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# Cognitive Functioning, Depression, and Strengths as Predictors of Quality of Life in Multiple Sclerosis

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Cognitive Functioning, Depression, and Strengths as Predictors of Quality of Life in Multiple  
Sclerosis

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A dissertation submitted in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

In

Clinical Psychology

Seattle Pacific University

School of Psychology, Family, & Community

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### **Abstract**

Patients with multiple sclerosis (MS) are at significant risk for decreased quality of life, partly due to associated cognitive impairment (Højsgaard Chow et al., 2018). A discrepancy often exists between objective and perceived measures of cognitive impairment (Middleton et al., 2006); the paths through which they predict quality of life for MS patients remain unclear (Baumstarck-Barrau, et al., 2011). Objective cognitive functioning as well as one's perceptions of it may differentially impact quality of life, and therefore may or may not act through the same mechanisms to impact quality of life. Depression is one possible mediator known to impact quality of life in MS patients (Göksel Karatepe et al., 2011). Additionally, strengths such as gratitude may impact quality of life in chronic diseases like MS. Gratitude allows patients to extend focus beyond themselves, increasing appreciation for other parts of life despite experiencing a medical condition (Büssing et al., 2014). The purpose of the present study was to examine the effects of cognitive impairment on quality of life via depression symptoms, and how these effects might be moderated by gratitude in a cross-sectional study with participants formally diagnosed with MS. Participants ( $N = 128$ ) completed a short battery to assess cognitive function and self-report measures of depression, perceived cognitive functioning, quality of life, and gratitude. Consistent with hypotheses, both perceived and objective cognitive functioning predicted quality of life through depression. This provides support for the idea that one's experience of cognitive impairment impacts depressed mood and might lead to impaired quality of life. Contrary to hypotheses, gratitude did not moderate links between cognitive functioning (perceived nor objective) and depression, depression and quality of life, nor the indirect effect between cognitive functioning (perceived nor objective) and quality of life via depression with

gratitude acting on the “A” and “B” paths. However, even after controlling for other study variables, gratitude predicted lower depression and higher quality of life. These results offer further understanding of cognitive functioning (objective and perceived) and the impact of depression on quality of life in MS, and bear implications for how gratitude may contribute to well-being beyond known processes.

*Keywords:* multiple sclerosis, cognition, depression, quality of life, gratitude

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## CHAPTER I

### Introduction and Literature Review

#### Overview

About 40-70% of patients with multiple sclerosis (MS) experience decreased cognitive functioning with impairment ranging from mild to severe (Romero, Shammi, & Feinstein, 2015). Evidence suggests that MS and cognitive impairment are consistently associated; however, the mechanisms by which the process of impairment occurs and impacts on quality of life are still not fully understood (Achiron et al., 2005; Jongen, Ter Horst, & Brands, 2012; Rahn, Slusher, & Kaplin, 2012; Rao, Leo, Bernardin, & Unverzagt, 1991).

Research studies document a common discrepancy between objective (i.e., cognitive testing) and perceived measures of cognitive impairment (i.e., self-reports) in patients with MS (Middleton, Denney, Lynch, & Parmenter, 2006). This suggests that either individuals have difficulty estimating their actual level of cognitive impairment, or that symptoms commonly experienced in MS (e.g., fatigue and depression) may contribute to how individuals perceive their abilities (Kinsinger, Lattie, & Mohr, 2011). For instance, in one study, patients' subjective ratings of depression, anxiety, fatigue, and level of disability predicted their perceived cognitive functioning, whereas objective measures of cognitive functioning did not predict their perceived cognitive functioning (Middleton et al., 2006). Factors outside of individuals' true level of cognitive functioning seem to influence how they perceive their cognitive abilities.

Objective and perceived cognitive functioning may have a differential impact on quality of life, and therefore may or may not act through the same mechanisms to impact quality of life. Some studies have found that objective measures of cognitive functioning predict quality of life for patients with chronic disease such as stroke (Barker-Collo & Feigin, 2006), end-stage liver

disease (Paulson, Shah, Miller-Matero, Eshelman, & Abouljoud, 2016), and minimal hepatic encephalopathy (Prasad et al., 2007), and in individuals specifically with MS (Benito-León, Morales, & Rivera-Navarro, 2002; Hoogs, Kaur, Smerbeck, Weinstock-Guttman, & Benedict, 2011; Mitchel, Benito-León, González, & Rivera-Navarro, 2005), whereas they had limited capacity to predict quality of life in other studies (Baumstarck-Barrau, et al., 2011; Giovannetti et al., 2016; Glanz et al., 2010). However, perceived cognitive functioning has consistently predicted quality of life, even when controlling for depression and disease severity (Giovannetti et al., 2016; Samartzis, Gavala, Zoukos, Aspiotis, & Thomaidis, 2014).

Given high comorbidity of depressed mood states with MS (Siegert & Abernethy, 2005) and their impact on quality of life in MS patients (Göksel Karatepe et al., 2011; Janardhan & Bakshi, 2002), it is possible that depression may act as a mediator in the relationship between cognitive functioning and quality of life, and particularly so for perceived cognitive functioning. On one hand, physical damage due to MS (demyelination lesions) in some studies has correlated with lower scores on objective measures of cognitive function (Popescu & Lucchinetti, 2012; Rahn et al., 2012; Stadelmann, Wegner, & Brück, 2011; Winkelmann, Engel, Apel, & Zettl, 2007), higher levels of depression (Feinstein et al., 2004; Feinstein et al., 2010; Pucak, Carroll, Kerr, & Kaplin, 2007), and lower quality of life specifically regarding aspects such as emotional well-being, and mental and physical fatigue (Mowry et al., 2009). This suggests the possibility that physical brain damage due to cognitive lesions might shape depression symptoms, and thereby quality of life. On the other hand, some studies have found that perceived cognitive functioning in MS patients was more highly associated with self-reported depression than were neuropsychological test scores (Kinsinger et al., 2011; Romero et al., 2015), and patients' emotional states (e.g., depression) may distort their perceptions of their cognitive functioning

(Kinsinger et al., 2011; Middleton et al., 2006). This implies the possibility that indirect effect of perceived cognitive functioning on quality of life may be more likely to be present than the effect of objectively measured cognitive functioning, although this is unknown. Patients' emotional states might explain part of the differential link between objective versus perceived cognitive functioning. Thus we need research to test depression as a mediating link between objective versus perceived cognitive functioning and quality of life directly. Directly assessing this mediating link may help to determine whether depression symptoms serve as a mediator between perceived and objective cognitive impairment and lower quality of life. Research is thereby warranted regarding: 1) the differential effects of perceived and objective cognitive functioning on quality of life in MS, and 2) the effect of depression as a possible mediator in the relationship between cognitive functioning and quality of life in MS (for both perceived and objective measures of cognitive functioning).

Whereas affectively negative processes such as depressive symptoms may predict lower quality of life in MS, the role of affectively positive processes such as personal strengths in predicting higher quality of life have largely gone unexplored in this population. Gratitude, for example, is a particular positive emotional state characterized by acknowledging and appreciating blessings received in one's life; it can be conceptualized as both a fleeting emotion (state) and as a trait whereby one is generally prone to experiencing the emotion (Tulbure, 2015). There is evidence to suggest that strengths such as gratitude may impact quality of life in chronic diseases other than MS (de Souza & Kamble, 2016; Swift, Ashcroft, Tadd, Campbell, & Dieppe, 2002; Tóthová et al., 2014). For instance, evidence suggests that the specific strength of trait gratitude positively predicts quality of life and factors related to quality of life (e.g., anxiety, depression, sleep, well-being) for individuals dealing with chronic diseases such as MS

(Allahbakhshian, Jafarpour, & Parvizi, 2011), cancer (Ruini & Vescovelli, 2013), asymptomatic heart failure (Mills et al., 2015), and chronic pain (Ng & Wong, 2012). Patients with a chronic illness such as MS often have a narrowed focus on their symptoms and finding relief from these symptoms (Büssing et al., 2014). Gratitude allows patients to extend their focus beyond themselves, to increase appreciation for other parts of life despite their medical condition, and to positively alter cognitions and perceptions regarding their quality of life (Büssing et al., 2014). However, there is a dearth of research investigating strengths such as gratitude within MS patients. In addition, there is a lack of research on how positive traits, such as gratitude, might affect the relationships between objective cognitive functioning, perceived cognitive functioning, and quality of life in MS patients.

In summary, the paths through which objective (Baumstarck-Barrau et al., 2011; Benito-León et al., 2002; Glanz et al., 2010; Gold, Schulz, Mönch, Schulz, & Heesen, 2003) and perceived cognitive functioning (Samartizis et al., 2014; Giovannetti et al., 2016) predict quality of life for MS patients are unclear, as is the question of whether strengths such as trait gratitude, might interact with these processes. Thus, the purpose of the present study is to better understand how individual differences in cognitive functioning, depression, and strengths are related to quality of life for individuals diagnosed with MS. Specifically, the study aims to serve the following goals in a sample of individuals diagnosed with MS: 1) To examine how cognitive functioning (both perceived and objective cognitive abilities) predicts quality of life; 2) to examine whether depression symptoms mediate the effects of cognitive functioning on quality of life (for both perceived and objective cognitive functioning); and 3) to examine whether personal strengths of gratitude moderate the relationship between cognitive functioning (both objective and perceived) and depression, as well as the relationship between depression and quality of life

for MS patients. The literature review that follows provides further background and justification for these aims.

## **Background**

### **Core Features of Multiple Sclerosis**

Multiple sclerosis (MS) is a relatively common neurological condition; in the United States about 400,000 individuals have been diagnosed with the disease—roughly 2 million people worldwide (Kingwell et al., 2013; Tullman, 2013). MS is an immune-mediated degenerative neurological condition in which an individual's immune system begins to attack the myelin that surrounds and insulates nerve fibers. When the myelin is attacked, nerve impulses may be interrupted and signals do not travel to their intended locations. Individuals experience symptoms such as dizziness, blurred vision, electric shock sensations, tremor, weakness in body limbs, spasticity, loss of balance, loss of coordination, and bladder and bowel dysfunction (World Health Organization, 2016).

Individuals can vary widely in the course of their disease; symptoms can be mild to severe and fluctuate over time. Initially, patients are typically diagnosed with relapsing-remitting MS, in which symptoms generally remain stable but are punctuated by intermittent attacks of more severe symptoms (Moore et al., 2012; Rolak, 2003). Individuals may be initially diagnosed with progressive MS where they do not have periods of remission; their symptoms continue to become worse from the onset of the disease. Individuals initially diagnosed with relapsing-remitting MS may eventually experience a progressive course of MS without periods of symptom remission called secondary progressive MS; in this subtype, individuals no longer experience remission from symptoms and symptoms progressively become worse. The cause of the disease remains unknown (Rolak, 2003). There is a significant amount of uncertainty in

disease progression due to the heterogeneous presentation of MS; there exists no clear long-term pattern or indicator to predict or determine the probable course of the disease (Gajofatto, Calabrese, Benedetti, & Monaco, 2013; Skoog, Tedeholm, Runmaker, Odén, & Andersen, 2014).

### **Health-Related Quality of Life in MS**

Although researchers in one atypical study found that 77% of MS patients in their sample reported a satisfactory to enjoyable quality of life, the literature collectively suggests that on average, quality of life scores in MS patients tend to be lower compared to both healthy controls and other chronic conditions (Ford, Gerry, Johnson, & Tennant, 2001; Nortvedt, Riise, Myhr, & Nyland, 1999; Pittock et al., 2004; Sprangers et al., 2000; Vickrey, Hays, Harooni, Myers, & Ellison, 1995). Individuals' quality of life (referred to interchangeably with health-related quality of life) refers to individuals' judgment of their overall well-being or perception of their condition in life. It is best understood within the context of physical, emotional, and psychosocial factors, in addition to individuals' perception of well-being, perceived functioning, and intrusiveness of disease-related symptoms (Benedict et al., 2005; Göksel Karatepe et al., 2011; Miltenburger & Kobelt, 2002).

Inconsistency exists regarding which aspects of quality of life are lower in MS patients compared to healthy controls, yet it is clear that individuals diagnosed with MS tend to have lower scores related to physical functioning (general health and fatigue) and mental/emotional functioning (depression, anxiety, pain, hopelessness) compared to non-MS controls (Benedict et al., 2005; Benito-León et al., 2002; Isaksson, Ahlström, & Gunnarsoson, 2005; Janardhan & Bakshi, 2000; Mitchell et al., 2005; Salehpoor, Rezaei, & Hosseini-zhad, 2014). Though depression may shape individuals' perception of quality of life, quality of life is distinct from depression. For example, depression can distort how individuals perceive their health or quality

of life and may increase difficulties in coping (Mitchell et al., 2005), yet quality of life reflects broader appraisals of functioning across multiple domains including physical, emotional, and psychosocial factors (Benedict et al., 2005; Göksel Karatepe et al., 2011; Miltenburger & Kobelt, 2002). Physical symptoms such as fatigue, for instance, are impairing and negatively affect quality of life for MS patients in terms of both employment and social functioning (Hakim et al., 2000; Hemmett, Holmes, Barnes, & Russell, 2004). Therefore, physical impairments can make daily functioning difficult for MS patients (Göksel Karatepe et al., 2011).

As the MS disease becomes more progressive, individuals experience increased impairment and decreased quality of life. Lower quality of life in MS patients is strongly associated with higher disability and disease progression; individuals with more progressive forms of MS have significantly lower reports of quality of life compared to individuals diagnosed with relapsing-remitting MS (Benito-León et al., 2002; Göksel Karatepe et al., 2011; Janardhan & Bakshi, 2000; Vermersch, de Seze, Delisse, Lemaire, & Stojković, 2002). This change in quality of life likely results from increased neurologic disability affecting mental and physical symptoms, and continually increasing difficulties with everyday activities, work, and social functioning without hope of symptom remission (Janardhan & Bakshi, 2000).

### **Cognitive Functioning in MS**

Despite heterogeneous symptom presentations and course, decreased cognitive function is relatively common in individuals diagnosed with MS. MS patients most commonly experience generalized dysfunction that cuts across domains including memory, information processing speed, attention, and executive functioning (Achiron et al., 2005; Javůrková, Zimová, Tomašovičová, & Raudenská, 2016). At earlier stages in the disease, the immune system begins to attack the central nervous system, causing inflammatory lesions in the brain, spinal cord, and

optic nerves as well as demyelination of the nerve fibers; this process leads to neurological symptoms including sensory, cognitive, visual, motor, cerebellar, and autonomic dysfunction (Popescu & Lucchinetti, 2012; Stadelmann et al., 2011; Winkelmann et al., 2007). However, at later stages however, neurological symptoms are associated with axonal degeneration (Su, Banker, Bourdette, & Forte, 2009; Winkelmann et al., 2007). However, the processes in MS that lead to these cognitive impairments (and the processes influencing the relationship between disease progression, cognitive functioning, and impact on quality of life) are poorly understood (Achiron et al., 2005; Jongen et al., 2012; Rao et al., 1991). Ongoing research, therefore, must further elucidate predictors of these outcomes in MS.

Most studies assessing objective cognitive functioning (Barker-Collo, 2006; Benito-León et al., 2002; Cutajar et al., 2000; Gold et al., 2003), though not all (Baumstarck-Barrau et al., 2011; O'Connor, Lee, Ng, Narayana, & Wolinsky, 2001), and perceived cognitive functioning (Giovannetti et al., 2016; Samartzis et al., 2014) find positive associations with quality of life in MS. Furthermore, lower cognitive functioning on objective measures is particularly impairing for MS patients' employment. It is extremely difficult for cognitively impaired individuals with MS to continue working; this tends to negatively affect their quality of life (Benedict et al., 2005; Rao et al., 1991). Additionally, MS patients' lower perceptions of their cognitive abilities related to planning/organizing and retrospectively remembering information, in particular, predicted lower quality of life above and beyond what disease severity predicted (Samartzis et al., 2014). Factors predicting quality of life are important as they may shape how MS patients manage and cope with an unpredictable disease on a daily basis (Buchanan, Huang, & Kaufman, 2010; Janardhan & Bakshi, 2000). However, the extent to which decreases in cognitive functioning impact quality of life in MS, and pathways by which it may do so, are not fully clear.



For individuals with MS, there is an evident discrepancy between individuals' perceived cognitive function and their objectively measured cognitive function (Middleton et al., 2006). It is uncontested that individuals with MS experience decreases in cognitive functioning. However, researchers' understanding of changes in cognitive functioning for individuals with MS may depend on the way that cognitive functioning is measured. Individuals with MS may subjectively experience cognitive impairment, however their subjective experience may not match their results on standardized neuropsychological tests. Objective cognitive performance and patients' perceptions of their cognitive performance often have a low correlation; individuals with MS tend to perceive their performance on cognitive abilities as lower than their level of functioning as estimated by objective cognitive performance tasks (Goverover, Genova, Griswold, Chiaravalloti, & DeLuca, 2014; Matotek, Saling, Gates, & Sedal, 2001; Middleton et al., 2006).

A variety of explanations are possible for why individuals' perceptions of their cognitive functioning are lower than their level of cognitive functioning as estimated by objective tests. Moreover, questions also remain about why cognitive functioning inconsistently predicts quality of life. First, variance in method or measurement of cognitive functioning may impact the relationship between objective and perceived cognitive functioning as well as the relationship between cognitive functioning and quality of life. Individuals with MS may experience a wide range of cognitive difficulties in domains including memory, processing speed, executive functioning, visuospatial skills, intellectual skills, and attention (Javůrková et al., 2016). Researchers may choose to measure select features of cognitive functioning in patients, perhaps using assessments measuring most typical forms of impairment (e.g., processing speed, memory, and executive function) (Javůrková et al., 2016). However, due to the unique process of

demyelination for each individual with MS, MS patients' composition of cognitive deficits may also be unique (Javůrková et al., 2016). Therefore, utilizing measures to assess only a few domains of cognitive functioning may not provide an accurate picture of individuals' objective cognitive function; however, an exhaustive neurological assessment however is rarely possible for research. Further, as individuals tend to observe their cognitive functioning as worse than is true, self-report measures of cognitive function may be a biased form of cognitive assessment (Maor, Olmer, & Mozes, 2001; Middleton et al., 2006). As objective and perceived cognitive functioning measures employ different assessment strategies and have a low correlation, they may differentially predict quality of life in MS. Results from a correlational study assessing objective cognitive functioning in MS patients showed a moderate relationship between objective cognitive functioning specific to visuospatial skills, as measured by an information processing speed task, and quality of life for MS patients (Glanz et al., 2010). However, in a cross-sectional study assessing MS patients with various subtypes, results evidenced only a weak relationship between objective cognitive functioning and quality of life (Baumstarck-Barrau et al., 2011).

Second, psychological factors may impact individuals' perception of cognitive functioning. A cross-sectional study assessing the joint effects of cognitive variables, psychological effects, disease severity, and disability in employed MS patients found that objective cognitive ability by itself did not predict quality of life, however psychological effects (anxiety and depression), disease severity, and disability were more effectively able to predict quality of life in patients (Giovannetti et al., 2016). In line with this finding, researchers have shown that individuals experiencing depression often have negative information-processing biases and cognitive distortions in terms of self-perception, perceptions of the world, and

perceptions of the future (Giordano et al., 2011; Gotlib & Joormann, 2010). These cognitive distortions, perceptions, and biases related to depression may help to explain why objective cognitive functioning alone is a less consistent predictor of quality of life. However, further research is warranted to clarify the nature of the relationship between cognitive functioning (objective and perceived) and quality of life for MS patients (Baumstarck-Barrau et al., 2011; Gold et al., 2003).

Third, physical brain damage from MS may impact individuals' objective cognitive functioning. Brain damage (demyelinating lesions and impaired immune system functioning) resulting from the MS disease directly shapes objective cognitive functioning (Feinstein et al., 2010; Popescu & Lucchinetti, 2012; Rahn et al., 2012; Stadelmann et al., 2011) and depression (Feinstein et al., 2004; Pucak et al., 2007). Depression and decreases in objective cognitive functioning can both affect individuals' quality of life as physical brain damage can result in decreases of individuals' attention, performance, energy, and ability to deal with physical distress (Rahn et al., 2012; Salehpoor et al., 2014). Such processes are also thought to impair patients' social functioning, mental health, daily energy, and overall quality of life (Salehpoor et al., 2014). Furthermore, the decreases in attention and memory resulting from physical brain damage (Rahn et al., 2012) may affect individuals' intellectual awareness and ability to estimate their actual cognitive functioning (Goverover et al., 2014; Matotek et al., 2001). Although it remains plausible that objective cognitive functioning (as a marker of organic brain pathology) would predict quality of life via depression symptoms, the evidence for this possibility has been inconsistent or minimal.

In contrast, there appears to be ample evidence for the relationships between perceived cognitive functioning, depression, and quality of life. Disease-related emotional (i.e., depression

and anxiety) and physical symptoms (i.e., fatigue and disability) in MS are consistently negatively associated with perceived cognitive functioning (Gilchrist & Creed, 1994; Kinsinger et al., 2011; Middleton et al., 2006). For example, patients who are depressed or under other emotional distress tend to perceive their cognitive functioning to be worse than is true (Maor et al., 2001; Middleton et al., 2006; Rohling, Green, Allen, & Iverson, 2002). Similarly, as patients' physical abilities decrease, patients' perception of their cognitive ability tends to become more negative (Middleton et al., 2006; Ray, Phillips, & Weir, 1993). With emotional distress, disability, or decreased physical functioning, patients seem to be less aware of their true level of cognitive functioning (Middleton et al., 2006). The lack of understanding regarding why there is a discrepancy between perceived and objective cognitive functioning suggests a gap in the literature. Depression (emotional distress) seems to affect both objective and perceived cognitive functioning; however, depression seems to be a particularly promising link in the relationship between perceived cognitive functioning and quality of life or well-being. To better understand the role of depression in mediating the relationship between cognitive functioning and quality of life or well-being, both perceived and objective cognitive impairment would need to be examined.

### **Depression**

Clinical depression generally manifests with five or more symptoms including negative mood state and/or lack of interest or pleasure, as well as hopelessness, excessive guilt, and related physical symptoms such as fatigue, sleep disturbance, appetite change, or change in psychomotor functioning, for a duration of at least two weeks (American Psychiatric Association, 2013). Depression is a common mood disturbance that individuals with MS typically experience at higher rates compared to other individuals with chronic illness. The

lifetime prevalence for depressive disorders for individuals with MS is approximately 50% (Giordano et al., 2011; Siegert & Abernethy, 2005).

Though the links of comorbid depression to MS are well-established, it is unclear exactly why MS patients tend to become depressed at such high rates (Janssens et al., 2003a). It is likely that depression in MS patients is caused by a number of factors. Physical effects from lesions on the central nervous system (CNS) in MS may partially account for increased rates of depression (Feinstein et al., 2004; Pucak et al., 2007). However, psychological influences may be present as well; depression may be a reaction to patients' deficits caused by MS (Rabins et al., 1986). For instance, a longitudinal study assessing MS patients at two time points over three years suggested that individuals with MS tended to become more depressed when they were not using active coping skills (e.g., making a plan of action, focusing on dealing with the problems at hand, and taking one step at a time) (Arnett & Randolph, 2006). A separate study (Giordano et al., 2011) suggested both physical and psychological influences on depression, finding that depression occurred later in the disease progression of MS with increased physical effects from lesions in the CNS. Researchers found that early signs of depression when patients are first diagnosed may be due to psychological influences such as immediate distress over the diagnosis (Janssens et al., 2003b). Additional studies have suggested that family environment (Schwartz & Kraft, 1999), loss of social support (Gulick, 1997), psychological impact of the disease (Kroencke, Lynch, & Denney, 2000), and illness beliefs (Jopson & Moss-Morris, 2003) may impact rates of depression in individuals with MS.

Depression in MS patients may also be impacted by somatic symptoms of MS such as cognitive impairment, pain, physical inactivity, or fatigue (Moore et al., 2012; Motl et al., 2010). For instance, depression appears to fluctuate with MS symptom relapses (e.g., increases in

neurological symptoms which may include decreased cognitive functioning, fatigue, pain, reduced mobility [Leary, Porter, & Thompson, 2005]) controlling for disease severity/disability (Dalos, Rabins, Brooks, & O'Donnell, 1983; Moore et al., 2012). Furthermore, in patients with MS, more neurological impairment is associated with greater depression symptoms (Rabins et al., 1986). In a longitudinal study assessing MS patients at baseline, 2, and 6 months after a relapse, depression rates increased during MS relapses and decreased post-relapse as MS symptoms remitted (Moore et al., 2012). A cross-sectional study assessing patients with primary progressive versus relapsing-remitting subtypes of MS found that individuals with relapsing-remitting MS were more likely to experience an episode of major depression at some point during their lives (Zabad, Patten, & Metz, 2005). These findings might be explained by differing biology of the sub-types of MS, the lack of unexpected relapses in primary progressive MS, and/or the typically later onset of primary progressive MS, allowing for increased psychological and social adjustment (Zabad et al., 2005). In another cross-sectional study, depression accounted for the negative relationship between overall MS symptoms and physical activity (Motl et al., 2010). However, a later longitudinal study found no such results (Motl et al., 2012). Although there are inconsistencies in the literature as to the nature of this relationship and why it exists, it is clear that a link between physical MS symptoms and depression exists.

As illness duration of MS increases patients often experience more severe and/or progressive somatic symptoms as well as psychological difficulties (e.g., depression and decreased cognitive function) characterized as “silent disabilities” for MS patients (Benito-León et al., 2002). Researchers assessing a cross-sectional sample of MS patients found that higher illness duration was associated with higher depression levels and lower quality of life (Benito-León et al., 2002). In a prospective study, even after accounting for the physical effects of fatigue

and disability, depression predicted quality of life for individuals with MS (Janardhan & Bakshi, 2002). Thus, depression is common in MS patients; it is associated with both physical and psychological symptoms as it plays an important and unique role in quality of life for individuals with MS.

Similar to the relationship between cognitive functioning and quality of life, there exist inconsistencies regarding the relationship between cognitive functioning and depression in MS. On one hand, some studies found no significant relationship between cognitive function and depression (Krupp, Sliwinski, Masur, Friedberg, & Coyle, 1994; Minden, Moes, Orav, Kaplan, & Reich, 1990; Ron & Logsdail, 1989; Schiffer & Caine, 1991). Other studies have found that individuals with MS who were depressed performed worse than non-depressed individuals on cognitive tasks related to attention, speed, and working memory (Arnett et al., 1999; Arnett, 2005; Barwick & Arnett, 2011; Landro, Celius, & Sletvold, 2004; Rabins et al., 1986;). Further, some researchers found depression was greater when individuals experienced cognitive deficits in areas such as occupational and relational functioning (Gilchrist & Creed, 1994). Researchers suggest that these discrepancies may be due to methodological differences such as longitudinal versus cross-sectional design, assessment of depression as a clinical diagnosis versus dimensional symptoms, and in particular, the assessment of cognitive function with objective versus self-report measures (Benito-León et al., 2002; Kinsinger et al., 2011). Therefore, studies aiming to understand the links of cognitive functioning to depression, as well as to quality of life, should assess measures of both objective and perceived cognitive functioning.

Depression may shape negative thoughts about one's MS symptoms suggesting that positive traits or strengths may be important in the context of MS as they might counteract the negative cognitions related to depression (Arnett, Barwick, & Beeney, 2008). One study

explored the utility of cognitive behavioral therapy (CBT) over 16 weekly sessions with MS patients, finding an inverse relationship between perceptions of cognitive functioning and depression; increased perception of cognitive ability was associated with decreases in depression while changes in objective cognitive measures and depression symptoms were not correlated (Kinsinger et al., 2011). For individuals with MS, higher levels of depression are typically associated with beliefs about the negative consequences of MS as well as beliefs about intrusiveness and lack of control of MS symptoms (Jopson & Moss-Morris, 2003). These findings, although not establishing causality, suggest the possibility that individuals who are able to cultivate and maintain a positive outlook may counteract some of the negative effects of MS on depression and quality of life. A trait-like disposition of gratitude, for instance, may facilitate this sort of predominantly positive outlook even amidst difficult circumstances (Tulbure, 2015). Therefore, gratitude may impact the relationship between MS symptoms and outcomes, specifically depression and quality of life.

### **Gratitude**

Gratitude is a positive social or moral emotion theorized to be elicited by attending to positive features of the present moment and making the best of what the individual has received (Tulbure, 2015). The perspective of gratitude can be experienced through many forms including but not limited to feeling grateful for or to people, nature, God, animals, events, and relationships (Tulbure, 2015). A daily focus on gratitude allows individuals to see the world through a positive lens and to view the self as a recipient of gifts (Wood, Maltby, Gillett, Linley, & Joseph, 2008a). Gratitude can exist as a state, temporary affect, or a trait related to individual differences in typical levels of grateful affect (Wood, Maltby, Stewart, Linley, & Joseph, 2008b). Individuals that have higher levels of trait gratitude tend to appreciate simple pleasures in life, appreciate



how other individuals invest in their well-being, and experience a feeling of abundance instead of feeling deprived (Watkins, Woodward, Stone, & Kolts, 2003). Individuals with higher levels of trait gratitude may feel more grateful in general, and they are more likely to feel grateful across a number of situations (Watkins et al., 2003).

Gratitude can be elicited by situations, emotions, and actions (Watkins, 2014). Two notable situations that tend to elicit gratitude are (1) when individuals recognize that an aversive event could have taken place but did not, or an event could have been worse than it was, and (2) when an individual recognizes that they have received a benefit/favor from another person (Watkins, 2014). Perceptions of the self as a recipient trigger the subjective feeling of gratitude which fosters an action tendency to make one want to reciprocate kindness to the giver (Emmons & McCullough, 2003). Furthermore, this cycle (i.e., being a recipient, feeling gratitude, desire to reciprocate kindness) is linked to outcomes characterized by positive emotions and a positive sense of well-being (Emmons & McCullough, 2003), and positively correlated to individuals' quality of life (de Souza & Kamble, 2016; Eaton, Bradley, & Morrissey, 2014). Indeed, high-gratitude individuals tend to experience more positive emotions, have higher overall psychological well-being, better social functioning, increased spirituality, decreased depression, increased ability to cope, and a stronger desire to give back to others, as suggested by both experimental and correlational studies (Disabato, Kashdan, Short, & Jarden, 2016; Emmons & McCullough, 2003; Tulbure, 2015; Wood et al., 2008a).

There is an abundance of research suggesting gratitude acts as a buffer against effects of depression (Lin, 2015; Lambert, Fincham, & Stillman, 2012; Wood et al., 2008a), and works to increase general well-being (Wood, Froh, & Geraghty, 2010) and quality of life (de Souza & Kamble, 2016; Eaton et al., 2014). Together, this evidence implies the possibility that gratitude

might moderate the link between depression and quality of life although such research has not been conducted within an MS population. Gratitude seems to promote a range of positive outcomes related to well-being as shown in studies of medically healthy individuals. Gratitude is significantly related to both eudaimonic well-being (i.e., meaning and fulfillment; Mills et al., 2015; Wood & Joseph, 2010) as well as hedonic well-being (subjective happiness) (Mills et al., 2015; Watkins et al., 2003), each predicting lower depression. Research assessing the role of gratitude in a longitudinal study found that when healthy individuals regularly practiced gratitude levels of stress and depression naturally decreased while social support increased; this appeared to be the case above and beyond effects of superordinate personality traits (e.g., Big 5 traits like extraversion; Wood et al., 2008b). In addition, in a medically healthy sample from a primary care setting, researchers found that individuals trained over a 6-week period in group sessions to exercise positive psychological skills such as gratitude (e.g., writing letters of gratitude, counting blessings) experienced decreased depression, decreased pain, increased general mental health, and increased vitality (Lambert D'raven, Moliver, & Thompson, 2015). Individuals who practiced gratitude reported increased feelings of happiness, personal growth, life purpose, autonomy, and self-acceptance (Ruini & Vescovelli, 2013). This increased well-being and social functioning may come about by both increasing pro-social behavior and decreasing maladaptive interpersonal behavior (Emmons & McCullough, 2003; McCullough, Kilpatrick, Emmons, & Larson, 2001). Such studies suggest the possibility that gratitude may contribute to higher quality of life, perhaps even in the context of MS.

There is a dearth of research regarding the relationships of gratitude with cognitive functioning, mood, and quality of life in MS populations. Only one study (Büssing et al., 2014) has assessed gratitude in individuals with MS gratitude. In a cross-sectional study assessing

experiences of beauty in life, gratitude, and awe in individuals with a diagnosis of MS, researchers observed relatively low gratitude levels in the participants. In addition, researchers found that gratitude was unable to explain variance related to life satisfaction, although individuals endorsing higher religiosity or spirituality reported higher levels of gratitude (Büssing et al., 2014). While this study offers some utility as the first study to examine the relationship between gratitude and individuals with MS, there are many limitations of this study. The outcome variable in this study, life satisfaction, is a construct related to generalized positive assessment of one's life (Peterson, Park, & Seligman, 2005), as opposed to a measure of quality of life that would encapsulate specific factors relevant to living with MS (mobility, MS symptoms, general contentment, thinking/fatigue, family and social well-being, and emotional well-being; Yorke & Cohen, 2015). In addition, in this particular sample, participants' low level of gratitude suggests limited variability, which may artificially limit effects of gratitude on life-satisfaction. Further, the study's measure of gratitude only used three unvalidated general items related to a combination of gratitude and awe (e.g., *I have learned to experience and value beauty, I have a feeling of great gratitude, I have a feeling of wondering awe*), whereas the present study will incorporate a well-validated measure of trait gratitude (McCullough, Emmons, & Tsang, 2002). As there is only one study in the literature assessing gratitude in individuals with MS more research is needed to better understand the nature of this relationship.

Despite scant research on gratitude in MS populations research on gratitude in the context of other chronic health conditions suggests further reasons for potential relevance to MS. Gratitude has predicted both physical symptoms and positive thinking for patients dealing with chronic medical conditions. In patients with asymptomatic heart failure, a condition that is often undetected yet increases an individuals' risk of heart failure and death (Goldberg & Jessup,

2006), gratitude acted as mediator or partial mediator between spiritual well-being and higher sleep quality, between spiritual well-being and higher cardiac-specific self-efficacy, between spiritual well-being and lower fatigue, and between spiritual well-being and lower depressed mood (Mills et al., 2015). Similarly, in patients with chronic pain, higher gratitude was associated with higher sleep quality and lower levels of depression and anxiety (Ng & Wong, 2012). In a separate correlational study assessing women with breast cancer, gratitude was positively related to positive affect (contentment and relaxation), post-traumatic growth, (finding meaning from the traumatic experience), positive social relationships, ideas about new possibilities, personal strength, spiritual changes, and appreciation of life, while negatively related to depression, anxiety, and hostility (Ruini & Vescovelli, 2013). Furthermore, Ruini and Vescovelli (2013) suggest that intentional reflection on ways to be grateful for oneself and the world promotes higher well-being, lower distress, and may promote feelings of a more meaningful life leading to resilience. Thus assessing the role gratitude plays in regard to MS is warranted, particularly its relation to depression symptoms and quality of life.

While gratitude has demonstrated evidence to enhance well-being (Emmons & McCullough, 2003) and buffer against negative emotion (Wood et al., 2008b), studies have not investigated the effects of gratitude as a buffer on the relationship between cognition and depression. Studies have found that positively valenced psychological variables such as gratitude are related to higher cognitive ability. For instance, individuals over the age of 70 years old who have increased satisfaction with life tend to have slower deterioration of perceptual speed (Gerstorf, Lövdén, Röcke, Smith, & Lindenberger, 2007). In addition, individuals have a decreased risk for mild cognitive impairment if they endorse a strong sense of purpose in life (Boyle, Buchman, Barnes, & Bennett, 2010). In another study assessing the effects of positive

well-being and cognition, after age and depression were controlled, a strong sense of positive well-being still predicted greater executive function, memory, and processing speed (Allerhand, Gale, & Deary, 2014). In experimental contexts, induction of positive affect (e.g., giving a package of candy, reading statements designed to elicit certain moods) increased creative problem solving (Estrada, Isen, & Young, 1994), flexibility (Isen, 2009), and decision-making (Isen, 2001). Thus, this research suggests the possibility that the positive-valenced process of gratitude might offset or buffer some of the effects of declining cognitive function on depression symptoms and quality of life in MS, though there is a lack of research directly examining such issues. These findings supply reasons to expect that gratitude may predict lower depression symptoms and higher quality of life in individuals with a chronic illness such as MS.

Evidence suggests that gratitude and related variables are inversely associated with cognitive functioning (Allerhand et al., 2014; Gerstorf et al., 2007) and depression (Disabato et al., 2016; Emmons & McCullough, 2003; Wood et al., 2008b), and positively associated with quality of life (de Souza & Kamble, 2016; Eaton et al., 2014; Emmons & McCullough, 2003); thus, it is reasonable to investigate the possibility that gratitude may simultaneously predict changes in these variables or moderate links between them. The research above lays the theoretical underpinnings to warrant assessment of the effects of cognitive functioning (both perceived [Giovannetti et al., 2016; Samartzis et al., 2014] and objective [Benito-León et al., 2002; Gold et al., 2003]) on quality of life through depression (Benito-Leon et al., 2002; Janardhan & Bakshi, 2002; Pucak et al., 2007). Within a mediation model where cognitive function (both perceived and objective) predicts quality of life through depression, gratitude may simultaneously function as a moderator between cognitive function (both perceived and objective) and depression, and between depression and quality of life. Breaking down the

moderated mediation, gratitude may function as a moderator between cognitive functioning (both perceived and objective) and depression. No research to date has assessed the impact of gratitude on the relationship between cognitive functioning (both perceived and objective) and depression. However, evidence suggests gratitude independently impacts each of these variables: buffering against decline in cognitive functioning (Boyle et al., 2010) and buffering against negative affect (Wood et al., 2008). Gratitude may also function as a moderator between depression and quality of life. No research has directly assessed if gratitude acts as a buffer on the relationship between depression and wellbeing or quality of life in an MS population. However, the practice of gratitude can lead to decreased depression and increased well-being (Wood et al., 2008a). The practice of gratitude tends to instill a positive outlook on life and increase life satisfaction and meaning through intentional reflection on what individuals are grateful for regarding oneself and the world (Ruini & Vescovelli, 2013). As well-being and life satisfaction typically increase as a result of practicing gratitude, it is therefore reasonable to assume quality of life might also be influenced by gratitude. This idea is bolstered through research by de Souza and Kamble (2016) and Eaton et al. (2014) who found gratitude to predict quality of life in patients with chronic illnesses.

In a mediation model linking cognitive functioning (objective and perceived) and quality of life through depression, gratitude may simultaneously act as a moderator on the relationships between cognitive functioning (objective and perceived) and depression, and between depression and quality of life. Moreover, assessing gratitude as a buffer within this context may offer insight about the impact of gratitude on symptoms of MS. As gratitude appears to impact multiple domains (e.g., lower depression, lower anxiety, higher positive affect, higher appreciation of life, higher positive social relationships [Ruini & Vescovelli, 2013], lower cognitive deterioration

[Allerhand et al., 2014; Gerstorf et al., 2007]), it is possible that gratitude may simultaneously impact the relationship between cognitive functioning (both perceived and objective) and depression, and the relationship between depression and quality of life. Assessing gratitude as a dual moderator may offer information regarding whether the magnitude of the indirect effect of cognitive functioning (both perceived and objective) on quality of life through depression varies based on individuals' trait gratitude. In addition, assessing how gratitude impacts the relationships between cognitive functioning, depression, and quality of life may be beneficial to further understand how strengths, such as gratitude, may offer a larger benefit to individuals experiencing MS, and may protect against or buffer the severity of common symptoms experienced by individuals with MS (e.g., decline in cognitive functioning, depression).

### **The Present Study**

Thus, questions remain about differential effects of objective and perceived cognitive functioning on quality of life, whether depression may account for effects of cognitive functioning on quality of life (and whether this is the case for both objective and perceived cognitive functioning), and the role of strengths such as gratitude in the lives of individuals with MS. The purpose of the present study is to address these questions in a cross-sectional study incorporating self-reported perceptions and objective measures of cognitive functioning, depression symptoms, and quality of life in a sample of individuals formally diagnosed with MS.

### **Hypotheses**

#### **Hypothesis 1a: Perceived cognitive functioning will positively predict quality of life.**

Based on the studies linking perceived cognitive functioning to quality of life in MS (Giovannetti et al., 2016; Samartzis et al., 2014), I hypothesized that higher perceived cognitive functioning would positively predict higher health-related quality of life (Figure 1).

**Hypothesis 1b: Perception of cognitive functioning will negatively predict depression.** Because individuals with lower perceptions of their cognitive functioning tend to endorse depressive symptoms (Romero et al., 2015), and individuals who endorse depressive symptoms tend to perceive their cognitive function to be lower than their true level of cognitive functioning (Maor et al., 2001; Middleton et al., 2006; Rohling et al., 2002), I expected that higher perceived cognitive functioning would predict lower depression (Figure 1).

**Hypothesis 1c: Depression will mediate the relationship between perceived cognitive functioning and quality of life.** Based on the aforementioned links as well as studies linking depression to lower quality of life in MS (Janardhan & Bakshi, 2002; Mitchell et al., 2005), I expected that perception of cognitive functioning would predict higher quality of life through lower scores on the mediating variable of depression (Figure 1).

**Hypothesis 2a: Objective cognitive functioning will positively predict quality of life.** I hypothesized that higher objective cognitive functioning would positively predict higher health related quality of life. I made this hypothesis based on the literature finding some positive associations between objective cognitive functioning and quality of life in MS (Benito-León et al., 2002; Cutajar et al., 200; Gold et al., 2003). However, I predicted this relationship would be weak, given the less consistent evidence of effects of objective cognitive functioning on well-being in MS (Baumstarck-Barrau et al., 2011; Glanz et al., 2010; O'Connor et al., 2001; Figure 2).

**Hypothesis 2b: Objective cognitive functioning will negatively predict depression.** Individuals diagnosed with MS who have decreased objective cognitive functioning may experience increased depressive symptoms, perhaps as a result of the negative relationship between cognitive functioning and depression due to demyelination lesions and immune system



dysfunction (Feinstein et al., 2004; Pucak et al., 2007; Rabins et al., 1986). I thus expected that higher objective cognitive functioning would predict lower depression (Figure 2).

**Hypothesis 2c: Depression will mediate the relationship between objective cognitive functioning and quality of life.** I hypothesized that effects of objective cognitive functioning on quality of life will be only be partially mediated by depression as depression appears to be inconsistently influential in this relationship (Benito-León et al., 2002; Feinstein et al., 2004; Pucak et al., 2007), compared to the stronger links of depression to subjective cognitive functioning and quality of life in the literature (Arnett & Randolph, 2006; Janardhan & Bakshi, 2002). I expected that objective cognitive functioning would predict higher quality of life through lower scores on the mediating variable of depression (Figure 2).

**Hypothesis 3a: Gratitude will have a main effect on depression and moderate the relationship between cognitive functioning and depression on the “A” path.** Based on studies suggesting adaptive effects of positive emotions and traits (relevant to gratitude) on cognition (Allerhand et al., 2014; Estrada et al., 1994; Gerstorf et al., 2007; Isen, 2009; Isen, 2001), and the evidence that gratitude may promote resilience (Lambert D’raven et al., 2015; Ruini & Vescovelli, 2013) and predict lower depression (Lin, 2015; Lambert et al., 2011; Wood et al., 2008a), I expected that trait gratitude have a positive main effect on depression. In addition, I expected gratitude would moderate the relationships between both perceived and objective cognitive functioning and depression on the “A” path. Specifically, I expected that higher trait gratitude would diminish the extent to which poorer cognitive functioning (both perceived and objective) predicted higher depressive symptoms (Figures 1, 2, and 3).

**Hypothesis 3b: Gratitude will have a main effect on quality of life and moderate the relationship between depression symptoms and quality of life on the “B” path.** Because

gratitude tends to buffer the effects of mental illness and promote greater higher appreciation of life (Lambert D'raven et al., 2015; Ruini & Vescovelli, 2013), I predicted that trait gratitude would moderate the relationship between depression and quality of life on the "B" path. Specifically, I expected that trait gratitude have a positive main effect on quality of life. In addition, I expected that higher trait gratitude would buffer the negative relationship between depression and cognitive functioning (Figures 1, 2, and 3).

**Hypothesis 4: Indirect effect of cognition on quality of life via depression will depend on the level of gratitude on both "A" and "B" paths.** No research to date has assessed the possible buffering effects of gratitude as part of a mediated moderation on the "A" and "B" paths of a conditional indirect effect between cognitive functioning (objective and perceived) and quality of life through depression: "A" path, between cognitive functioning (both perceived and objective) and depression, and "B" path, between depression and quality of life. Research in the literature suggests gratitude independently impacts each of these variables: buffering against cognitive decline (Boyle et al., 2010) and negative affect/depression (Wood et al., 2008a) as well as increasing well-being (Wood et al., 2008a) and quality of life (de Souza & Kamble, 2016; Eaton et al., 2014). Based on the links of perceived (Giovannetti et al., 2016) and objective cognitive functioning to depression (Benito-Leon et al., 2002; Feinstein et al., 2004), and to quality of life (Arnett & Randolph, 2006; Benito-Leon et al., 2002; Janardhan & Bakshi, 2002), as well as the idea of gratitude's buffering properties on the "A" (Allerhand et al., 2014; Estrada et al., 1994; Gerstorf et al., 2007) and "B" paths (Lambert D'raven et al., 2015; Ruini & Vescovelli, 2013), I hypothesized that the indirect effect of cognitive functioning on quality of life via depression would be weaker for those with higher trait gratitude (Figure 1, 2, and 3).

**Hypothesis 5: When both indirect effects are tested simultaneously, only the indirect effect of perceived cognitive functioning on quality of life via depression will remain significant.** Past research suggests strong evidence for the links of perceived cognitive functioning to depression (Kinsinger et al., 2011; Middleton et al., 2006) and quality of life (Middleton et al., 2006; Mitchell et al., 2005). However, there is weaker evidence in the literature assessing the links of objective cognitive functioning to depression (Feinstein et al., 2004; Pucak et al., 2007) and quality of life (Baumstarck-Barrau et al., 2011; Benito-León et al., 2002; Gold et al., 2013; O'Connor et al., 2001). Based on this evidence in the literature, I hypothesized that when utilizing a conservative path model analysis with both perceived and objective cognitive function acting as predictors in the same model, the unique indirect effect of perceived cognitive functioning predicting quality of life through depression would be significant and that the unique indirect effect of objective cognitive functioning predicting quality of life through depression would *not* be significant (Figure 4).

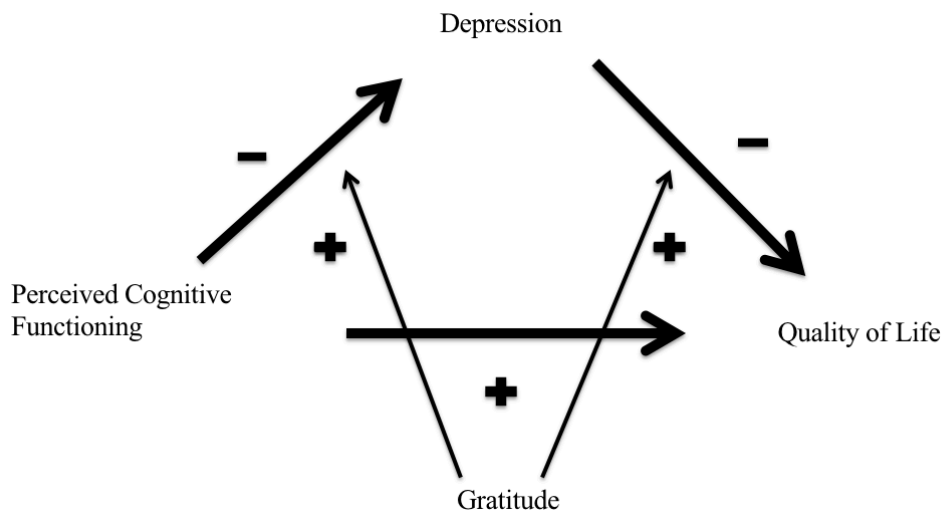


Figure 1. Hypothesized relationships between perceived cognitive functioning, quality of life, depression, and gratitude. Increased thickness in lines indicates stronger hypothesized relationship.

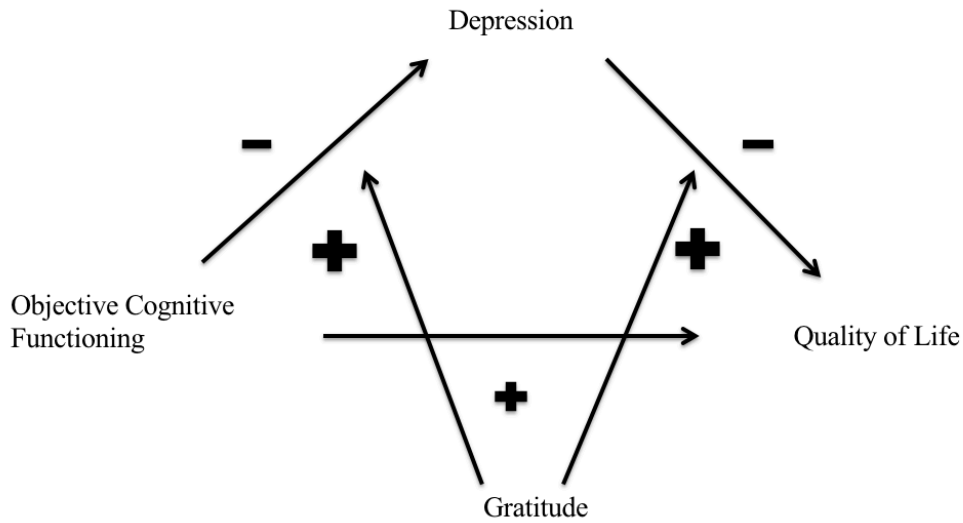
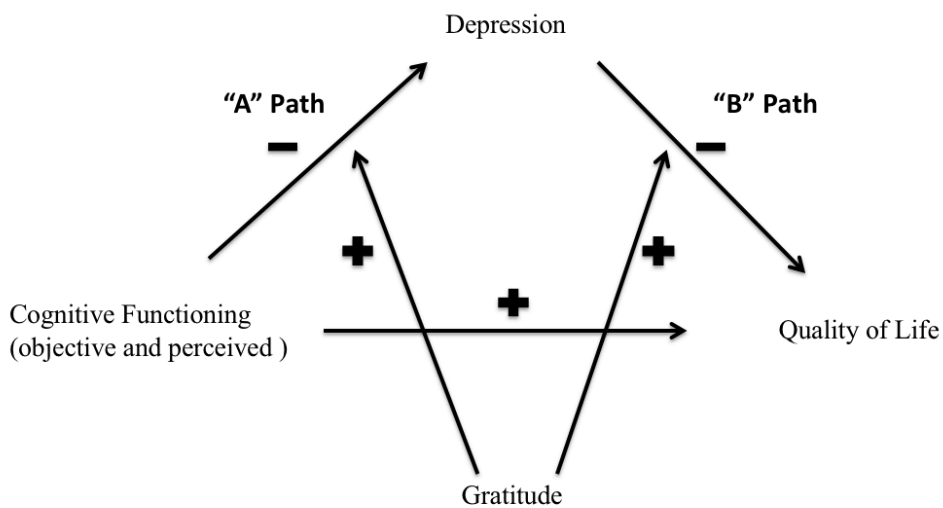
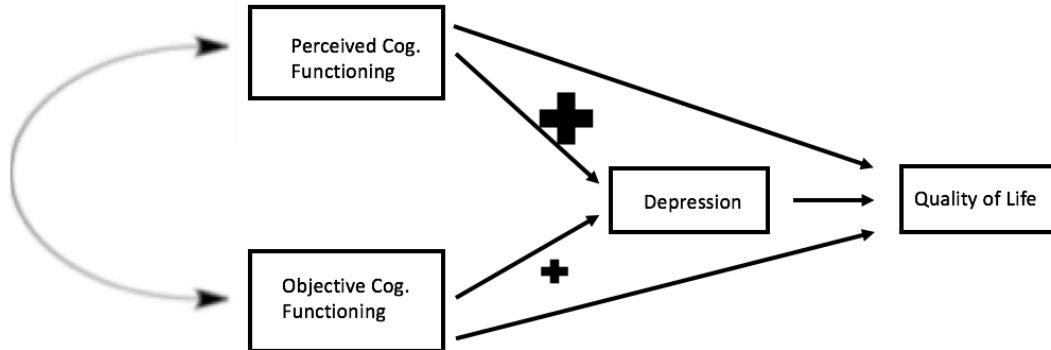


Figure 2. Hypothesized relationships between objective cognitive functioning, quality of life, depression, and gratitude. Increased thickness in lines indicates stronger hypothesized relationship.



*Figure 3.* Hypothesized moderated mediation model: mediation between cognitive functioning (objective and perceived) and quality of life through depression, with gratitude moderating “A” and “B” pathways.



*Figure 4.* Hypothesized path model of the relationships between perceived cognitive functioning, objective cognitive functioning, quality of life, and depression.

## CHAPTER II

### Method

#### Sample and Participant Selection

**Participants.** A total of 128 individuals diagnosed with MS (69.5% female, 30.5% male) participated in this study, ranging from 21-78 years old ( $M = 48.9$ ;  $SD = 13.2$ ). All participants were formally diagnosed, or had their diagnosis confirmed by one of the neurologists at the MS center where the study was conducted. MS patients are diagnosed by physicians through objective evidence of damage to the patients' central nervous system (CNS) in at least two brain regions, as assessed at two or more separate time points. Symptom assessment, patient history, magnetic resonance imaging (MRI), cerebrospinal fluid analysis (CSF), and visual evoked

potentials (EP) may all be used to assess damage to the CNS (National Multiple Sclerosis Society, n.d.). Other possible diagnoses were ruled out. Participants were diagnosed with relapsing-remitting MS (82%), primary progressive MS (10.2%), and secondary progressive MS (7.8%). Time since diagnosis ranged from 3 months to 52 years. Patients' years of education ranged from 9 to 23. Participants described themselves as Caucasian (82%), Asian-American (3.1%), Hispanic/Latino (3.1%), African American (5.5%), American Indian/ Alaska Native (0.8%), bi-racial (2.3%), or other (3.1%).

**Sample size, power, and precision.** I expected to recruit at least 121 participants, assuming 5 predictors (cognitive functioning, depression, gratitude, gratitude  $\times$  cognition, gratitude  $\times$  depression) in multiple regression and relatively small effect sizes ( $r = .1$ ), with  $\alpha = 0.01$ , and power of .80.

### **Procedure**

Participants were recruited through an urban MS treatment center in the Pacific Northwest. Patients who were formally diagnosed by a neurologist at the MS center based on their symptoms, history, and evidence of damage to the central nervous system (CNS) in at least two places (occurring at two separate time points) were recruited to participate in this study.

Researchers called patients with already scheduled ongoing care appointments at the clinic to inquire if the patient would be interested in participating in a 40-minute assessment for research purposes. Participants were informed that the study would assess cognitive functioning and related aspects of cognitive functioning such as depression and quality of life. Individuals that were interested in participating were scheduled for a 40-minute appointment immediately prior to or following their upcoming clinical appointment.

The present study employed a cross-sectional, single time-point design. Consenting participants visited the MS treatment clinic for a clinical appointment. During the 40-minute assessment, which was either before or after the participants' medical appointment at the MS clinic based on the participants' availability, researchers first administered the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) as an objective cognitive assessment. The BICAMS battery consists of three assessment measures specifically chosen as a screen for individuals diagnosed with MS based on common areas of decreased cognitive function seen in MS patients (Langdon et al., 2012). A trained graduate or undergraduate student working at the Multiple Sclerosis Center as part of this study administered the BICAMS battery. Participants were next asked to complete seven short self-report assessment measures of depression, anxiety, quality of life, gratitude, and perceived cognitive functioning. All self-report measures were completed in paper and pencil format with participants. Graduate and undergraduate students working at the MS Center underwent training to work with human subjects in general, to work specifically with individuals with MS, and to administer the BICAMS assessment. Participation was completely voluntary; participants did not receive compensation for participation.

### **Measures**

**Perceived cognitive functioning.** The Perceived Deficits Questionnaire (PDQ; Ritvo et al., 1997) is a 20-item self-report questionnaire that was developed in a population of individuals who had been diagnosed with MS. The purpose of this scale is to measure subjective cognitive functioning on a dimensional level for individuals with MS in four domains: attention/concentration, prospective memory, retrospective memory, and organization/planning (Takasaki, Chien, Johnston, Treleaven, & Jull, 2012). The scale is composed of five items designed to assess for attention/concentration, five items for retrospective memory, five items for

prospective memory, and five for organization planning. Participants are asked to rate the extent to which they agree with each item on a 5-point Likert scale ranging from zero (*never*) to four (*almost always*). Examples of the items include “During the last four weeks, how often did you forget what you talked about after a telephone conversation?” (assessing for retrospective memory), and “During the last four weeks, how often did you have trouble getting things organized” (assessing for organization/planning; Ritvo et al., 1997). Scale scores range from 0 to 20, and total scores range from zero to 80. Scores were reverse coded in the present study for ease of interpretation and for parallelism with our objective cognition index; thus higher scores reflect higher cognitive function.

The PDQ showed acceptable psychometric properties in MS samples for purposes of assessing individuals’ perceptions of their cognitive abilities (Ritvo et al., 1997). Using the PDQ in a sample of MS patients, Ritvo et al. (1997) demonstrated the PDQ has good reliability reported ( $\alpha = 0.93$ ). The total score has been validated for interpretation (Ritvo et al., 1997). In our study, the coefficient  $\alpha = .95$ .

**Objective cognitive functioning.** The Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS; Langdon et al., 2012) is a battery of assessments comprised of the Symbol Digit Modalities Test (SDMT; Smith, 1982), the California Verbal Learning Test-II (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000), and the Brief Visual Spatial Memory Test-Revised (BVMT-R; Benedict, 1997). The BICAMS assessment battery was designed as a screening tool and designed for research purposes to assess for cognitive function in individuals with a diagnosis of MS (Benedict et al., 2012a; Goretti, et al., 2014).

The SDMT task is an assessment designed to measure information-processing speed. It is a coding task in which the participants are given a key with nine symbols at the top of a page;



each symbol is paired with a number from one to nine. The remainder of the page is filled with the same symbols presented in the key, but no numbers. Participants are asked to fill in the number paired with each symbol and are given 90 seconds to complete as many pairs as possible. The task can be done in written or oral form (Benedict et al., 2012a). To score the SDMT task participants are given one point for every correct pair of numbers and symbols completed. Scores may range from zero to 110 (Strauss, Sherman, & Spreen, 2006).

The CVLT-II task is an assessment measuring immediate verbal recall. Participants are asked to recall words read to them by the examiner from a 16-item list. The words in the list conform to four different categories (e.g., animals, vegetables, furniture, and modes of transportation). Following initial patient recall, the examiner repeats the list and the participant is asked to again recall any words from the list they can including words they said in previous trials. This scenario is repeated for a total of five trials (Langdon et al., 2012). Participants are given one point for every correct word recalled; each trial is scored separately, yielding a total of five scores ranging from zero to 16; a total score for the assessment is computed by adding the scores from the five trials (Langdon et al., 2012). In our study, the coefficient  $\alpha = .92$

The BVMT-R task is an assessment of immediate visual recall. During the BVMT-R task, participants are presented with a sheet with six abstract images (two columns, with three images in each column) for ten seconds. After the sheet is taken away, participants are asked to draw from memory the shapes presented to them on a blank page— drawing the same images that appeared on the presented sheet of paper, in the same places that images appeared. Each abstract image is given a score from zero to two points based on location placement (one point if correct) and accuracy of drawing (one point if correct). Scores from each drawing are added

together for a total score; total scores for this task can range from 0 to 12 (Benedict et al., 2012a; Langdon et al., 2012). In our study, the coefficient  $\alpha = .91$

The BICAMS battery was developed as a brief assessment to monitor cognitive functioning in patients with MS. Studies have demonstrated strong psychometric properties for use of the BICAMS assessment in samples with MS. To assess BICAMS scores, raw scores from each of the three tasks are turned into  $z$ -scores; if participants score at or below 1.5 SD below the mean on at least one of the three tasks, they are considered to be cognitively impaired (Dusankova, Kalincik, Havrdova, & Benedict, 2012; O'Connell, Langdon, Tubridy, Hutchinson, & McGuigan, 2015). Additionally, there exists a precedent in the literature for utilizing a continuous total BICAMS score created via summing  $z$ -score scale totals for the SDMT, CVLT, and BVMT to provide an objective broad assessment of cognitive functioning. Supporting this practice, intercorrelations among the three scales were moderate to large; they range from .49 to .65 (see Table 1). Similarly, measures such as the Wechsler Adult Intelligence Scale (WAIS) and Wechsler Memory Scale (WMS) utilize multiple types of measures assessing several components of a broader construct, such as intelligence, creating totals through combining  $z$ -scores (Dawis, 2000; Holdnack, Zhou, Larrabee, Millis, & Salthouse, 2011).

The BICAMS assessment is not intended to be diagnostic (Langdon, et al., 2012). It is intended for regular use by professionals working with MS patients to help manage patient care. By annually assessing patients with the BICAMS assessment, professionals can observe changes or trends in patients' scores and assess participants' abilities on specific domains of cognitive functioning (Langdon et al., 2012). Professionals can also monitor for decreasing score trends or task scores 1.5 SD below the mean (Dusankova et al., 2012; O'Connell et al., 2015). This data may be used by professionals as an aid to determine if individuals may benefit from receiving

information about cognitive functioning, cognitive rehabilitation, engaging in individual or group counseling, or obtaining help with making adjustments in school, work, or home life, to facilitate daily functioning (e.g., based on patients' relative strengths and weaknesses on BICAMS tasks; Dusankova et al., 2012; Langdon et al., 2012).

The BICAMS has demonstrated good psychometric properties. Using the BICAMS in an MS sample, Walker et al. (2016) reported good test-retest reliability over two weeks in the BVMT-R ( $r = 0.69$ ), CVLT-II ( $r = 0.74$ ), and SDMT ( $r = 0.87$ ). The SDMT task was originally normed in 1982, the BVMT-R in 1997, and the CVLT-II in 2000; all three tests were recently re-normed in 2009 on a sample of 395 MS patients and 100 healthy U.S. volunteers (Benedict, 1997; Delis et al., 2000; Parmenter, Testa, Schretlen, Weinstock-Guttman, & Benedict, 2010; Smith 1982). The SDMT demonstrated high test-retest reliability in a study assessing MS patients, with a Cronbach's alpha value of 0.97. The CVLT-II and BVMT-R both demonstrated good retest reliability over two weeks with Cronbach's alpha values of 0.78 and 0.91 respectively (Benedict, 2005). There is strong support for alternate forms reliability for the BVMT-R, CVLT-II (Benedict et al., 2012a), and for the SDMT (Benedict et al., 2012b). The SDMT (Benedict et al., 2006; Walker et al., 2016), CVLT-II (Walker et al., 2016), and BVMT-R (Benedict et al., 2006; Walker et al., 2016) have demonstrated concurrent validity in the ability to discriminate between MS and healthy control groups. In terms of predictive validity, lower scores on the CVLT and SDMT are associated with poorer vocational outcomes and job loss (Morrow et al., 2010). The BICAMS battery has demonstrated 58.2% sensitivity and 86.7% specificity in predicting the presence of cognitive deficits (Niccolai et al., 2015). The BICAMS battery also demonstrated 94% sensitivity and 86% specificity in predicting a cognitive deficit,

as defined by a score 1.5 SD below the mean on at least one of the three BICAMS tasks (Dusankova et al., 2012; O'Connell et al., 2015).

Table 1.

| <i>BICAMS Intercorrelations</i> |       |       |    |
|---------------------------------|-------|-------|----|
| <i>Variables</i>                | 1     | 2     | 3  |
| 1. SDMT                         | --    |       |    |
| 2. CVLT                         | .57** | --    |    |
| 3. BVMT                         | .73** | .67** | -- |

*Note.* \* $p < .05$ , \*\* $p < .01$ .

**Depression symptoms.** The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) depression subscale is a seven item self-report questionnaire that was designed to assess depression in non-psychiatric patient populations. Participants were asked to rate the extent to which they agree with each item on a 4-point Likert scale ranging from zero (*not at all*) to three (*most of the time*). Examples of the items include “I still enjoy the things I used to enjoy” (assessing for anhedonia), and “I can laugh and see the funny side of things” (assessing for depressed mood; Zigmond & Snaith, 1983).

This scale was developed using a general medical population. The purpose of the scale is not for diagnostic purposes, but rather to identify medical patients who are more likely to be depressed and in need of further psychiatric evaluation (Michopoulos et al., 2008). The HADS was administered to 521 patients at a large general hospital and outpatients ( $n = 275$  controls,  $n = 246$  inpatients; Michopoulos et al., 2008). Participants were about equally male (53%) and female. The mean age of participants was 50 years old ( $SD = 18.94$ ). No indication of ethnicity was noted. The HADS had high internal consistency with a Cronbach's alpha value of 0.88 for anxiety and 0.83 for depression. Test-retest reliability assessed at two time points, 20 days apart,

showed high stability (ICC= 0.94). Construct validity was assessed using inter-scale correlations; values for the inter-scale correlations ranged from 0.54 to 0.80. Factor analysis for the HADS scale showed a two-factor solution, with the intended items loading on to their respective factors; one exception to this was item 14 of the scale (*I can enjoy a good book or radio or TV program*), which loaded equally onto both factors. The depression subscale of the HADS additionally showed concurrent validity with the Beck Depression Inventory ( $r = 0.75$ ), which is considered to be the gold standard of depression measurement (Michopoulos et al., 2008). Additionally, the HADS scale has shown 90% sensitivity and 87.3% specificity with a threshold score of eight or more to designate clinical depression (Honarmand & Feinstein, 2009). This scale has been validated to detect depression in MS populations (Honarmand & Feinstein, 2009). In our study, the coefficient  $\alpha = .79$ .

**Quality of life.** The Functional Assessment of Multiple Sclerosis (FAMS; Cella et al., 1996) is a 37-item self-report questionnaire designed to assess health-related quality of life in individuals diagnosed with MS. The questionnaire was shortened from the original 59 items. Two subscales were eliminated from the quality of life measure for the purpose of this study: the additional concerns subscale (15 items), which is never used as part of the total score (Yorke & Cohen, 2015), and the emotional well-being subscale (seven items). The emotional well-being subscale, which includes items assessing depression symptoms, was removed to avoid risk of construct overlap with the HADS depression measure which is a predictor/mediator variable in our model.

The FAMS measure was developed by principle components analysis, and the subscales were created to be distinct factors by principle components analysis as well (Cella et al., 1996). Each scale has demonstrated reliability and construct validity individually and as part of a total

scale score; this makes it reasonable to selectively utilize subscales of interest for the present study (Cella et al., 1996). The scale is composed of seven items designed to assess mobility, seven items designed to assess MS symptoms, seven items designed to assess general contentment, nine items designed to assess cognitive and physical fatigue, and seven items designed to assess for family and social well-being. For each item, participants are asked to rate the extent to which they agree with each item on a 5-point Likert scale ranging from zero (*not at all*) to four (*very much*). Examples of the items include “I have accepted my illness” (general contentment) and “I have a lack of energy” (thinking and fatigue) (Cella et al., 1996). Total scores typically range from 0 to 176, however with the exclusion of the emotional well-being subscale the total score ranges from 0 to 169, with lower scores reflecting decreased quality of life. The FAMS has shown strong psychometric properties in MS for assessing health related quality of life (Yorke & Cohen, 2015). Using the FAMS in an MS sample, Yorke and Cohen (2015) reported high retest reliability (ICC= 0.81-0.91). The FAMS subscales show high internal consistency ( $\alpha = 0.82-0.96$ ) (Cella et al., 1996; Sørensen et al., 2011) and high construct validity with more progressive MS disease subtypes reflecting lower scores. The FAMS subscales have also shown high criterion validity between FAMS Mobility scale and the SF-36 Physical Component Scale ( $r = 0.62-0.78$ ) and between the FAMS Emotional Scale and SF-36 Mental Component Scale ( $r = 0.59-0.62$ ) (Cella et al., 1996). In our study, the coefficient  $\alpha = .94$ .

In addition, fatigue is often used as part of the quality of life measure for MS, measured in the FAMS assessment by the thinking and fatigue subscale. However, fatigue can represent a symptom of depression (Bakshi et al., 2000; Ford, Trigwell, & Johnson, 1998), or it could affect cognition function or complex reasoning (DeLuca, Johnson, Belowicz, & Natelson, 1995; DeLuca, Johnson, & Natelson, 1993). Therefore, measures of depression including fatigue items

and measures of quality of life including fatigue items may create a confound in the relationship between depression and quality of life due to the overlapping nature of the variables. In addition, as fatigue may impact cognitive function or complex reasoning, fatigue may impact the BICAMS cognitive assessment measuring objective cognitive functioning resulting in an artificially deflated score. Therefore, it is important to address this confounding effect in the following ways: 1) utilizing a measure of depression that does not overlap with physical fatigue (Ford et al., 1998) such as the HADS measure chosen for this study (Honarmand & Feinstein, 2009; Michopoulos et al., 2008), 2) ensuring that participants complete the neurocognitive testing prior to self-report assessment, as the protocol for this study stipulated, and 3) conducting analyses with and without fatigue controlled, as executed in the present study.

**Gratitude.** The Gratitude Questionnaire-Six Item Form (GQ-6; McCullough, Emmons, & Tsang, 2002) is a six item self-report measure that assesses a general trait-like tendency to experience gratitude or thankfulness. For each item, participants are asked to rate the extent to which they agree on a 7-point Likert scale ranging from one (strongly disagree) to seven (strongly agree). Examples of the items include “I have so much in life to be thankful for,” and “I am grateful to a wide variety of people” (McCullough et al., 2002). Total scores range from 6 to 42 with higher scores reflecting higher feelings of gratitude. The psychometric properties of the GQ-6 were demonstrated in a sample of 1,228 adults (McCullough et al., 2002). McCullough et al. (2002) reported excellent internal consistency ( $\alpha = .87$ ) and convergent validity via correlations of the GQ-6 with positive affect and wellbeing ( $r = .31$ ), life satisfaction ( $r = .53$ ), and discriminant validity with depression ( $r = -.30$ ) and neuroticism ( $r = -.30$ ; McCullough et al., 2002). Cronbach’s  $\alpha$  ranged from .76 to .84 for GQ-6 total scale (McCullough et al., 2002; McCullough, Tsang, & Emmons, 2004). In our study, the coefficient  $\alpha = .82$ .

## Data Analytic Plan

### Overview of Statistical Approach

After preliminary data screening, I analyzed data via PROCESS macro for SPSS (Hayes, 2013) to evaluate the moderated mediation model theorized in this study. I initially tested a basic mediation analysis using Model 4, which assumes a single mediator between the predictor and outcome variable (see Appendix A for a visual representation of PROCESS model 4). In the initial mediation analysis, I specified a model predicting quality of life as the outcome variable, cognitive functioning (perceived or objectively measured) as the focal predictor, and depression as the mediator. Next, I utilized Model 58 to test the moderated mediation. Model 58 assumes a single mediator between the predictor and outcome variable, with a single moderator variable interacting on both the “A” path between the predictor and the mediator and the “B” path between the mediator and the outcome variable (see Appendix A for a visual representation of PROCESS models 4 and 58). Thus, I conducted each mediation and moderated mediation model twice: once with perceived cognitive functioning as a predictor variable, and then with objective cognitive functioning as the predictor (for a total of four models). For significant moderation effects I planned to conduct follow-up tests to probe the interactions (e.g., simple slope analyses at high [1 *SD* above the sample mean] and low [1 *SD* below the mean] levels of the moderator, trait gratitude).

Following core analyses, I conducted a more conservative supplemental analysis to assess the unique indirect effects of perceived and objective cognitive functioning on quality of life via depression with both perceived and objective cognitive functioning set as predictors in the same model. As PROCESS only allows models testing one predictor at a time, I used a path analysis model in AMOS 23.0 (Arbuckle, 2014). Through AMOS I was able to assess perceived and



objective cognitive functioning as simultaneous predictors in the same model, controlling for one another, and estimated unique indirect effects. This path analysis was specifically used to test the hypothesis that the unique indirect effect of perceived cognition on quality of life would be significant, whereas the unique indirect effect of objective cognition would be insignificant (when both were simultaneously in the model). In conducting this path analyses, I worked to specify the model with both perceived and objective cognitive functioning as predictors, depression as the mediator, and quality of life as the outcome variable. I assessed for the (a) unique indirect effects from perceived and objective cognitive functioning on quality of life through depression, (b) the direct effects from perceived and objective cognitive functioning to depression, (c) the direct effect from perceived and objective cognitive functioning to quality of life. I did not examine model fit as the goal was to estimate the predictive effects of the variables rather than to test a model. In addition, with the paths in the model discussed above, the model was “saturated” (did not have excess degrees of freedom required to test model fit). I calculated indirect effects and bootstrapped 95% confidence intervals to test for unique indirect and direct effects.

## **CHAPTER III**

### **Results**

#### **Preliminary Analyses**

Preliminary data pre-screening included evaluating assumptions of normality (e.g., calculating skew and kurtosis) and checking the data for outliers. The univariate skew ranged from -.726 to .458 and kurtosis ranged from -.751 to -.167 across major variables, within normal limits. Scatterplots suggested no evidence of nonlinear relationships. Means, standard deviations, and reliability estimates for each variable are represented in Table 2. The dataset consisted of

128 participants. Screening for missing data revealed that data were 99.4% complete (one participant completed the objective, but not self-reported, cognitive measure). Given very low missing data in this study, and the notion that data imputation tends to have inconsequential effects when less than 5% of data are missing (Cheema 2014; Schafer, 1999), I analyzed raw data without imputation.

Table 2.

*Means and Standard Deviations, and Reliability*

| Variable        | Range |        | <i>M</i> | <i>SD</i> | $\alpha$ |
|-----------------|-------|--------|----------|-----------|----------|
|                 | Min   | Max    |          |           |          |
| BICAMS          | -2.80 | 2.31   | -0.04    | 1.01      | .77      |
| PDQ             | 8.00  | 78.00  | 45.99    | 15.98     | .95      |
| GQ-6            | 18.00 | 42.00  | 34.56    | 6.04      | .82      |
| HADS Depression | 0     | 14.00  | 5.38     | 3.56      | .79      |
| FAMS            | 16.44 | 141.00 | 87.38    | 27.28     | .94      |

*Note.* BICAMS = Brief International Cognitive Assessment for Multiple Sclerosis; PDQ= Perceived Deficit Questionnaire; GQ-6= Gratitude Questionnaire; HADS Depression = Hospital Anxiety and Depression Scale, depression subscale; FAMS = Functional Assessment of Multiple Sclerosis total scale without fatigue subscale.

Zero-order associations between the study variables are displayed in Table 3.

Table 3.

*Bivariate Correlations Among All Study Variables*

| Variable           | 1     | 2      | 3      | 4  | 5 |
|--------------------|-------|--------|--------|----|---|
| 1. BICAMS          | --    |        |        |    |   |
| 2. PDQ             | .21*  | --     |        |    |   |
| 3. GQ-6            | .14   | .37**  | --     |    |   |
| 4. HADS Depression | -.23* | -.59** | -.53** | -- |   |

|         |       |       |       |        |    |
|---------|-------|-------|-------|--------|----|
| 5. FAMS | .36** | .71** | .54** | -.73** | -- |
|---------|-------|-------|-------|--------|----|

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*Note.* \* $p < .05$ , \*\* $p < .01$ . BICAMS= Brief International Cognitive Assessment for Multiple Sclerosis; PDQ= Perceived Deficit Questionnaire; GQ-6= Gratitude Questionnaire; HADS Depression= Hospital Anxiety and Depression Scale, depression subscale; FAMS= Functional Assessment of Multiple Sclerosis.

Because fatigue manifests as a symptom of both MS (American Psychiatric Association, 2013; Braley & Chervin, 2010) and depression (Hind et al., 2016; Skokou, Soubasi, & Gourzis, 2012), fatigue might reflect a confound in the model. This concern was minimized in part by the use of a depression measure that excludes physiological symptoms and does not include fatigue items (Honarmand & Feinstein, 2009; Zigmond & Snaith, 1983). Additionally, the models were analyzed with fatigue items both included and excluded from the quality of life total score for comparison; the direction and pattern of significance for effects was similar. As a result, here I report the results with fatigue items included in the quality of life variable.

Initially, I conducted analyses with covariates in the model including gender, age, years of MS, and years of education. However, given that only years of education was a significant predictor in the model (see Table 4 and 5), and inclusion of covariates did not markedly change the pattern of results, I report the models without covariates, with the exception of years of education, in the model in order to optimize the degrees of freedom and statistical power.

Table 4.

Correlations Among Covariates

| Variable              | 1    | 2     | 3    | 4     | 5      | 6  |
|-----------------------|------|-------|------|-------|--------|----|
| 1. Gender             | --   |       |      |       |        |    |
| 2. Age                | .02  | --    |      |       |        |    |
| 3. Years of MS        | -.10 | .52** | --   |       |        |    |
| 4. Years of Education | -.03 | .04   | -.05 | --    |        |    |
| 5. HADS Depression    | .01  | .04   | .02  | -.16  | --     |    |
| 6. FAMS               | -.04 | -.11  | -.06 | .32** | -.73** | -- |

*Note.* \* $p < .05$ , \*\* $p < .01$ . HADS Depression= Hospital Anxiety and Depression Scale, depression subscale; FAMS= Functional Assessment of Multiple Sclerosis.

**Hypothesis 1a: Perceived cognitive functioning predicting quality of life.** In the first model, I analyzed the basic relationship, or total effect, between the predictor and outcome variables, perceived cognitive functioning and quality of life, prior to assessing these variables in a mediated model. As hypothesized (see Table 5), higher perceived cognitive functioning predicted higher quality of life, such that individuals who perceived themselves to have higher levels of cognitive functioning also tended to endorse a higher quality of life.

**Hypothesis 1b: Perceived cognitive functioning predicting depression.** In the next step within the second model, I analyzed the basic relationship between the predictor and mediator variables—perceived cognitive functioning and depression. As hypothesized, higher perceived cognitive functioning negatively predicted lower depressive symptoms, such that individuals who perceived themselves to have higher levels of cognitive functioning also tended to have a fewer depressive symptoms.

**Hypothesis 1c: Depression mediation between perceived cognitive functioning and quality of life.** In the next step, I analyzed the model testing depression symptoms as a mediator between perceived cognitive functioning and quality of life. Even after accounting for a negative (as hypothesized) effect of depression on quality of life, perceived cognitive functioning continued to predict the outcome. As hypothesized, a significant indirect effect showed that higher perceived cognitive functioning predicted higher quality of life through lower scores on the mediating variable of depression. In other words, individuals with MS who perceive their own cognitive functioning to have decreased may be at risk for lower quality of life because they experience higher depression (Table 5 and 6).

Table 5.

*Regressions of Quality of Life on Perceived Cognitive Functioning and Depression*

| Outcome         | Predictor          | <i>B</i> | <i>SE</i> | <i>t</i> | <i>p</i> | LLCI  | ULCI  |
|-----------------|--------------------|----------|-----------|----------|----------|-------|-------|
| HADS Depression | PDQ                | -0.13    | .02       | -7.84    | <.001    | -0.17 | -0.10 |
|                 | Years of Education | -0.04    | .11       | -0.33    | .740     | -0.26 | 0.18  |
| FAMS            | HADS Depression    | -3.57    | .50       | -7.17    | <.001    | -4.55 | -2.58 |
|                 | PDQ                | 0.67     | .11       | 5.93     | <.001    | 0.45  | 0.90  |
|                 | Years of Education | 1.81     | .61       | 2.97     | .004     | 0.61  | 3.02  |

*Note.* PDQ= Perceived Deficits Questionnaire; HADS Depression = Hospital Anxiety and Depression Scale, depression subscale; GQ-6= Gratitude Questionnaire-6; FAMS= Functional Assessment of Multiple Sclerosis total scale.

Table 6.

*Indirect Effects of Perceived Cognitive Functioning on Quality of Life via Depression*

| Mediator        | Moderator | Boot SE | Boot LLCI | Boot ULCI |
|-----------------|-----------|---------|-----------|-----------|
| HADS Depression | .47       | .095    | .31       | .68       |

*Note.* HADS Depression = Hospital Anxiety and Depression Scale, depression subscale; GQ-6= Gratitude Questionnaire-6.

**Hypothesis 2a: Objective cognitive functioning predicting quality of life.** In the second model, I analyzed the basic relationship between objective cognitive functioning and quality of life prior to assessing these variables in a mediated model. As hypothesized, higher objective cognitive functioning predicted higher quality of life, such that individuals who obtained higher scores on the measure of objective cognitive functioning also tended to endorse better quality of life (see Table 7 for all parameter estimates for this analysis).

**Hypothesis 2b: Objective cognitive functioning predicting depression.** In the next step, I analyzed the relationship between objective cognitive functioning and depression. As hypothesized, higher objective cognitive functioning predicted lower depressive symptoms, such that individuals who obtained higher scores on the measure of objective cognitive functioning also tended to have fewer depressive symptoms.

**Hypothesis 2c: Depression mediation between objective cognitive functioning and quality of life.** Next, I analyzed the model testing depression as a mediator between objective cognitive functioning and quality of life. Even after accounting for higher depression predicting lower quality of life (as expected), objective cognitive functioning continued to predict higher quality of life. Moreover, results indicated a significant indirect effect of objective cognitive functioning on quality of life through depression as hypothesized; specifically, higher levels of objective cognitive functioning predicted fewer depressive symptoms, which in turn predicted higher quality of life (Table 7 and 8).

Table 7.

| <i>Regressions of Quality of Life on Objective Cognitive Functioning and Depression</i> |                       |          |           |          |          |       |       |
|-----------------------------------------------------------------------------------------|-----------------------|----------|-----------|----------|----------|-------|-------|
| Outcome                                                                                 | Predictor             | <i>B</i> | <i>SE</i> | <i>t</i> | <i>p</i> | LLCI  | ULCI  |
| HADS<br>Depression                                                                      | BICAMS                | -0.71    | 0.33      | -2.16    | .030     | -1.36 | -0.06 |
|                                                                                         | Years of<br>Education | -0.16    | 0.14      | -1.17    | .240     | -0.43 | 0.11  |

|      |                    |       |      |        |       |       |       |
|------|--------------------|-------|------|--------|-------|-------|-------|
| FAMS | HADS Depression    | -5.01 | 0.45 | -11.02 | <.001 | -5.91 | -4.11 |
|      | BICAMS             | 4.98  | 1.67 | 2.98   | .003  | 1.68  | 8.28  |
|      | Years of Education | 1.93  | .68  | 2.83   | .005  | 0.58  | 3.28  |

*Note.* BICAMS=Brief International Cognitive Assessment of Multiple Sclerosis; HADS depression = Hospital Anxiety and Depression Scale, depression subscale; GQ-6= Gratitude Questionnaire-6; FAMS= Functional Assessment of Multiple Sclerosis total scale.

Table 8.

*Indirect Effects of Objective Cognitive Functioning on Quality of Life via Depression*

| Mediator        | Moderator | Boot SE | Boot LLCI | Boot ULCI |
|-----------------|-----------|---------|-----------|-----------|
| HADS Depression | 3.55      | 1.75    | .12       | 6.96      |

*Note.* HADS Depression = Hospital Anxiety and Depression Scale, depression subscale; GQ-6= Gratitude Questionnaire-6.

**Hypothesis 3a: Gratitude moderates the effect of relationship between cognitive functioning on depression.** After establishing the aforementioned mediation effects, I examined whether gratitude had a main effect on depression. I expected higher gratitude would predict lower depression. In line with hypotheses gratitude negatively predicted depression within the model assessing perceived cognitive functioning, such that at higher levels of gratitude individuals tended to have less depression (Table 9). Gratitude did not predict depression in the model with objective cognitive functioning as the predictor (Table 10). I also examined whether gratitude might moderate the effects of cognitive functioning on depression on the “A” path. Specifically, I expected that higher trait gratitude would diminish the extent to which poorer cognitive functioning (both perceived and objective) predicted higher depressive symptoms. Contrary to the hypothesis, gratitude did not moderate the effects of cognitive functioning (perceived nor objective) on depression (Table 9).

Table 9.

*Moderation Analysis Parameter Estimates for Perceived Cognitive Function*

| Outcome         | Predictor            | <i>B</i> | <i>SE</i> | <i>t</i> | <i>p</i> | LLCI   | ULCI   |
|-----------------|----------------------|----------|-----------|----------|----------|--------|--------|
| HADS Depression | PDQ                  | -0.100   | .020      | -6.07    | <.001    | -0.130 | -0.070 |
|                 | GQ-6                 | -0.220   | .040      | -4.92    | <.001    | -0.310 | -0.130 |
|                 | PDQ*GQ-6             | -0.001   | .003      | -0.49    | .630     | -0.006 | 0.004  |
|                 | Years of Education   | 0.002    | .100      | 0.02     | .980     | -0.200 | 0.200  |
| FAMS            | HADS Depression      | -3.050   | .540      | -5.68    | <.001    | -4.120 | -1.990 |
|                 | PDQ                  | 0.650    | .110      | 5.82     | <.001    | 0.430  | 0.870  |
|                 | GQ-6                 | 0.750    | .290      | 2.61     | .010     | 0.180  | 1.310  |
|                 | HADS Depression*GQ-6 | -0.050   | .060      | -0.89    | .380     | -0.170 | 0.070  |
|                 | Years of Education   | 1.710    | .600      | 2.85     | .010     | 0.520  | 2.890  |

*Note.* PDQ= Perceived Deficits Questionnaire; HADS Depression = Hospital Anxiety and Depression Scale, depression subscale; GQ-6= Gratitude Questionnaire-6; FAMS= Functional Assessment of Multiple Sclerosis total scale.

**Hypothesis 3b: Testing gratitude as a moderator of depressive symptoms on quality of life.** In our next model, I examined whether gratitude had a main effect on quality of life. I expected higher gratitude would predict higher quality of life. As hypothesized, gratitude positively predicted higher quality of life within the model assessing perceived cognitive functioning as the predictor (Table 9) and the model assessing objective cognitive functioning as the predictor (Table 10), such that at higher levels of gratitude individuals tended to have better quality of life. I also analyzed the effects of gratitude moderating the impact of depression on quality of life on the “B” path. I hypothesized that higher trait gratitude would diminish the extent to which depression predicted lower quality of life. Contrary to the hypothesis, gratitude did not moderate the relationship between depression and quality of life. However, gratitude did predict quality of life, such that at higher levels of gratitude individuals tended to report higher quality of life (in both perceived and objective cognitive functioning models) (Tables 9 and 10).



Table 10.

*Moderation Analysis Parameter Estimates for Objective Cognitive Function*

| Outcome            | Predictor            | <i>B</i> | <i>SE</i> | <i>t</i> | <i>p</i> | LLCI  | ULCI  |
|--------------------|----------------------|----------|-----------|----------|----------|-------|-------|
| HADS<br>Depression | BICAMS               | -0.42    | 0.29      | -1.44    | .150     | -1.01 | 0.16  |
|                    | GQ-6                 | -0.30    | 0.05      | -6.52    | <.001    | -0.40 | -0.21 |
|                    | BICAMS*GQ-6          | 0.01     | 0.04      | 0.16     | .870     | -0.07 | 0.08  |
|                    | Years of Education   | -0.07    | 0.12      | -0.56    | .580     | -0.30 | 0.17  |
| FAMS               | HADS Depression      | -4.35    | 0.52      | -8.31    | <.001    | -5.38 | -3.31 |
|                    | BICAMS               | 4.85     | 1.64      | 2.96     | .004     | 1.61  | 8.09  |
|                    | GQ-6                 | 0.85     | 0.31      | 2.73     | .010     | 0.23  | 1.47  |
|                    | HADS Depression*GQ-6 | -0.05    | 0.07      | -0.77    | .440     | -0.18 | 0.08  |
|                    | Years of Education   | 1.80     | 0.67      | 2.69     | .010     | 0.47  | 3.12  |

*Note.* BICAMS= Brief International Cognitive Assessment of Multiple Sclerosis; HADS Depression = Hospital Anxiety and Depression Scale, depression subscale; GQ-6= Gratitude Questionnaire-6; FAMS= Functional Assessment of Multiple Sclerosis total scale.

**Hypothesis 4: Indirect effect of cognition on quality of life via depression will depend on the level of gratitude.** Additionally, I tested for the presence of a moderated mediation. Contrary to the hypothesis, the indirect effect of cognition on quality of life via depression did not depend on the level of gratitude. The indirect effects of perceived cognitive functioning on quality of life through depression were significant at multiple levels of the moderator (1 standard deviation below the mean, at the mean, and one standard deviation above the mean) (Table 11). The indirect effect of objective cognitive functioning on quality of life through depression was not significant at any level of the moderator (Table 12). Although the indirect effect on objective cognitive functioning on quality of life through depression was significant without gratitude in the model (In Hypothesis 2C above), once gratitude was added to the model as a moderator the indirect effect was no longer significant. Therefore, the indirect effect of cognitive functioning (perceived and objective) via depression on quality of life did not depend on gratitude level, suggesting no moderated mediation (Table 11 and 12).

Table 11.

*Testing Conditional Indirect Effects of Perceived Cognitive Functioning on Quality of Life*

|                 | Moderator<br>GQ-6 | Effect | Boot SE | Boot LLCI | Boot ULCI |
|-----------------|-------------------|--------|---------|-----------|-----------|
| HADS Depression | -6.03             | .26    | .12     | .07       | .54       |
| HADS Depression | .000              | .31    | .08     | .17       | .50       |
| HADS Depression | 6.03              | .37    | .10     | .20       | .57       |

*Note.* HADS Depression = Hospital Anxiety and Depression Scale, depression subscale; GQ-6= Gratitude Questionnaire-6.

Table 12.

*Testing Conditional Indirect Effects of Objective Cognitive Functioning on Quality of Life*

|                 | Moderator<br>GQ-6 | Effect | Boot SE | Boot LLCI | Boot ULCI |
|-----------------|-------------------|--------|---------|-----------|-----------|
| HADS Depression | -6.05             | 1.86   | 1.80    | -1.06     | 6.00      |
| HADS Depression | .000              | 1.84   | 1.25    | -0.46     | 4.46      |
| HADS Depression | 6.05              | 1.80   | 1.66    | -1.49     | 5.09      |

*Note.* HADS Depression = Hospital Anxiety and Depression Scale, depression subscale; GQ-6= Gratitude Questionnaire-6.

**Hypothesis 5: When both indirect effects are tested simultaneously, only the indirect effect of perceived cognitive functioning on quality of life via depression will remain significant.** The fifth model tested the relationship between perceived cognitive functioning, objective cognitive functioning, depression, and quality of life via a path analysis model. I utilized a path analysis to calculate the indirect effects but not with the intention of model fit (Figure 4). As hypothesized, the *unique* indirect effect from perceived cognitive functioning to quality of life through depression was significant (controlling for effects of objective cognitive functioning), whereas the *unique* indirect effect from objective cognitive functioning to quality of life through depression was not significant (controlling for perceived cognitive functioning) (Table 13). There was a significant *unique* direct effect of perceived cognitive functioning on depression, such that higher perception of cognition functioning significantly predicted fewer depressive symptoms. However, there was not a significant *unique* direct effect from objective cognitive functioning to depression. There was a significant direct effect from depressive

symptoms to quality of life, such that fewer depressive symptoms predicted higher quality of life for both perceived and objective cognitive functioning. Finally, even after controlling for indirect effects via depression, there was still a *unique* direct effect for perceived cognition on quality of life and for objective cognition on quality of life, such that higher cognitive functioning predicted higher quality of life (for both objective and perceived cognitive functioning). Also, perceived cognition and objective cognition covaried positively.

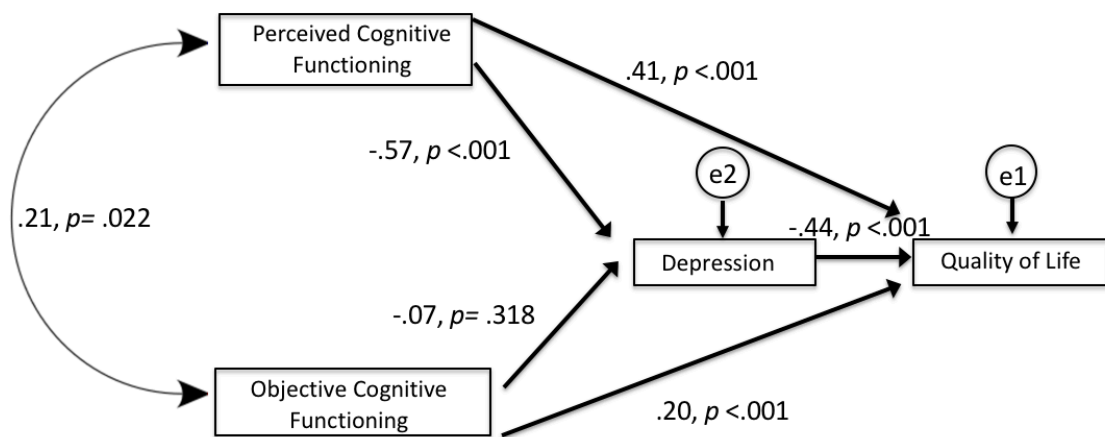


Figure 5. Final model with standardized parameter estimates via path analyses.

Table 13.

*Path Analyses: Indirect Effect of Cognition on Quality of Life via Depression*

| Outcome | Predictor | B    | p    | LLCI  | ULCI |
|---------|-----------|------|------|-------|------|
| FAMS    | BICAMS    | .049 | .079 | -.017 | .159 |
|         | PDQ       | .256 | .010 | .115  | .355 |

Note. BICAMS= Brief International Cognitive Assessment of Multiple Sclerosis; PDQ= Perceived Deficit Questionnaire; FAMS= Functional Assessment of Multiple Sclerosis total scale.

## CHAPTER IV

### Discussion

#### Purpose of the Study

The purpose of the present study was to better understand how individual differences in cognitive functioning, depression, and strengths are related to quality of life for individuals diagnosed with MS. Research to date has examined the impact of cognitive functioning on quality of life. However the existing research has not simultaneously examined the impact of perceived and objective cognitive functioning on quality of life for individuals diagnosed with MS, nor has the literature established mechanisms through which cognitive functioning predicts quality of life. The results of this study therefore offer a unique perspective allowing a direct comparison of objective cognitive functioning and perceived cognitive functioning as differential predictors of quality of life through a shared mechanism, depression. A secondary purpose of this study was to examine the potential impact of gratitude as a strength that might buffer against the effects of lower cognitive function on depression symptoms, and of depression on quality of life in MS. Strength related constructs, particularly gratitude, have received little attention in the literature regarding their impact on the MS population. This study therefore examined (a) how cognitive functioning (both perceived and objective cognitive abilities) predicted quality of life, (b) whether depression symptoms mediated the effects of cognitive functioning on quality of life (for both perceived and objective cognitive functioning), (c) and whether gratitude moderated the relationship between cognitive functioning (both objective and perceived) and depression, the relationship between depression and quality of life, and the indirect effect of cognitive functioning on quality of life in MS through depression (i.e., moderated mediation).

## Major Findings

**Perceived cognitive functioning predicting quality of life through depression.** As hypothesized, higher perceived cognitive functioning predicted lower depressive symptoms. This result replicates past studies that have consistently found perceived cognitive functioning to be a negative predictor of depression (Gilchrist & Creed, 1994; Romero et al., 2015). The awareness of decreased cognitive functioning and the daily impact of these perceived deficits may contribute to individuals' feelings of depression as they experience a loss of ability. Evidence exists for this relationship between disability, or illness severity, and depression in the literature (Chwastiak et al., 2002; Lynch, Kroencke, & Denney, 2001).

As hypothesized, higher perceived cognitive functioning also predicted higher quality of life replicating past studies that have consistently found perceived cognitive functioning to be a positive predictor of quality of life (Giovannetti et al., 2016; Samartzis et al., 2014). As existing literature (Giovannetti et al., 2016; Samartzis et al., 2014) and results from this study suggest, perceived cognitive functioning significantly impacts individuals' quality of life. Individuals who perceive increased cognitive impairment may experience increased problems in areas such as occupational settings, or personal relationships or engaging in daily tasks (Samartzis et al., 2014). These increased problems may be due to perceived diminished cognitive capacity in areas such as concentration, decreased memory, losing one's train of thought, and difficulty planning or making decisions (Ritvo et al., 1997).

In addition, as hypothesized, higher perceived cognitive functioning predicted higher quality of life via lower depressive symptoms (indirect effect). As individuals see a negative change in their cognitive ability at work, socially, or in daily tasks, individuals may be experiencing psychological symptoms (e.g., depressive symptoms) associated with adjustment to

their MS. As cognitive abilities play a role in all life tasks, individuals seem to experience decreased quality of life as their daily functioning appears to have changed. In addition, individuals may experience uncertainty regarding future changes in ability leading to depressed mood. Each new experience of symptoms or perceived deficits may represent a new period of adjustment in life and uncertainty in disease progression. Previous research by Kroencke, Denney, and Lynch (2001) supports this idea. Researchers found depression positively fluctuated with MS symptom exacerbations. Further, researchers found that it was patients' levels of uncertainty that specifically influenced depressive symptoms (Kroencke et al., 2001). It is possible that the depression symptoms individuals experience reflect their continued adjustment to changes or perceived changes in ability due to MS.

To my knowledge there is no study directly assessing depression as a mediator between perceived cognitive function and quality of life in an MS population. Past research has shown associations between variables: perceived cognitive functioning and depression (Maor et al., 2001; Middleton et al., 2006; Rohling et al., 2002), perceived cognitive functioning and quality of life (Giovannetti et al., 2016; Samartzis et al., 2014) and depression and quality of life (Janardhan & Bakshi, 2002; Mitchell et al., 2005). Results in the literature suggest that in an MS population, decreased perceived cognitive functioning is related to higher depressive symptoms and lower quality of life in individuals with MS. Similar to the present study, Samartzis et al. (2014) found a significant relationship between perceived cognitive functioning and depression, though they found perceived cognitive functioning predicted quality of life independent of depression; however, that study did not directly test for a mediation effect. Conversely, my results suggest that depression, in part, may account for the relationship between perceived cognitive functioning and quality of life.

As Samartzis et al. (2014) found perceived cognitive functioning predicted quality of life independent of depression, and the present study found depression to act as only a partial mediator, future studies may consider examining other potential mechanisms by which we can understand the relationship between perceived cognitive functioning and quality of life. For instance, other predictors of quality of life, which may be impacted by changes in perceived cognitive functioning, include disability (Goksel Karatepe et al., 2011; Rao et al., 1991), social support (Yamout et al., 2013; Rao et al., 1991), employment (Yamout et al., 2013; Rao et al., 1991), and fatigue (Kinsinger et al., 2010; Yamout et al., 2013). Future studies should examine these variables as potential mediators, above and beyond effects of depression symptoms, with potential to garner greater understanding of the relationship between perceived cognitive functioning and quality of life.

**Objective cognitive functioning predicting quality of life through depression.** Next, as hypothesized, higher objective cognitive function predicted lower depressive symptoms in line with previous studies (Feinstein et al., 2004; Pucak et al., 2007). This finding may indicate that brain lesions (caused by demyelination) may contribute to depressive symptoms (Feinstein et al., 2004; Pucak et al., 2007). However, some studies have failed to find a significant relationship between objective cognitive functioning and depression (Julian, Merluzzi, & Mohr, 2007; Srisurapanont, Suttajit, Eurviriyankul, & Varnado, 2017). The results of the present study bolster evidence that objective cognitive functioning in MS predicts lower depression.

As hypothesized, higher objective cognitive functioning also predicted higher quality of life, even when controlling for depression. This finding replicates past studies which have consistently found objective cognitive functioning to positively predict quality of life (Benito-León et al., 2002; Cutajar et al., 2000; Gold et al., 2003). Lower cognitive functioning may

impact individuals' ability to work, relate to others, plan, organize, and engage in daily tasks as was possible prior to having MS (Hakim et al., 2000; Javůrková et al., 2016).

In addition, parallel to the findings for perceived cognition, higher objective cognitive functioning predicted higher quality of life via lower depressive symptoms (indirect effect). Depression whether impacted by perceived or objective cognitive functioning exhibits similar symptoms (e.g., fatigue, depressed mood, loss of interest or pleasure, sleeping difficulties, psychomotor retardation or agitation, change in weight, negative self-image, feelings of guilt and self-blame, reduced concentration, and sometimes suicidal ideation) and can be impairing for individuals impacting quality of life (Siegert & Abernethy, 2005). Depression impacted by physical brain damage may mean more resistant depression or depression needing specific forms of treatment as individuals' depression relates to a physical cause rather than purely due to adjustment. If this is the case, depression symptoms resulting from physical brain damage may be impacting quality of life due to the typically impairing symptoms present with Major Depressive Disorder, addressed above, in addition to patients' co-occurring MS symptoms. Depression and quality of life impacted from brain damage may respond best to particular forms of treatment given the source of depressive symptoms through disease modifying therapies, antidepressants, and psychotherapy based on coping skills (Mohr, Goodkin, & Islar, 2001; Schiffer & Wineman, 1990).

The present study uniquely offers this new finding not assessed previously in the literature. Previous research has found associations between objective cognitive functioning, depression, and quality of life, such that lower cognitive functioning and higher depression predict lower health related quality of life (Benito-León et al., 2002) and physical quality of life (Seidel et al., 2014). Similarly, Baumstarck-Barrau et al. (2011) found objective cognitive



impairment only weakly associated to quality of life once depression and fatigue were controlled. Consistent with this assertion, Giovannetti et al., (2016) found cognitive function poorly predicted quality of life without additional variables such as anxiety, depression, or level of disability. However, no study to my knowledge directly assesses the relationship between objective cognitive function and quality of life through depression as a mediator in an MS population. The indirect effect found in the present study suggests that physical aspects of demyelination, such as brain lesions, may contribute to both decreased cognitive functioning and symptoms of depression (Feinstein et al., 2004; Feinstein et al., 2010; Popescu & Lucchinetti, 2012; Pucak et al., 2007; Rahn et al., 2012). If this is the case, the unique demyelination course occurring for each individual with MS may be having an effect on their depressive symptoms in addition to their cognitive symptoms. It is possible that the progressiveness of the disease, and specific areas which the demyelination are occurring, may be impacting depressive symptoms. Researchers may consider studying the impact disease modifying treatment (i.e., drug therapies) have on patients' depressive symptoms.

Depression did not fully mediate the effects of objective cognitive functioning in this study, which suggests that other mediators may be operating on this pathway. Disability, for example, may be a possible mediator given its impact on quality of life (Janardhan & Bakshi, 2002) and the fact that it has been predicted by objective cognitive functioning (Miller & Dishon, 2006). Researchers may also find utility in investigating a moderated mediation model assessing whether brain lesion surface area moderates the indirect effect of objective cognitive functioning on quality of life. Greater understanding of the mechanisms through which cognitive functioning (both objective and perceived) impact quality of life, and variables which moderate those mechanisms, will lead to further knowledge of the underlying processes occurring for MS

patients. In addition, added knowledge in this area may lead to strategies for clinical intervention to improve patients' quality of life.

**Gratitude moderating the relationship of cognitive functioning and depression.** In the next model, contrary to my hypothesis, gratitude did not act as a moderator on the relationship between cognitive functioning (perceived nor objective) and depression. The absence of an interaction in the study is somewhat inconsistent in the literature. There is no literature to my knowledge directly assessing gratitude as a moderator of the relationship between cognitive functioning and depression within or outside of an MS population. However, there is evidence showing that positively valenced psychological variables (e.g., positive well-being, positive affect) impact objective cognitive functioning (Allerhand et al., 2014; Estrada et al., 1994; Gerstorf et al., 2007; Isen, 2009; Isen, 2001). Specifically, evidence in the literature suggests that positive well-being, related to gratitude, is related to higher cognitive ability, particularly slower deterioration of perceptual speed, greater executive function, and memory (Allerhand et al., 2014; Gerstorf, et al., 2007). In addition, the literature shows considerable evidence suggesting gratitude promotes resilience (Lambert D'raven et al., 2015; Ruini & Vescovelli, 2013) and predicts lower depression (Lin, 2015; Lambert et al., 2011; Wood et al., 2008a). I had therefore expected gratitude to act as a buffer between cognitive functioning and depression. It is possible that positively valenced variables such as gratitude do not in fact influence MS symptoms (e.g., cognitive functioning, depression, and quality of life). However, based on the evidence in the literature, there may be other reasons for the lack of significant indirect effects between cognitive functioning and depression found in the present study.

One possible reason the present study did not find gratitude to moderate the relationship between cognitive functioning and depression may be due the research design of assessing trait

gratitude versus utilizing a gratitude-focused intervention. There is evidence in the literature supporting the design used in the present study indicating that measuring trait gratitude, or self-reported gratitude not induced through an intervention, can be sufficient to detect an effect (Disabato et al., 2017; Mofidi, El-Alayli, & Brown, 2014; Ruini & Vescovelli, 2013; Wood, Joseph, Lloyd, & Atkins, 2009). However, the literature offers more substantial support for a study design utilizing gratitude induction, implementing a gratitude-focused intervention, to detect an effect (Emmons & Stern, 2013; Froh, Kashdan, Ozimkowski, & Miller, 2008; Witvliet et al., 2018; Wood et al., 2008a). Trait measures of gratitude without intervention may not be enough to *significantly* impact change in areas such as mood or quality of life, yet gratitude may still have an impact on these processes. The studies in the literature utilizing a gratitude-focused intervention suggest individuals who *practice* gratitude report increased feelings of happiness, self-acceptance, and well-being (de Souza & Kamble, 2016; Emmons & McCullough, 2003; Ruini & Vescovelli, 2013; Watkins et al., 2003). Further, research studying potential reciprocal effects found that while gratitude leads to many positive increases regarding psychological well-being, nothing seems to naturally lead to gratitude (Wood et al., 2008a). This may indicate the possibility of differing impacts of trait versus induced gratitude. Specifically, individuals may need to actively practice gratitude (e.g., writing a gratitude journal, writing a thank you note) or engage in an intervention to see a significant impact on areas such as quality of life or mood. Future research may consider creating a longitudinal experiment offering a gratitude focused intervention to assess the differing impact induced gratitude may play for individuals with MS versus trait gratitude as reported in the present study.

While gratitude did not act as a moderator in the present study, gratitude did have a significantly negative association with depression consistent with findings in the literature (Lin,

2015; Lambert et al., 2012; Wood et al., 2008a). In line with this finding, evidence in the literature shows it is effective for individuals with health concerns experiencing depression to practice gratitude. Results show practicing gratitude increases mental health and vitality even for individuals with health concerns (Lambert D'raven et al., 2015). In addition, in the present study, gratitude predicted outcomes (e.g., depression and quality of life) in both models of cognitive functioning (perceived and objective); this suggests gratitude may be an important process to understand regarding its contribution to depression and quality of life for individuals with MS beyond well-established mechanisms. Though perceived cognitive functioning may be more related to individual psychological variables (e.g., depression) (Kinsinger et al., 2011; Middleton et al., 2006) and objective cognitive functioning may be more related to lesions in the brain (Popescu & Lucchinetti, 2012; Stadelmann et al., 2011; Winkelmann et al., 2007), gratitude remained a predictor in each model (perceived and objective) for depression and quality of life; this may suggest gratitude cuts across psychological and physical variables. This is consistent with previous research indicating practicing gratitude can impact variables including sleep, depression, anxiety, fatigue, and self-efficacy (Mills et al., 2015; Ng & Wong, 2012). The knowledge that gratitude may act on both psychological and physiological levels further suggests gratitude may contribute to the treatment of MS patients – potentially impacting multiple symptoms simultaneously (e.g., fatigue, depression, anxiety, sleep). This study did not find evidence for gratitude as a moderator on the relationship between cognitive functioning and depression, however gratitude may have a downstream effect on mood.

The present study did not use an intervention to induce gratitude and though data is correlational, the results do suggest gratitude might have a downstream effect on depression. Trait gratitude or individuals' practice of gratitude without the use of intervention may still

positively impact individuals' negative mood for individuals with MS. Though individuals with MS may still experience feelings of depression, gratitude centered thought content may allow individuals to appreciate people, events, and situations in life, and to feel thankful for their life and social relationships, compared to those with low levels of gratitude (McCullough et al., 2002). Thought content infused with gratitude may act as a strength for individuals and lead to a more positive outlook on life (Wood et al., 2010), hope (Witvliet et al., 2017), and motivation to engage positively with others (Froh, Bono, & Emmons, 2010; Simão & Seibt, 2014). These downstream effects may impact the way individuals with gratitude perceive each day, thereby influencing their thoughts, emotions, and behaviors; this may also impact the ways they interact with others, the way they view themselves and the world, and perhaps the way they manage and/or perceive their illness.

The findings of the present study suggest gratitude may play a role in patients' experience of negative mood symptoms, although I found no evidence for gratitude as a buffer against negative mood symptoms as related to cognitive functioning. This study is one of two studies on gratitude in the field of MS. Results warrant further assessment of the impact of gratitude in MS.

**Gratitude moderating the effect of depression on quality of life.** Next, contrary to hypotheses, gratitude did not moderate the link between depression and quality of life. The non-significant interaction is somewhat inconsistent with the literature. Evidence in the literature suggested a positive relationship between gratitude and quality of life/well-being (Emmons & McCullough, 2003) and a negative association between gratitude and depression (Wood et al., 2008a), as well as a negative relationship between quality of life and depression (Benito-León et al., 2002). I had therefore expected gratitude to act as a buffer between depression and quality of life. Some evidence in the literature suggests gratitude must be practiced or induced to impact

negative affect or quality of life (Wood et al., 2008a). It is possible that, had the present study utilized a gratitude-focused intervention, the impact of gratitude on the relationship between depression and quality of life may have been stronger or significant.

While gratitude did not act as a buffer in the present study, gratitude did have a significant positive direct association with quality of life. If gratitude is able to predict quality of life despite not moderating the relationship between depression and quality of life, it may nonetheless contribute to well-being in the context of MS. Gratitude can impact the way individuals think, feel, and behave (Wood et al., 2008a). In line with a cognitive behavioral perspective gratitude could play a more causal role in impacting quality of life by altering individuals' perceptions of the world, themselves, others, and their illness (Emmons & McCullough, 2003; Wood et al., 2008a). Perceiving life through a perspective of gratitude may directly alter individuals' negative affect and quality of life without changing the nature of the relationship of depression to quality of life or buffering the effects of cognitive functioning or negative affect (Wood et al., 2008a).

The present study is the second to assess gratitude in an MS population, and the first study to find significant main effects (Büssing et al., 2014). The Büssing et al. (2014) study found relatively low levels of gratitude in the MS sample assessed and found that gratitude was unable to explain variance related to life satisfaction. The results of the present study uniquely contribute to the literature showing that gratitude impacts quality of life. A grateful mindset impacts how individuals think, behave, and feel (Wood et al., 2008a). If individuals perceive their world through this positive lens, recognizing and appreciating the positive things in themselves, the world, and others, both positive mood and increased motivation to engage in

prosocial behaviors may result. However, it remains for future studies to directly test that idea in the context of MS.

Additionally, this study is the first of its kind to assess gratitude in patients with MS in the context of cognitive functioning and depressed affect. Previous research has shown a negative association between gratitude and depression in other chronic health conditions (Mills et al., 2015; Ng & Wong, 2012) and a positive association between positively valenced psychological variables (positive well-being and affect) and cognitive functioning (Allerhand et al., 2014; Gerstorf et al., 2010). However, there is no research within the field of MS assessing gratitude within the context of cognitive functioning or depression, two of the most common symptoms associated with MS (Giordano et al., 2011; Kinsinger et al., 2011; Romero et al., 2015; Siegert & Abernethy, 2005). More research is needed to gain clarity on the role or function of gratitude for MS patients within the context of cognitive functioning, depression, and quality of life. By increasing understanding of the impact of gratitude on constructs related to quality of life, cognitive function, and other types of disability (physical, affective), clinicians may be able to effectively integrate gratitude-based interventions for individuals diagnosed with MS—potentially offering a cost-free and potentially life-enhancing therapeutic tool. For instance, gratitude predicted quality of life even after accounting for variables previously shown to predict quality of life in MS (e.g., cognitive functioning, depression). This suggests that in addition to medical strategies targeting MS symptoms (e.g., mental and physical exercises, antidepressants), teaching gratitude interventions may impart additional incremental benefits.

Gratitude is one strength that has shown utility in positively impacting negative mood states and quality of life; however, there may be other strengths positively influencing individuals with MS. Strengths such as spirituality, love of learning, bravery, creativity,

curiosity, forgiveness, or humor, may also positively impact negative mood or quality of life. Researchers studying creativity in individuals with MS found that making art increased individuals' ability to maintain identity, cope with loss of function by opening up new opportunities, and increase positive traits of fulfillment, hope, self-esteem, and social support (Fraser & Keating, 2014; Hunt, Nikopoulou-Smyrni, & Reynolds, 2014). Similarly, spirituality has sometimes positively predicted adaptation to MS (McNulty, Livneh, & Wilson, 2004), though not always (Makros & McCabe, 2003). Research on these and other strengths would be beneficial to build a greater understanding of the impact of strengths for individuals with MS. In addition, the field of MS may benefit from research assessing how strengths might act as potential buffers against negative mood states (depression, anxiety) and/or as potential buffers against the impact of negative mood states on patients' quality of life. There is ample evidence in the literature suggesting that strengths are beneficial for similar chronic illness populations. These previous findings offer precedence for strength-based research in MS populations (Carson et al., 2005; Christie & Moore, 2005; Kristjansdottir et al., 2018; O'Neill & Kenny, 1998; Thompson, 2014).

**Indirect effect of cognition on quality of life via depression will depend on the level of gratitude.** Contrary to my hypothesis, the indirect effect of cognition on quality of life via depression did not depend on the level of gratitude, suggesting no moderated mediation. This finding was somewhat surprising given evidence in the literature which suggests that factors associated with gratitude (e.g., positive affect, positive well-being) are positively associated with cognitive functioning (Allerhand et al., 2014; Isen, 2001). In addition, the literature suggests that gratitude is negatively associated with depression (Benito-León et al., 2002; Ng & Wong, 2012), and positively associated with factors impacting quality of life for a number of chronic health



conditions (e.g., asymptomatic heart failure, arthritis, chronic obstructive pulmonary disease, diabetes; Eaton et al., 2014; Mills et al., 2015). Therefore, I had reasonably expected an indirect effect of cognition on quality of life via depression, such that gratitude would blunt the extent to which depression mediated the relationship between cognitive functioning and quality of life.

Results of earlier models suggested a significant indirect effect of the relationship between cognitive functioning (perceived and objective) and quality of life through depression. The current indirect effect with *perceived* cognitive functioning on quality of life through depression remained significant, though gratitude did not moderate this relationship on either the “A” or “B” path. However the indirect effect of *objective* cognitive functioning on quality of life through depression lost significance once gratitude was accounted for in the model. Thus, once gratitude was in the model the indirect effect of objective cognitive function on quality of life through depression was no longer significant; gratitude did not significantly moderate this relationship on either the “A” or “B” path. As gratitude is such a strong predictor of depression, when gratitude became a predictor in the relationship between objective cognitive functioning and depression, the presence of gratitude in the model likely made it more difficult for the indirect effects between objective cognitive functioning on quality of life through depression to remain significant.

Several potential reasons for the lack of moderated mediation are plausible. First, trait gratitude rather than induced gratitude was measured in the present study. As noted earlier, the impact of trait gratitude may not be strong enough to detect an effect. Gratitude may need to be practiced to have a significant impact on an individual’s mood, well-being, or demonstrate other adaptive benefits (de Souza & Kamble, 2016; Emmons & McCullough, 2003; Ruini & Vescovelli, 2013). Therefore, future studies may consider utilizing a gratitude-focused

intervention when assessing the impact of gratitude in MS populations. Second, the present study utilized a cross-sectional study design to assess gratitude. Gratitude may need to be assessed at multiple time points to assess changes in individuals' level of gratitude over time (Toepfer & Walker, 2009) or to allow opportunity for individuals to regularly practice of gratitude (Lyubomirsky, Dickerhoof, Boehm, & Sheldon, 2011). Third, although my sample size was adequately powered to detect main effects, interactions often require much larger samples to be fully powered. Further research on gratitude in MS populations, particularly study designs including longitudinal data collection or gratitude induction (with large samples), would be beneficial to increase the understanding of strengths such as gratitude and its relevance to coping with MS.

**Differential predictive nature of unique perceived and unique objective cognitive functioning when predictors control for one another in the same model.** Finally, as hypothesized, when indirect effects of both perceived and objective cognitive functioning on quality of life were *simultaneously* estimated in the same model, only the unique indirect effect of perceived cognitive functioning to quality of life through depression was significant (Figure 5). Although both indirect effects were significant when examined independently as reviewed above (Figure 1 and 2), once shared variance was accounted for, only the effect of perceived cognition remained. The present study is the first to our knowledge to simultaneously test indirect effects of perceived and objective cognitive functioning on quality of life, providing a more conservative estimate of effects.

The indirect effect from objective cognitive functioning to quality of life through depression lost significance once both predictors (perceived and objective cognitive functioning) were set in the same model controlling for one another. This suggests that perceived cognitive

functioning may act as a stronger predictor for quality of life when depression is mediating the relationship. As strong evidence exists in the MS literature for the link between decreased perceived cognitive functioning and depression (Gilchrist & Creed, 1994; Kinsinger et al., 2011; Middleton et al., 2006) and for the link between perceived cognitive functioning and quality of life (Giovannetti et al., 2016; Janardhan & Bakshi, 2002; Samartizis et al., 2014) this idea is likely. Because depression and perceptions of poor cognitive functioning both entail negative perspectives of oneself, it makes sense that depression would serve as a stronger mediator for perceived cognition relative to actual cognitive performance. Evidence in the literature, though mixed (Baumstarck-Barrau, et al., 2011; Glanz et al., 2010), still exists for the link between objective cognitive functioning as a positive predictor of quality of life (Benito-León et al., 2002; Cutajar et al., 2000; Gold, 2003) and depression (Feinstein et al., 2004; Pucak et al., 2007) for individuals with MS. However, the indirect effect of cognitive functioning on quality of life through depression may be stronger for perceived cognitive functioning than for objective cognitive functioning. These results suggest that while perceived and objective cognitive function share some variance through depression on their impact on quality of life, they may each have unique mechanisms accounting for their impact on quality of life (e.g., depression impacted by objective cognition may relate to neurological demyelination whereas depression impacted by perceived cognition may relate to individuals' reactions to decreased ability or adjustment to illness). In addition to unique influences of depression as a mediator on the relationship between cognition (objective versus perceived) and quality of life, there may be an amalgam of mechanisms mediating this relationship. Specifically, mechanisms apart from depression may be required to account for the unique impact of objective cognition functioning

on quality of life, such as disability (Janardhan & Bakshi, 2002; Miller & Dishon, 2006) and the unique impact of perceived cognitive functioning, such as fatigue (Kinsinger et al., 2011).

Past findings have clearly indicated a low association between patients' perceptions of their objective cognitive performance and their actual cognitive performance (Goverover et al., 2014; Matotek et al., 2001; Middleton et al., 2006). The results from the current study showed a positive and significant relationship between perceived and objective cognitive functioning (Figure 5). However, it is evident that each contributed unique variance to quality of life, even apart from the path through depression. This implies that both objective cognitive functioning and perceived cognitive functioning uniquely impact quality of life for individuals diagnosed with MS. More research is needed to elucidate (or disentangle) the unique impact objective cognitive functioning and perceived cognitive functioning have on individuals' quality of life.

### **Implications**

**Clinical Implications.** Research to date has not found reproducible evidence-based pharmacological treatments to significantly improve cognitive functioning or reverse impairments for individuals with MS (He, Zhou, Guo, Hao, & Wu, 2011; Rahn et al., 2012). Cognitive rehabilitation therapy, however, has shown promise for MS patients in reducing fatigue and improving cognitive functioning in areas such as working memory and attention. In cognitive rehabilitation, patients are provided training and work to practice a specific cognitive skill. This process works to strengthen neurological connections required for the cognitive skill being practiced (Charvet, et al., 2017; Güçlü Altun, et al., 2015; Rahn et al., 2012). With irreversible brain damage, however, training and practice may focus on compensating for cognitive deficits rather than restoring cognitive functioning (Rahn, et al., 2012). Nonetheless, research offers inconsistent evidence on the effect of cognitive rehabilitation on mood/emotional

functions (Brenk, Laun, & Haase, 2008; Lincoln et al., 2002; Mattioli, Stampatori, Zanotti, Parrinello, & Capra, 2010; Mitolo, Venneri, Wilkinson, & Sharrack, 2015; Rosti-Otajärvi, & Hämläinen, 2014); this seems to represent a potential gap in treatment. However, it may be that supplementing cognitive rehabilitation with intervention focused on improving mood may benefit patients. Some evidence has suggested that patients' own perceived cognitive deficits are related to internalized stigma and quality of life (Shin, Joo, & Kim, 2016). The results from the present study may indicate possibilities for intervention that come from standard evidence-based interventions (e.g., challenging patients' beliefs regarding their cognitive functioning, reframing cognitions to attend to positive features of patients' cognitive functioning rather than deficits, or directly targeting depression via strategies such as behavioral activation).

In addition, clinical interventions may need to target the source of depression relative to cognition (perceived and/or objective). As individuals with MS tend to perceive their cognitive abilities as worse than is true, they may benefit from gaining a more realistic understanding of their actual cognitive function (e.g., via feedback from cognitive assessment). For individuals experiencing true decline in cognitive functioning, it may be beneficial to increase knowledge of resources for coping with cognitive dysfunction (e.g., cognitive behavioral therapy, exercise, education programs, problem-focused coping) to increase their sense of competence to deal with real cognitive deficits (Jongen, Ter Horst & Brands, 2012; Rahn et al., 2012). Further knowledge of the relationship between cognitive functioning (objective and perceived) and depression and knowledge of the impact of depression on quality of life may aid clinicians to provide specific and focused interventions targeted to improve depression and quality of life.

In addition, implementing a gratitude-focused intervention for individuals with MS may offer added benefit in treatment. Individuals with higher levels of gratitude tend to experience

more positive emotions, lower depression, better social functioning, increased ability to cope, and stronger desire to give back to others (Disabato et al., 2016; Emmons & McCullough, 2003; Tulbure, 2015; Wood et al., 2008a). Experiencing and practicing gratitude, and related strengths, has also been linked to improved physical (Goldberg & Jessup, 2006; Mills et al., 2015), cognitive (Allerhand et al., 2014; Gerstorff, et al., 2007), and emotional well-being (Emmons & McCullough, 2003; Ruini & Vescovelli, 2013). Researchers asked adults, recruited in a convenience sample from visitors to researcher Seligman's Web site dedicated to his book *Authentic Happiness*, to practice relatively simple exercises foster gratitude, such as writing and delivering a letter of gratitude to someone, writing down three good things in life, counting one's blessings, or identifying signature strengths and using them in a new way (Emmons & McCullough, 2003; Seligman, Steen, Park, & Peterson, 2005). These exercises increased happiness and decreased depressive symptoms when practiced daily for one week in a population of mildly depressed individuals— effects persisted six months following the study (Sin, Della Porta, & Lyubomirsky, 2011). Furthermore, positive psychotherapy (PPT) and well-being therapy (WBT), which feature strength based activities, have shown promise in reducing depressive symptoms in clinical populations compared to both treatment as usual and treatment as usual with medication (Sin et al., 2011).

Researchers have begun to examine the impacts of gratitude in populations experiencing chronic illness (such as asymptomatic heart patients and chronic pain) as gratitude seems to have a versatile impact on diverse aspects of well-being (Mills et al., 2015; Ng & Wong, 2012). For instance, researchers found that having patients regularly practice gratitude by having patients write about ways they were better off than others led to positive impacts for patients diagnosed with neuromuscular disease. Outcome effects included higher positive affect, lower negative

affect, higher well-being, and higher life satisfaction (Emmons & McCullough 2003). It is possible that pairing cognitive rehabilitation with positive psychology strategies focused on strengths, such as gratitude exercises, may enhance patients' perception of their cognitive functioning, mood, and/or quality of life. However, further research is warranted to directly examine applications for individuals with MS.

### **Limitations and Future Research**

There are several limitations notable for the present study. First, gratitude was measured as a self-report measure of trait gratitude without intervention. Some evidence in the literature suggests that while gratitude leads to positive outcomes (e.g., increased well-being, decreased negative affect) no particular constructs or processes (aside from gratitude exercises) naturally lead to gratitude (Wood et al., 2008a). Therefore, to have a measureable impact, gratitude may need to be induced through gratitude-focused interventions to observe effects in line with those found in the literature (Mills et al., 2015; Ng & Wong, 2012; Ruini & Vescovelli, 2013). However, given the constraints of patient time and clinic capacity, including a gratitude-focused intervention was not feasible in the present study: (a) the MS center where the study was conducted serves MS patients from the North West region of the U.S., therefore many patients come into the clinic infrequently often traveling long distances; (b) study researchers desired to limit research materials to limit cognitive fatigue and/or added burden for patients; and (c) patient willingness to participate would likely have decreased with increased study requirements (e.g., added time during visit, increased visits); thereby decreasing study sample size, data collected, and study power. Therefore, with the given time and visit constraints, trait gratitude, a single time point self-report measure, was used as it has well-validated psychometric properties (McCullough et al., 2002). However, future studies may benefit from investigating dynamic

within-person variability in state gratitude to obtain a greater understanding of the possible impact gratitude may have for individuals with MS.

Second, this study was conducted at a single time point, again due to constraints of the clinic, constraints of patients, and available study resources. A longitudinal study design with opportunity for tracking mood, cognitive functioning (perceived and objective), and quality of life would offer a greater understanding of the prospective relationships between these variables (i.e., testing lagged effects). However, given the constraints discussed above, adding additional time points to the study would have likely decreased the study sample size due to expectable attrition and increased patient burden (likely dissuading patients from committing to a voluntary study). I chose to utilize a less burdensome approach to patient assessment for the present study of gratitude in MS, viewing it as a pilot study that should be followed by longitudinal designs in the future. Thus findings of this study may help to inform future studies and provide precedence for a longitudinal design.

Third, for generalizability to the broader MS population, inclusion of additional participants diagnosed with primary progressive or secondary progressive MS would have been beneficial. Patients with existing appointments at the MS center were called about participation in the present study one week before their appointment. Though researchers systematically worked to call all eligible patients, patients participating in the study largely experienced relapsing-remitting MS (82.0%), as compared to primary progressive (10.8%) or secondary progressive MS (7.2%). Some research has found that patients experiencing progressive forms of MS significantly report lower quality of life (Benito-León et al., 2002; Göksel Karatepe et al., 2011), though other research has shown individuals with the Relapsing-Remitting subtype are more likely to experience an episode of major depression at some point during their lives (Zabad



et al., 2005). In addition, an estimated 85% of individuals are initially diagnosed with MS experience relapsing remitting MS, with about 60 to 75% of patients eventually transitioning to secondary progressive MS by roughly 10 to 20 years after diagnosis, and only about 15% of patients having primary progressive MS (Spain, n.d.). Therefore, there are fewer individuals experiencing primary progressive MS, and those with secondary progressive MS tend to experience it much later in their disease course. Thus, a sample with a majority of patients experiencing relapsing remitting MS is consistent with these disproportionate diagnoses seen in the population. Research also suggests significant variability and diversity in patient symptoms despite subtype (Rolak, 2003). Therefore, given the constraints of those who chose to participate, the distribution of MS subtype diagnosis across individuals with MS, the small population size of patients diagnosed with primary and secondary progressive MS relative to patients diagnosed with relapsing remitting MS, and the understanding that each MS case is unique despite diagnosis subtype, the composition of the study sample was reasonable.

Fourth, the BICAMS serves as an excellent screen for cognitive functioning (information processing speed, verbal recall, and visual recall), but does not provide a thorough neurocognitive assessment of intellectual ability, visuomotor skills, visuospatial skills, attention, memory and learning, verbal ability, and executive functioning (Javůrková et al., 2016). However, while individuals with MS may experience a diverse range of cognitive impairment (intellectual ability, visuomotor skills, visuospatial skills, attention, memory and learning, verbal ability, and executive functioning), information processing speed, verbal recall, and visual recall, measured by the BICAMS, are the three most commonly impaired forms of cognitive functioning for individuals with MS (Javůrková et al., 2016). In addition, the BICAMS cognitive screen used to assess objective cognitive function of patients is considered to be a screening tool

rather than a diagnostic assessment of cognitive functioning (Benedict et al., 2012a; Goretti, et al., 2014). This compilation of measures (SDMT, CVLT, and BVMT), however, have been well validated (Walker et al., 2016) and frequently used in research as a measure of cognitive functioning due to its brief format and validity in MS populations (Benedict et al., 2012; Campbell, Rashid, Cercignani, & Langdon, 2016; Cinar, Kösehasanoğulları, Yigit, & Ozakbas, 2017; Walker et al., 2016). Therefore, I was justified in utilizing the BICAMS assessment as a measure of cognitive functioning. Future studies may consider utilizing alternative measures of objective cognitive function, although cognitive fatigue, burden to patients, specificity to MS, and comprehensiveness of cognitive functioning should be accounted for when considering alternative measures.

Finally, as fatigue is highly comorbid with depression and impacts patients' cognitive functioning, it may have impacted patients' (a) cognitive assessment scores, (b) report of depression, and (c) report of quality of life. MS patients frequently report experiencing fatigue and consider it one of their most debilitating symptoms (Bol et al., 2010; Branas, Jordan, Fry-Smith, Burls, & Hyde, 2000; Braley & Chervin, 2010). However, I took several steps to limit the effect of fatigue in this study. I assessed patients with the BICAMS measure prior to providing patients with self-report measures to limit cognitive fatigue. Additionally, I purposefully chose to use the BICAMS assessment as it is a brief assessment typically lasting about 15 minutes, minimizing cognitive fatigue. To reduce the possibility that associations between constructs would be contaminated by variance related to fatigue (i.e., as a symptom common to both depression and MS), I purposefully chose the HADS measure of depression. The HADS does not include physical symptoms of depression, it was normed on hospital populations, and it demonstrated valid use in MS populations (Honarmand & Feinstein, 2009; Michopoulos et al.,

2008). In addition, I measured patient fatigue via self-report and conducted the data analyses with and without fatigue included as a variable impacting quality of life. The results were similar in direction and significance with and without fatigue controlled, so I decided to include fatigue as part of the measure of quality of life from the analyses to allow a robust measure of patients' quality of life.

### **Conclusion**

Despite the limitations addressed, the present study speaks to a number of gaps existing in the literature regarding the differential impact of strengths and depression in the relationship between perceived and objective cognition on quality of life for MS patients. First, this study provides support for both perceived and objective cognitive functioning as predictors of quality of life. Second, there is a lack of understanding in the literature as to why there is a discrepancy between perceived and objective cognitive functioning and why they differentially predict quality of life. This study suggests that depression symptoms are one mechanism that may explain this relationship. In addition to examining perceived and objective cognitive functioning separately, examining their unique indirect and direct effects on health-related quality of life simultaneously in the same model provided novel insight into the fact that depression may be a more important mediator for perceived cognitive functioning than for objective cognitive functioning.

This study was the second study to assess gratitude in the context of MS patients, and the first study to assess the impact of gratitude on MS patients' symptoms of depression, cognitive functioning, and quality of life. This study was uniquely able to provide evidence that MS patients experience gratitude, and that gratitude is associated with less depression and higher quality of life for MS patients. Finally, these findings offer precedence for future studies to

assess strengths impacting MS patients' quality of life, and symptoms of MS as well as potential differential effects of states, traits, and interventions related to gratitude. Overall, this study increases our understanding of *why* perceived and objective cognitive functioning differentially impact quality of life as well as providing further reason to study strengths in individuals with MS with the ultimate goal of improving their quality of life and functioning.

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