. Future studies should address some present limitations in this project, such as those that involve generalization by including more minorities, and a combination of clinical and non-clinical groups. Additionally, further studies should make use of other measures of autobiographical memory specificity, such as the Sentence Completion for Events from the Past test (Raes, Hermans, Williams, & Eelen, 2007), which might be more sensitive to a non-clinical older adult population than the AMT. With respect to the study of vascular depression, future research should continue to look at rumination and executive functioning scores, and their role with other variables on the development of vascular depression.

These findings add to prior research cognition and depression in older adults in general and as it relates to the vascular depression hypothesis in particular. Through a better understanding of contributing factors to the exacerbation of depression, better treatments can be designed to mitigate the damaging effects of this disorder in older adults, their caregivers and their families in general.

APPENDIX A: FIGURES

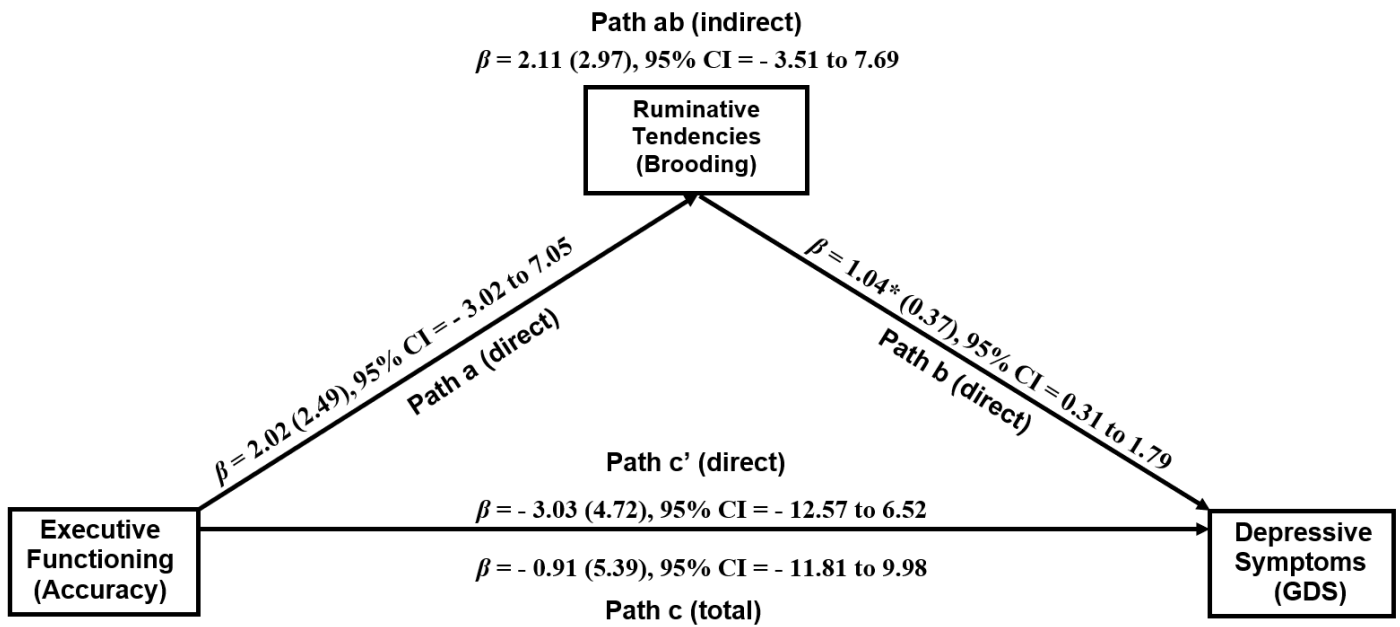


Figure 1. Mediation analysis on the relationship between executive functioning using accuracy values and depression with rumination as a mediator. CI = confidence interval. Standard errors for standard coefficients are enclosed in parentheses; executive functioning refers to interference control more specifically. * $p = .01$

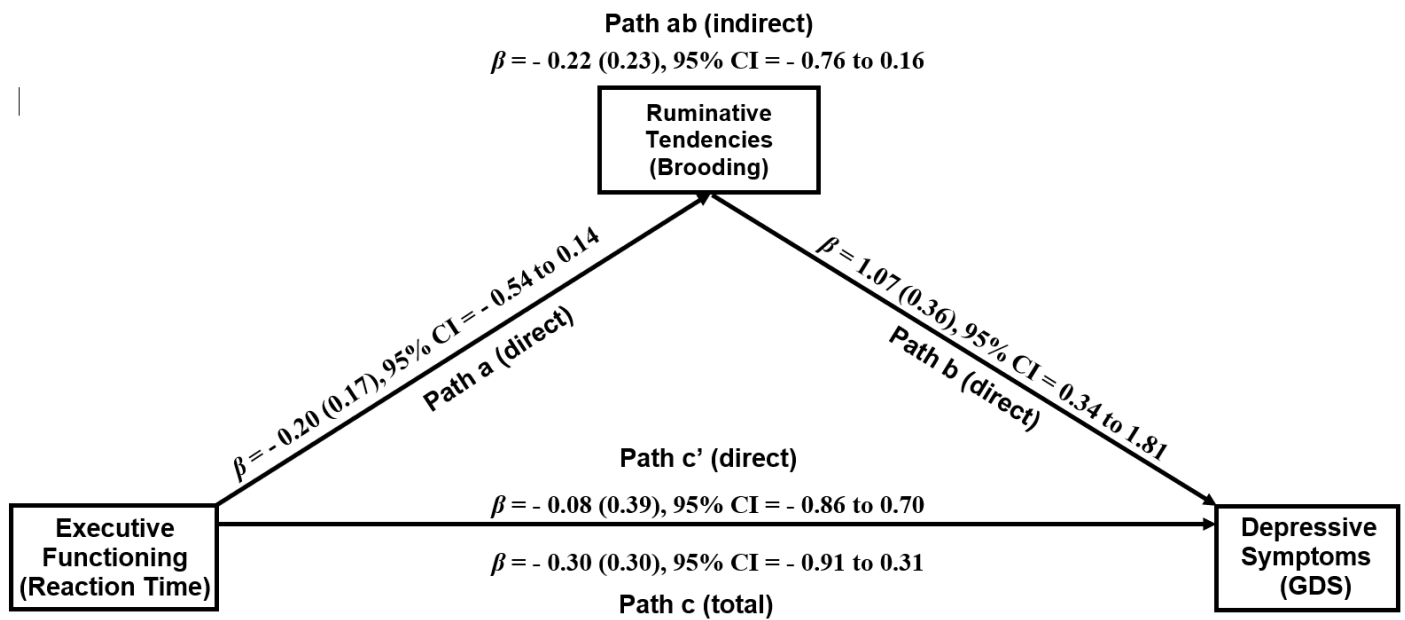


Figure 2. Mediation analysis on the relationship between executive functioning using reaction time values and depression with rumination as a mediator. CI = confidence interval. Standard errors for standard coefficients are enclosed in parentheses; executive functioning refers to interference control more specifically. * $p = .01$

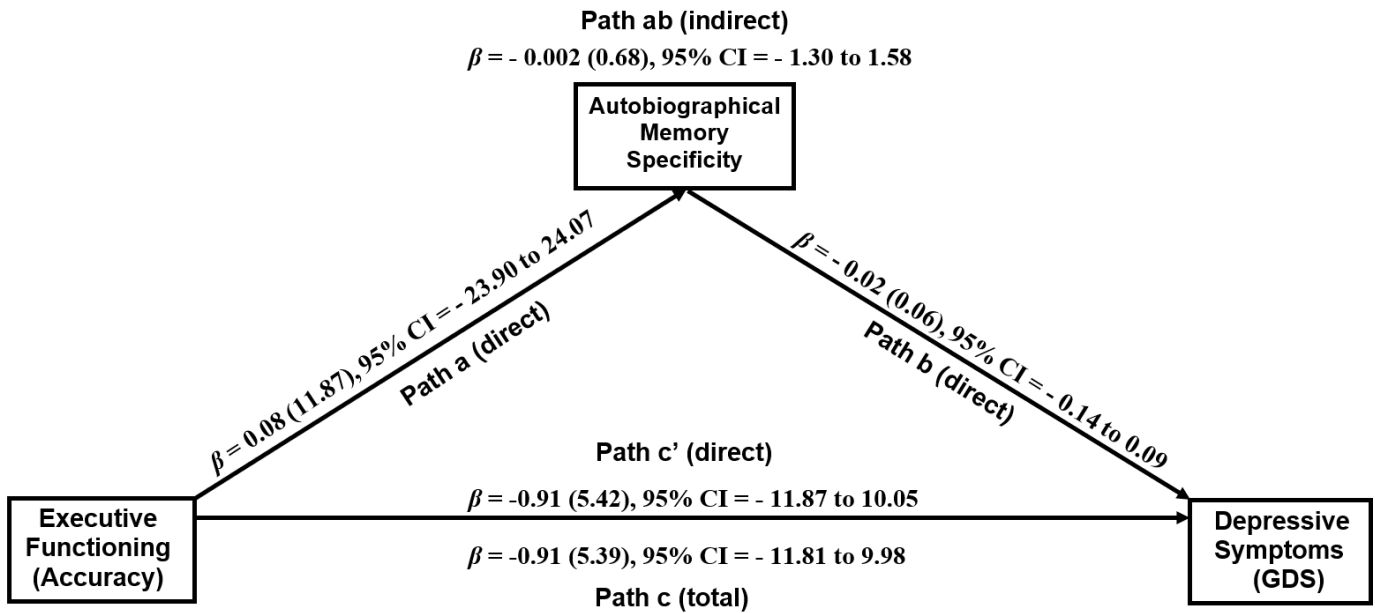


Figure 3. Mediation analysis on the relationship between executive functioning using accuracy values and depression with autobiographical memory specificity as a mediator. CI = confidence interval. Standard errors for standard coefficients are enclosed in parentheses; executive functioning refers to interference control more specifically.

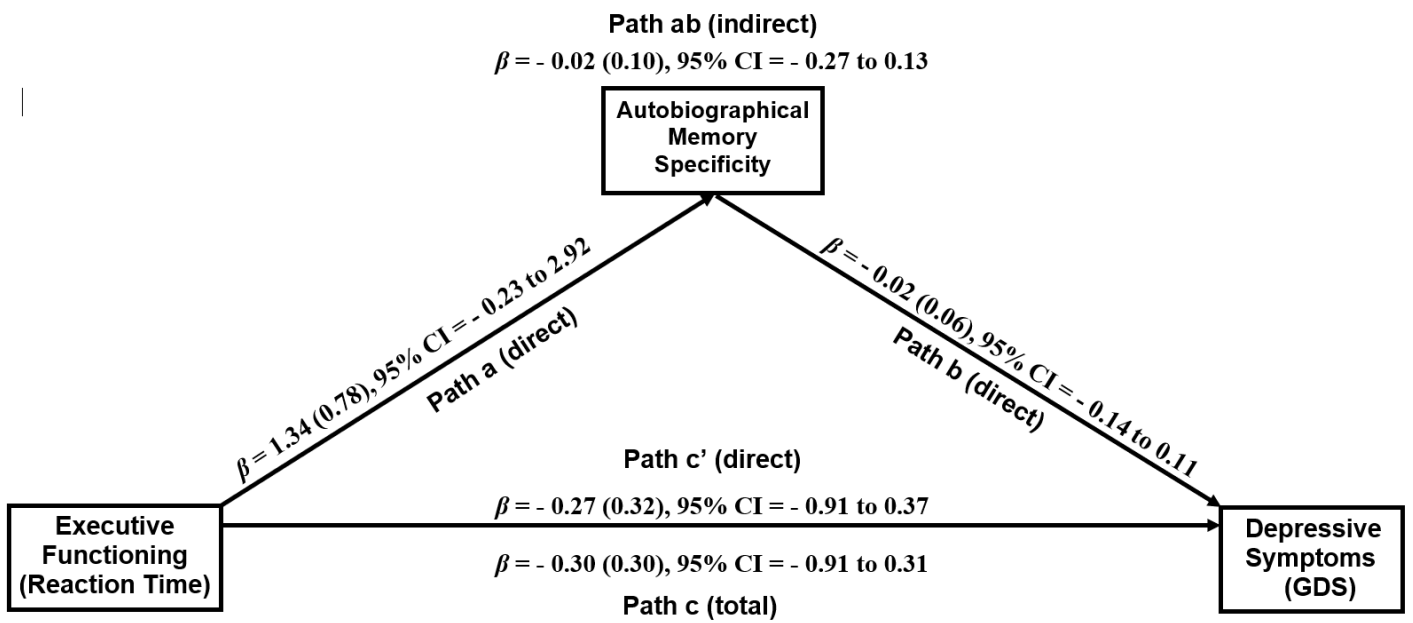


Figure 4. Mediation analysis on the relationship between executive functioning using reaction time values and depression with autobiographical memory specificity as a mediator. CI = confidence interval. Standard errors for standard coefficients are enclosed in parentheses; executive functioning refers to interference control more specifically.

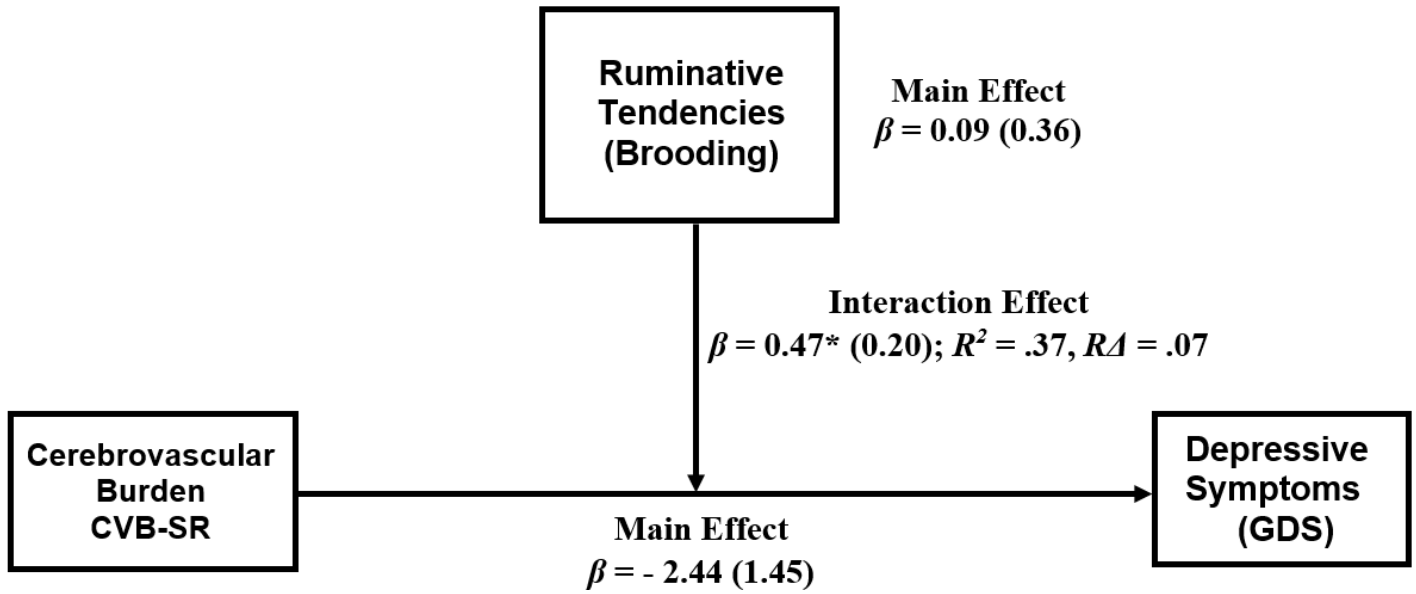


Figure 5. Moderation analysis on the relationship between cerebrovascular burden and depression with rumination as a moderator. CVB-SR = cerebrovascular burden as defined by self-report health conditions. Standard errors for standard coefficients are enclosed in parentheses. * $p = .02$

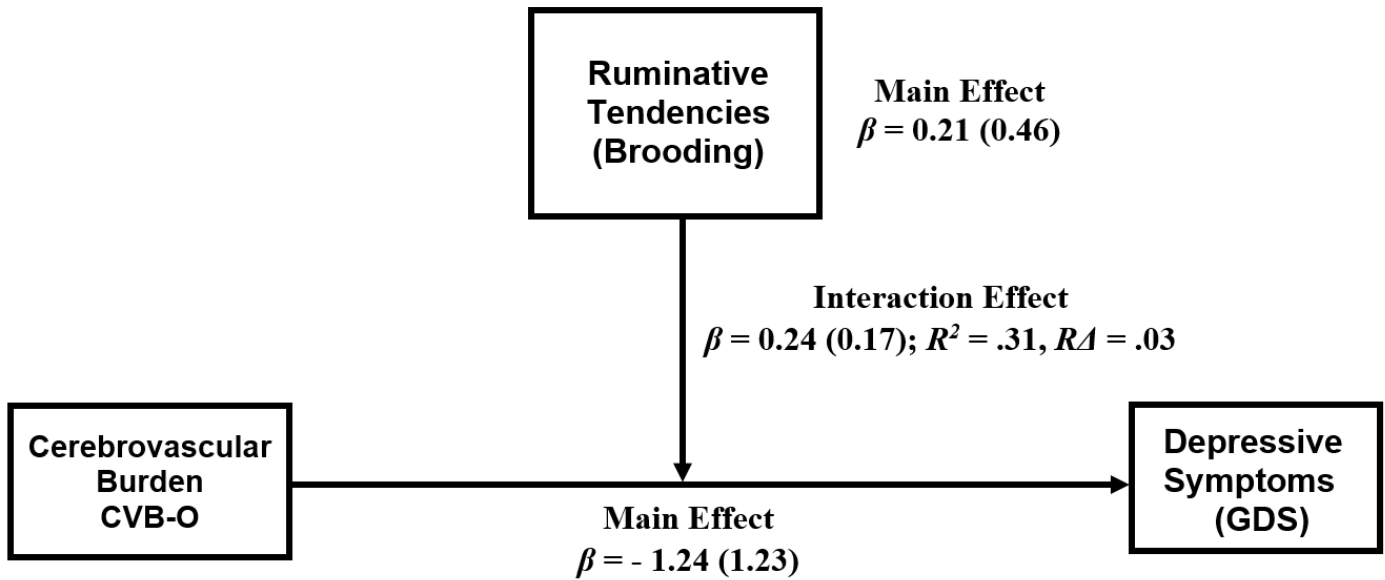


Figure 6. Moderation analysis on the relationship between cerebrovascular burden and depression with rumination as a moderator. CVB-O = cerebrovascular burden as defined by self-report health conditions and biomarker data. Standard errors for standard coefficients are enclosed in parentheses.

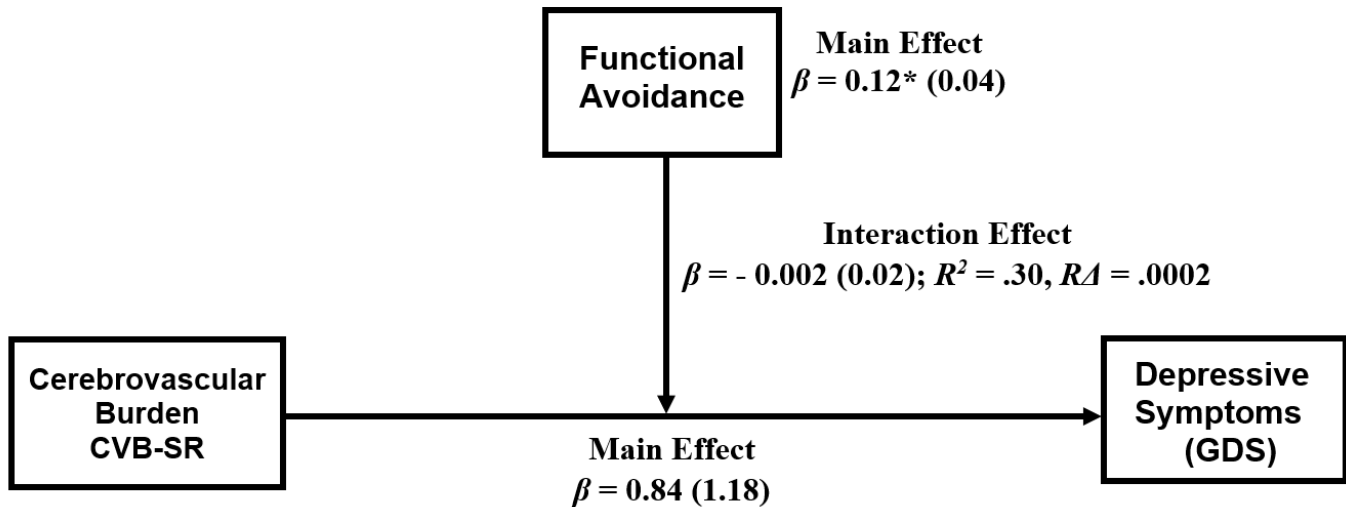


Figure 7. Moderation analysis on the relationship between cerebrovascular burden and depression with functional avoidance as a moderator. CVB-SR = cerebrovascular burden as defined by self-report health conditions. Standard errors for standard coefficients are enclosed in parentheses. * $p = .01$

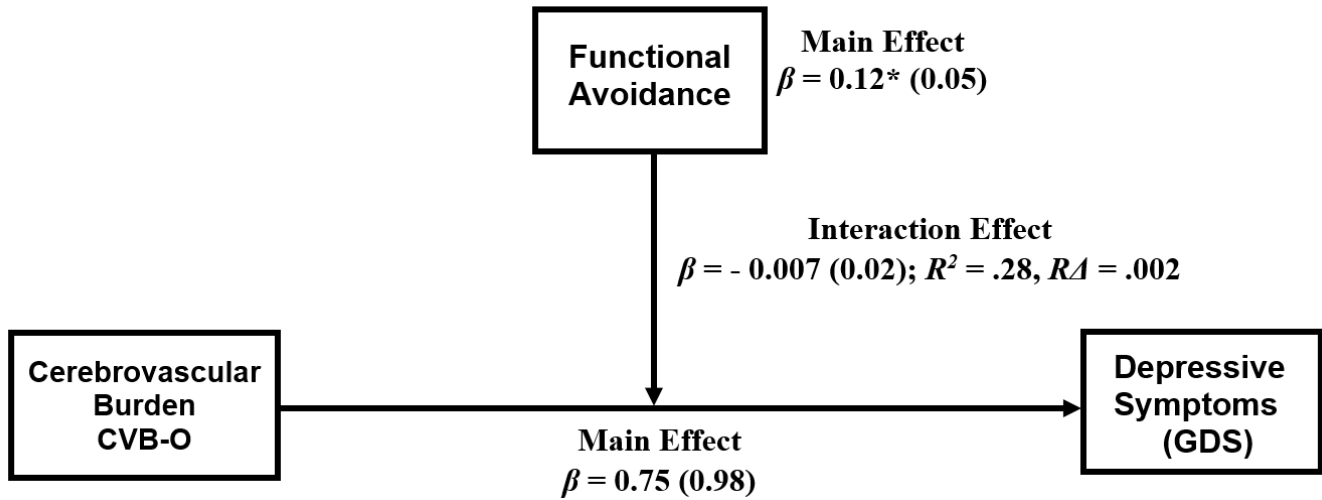


Figure 8. Moderation analysis on the relationship between cerebrovascular burden and depression with functional avoidance as a moderator. CVB-O = cerebrovascular burden as defined by self-report health conditions and biomarker data. Standard errors for standard coefficients are enclosed in parentheses. * $p = .01$

APPENDIX B: TABLES

Table 1: Demographic characteristics of the sample

Demographic Data (N = 52)	
Variables	Mean (SD) or % (Unless indicated otherwise)
Age	76.40 (4.60)
Gender (Female)	63.46
Race	
White	90.39
Hispanic/Latino	7.69
Native American	1.92
Education Level (Years)	16.46 (2.94)
Income (Interquartile Range)	\$42,500.00
Marital Status	
Married	55.77
Divorced	17.31
Widowed	26.92
Employment Status	
Employed Part-Time	5.77
Retired	94.23
Number of People in Household	
One – I live alone	36.54
Two	61.54
Five	1.92
Handedness (Right)	92.31
Depressive Symptomatology (GDS)	6.23 (4.10)
Heart rate	71.67 (13.71)
Oxygen Saturation	95.02 (5.43)
Systolic Blood Pressure	134.77 (16.63)
Diastolic Blood Pressure	71.58 (10.05)
Self-Reported Health Complaints ††	
High Blood Pressure	40.39
Hearth and Circulation Problems	19.23
Chest Problems	9.62
Diabetes	19.23

† Income Amount in U.S. Dollars

†† Health Complaints During the Past Year

Table 2: Bivariate correlation analysis of main variables in the study

	CVB-SR	CVB-O	GDS	AMS	CaR	FA	X(Time)	X(Accuracy)
CVB-SR	-							
CVB-O	.91***	-						
GDS	.30*	.26	-					
AMS	-.09	-.17	-.004	-				
CaR	.12	.13	.49***	.04	-			
FA	.19	.22	.51***	-.02	.67***	-		
X (Time)	.13	.09	-.11	.25	.14	-.20	-	
X (Accuracy)	.02	-.06	-.03	.001	.11	.16	-.02	-

CVB-SR = Cerebrovascular burden as defined by self-reported health conditions; CVB-O = cerebrovascular burden as defined by self-reported health conditions and biomarker data; GDS = Depression as measured with the Geriatric Depression Scale; AMS = Autobiographical Memory Specificity; CaR = Rumination (Brooding); FA = Functional Avoidance; X = Executive Functioning (Interference Control); * $p < .05$; ** $p < .01$

APPENDIX C: APPROVAL LETTER



University of Central Florida Institutional Review Board
 Office of Research & Commercialization
 12201 Research Parkway, Suite 501
 Orlando, Florida 32826-3246
 Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Human Research

From: UCF Institutional Review Board #1
 FWA00000351, IRB00001138

To: Daniel Lee Paulson and Co-PIs: David Brush & Manuel Herrera Legon

Date: January 05, 2017

Dear Researcher:

On 01/05/2017 the IRB approved the following human participant research until 01/04/2018 inclusive:

Type of Review: IRB Continuing Review Application Form
 Expedited Review

Project Title: UCF Vascular Aging Study

Investigator: Daniel Lee Paulson

IRB Number: SBE-15-11791

Funding Agency: College of Sciences, Learning Institute for Elders at UCF

Grant Title:

Research ID: N/A

The scientific merit of the research was considered during the IRB review. The Continuing Review Application must be submitted 30 days prior to the expiration date for studies that were previously expedited, and 60 days prior to the expiration date for research that was previously reviewed at a convened meeting. Do not make changes to the study (i.e., protocol, methodology, consent form, personnel, site, etc.) before obtaining IRB approval. A Modification Form **cannot** be used to extend the approval period of a study. All forms may be completed and submitted online at <https://iris.research.ucf.edu>.

If continuing review approval is not granted before the expiration date of 01/04/2018, approval of this research expires on that date. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

Use of the approved, stamped consent document(s) is required. The new form supersedes all previous versions, which are now invalid for further use. Only approved investigators (or other approved key study personnel) may solicit consent for research participation. Participants or their representatives must receive a signed and dated copy of the consent form(s).

All data, including signed consent forms if applicable, must be retained and secured per protocol for a minimum of five years (six if HIPAA applies) past the completion of this research. Any links to the identification of participants should be maintained and secured per protocol. Additional requirements may be imposed by your funding agency, your department, or other entities. Access to data is limited to authorized individuals listed as key study personnel.

In the conduct of this research, you are responsible to follow the requirements of the [Investigator Manual](#).

On behalf of Sophia Dziegielewski, Ph.D., L.C.S.W., UCF IRB Chair, this letter is signed by:

Signature applied by Kamille Chaparro on 01/05/2017 04:52:12 PM EST

IRB Coordinator

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