

Cognitive Impairment, Depression, Anxiety, and Personality and MS Patient Estimations of Memory Function

Jordan Charboneau
Marquette University

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Cognitive Impairment, Depression, Anxiety, and Personality and MS Patient Estimations
of Memory Function

by

Jordan Charboneau

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ABSTRACT
COGNITIVE IMPAIRMENT, DEPRESSION, ANXIETY, AND PERSONALITY AND
MS PATIENT ESTIMATIONS OF MEMORY FUNCTION

Jordan Charboneau

Marquette University, 2017

Multiple Sclerosis (MS) is an autoimmune disease of unknown etiology, characterized by a wide range of physical, cognitive, psychological, and behavioral symptoms. To effectively diagnose and treat MS, clinicians rely on patient reports of function to help identify and treat their problems (Kinsinger, Lattie, & Mohr, 2010). Specifically, self-reports of cognitive symptoms are a valuable source of information upon which clinicians depend (Van der Hiele, Spliethoff-Kamminga, Ruimschotel, Middelkoop, & Visser, 2012). While patient reports of cognitive functioning, including memory, are important, there has been substantial debate about the accuracy of such information. The present study investigated the association between general cognitive impairment, depression, anxiety, and personality function among MS patients, and determined how such variables related to the accuracy of MS patient reports of memory function. Findings indicated that increases in anxiety, depression, somatization, and negative impression management were all associated with a decrease in the estimation of memory function. Alternatively, an increase in positive impression management was associated with an increase in estimation of memory function. Cognitive function was not significantly correlated with estimation of memory function, though emerged as the only significant predictor of estimation of memory in the regression analysis. Findings highlight the presence of psychological concerns among MS patients and support the impact of cognitive function on the estimation of patient reported memory symptoms. To comprehensively, and efficaciously, treat individuals with MS, clinicians should interpret self-reports of cognitive function with caution and assess for psychological disturbance when possible.

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CHAPTER I: INTRODUCTION

Background Context

Multiple Sclerosis (MS) is an autoimmune disease of unknown etiology characterized by a wide range of physical, cognitive, psychological, and behavioral symptoms. It is among the most frequent causes of disability in early to middle adulthood, impacting 100-130 per 100,000 people in the United States (Kurtzke & Wallin, 2000). In fact, Ogden (2005) noted that MS is the most common nontraumatic neurological disorder impacting young adults. MS onset occurs, on average, at around 30 years of age (Kurtzke, Page, Murphy, & Norman, 1992), with fewer than 10% of MS patients experiencing disease onset before puberty or after 55 years of age (Ogden, 2005). MS is twice as common in women relative to men (Beatty, 1996) and twice as common among White ethnic groups relative to Black ethnic groups (Ogden, 2005).

To effectively diagnose and treat MS, clinicians rely on patient reports of function to help identify and treat their problems (Kinsinger, Lattie, & Mohr, 2010). Specifically, self-reports of cognitive symptoms are a valuable source of information upon which clinicians depend (Van der Hiele, Spliethoff-Kamminga, Ruimschotel, Middelkoop, & Visser, 2012). While patient reports of cognitive functioning are important, there has been substantial debate about the accuracy of such information.

Multiple studies (Basso et al., 2008; Marrie, Chelune, Miller, & Cohen, 2005; Matotek, Saling, Gates, & Sedal, 2001; Randolph, Arnett, & Higginson, 2001) have found that patient reported cognitive difficulty is related to neuropsychological test performance, while others (Beatty & Monson, 1991; Maor, Olmer, & Mozes, 2001; Middleton, Denny, Lynch, & Parmenter, 2006) have not. In fact, MS patients have been

found to both underestimate and overestimate their cognitive performance. A careful review of the available literature suggests there are multiple factors that influence MS patients' ability to accurately report their cognitive functioning, including level of cognitive impairment, depression, anxiety, and personality dysfunction. The relationship between each of these variables and the accuracy of cognitive symptom reporting has been investigated, though the literature on anxiety and personality is notably sparse. While it is generally understood how each of these variables individually influences cognitive symptom reporting, there have been no comprehensive studies examining the manner in which cognitive impairment, depression, anxiety, and personality dysfunction collectively relate to the accuracy of cognitive symptom reporting.

Statement of the Problem

As noted above, there is limited research investigating the manner in which anxiety and personality are related to the accuracy of MS patient cognitive symptom reporting. Given that anxiety and personality dysfunction are common among MS patients (Rintell, 2012; Stathopoulou, Christopoulos, Soubasi, & Gourzis, 2010), it is necessary to understand how such variables are related to the accuracy of cognitive symptom reporting. Additionally, the available evidence suggests that cognitive impairment, depression, anxiety, and personality function influence each other (Bruce & Lynch, 2011). However, extant research is limited in that it has not fully examined the manner in which cognitive impairment, depression, anxiety, and personality function collectively influence the accuracy of symptom reporting. While the individual impact of the aforementioned factors has been examined to varying degrees, the relationship between them and their collective influence on cognitive symptom reporting remains a

relative mystery, potentially leading to misdiagnosis or improper treatment of individuals with MS. Additionally, there have been no investigations of the manner in which cultural and demographic factors influence MS patient reports of cognitive symptoms.

Purpose of the Present Study

The purpose of the present study is to investigate the association between cognitive impairment, depression, anxiety, personality function, and cultural factors among MS patients, and determine how such variables relate to the accuracy of MS patient reports of memory function. Memory function is the primary cognitive domain of interest due to the fact that memory difficulties are common and often clinically reported as a domain of cognitive difficulty by MS patients (Rao, Grafman, & Dijkerman, 1993). The present study will thus investigate the role of each of the aforementioned variables, and explore their relation to the accuracy of cognitive symptom reporting.

Research Questions

The present study will investigate the following research questions:

1. How do cognitive impairment, depression, anxiety, and personality function individually and collectively relate to the accuracy of MS patient reported memory function?
2. Does the accuracy of patient reported memory function differ by race/ethnicity, sex, educational level and age?

Clinical Implications

From both an assessment and treatment perspective, it is important for clinicians to be aware of how factors such as cognitive impairment, depression, anxiety, and personality may influence the accuracy of patient reports of cognitive function.

Determining what factors influence cognitive symptom reporting will inform clinical practice by helping clinicians diagnosing MS determine the appropriate battery of neuropsychological tests to administer. For example, a patient who presents with depression and anxiety may be more likely to report a high number of cognitive symptoms, relative to a patient who is free of psychological difficulty. In this case, the high number of reported cognitive symptoms may lead the clinician to more thoroughly assess the patient's psychiatric functioning. As previously noted, cognitive and psychological impairment may result in patients under- or over-reporting their cognitive symptoms, and knowing such information may lead to more appropriately tailored assessments. Clinicians may want to include or exclude various psychological or cognitive assessments in their exam, depending on the degree to which depression, anxiety, personality, and cognitive function possibly contribute to patients' reports of cognitive symptoms.

Perhaps more significantly, the knowledge produced by the present research may impact the focus of treatment for MS patients. Treatment professionals frequently rely on patient self-report for evaluation and treatment planning. If a patient's cognitive complaints are largely influenced by mood, the appropriate treatment may be psychotherapy rather than cognitive rehabilitation. For example, a patient may report multiple cognitive difficulties, though may not demonstrate any when formally assessed. If the patient were not cognitively impaired, it would be useful for the clinician to know what factors were contributing to the patient's report of symptoms so that the appropriate treatment may be recommended. Alternatively, if a patient with MS reports cognitive deficits and is free of psychological difficulty, clinicians may be more confident in

directing treatment towards alleviating the cognitive difficulties rather than recommending psychotherapy or psychopharmacologic intervention. It is thus important for individuals involved in MS patient treatment to understand what factors influence patient reports of cognitive function.

CHAPTER II: LITERATURE REVIEW

Multiple Sclerosis

While cases of MS have potentially been observed for hundreds of years, the scientific community has, until recently, failed to fully understand the multidimensional nature of the disease. For instance, it was only within the last 30-40 years that cognitive dysfunction was recognized as a major component of MS, and even more recently that the impact of psychological variables on MS was even considered. Given that MS impacts most areas of afflicted individuals' lives, it is important that researchers and practitioners assess and treat patients in a comprehensive and sensitive manner.

MS is a complex disease of unknown etiology. While the cause remains unknown, a wide variety of epidemiologic studies have identified various risk factors for developing the disease. Individuals who live further from the equator, smoke cigarettes, are deficient in vitamin D, are between the ages of 30-50 years old, are female, are Caucasian, or have a relative with MS are at increased risk of developing MS.

Currently, there is no single assessment used to determine the presence of MS. Instead, MS is defined by the presence of neurological symptoms distributed in time and space within the CNS, without a better explanation (Miller, 2006). While multiple diagnostic criteria have been used to diagnose MS (McDonald et al., 2001; Polman, Reingold, Banwell et al., 2011; Polman, Reingold, Edan et al., 2005; Poser, Paty, & Scheinberg, 1983), the most recent criteria for the diagnosis of MS are the revised 2010 McDonald criteria (Polman et al., 2011). These criteria state that MS can be diagnosed when there is evidence of two separate attacks that involve multiple, discrete locations within the CNS. An attack is defined as any neurological disturbance lasting more than

24 hours and may include symptoms reported by patients themselves or discovered on clinical exam. While MS can be diagnosed on patient report alone, in most circumstances an MRI of the brain or cerebral spinal fluid testing is also recommended, which allows clinicians to rule out alternative explanations for the neurologic symptoms (e.g. stroke, brain tumor, infection). In fact, more than 95% of people with MS demonstrate CNS abnormalities on MRI findings (Sahraian & Radue, 2008).

MS is characterized by the formation of sclerotic plaques that develop as a result of tissue damage in the CNS. Such plaques tend to form in the white matter areas of the CNS, though the lesions can be found in any part of the CNS (Kidd et al., 1999; Noseworthy, Lucchinetti, Rodriguez, & Weinshenker, 2000). In many areas of the CNS, myelin wraps around the axons of neurons and facilitates more rapid nerve conduction. MS interferes with this process by damaging the myelin, which initially slows nerve conduction. However, if the demyelination is more severe or there is axonal damage, impulse conduction maybe lost completely, leaving afflicted individuals with more permanent loss of neurological function (Noseworthy et al., 2000).

Most commonly, lesions are found in the periventricular areas, subcortical white matter of cerebral hemispheres, corpus callosum, and the spinal and optic nerves (Ogden, 2005), though they can occur in any area of the central nervous system where there is myelin. In addition to variation in location, lesions may also vary by type. They may be inflammatory and acute with improvement occurring over a period of days to weeks, or may remain permanently without resolution of symptoms (Ogden, 2005). Both the location and type of lesions can vary greatly between individuals and even within the same individual, which can subsequently produce a wide variety of symptoms.

Although Charcot described memory and concept formation difficulty in his initial lectures (Charcot, 1877), the cognitive manifestations of MS were underestimated and rarely discussed in the literature for multiple decades (Ari, Benedict, LaRocca, & Caruso, 2013). In fact, MS was previously thought to be primarily a gait and sphincter (i.e., bowel and bladder) disorder (Scheinberg & Smith, 1987). Fischer (2001) suggested that the medical community has historically underestimated the cognitive dysfunction associated with MS because cognitive deficits were difficult to detect, and it was prevailing knowledge, albeit inaccurate, that cognitive dysfunction rarely occurred in MS and if it did, it was only in severe cases.

With advances in technology, assessment procedures, and the scientific understanding of the disease, it is now known that approximately 40-60% of individuals with MS experience cognitive dysfunction (Demaree, Deluca, Gaudino, & Diamond, 1999; van der Hiele et al., 2012). Although cognitive dysfunction is relatively common, cognitive difficulties are rarely reported among the presenting symptoms of MS (Patty, 2000), presumably due to the overwhelming presence of physical symptoms. Additionally, cognitive symptoms are easily overlooked in routine neurological exams (Rao, 1995), as brief screening measures tend to lack the sensitivity to detect subtle cognitive changes.

Specific cognitive symptoms experienced largely depend on the location of an individual's lesions. However, the most common cognitive problems associated with MS involve speed of information processing, memory, and executive functioning (Ari et al., 2013; Bobholz & Gremley, 2011; Van der Hiele et al., 2012).

As noted above, information processing difficulties are thought to be common among MS patients (Bobholz & Gremley, 2011). MS patients have consistently been found to perform more poorly than controls on tasks requiring rapid information processing (DeLuca, Berbieri-Berger, & Johnson, 1994; Rao, Leo, Bernardin, & Unverzagt, 1991). However, studies have shown that information processing difficulty in MS is primarily related to speed, not necessarily comprehension. When patients were given adequate time to process test stimuli, they performed similarly to controls on memory tasks (Arnett, 2004; DeLuca, Chelune, Tulskey, Lengenfelder, & Chiaravalloti, 2004; Demaree et al., 1999; Denney, Lynch, & Parmenter, 2008).

Memory decline is also among the most common MS-related cognitive difficulties, impacting 40 to 60% of MS patients (Rao et al., 1993). The most notable difficulty tends to be with explicit memory tasks, while autobiographical and implicit memory are generally left intact. Working memory deficits have also been observed in MS patients, though these are thought to be related to processing speed difficulties (Rao et al., 1993).

Lastly, individuals with MS tend to have more difficulty than those without MS on tests of executive functioning, showing more difficulty with decision making and problem solving (Birnboim & Miller, 2004; Brassington & Marsh, 1998). Related to executive functioning, MS patients have also been found to have difficulty with semantic and phonemic fluency (Henry & Beatty, 2004). Deficits in executive function can impact one's ability to plan for and manage the demands of daily life, and have also been associated with self-awareness and self-monitoring (Smith, 2007).

Cognitive Symptom Reporting

There are many methods used to obtain information regarding cognitive symptoms, one of which is patient self-report. Self-reports of cognitive symptoms are a valuable source of information that clinicians use to help identify and treat their patients' cognitive problems (Kinsinger, Lattie, & Mohr, 2010). Understanding what factors contribute to the accuracy of MS patient reports of cognitive functioning will allow clinicians to more effectively assess and treat individuals with MS. As noted previously, there is a high degree of inconsistent findings regarding the accuracy of MS patient reports of cognitive impairment. The available literature indicates that cognitive impairment itself, as well as depression, anxiety, and personality function may account for such variability in findings, as each may relate to the manner in which MS patients report cognitive function.

Additionally, research suggests that cultural and demographic variables such as sex, race, or ethnic background may influence the manner in which individuals express psychological and cognitive symptoms. For example, relative to the U.S. where an emphasis is placed on the open expression of emotion, many other cultures value non-confrontation and social harmony, which may result in individuals being less likely to report concerns to health care providers (Kirmayer, 2001). In fact, cultural expression of depression and anxiety, and subsequently cognitive symptoms, likely varies widely even within the U.S. given the unique cultural variability of the population. However, there have been no investigations of the manner in which cultural and demographic factors influence MS patient reports of cognitive symptoms. The available literature investigating the relationship between cognitive impairment, depression, anxiety, personality function, and cognitive symptom reporting will be reviewed below.

Cognitive impairment. The available literature investigating the relationship between cognitive dysfunction and symptom reporting is relatively sparse. Multiple studies have found that MS patients with cognitive impairment are, in fact, able to accurately report the nature of their cognitive difficulties. However, as will be demonstrated below, the severity of cognitive impairment appears to significantly influence how patients perceive their own cognitive function.

Multiple studies have consistently found that cognitively impaired patients with MS can accurately report the nature of their difficulties. In fact, some studies have found that MS patients' reports of cognitive difficulty were more accurate than informant reports of MS patient cognitive difficulty (Randolph, Arnett, & Higginson, 2001). Similar studies (Matotek, Saling, Gates, & Sedal, 2001; Smith & Arnett, 2010) investigating the relationship between MS patient complaints of cognitive difficulty, specifically memory and executive function difficulty, and actual cognitive performance also found that MS patients are generally able to accurately report their level of cognitive impairment. Adding to the robustness of these findings is the fact that each study utilized different measures of cognition and patient report of cognitive difficulty, and investigated different domains of cognition. Notably, both Matotek et al. (2001) and Smith and Arnett (2010) studied participants who experienced a mild form of MS and were subsequently only mildly cognitively impaired. While Randolph et al. (2001) did not report participant disease severity or level of impairment, they do note that all patients were capable of being seen in an outpatient clinic and none of them were experiencing symptom exacerbation, facts that lead to the assumption that they were a relatively high functioning and unimpaired group. This is an important fact because, as will be shown below, the

level of cognitive impairment appears to significantly influence patients' abilities to perceive and report their own cognitive difficulties.

Determining whether MS patients can accurately report their own cognitive difficulties has been a hotly debated topic. Studies, such as those listed above, suggest that MS patients are good reporters of their own cognitive function. Others, such as Beatty and Monson (1991), found that MS patients failed to acknowledge their memory difficulties on self-report measures, suggesting that MS patients are poor reporters of their own impairment. While each of these studies is compelling, it seems that they do not tell a comprehensive story. In fact, MS patients can be both inaccurate and accurate reporters of their own cognitive abilities. For example, Goverover, Chiaravalloti, and DeLuca (2005) found that as MS patient reports of cognitive function became more inaccurate, so too did their level of cognitive impairment, implying that more cognitively impaired MS patients failed to perceive their own cognitive symptoms, a finding supported by the following studies.

Carone, Benedict, Munschauer, Fishman, & Weinstock-Guttman (2005) found that MS patients who overestimated their cognitive function were less depressed and experienced a greater degree of cognitive impairment, relative to those who accurately perceived or underestimated their cognitive abilities. Such findings indicate that mood may influence patient reports of cognitive difficulty, but perhaps more significantly, a greater degree of cognitive impairment may be related to overestimation of cognitive function. Notably, accuracy of patient reports was determined by the degree that patients' reports of cognitive difficulty differed from informant ratings of patient cognitive impairment. Unfortunately, as Randolph et al. (2001) noted, informant reports of patient

cognitive difficulties are not necessarily more accurate. While this is a relatively common way to determine patient accuracy, it is important to note that informant reports can be influenced by multiple factors as well and should not be considered the standard measure of accuracy. Preferably, MS patient reports of cognitive difficulty should be compared to neuropsychological test results for an indication of accuracy.

Similarly, Marrie, Chelune, Miller, and Cohen (2005) examined the relationship between objectively measured and patient-reported cognitive impairment and found that among patients with mild or no cognitive impairment, perceptions of impairment were consistent with actual cognitive deficits. However, patients with more severe deficits tended to perceive themselves as unimpaired. Additionally, the relationship between memory impairment and patient reports of cognitive difficulty was modified by age, such that among young individuals, decreased memory ability was associated with increased reports of cognitive impairment, though there was no association for individuals over age 65 years with memory ability.

As demonstrated above, MS patients who are mildly impaired tend to accurately perceive and report their cognitive difficulties. However, consistent with Carone et al. (2005), Goverover, Chiaravalloti et al. (2005), and Marrie et al. (2005), as cognitive impairment becomes more severe and patients age, they tend to lack awareness and underestimate their cognitive difficulty. The findings also suggest that older age, presumably associated with greater cognitive impairment, is associated with less awareness of cognitive difficulty.

The available literature investigating the relationship between patient-reported cognitive impairment and actual cognitive impairment is both limited and seemingly

conflicting. However, a closer review has revealed that MS patients' abilities to report their level of cognitive difficulty are dependent on their level of cognitive impairment. A greater degree of cognitive impairment among MS patients is associated with overestimating one's cognitive ability and reporting fewer cognitive symptoms.

Depression. Depression is, by far, the most studied psychological aspect of MS. It was the first recognized psychological consequence of MS, and for many years was thought to be the only psychological difficulty experienced by MS patients. While depression affects approximately 6% of the U.S. population annually (Kessler, Chiu, Demler, & Walters, 2005; U.S. Census Bureau, 2005), its rates in the MS population are much higher. It is estimated that more than 50% of patients with MS experience depression during the disease course (Feinstein & Feinstein, 2001; Minden, Orav, Reich, 1987; Mohr & Cox, 2001), with annual prevalence rates around 20% (Patten, Beck, Williams, Barbui, & Metz, 2003). However, lifetime prevalence rates of depression are estimated as high as 64% when patients who do not meet diagnostic criteria for depression, though express depressive symptoms, are included in analyses (Feinstein & Feinstein, 2001; Fischer et al., 1994). While depression is common among patients with MS, it is unfortunately not often detected or treated (Feinstein, 2004; Siegert & Abernethy, 2005). In fact, McGuigan and Hutchinson (2006) examined a community-based MS sample and found that 25% of patients reached clinically diagnosable levels of depression, though were unaware of their depression and had not received treatment for it.

While it has been recognized that depression is common among MS patients, it has only been within the last 10-15 years that researchers began to investigate the manner in which depression influenced patient reports of cognitive difficulty. Overwhelmingly,

studies have consistently found that self-report of cognitive symptoms is more highly correlated with depressive symptoms than with neuropsychological test performance. In general, MS patients who present as more depressed tend to report a greater degree of symptoms associated with cognitive impairment, a trend supported by the work of Christodoulou et al. (2005), Goverover, Kalmar et al. (2005), Lovera et al. (2006), Maor et al. (2001), and Middleton et al. (2006). Each of these authors investigated the relationship between self-reported cognitive complaints and objective measures of cognitive impairment and found that depression was positively correlated with patient reports of cognitive impairment. Additionally, both Maor et al. (2001) and Middleton et al. (2006) conducted stepwise regression analyses and found that depression emerged as the strongest predictor of MS patient-reported cognitive impairment. Interestingly, to minimize the impact of depression, Christodoulou et al. (2005) and Lovera et al. (2006) excluded patients with moderate to severe depression. However, depression inventory scores were still significantly correlated with patient-reported cognitive difficulty, highlighting the robustness of the impact of depressive symptoms among MS patients. It should be noted that the strength of the association in these two studies was likely underestimated as a result.

Consistent with the aforementioned studies, Kinsinger, Lattie, and Mohr (2010) and Julian, Merluzzi, and Mohr (2007) also found that depression was associated with an increase in MS patient-reported cognitive dysfunction. However, both studies additionally found that after receiving successful treatment for depression, MS patients reported fewer symptoms of cognitive dysfunction, suggesting that treating depression

may result in more accurate self-reports and supporting the theory that depressive symptoms distort patients' perceptions of their cognitive and functional abilities.

As evidenced above, the available literature on cognitive symptom reporting and depression indicates that depression seems to have a significant impact on the manner in which patients perceive their own cognitive function, a finding consistent with multiple studies (Bruce & Arnett, 2004; Fischer, LaRocca, Miller, Rivto, Andrews, & Paty, 1999; Gold, Schulz, Monch, Schulz, & Heesen, 2003). In fact, depression was consistently more correlated with self-reports of cognitive functioning than actual neuropsychological performance. Overwhelmingly, patients experiencing depression perceived their cognitive impairment as more severe than it actually was. Further strengthening this relationship is evidence from Kinsinger et al. (2010) and Julian et al. (2007), who found that successful treatment of depressive symptoms was associated with a more accurate self-report of cognitive function.

The consistency of the above findings regarding depression is even more notable considering the variety of methods utilized in these studies. Studies utilized large and small samples, community and clinical samples, participants from locations throughout the United States, and participants with all forms of MS. Studies were also varied in the measures they used to assess cognitive symptom reporting, depressive symptoms, and cognitive function.

Anxiety. In contrast to the large body of research examining depression, much less attention has been paid to anxiety, which Sa (2008) noted is also a cause of disability among patients with MS. Extant literature indicates that rates of anxiety among MS patients vary widely from 19 to 90% (Feinstein, O'Connor, Gray, & Feinstein, 1999;

Korostil & Feinstein, 2007; Minden & Schiffer, 1991; Noy et al., 1995; Pepper, Krupp, Friedberg, Doscher, & Coyle, 1993; Stenager, Knudsen, & Jensen, 1994). In contrast to 18% in the U.S. population, the lifetime prevalence rate of any anxiety disorder among MS patients is estimated to be 36% (Korostil & Feinstein, 2007). Interestingly, Feinstein et al. (1999) and Noy et al. (1995) found that individuals with MS experienced higher rates of anxiety than depression. Such high rates of anxiety among MS patients are not surprising given the chronic and unpredictable nature of MS. Individuals with MS must deal with the progressive limitations imposed by the disease, adapt to family and social demands, deal with unpleasant self-injectable medications, and continually adjust their sense of self as they live with MS on a daily basis (Sa, 2008). Available evidence suggests that anxiety is common among patients with MS, though like depression, it is not often detected or treated (Rintell, 2012). For example, Korostil and Feinstein (2007) found that none of the MS patients in their study, who were experiencing clinical anxiety, were previously diagnosed or treated. Below is a review of the available literature addressing the manner in which anxiety influences the accuracy of patient reports of cognitive difficulty.

Within the available literature there are three investigations of the manner in which anxiety influences patient self-reports of cognitive functioning. Similar to findings regarding depression and self-report of cognitive symptoms, the available literature indicates that those with higher levels of anxiety also tend to report a greater degree of cognitive impairment, generally incongruent with their actual cognitive performance.

Akbar et al. (2011) and Middleton et al. (2006) examined perceptions of cognitive functioning relative to performance on cognitive tests among MS patients. Both authors

found that self-reports of cognitive difficulties were not matched by objective data obtained from neuropsychological testing and that anxiety was positively correlated with patient reports of cognitive difficulties. Additionally, Akbar et al. (2011) and Middleton et al. (2006) each conducted a hierarchical regression analysis and found that anxiety was a better predictor of patient-reported cognitive impairment than depression. Consistent with the findings of Akbar et al. (2011) and Middleton et al. (2006) are the findings of van der Hiele et al. (2012), who examined the psychological characteristics of MS patients who underestimated and overestimated their executive function abilities. While many participants were able to accurately report their cognitive difficulties, those who reported more executive dysfunction than was evidenced by neuropsychological testing were characterized by more depression, anxiety, and psychosocial stressors than those who were accurate or underestimated their executive function performance.

The available literature investigating the relationship between anxiety and self-reported cognitive function is sparse, but consistent. Despite the use of different self-report measures of depression, anxiety, and cognitive abilities, each of these studies found that anxiety was positively associated with self-reported cognitive impairment. In fact, both Akbar et al. (2011) and Middleton et al. (2006) found that anxiety was more strongly associated with patient-reported cognitive impairment than depression. Similar to the trend in the depression literature, higher rates of anxiety are associated with higher levels of patient-reported cognitive impairment. It is important to note, however, that elevated levels of depression and anxiety do not relate to poorer cognitive performance.

Notably, there is a significant lack of research on this topic, and more studies investigating the role of anxiety in cognitive symptom reporting are needed to support the

present trend. Historically, depression was the only psychological variable thought to impact MS patients. Interestingly, two of the three studies presented above suggest that anxiety may be a prominent feature of the disease and influence cognitive symptom reporting more than depression. Future studies should include a variety of anxiety measures, and investigate the manner in which anxiety relates to both depression and specific areas of cognitive difficulty.

Personality. In addition to depression and anxiety, MS patients also experience personality disturbances (Stathopoulou, Christopoulos, Soubasi, & Gourzis, 2010). In a review of available literature, Stathopoulou et al. (2010) found that personality changes were relatively common in MS, affecting 20 to 40% of patients. Relative to controls, MS patients commonly have increased levels of neuroticism (Merkelbach, Konig, & Sittinger, 2003; Ozura, Erdberg, & Sega, 2010) as well as increased social inappropriateness, disinhibition, apathy, emotional lability, and impulsivity (Bruce & Lynch, 2011). Alternatively, approximately 25% of MS patients present with a euphoric mood that is incongruent with their situation and not necessarily congruent with their disposition before the onset of MS (Mitsonis, Potagas, Zervas, & Sfagos, 2009).

While many studies have documented personality changes in MS patients, very few have examined the manner in which personality changes impact patient reports of cognitive difficulty. The following three studies address the impact of personality factors on self-report measures of cognition. Although each uses the NEO Five Factor Inventory (NEO-FFI; Costa & McCrae, 1992), Carone et al. (2005) restricted their investigation to the agreeable and conscientiousness scales, making comparisons limited.

In addition to investigating the impact of anxiety, Akbar et al. (2011) investigated the role of personality on self-report measures of cognition and found that higher self-reported cognitive difficulty was associated with higher neuroticism (i.e. high reactivity to stress; unstable) and lower conscientiousness (i.e. careful, vigilant, efficient, organized). Beyond the predictive value of anxiety, conscientiousness was the only other significant predictor of patient-reported cognitive impairment. Neuroticism and conscientiousness were the only personality factors that were related to self-reported cognitive difficulty, such that increased reported cognitive difficulty was associated with higher neuroticism and lower conscientiousness.

Carone et al. (2005) separated MS patients into groups that overestimated, underestimated, and accurately estimated their own cognitive ability. MS patients who overestimated their cognitive function were more conscientious relative to those who were accurate or underestimated cognitive performance, while the opposite trend was observed for informant ratings of patient conscientiousness. Unfortunately, the authors limited their investigation to the agreeable and conscientiousness scales from NEO-FFI, making comparisons to other studies difficult.

Bruce and Lynch (2011) recently examined the association between anxiety, depression, and personality disturbances in MS patients and suggested that a diagnosis of MS alone is not significantly associated with personality change, noting the possible contributory influence of other factors. They found that patients with clinically diagnosed anxiety or depression exhibited higher neuroticism and less conscientiousness than MS patients without anxiety or depression, a finding consistent with studies previously discussed. While these authors did not investigate cognitive symptom reporting, based on

previously discussed studies, it seems reasonable to conclude that higher levels of cognitive symptom reporting are associated with increased depression, anxiety, and likely increased neuroticism and decreased conscientiousness. In other words, the manner in which personality factors influence cognitive symptom reporting is moderated by other psychological variables such as depression and anxiety. Notably, Bruce and Lynch (2011) did not include measures of cognitive function in their analysis. As demonstrated previously, level of cognitive impairment seems to significantly influence the accuracy of MS patient reports of cognitive function.

Together, these three studies suggest that cognitive impairment, depression, anxiety, and personality function interact to collectively influence cognitive symptom reporting. Although they each used the NEO Five Factor Inventory (NEO-FFI), a self-report measure of personality function, comparisons between these studies must be made with caution. Both Akbar et al. (2011) and Carone et al. (2005) directly examined the relationship between cognitive symptom reporting and personality. However, Carone et al. (2005) limited their investigation to the agreeable and conscientiousness scales from NEO-FFI, while Akbar et al. (2011) examined all scales of the NEO-FFI. However, they were consistent in finding that a higher reported level of cognitive difficulty was associated with less conscientiousness, while reporting fewer cognitive difficulties (i.e., overestimating one's cognitive ability) was associated with higher conscientiousness. Bruce and Lynch (2011) did not investigate cognitive function or cognitive symptom reporting, but did find that MS patients with clinically diagnosed anxiety or depression exhibited higher neuroticism and less conscientiousness. The available literature examining the relationship between personality and cognitive symptom reporting is

notably lacking. Future studies investigating the relationship between personality and the accuracy of MS patient cognitive symptom reporting should account for the influence of cognitive function, depression, and anxiety, as each has been shown to have an influence.

Conclusion

As outlined in the introduction, patient self-reports of cognitive function are an important source of information for clinicians and help guide the assessment and treatment of MS. While patient reports of cognitive functioning are important, there has been a substantial debate about the accuracy of such information. The present review has identified the manner in which cognitive impairment, depression, anxiety, and personality can influence the accuracy of MS patient reports of cognitive functioning.

After reviewing the available literature investigating the relationship between patient-reported cognitive impairment and actual cognitive impairment, it is clear that MS patients with cognitive impairment can both accurately and inaccurately report their level of cognitive impairment, depending on their level of impairment. At a mild level of impairment, MS patients are able to accurately report their level of cognitive difficulty. However, increasing cognitive impairment appears to be associated with less awareness, such that cognitively-impaired patients report fewer problems than they are actually experiencing. In general, a greater degree of cognitive impairment among MS patients is associated with overestimating one's cognitive ability and reporting fewer cognitive difficulties.

The opposite trends were observed for depressed and anxious MS patients. A large body of research supports the finding that depression has a significant impact on the manner in which patients perceive their own cognitive function, such that depressed MS

patients over-report the extent of their cognitive difficulties. In fact, two studies (Julian et al., 2007; Kinsinger et al., 2010) found that successfully treating depressed MS patients was associated with more accurate self-report of cognitive function. Although there is a significant lack of research investigating the relationship between anxiety and self-reported cognitive function, the findings are consistent. Congruent with trends noted with depressed MS patients, increased anxiety is also associated with higher levels of patient-reported cognitive impairment. Notably, the majority of studies reviewed found that anxiety was more predictive of cognitive symptom reporting than depression.

The trends noted in the personality literature were less prominent, though revealing nonetheless. The studies that allowed for comparison revealed that a higher reported level of cognitive difficulty was associated with less conscientiousness. When studies integrating depression, anxiety, report of cognitive function, and personality were examined, the trend became more prominent and revealed that MS patients who over-reported their cognitive difficulties were characterized by higher depression, anxiety, neuroticism, and lower conscientiousness. Interestingly, these studies suggest that there are complex interactions among these variables, and the manner in which each of them influences cognitive symptom reporting is likely influenced by the others.

In addition to the diagnostic and treatment implications discussed in the introduction, this information has ethical implications as well. To comprehensively treat patients in the most efficacious and ethical manner possible, clinicians have a duty to understand how psychological and cognitive factors interact and collectively influence patient reports of cognitive function. Given the consistent relationships demonstrated above, it is not difficult to imagine MS patients being misdiagnosed or mistreated as a

result of their presentation and report of symptoms, likely the result of many variables that may or may not be recognized. Knowing how cognitive impairment, depression, anxiety, and personality impact cognitive symptom reporting is thus critical for ethical treatment of MS patients.

In conclusion, both cognitive and psychiatric difficulties (e.g., depression, anxiety, personality changes) occur frequently in patients with MS, and are attributed to both cerebral demyelination and the psychosocial impact of a chronic, usually progressive, disabling illness (Stathopoulou et al., 2010). The evidence presented above suggests that cognitive impairment, depression, anxiety, and personality function influence each other. However, extant research is limited in that it has not fully examined the manner in which cognitive impairment, depression, anxiety, and personality function collectively influence symptom reporting. While the individual impact of the aforementioned factors has been examined to varying degrees, the relationship between them and their collective influence on cognitive symptom reporting remains a relative mystery, and is a notable area of needed future study.

CHAPTER III: METHOD

Participants

Participants in the present study were retrospectively identified from the Center for Neuropsychological Services at the Aurora St. Luke's Medical Center in Milwaukee, WI. All participants were referred for neuropsychological evaluation to assist with MS diagnosis or track MS progression.

Participant eligibility. Participants were eligible for inclusion if they meet the following criteria: (1) the patient had a diagnosis of MS; (2) the patient was evaluated at the Center for Neuropsychological Services at the Aurora St. Luke's Medical Center; (3) the patient produced a valid personality profile based on the validity scales of the Personality Assessment Inventory; and (4) complete data were available for the patient. The patient was excluded from participation if s/he did not have complete test scores (i.e. missing data) or produced an invalid personality profile, as the inclusion of invalid personality profiles could bias the results. Only data from the patient's initial evaluation was used in cases in which testing occurred more than once.

Variables and Measures

Patient-reported memory impairment. The Structured Inventory of Malingered Symptomatology (SIMS; Smith & Burger, 1997) was used to assess patient-reported memory impairment. The SIMS is a multi-axial, self-administered measure developed as a screening tool for detecting feigned or exaggerated psychiatric disturbance and cognitive dysfunction. It consists of five non-overlapping scales including Psychosis, Neurologic Impairment, Amnesic Disorders, Low Intelligence, and Affective Disorders. For the purposes of the present study, only data from the 15-item true/false Amnesic

Disorders scale was utilized, as items included in this scale specifically relate to memory function. Raw scores range from 0-15, with 0 indicating all false responses and 15 indicating all true responses, and were converted to standard scores for analysis. Internal consistency for the Amnestic Disorders scale is satisfactory ($\alpha = .83$) (Windows & Smith, 2005). Total score test-retest reliability is adequate ($r = .72$) (Windows & Smith, 2005). Convergent validity is supported by high correlations between SIMS scores and similar measures such as the MMPI F Scale ($r = .84$) and F-K index ($r = .81$) (Schretlen & Arkowitz, 1990).

Personality. The Personality Assessment Inventory (PAI; Morey, 1991) is an assessment of personality consisting of 344 items and 22 non-overlapping scales. The four validity scales include the Inconsistency and Infrequency scales designed to detect deviations in responding, as well as the Negative and Positive Impression Management scales designed to assess patients' attempts to present themselves in an unfavorable or favorable manner. The clinical scales include the Somatic, Anxiety, Anxiety-Related Problems, Depression, Mania, Paranoia, Schizophrenia, Borderline Features, Antisocial Features, Alcohol Problems, and Drug Problems. Additionally, there are 5 treatment consideration scales and two interpersonal scales. For the purposes of the present study, analysis was limited to the Somatic, Negative Impression Management (NIM), and Positive Impression Management (PIM) scales, as these are the only scales hypothesized to relate to the accuracy of cognitive symptom reporting.

The median internal consistency across full sales is satisfactory ($\alpha = .81$). Test-retest reliability is .83. The Somatic scale is correlated with the Wiggins Health Concerns ($r = .80$) and Organic Problems ($r = .82$) content scales, and the Wahler Inventory (r

= .72), indicating satisfactory convergent validity (Morey, 1996). The NIM is significantly correlated with the MMPI F scale ($r = .54$) and the PIM is associated with Marlow-Crowne Social Desirability scale ($r = .56$) and the MMPI K ($r = .47$) and L ($r = .41$) scales (Morey, 1991), all indicating acceptable levels of convergent validity.

Depression. The Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996) is a 21-item, multiple-choice, self-report measure of depression. Each of the 21 items includes a list of four statements arranged in increasing severity about a particular symptom of depression (i.e., I do not feel sad, I feel sad much of the time, I am sad all the time, I am so sad or unhappy that I can't stand it). Scores of 0-13 indicate minimal depression, 14-19 mild depression, 20-28 moderate depression, and 29-63 severe depression. Internal consistency values have ranged from .84-.93 (Al-Musawi, 2001; Beck, Steer, Ball, & Ranier, 1996; Schulenberg & Yutrzenka, 2001). Test-retest reliability ranges from .74 to .96 (Al-Musawi, 2001, Beck et al., 1996). The BDI-II is highly correlated with other measures of depression including the SCID-I ($r = .83$), CES-D ($r = .69$), and the Reynolds Adolescent Depression Scale ($r = .84$), indicating strong convergent validity. Divergent validity is supported by findings that the BDI-II is negatively correlated ($r = -.10$ to $-.46$) with measures of happiness, ego strength, and boldness (Al-Musawi, 2001).

Anxiety. The Beck Anxiety Inventory (BAI; Beck & Steer, 1993) is 21-item, multiple-choice, self-report measure of anxiety. Each of the 21 items is composed of a symptom of anxiety (i.e. nervous, shaky, heart pounding) and four possible patient endorsements (not at all, mildly, moderately, severely). Scores of 0-7 indicate minimal anxiety, 8-15 mild anxiety, 16-25 moderate anxiety, and 26-63 severe anxiety. Internal

consistency is high ($\alpha = .94$), and test-retest reliability is acceptable ($r = .67$) (Fydrich, Dowdall, & Chambless, 1992). Convergent validity is acceptable with the Hamilton Anxiety Rating Scale, ($r = .51$) and the State-Trait Anxiety Inventory ($r = .58$ for the State and $r = .47$ for the Trait subscales (Leyfer, Ruberg, & Woodruff-Borden, 2006).

Memory function index score. Data from the following measures was combined into an index of overall memory function. Combining individual assessment scores according to Rohling's Interpretive Method (RIM; Miller & Rohling, 2001) is common practice and creates an easily interpreted score produced from a flexible battery approach to neuropsychological testing. The memory function index score was used in conjunction with the SIMS score to create a difference score representing the accuracy of patient-reported memory function.

Wechsler Memory Scale – IV (WMS–IV). The WMS-IV (Wechsler, 2009) is a standardized assessment of memory consisting of 7 subtests. For the purposes of the present study, only the Logical Memory (LM) and Visual Reproduction (VR) subtests were utilized, as they were the only 2 subtests administered to patients. The LM subtest is a measure of immediate, delayed, and recognition auditory memory, while the VR subtest is a measure of immediate, delayed, and recognition visual memory (The Psychological Corporation, 2002). LM scores include LM I Immediate Recall Total, LM II Delayed Recall Total, and LM II Recognition Total. Each raw score is converted to a scaled score ($M = 10$, $SD = 3$). VR scores include VR I Immediate Recall Total, VR II Delayed Recall Total, and VR II Recognition Total. Again, each raw score is converted into a scaled score ($M = 10$, $SD = 3$). Internal consistency was high for VR II ($\alpha = .97$) and VR I ($\alpha = .93$) (Wechsler, 2009). Additionally, internal consistency was adequate for LM II ($\alpha =$

.85) and LM I ($\alpha = .82$) (Wechsler, 2009). The VR and LM subtests were only moderately correlated, indicating reasonable discriminant validity. Concurrent validity is supported by strong correlations between the WMS-IV auditory memory index and the California Verbal Learning Test-II ($r = .63$) (Wechsler, 2009).

Hopkins Verbal Learning Test–Revised (HVLTR). The HVLTR (Brandt & Benedict, 2001) is a brief word list designed to assess memory. Patients' immediate, delayed, and recognition memory of words are assessed. Scores include recall total, delayed recall, and recognition/discrimination. Raw scores are converted into T-scores ($M = 50$, $SD = 10$). Test-retest reliability is .74 for recall total, .66 for delayed recall, and .40 for recognition (Benedict & Zgalijardic, 1998). Shapiro, Benedict, Schretlen, and Brandt (1999) note a correlation of .77 between the HVLTR and Wechsler Memory Scale – Revised (WMS-R; Wechsler, 1987) LM delayed recall, and a correlation of .69 between HVLTR and WMS-R VR delayed recall, indicating adequate convergent validity. Recognition/discrimination scores were excluded from analysis due to inconsistent inclusion in patient records.

Brief Visuospatial Memory Test–Revised (BVMT-R). The BVMT-R (Benedict, 1997) is a brief test of visual memory. Although initially intended to be included, the BVMT-R was not used in the present study because it was only administered to a minority study participants. Including BVMT-R data would have severely limited the number of participants included in the analyses.

Overall cognitive function index. The measures below represent a wide range of cognitive domains and will be combined into an index of overall cognitive function. The

cognitive function index score produced by the following tests was used to predict variance in the criterion variable.

Wisconsin Card Sorting Test (WCST). The WCST (Berg, 1948) is a measure of cognitive set shifting, or the ability to maintain flexibility as situational demands change. It is thought to be a general test of executive function and abstract reasoning (Heaton, Chelune, Talley, Kay, & Curtiss, 1993), and requires patients to match a stimulus card to one of four key cards based on a changing set of criteria. Scores are calculated for number of categories completed, perseverative responses, failure to maintain set, and total number of errors. Heaton et al. (1993) found that generalizability coefficients ranged from .39 to .72, indicating acceptable internal consistency. Additionally, Heaton et al. (1993) also found that patients with MS consistently performed worse than healthy controls on the WCST.

Boston Naming Test (BNT). The BNT (Kaplan, Goodglass, & Weintraub, 1983) is a measure of confrontational naming and consists of 60 pictures that patients are asked to name. The BNT is sensitive to individuals with frontal or temporal lobe impairment (Mitchell & Crow, 2005), though picture-naming difficulty is often used as an indirect measure of more global cognitive impairment. Internal consistency is .96 (Huff, Collins, Corkin, & Rosen, 1986) and test-retest reliability is .94 (Sawrie, Chelune, Naugle, & Luders, 1996). Convergent validity is supported by correlations between the BNT and the Gates-McGinite Reading Vocabulary Test ranging from .74 to .87 (Hawkins et al., 1993). The BNT is poorly correlated with the Facial Recognition Test ($r = .27$; Benton & Van Allen, 1968), evidence of strong divergent validity.

Judgment of Line Orientation (JLO). The JLO (Benton, Hannay, & Varney, 1975) is a measure of visuo-spatial processing. It consists of 30 items and tests patients' abilities to estimate angular relationships between line segments. Test-retest reliability is .90 (Benton, Sivan, Hamsher, Varney, & Spreen, 1994).

Controlled Oral Word Association Test (COWAT). The COWAT (Benton, Hamsher, & Sivan, 1994) assesses verbal fluency. It consists of three word-naming trials in which the patient is told a letter (i.e. c, f, l) and asked to name as many words as s/he can think of that begin with that letter within a 60-second time period. Divergent validity is evidenced by a moderate correlation ($r = .56$) between the COWAT and Multilingual Aphasia Examination (MAE) Visual Naming (Benton et al., 1994). Benton et al. (1994) stated that the moderate correlation was likely the result of the similar word retrieval demands of each test. Additionally, a weak correlation ($r = .34$) between the COWAT and Sentence Repetition further supports strong divergent validity (Benton et al., 1994).

Wide Range Achievement Test: Fourth Edition (WRAT-4). The WRAT-4 (Wilkinson & Robertson, 2006) is a measure of academic function including word reading, sentence comprehension, spelling, and math computation. Although initially intended to be included, the WRAT-4 was not used in the present study because it was only administered to a minority study participants. Including WRAT-4 data would have severely limited the number of participants included in the analyses.

Trail Making Test (TMT). The TMT (Partington & Leiter, 1949) measures scanning and visuo-motor tracking, divided attention, and cognitive flexibility (Reitan & Wolfson, 1993). Although initially intended to be included, the TMT was not used in the present study because it was only administered to a minority study participants. Including

TMT data would have severely limited the number of participants included in the analyses.

Demographic variables. Data was collected regarding patients' age, age at diagnosis, sex, race, marital status, duration of MS, and level of education.

Procedure

Approval for the present study was obtained from Marquette University's IRB and Aurora St. Luke's Medical Center RSPP/IRB. All participants completed a neuropsychological evaluation consisting of a clinical interview and the administration of a standard battery of neuropsychological tests. Order of test administration was not controlled, though tests were administered according to standardized test administration instructions, which are described in their respective administration manuals. Following test administration, individual tests were scored according to standardized procedures outlined in their respective manuals.

Data Analysis

When necessary, raw scores from the neuropsychological test data were transformed into z-scores, allowing for the computation of two index scores from scores on different original scales. The memory index score was composed of the Wechsler Memory Scale and the Hopkins Verbal Learning Test–Revised. The cognitive ability index score consisted of the Controlled Oral Word Association Test, Judgment of Line Orientation, Boston Naming Test, and the Wisconsin Card Sorting Test. Both indices were generated according to the steps of Rohling's Interpretive Method (RIM; Miller & Rohling, 2001). RIM was designed to allow for a more easily understood interpretation of neuropsychological assessment data generated from a flexible battery approach to

neuropsychological testing. Generally, it involves assigning test scores to a specific conceptual domain, converting to a standardized metric, and computing an overall domain score. The cognitive ability index score was used as a predictor variable and did not include memory assessment data. The BAI, BDI, and personality scores remained in their original scale of measurement.

The memory index score was used in conjunction with the SIMS data to generate a difference score, representing the accuracy of patient-reported memory function and acting as the primary criterion variable in the present study. The difference score was calculated by transforming the SIMS raw score and memory index raw score into standardized scores, and calculating the difference between them (perceived – actual performance). A score of zero indicated that the participant was completely accurate. Any deviation from zero indicated inaccuracy, and the direction (i.e., positive or negative) of the difference indicated whether the participant was over- or underestimating his or her memory function. Possible accuracy scores ranged from -4 to 4. SIMS data were reversed scored so that higher scores in both perceived and actual performance represented better functioning, and visa versa. Negative scores indicated that participants underestimated their performance (i.e., reported more memory problems than testing showed), while positive scores indicated that participants' overestimated their memory performance (i.e., reported fewer memory difficulties than testing revealed).

First, descriptive statistics were examined in order to better understand the characteristics of the sample. Then, bivariate correlations of the predictors and dependent variable were run to investigate how the variables related to each other in the absence of other predictors.

To address the research questions, a model was created to investigate the predictors in combination. The PAI, BDI, BAI, and index of cognitive function were used to account for variance in the accuracy score generated from the SIMS and memory function index. This was done with a hierarchical regression analysis with block variable entry. There were four total blocks, including an anxiety block with data from the BAI, a depression block consisting of data from the BDI, cognitive function block with data from the cognitive function index score, and a personality block with data from the PAI. Anxiety was entered first because it was predicted that it would account for the most variance in the estimation of memory performance. Depression scores were entered second to determine if they accounted for unique variance beyond the variance accounted for by anxiety scores. Depression and anxiety were predicted to account for the most variance in estimation of memory function. Cognitive function scores were entered next to determine if they accounted for variance beyond the variance explained by the depression and anxiety scores. Personality function was the most novel aspect of the analysis and was entered last to determine if there was any additional contribution.

Assumptions of linearity, normality, and multicollinearity were tested. Histograms were used to assess normality, and linearity was assessed with plots of residuals verses predicted values. Non-parametric bootstrapping was utilized (1000 sample) due to concerns regarding small sample size and multicollinearity. Bootstrapped regression results did not significantly differ from non-bootstrapped results, indicating that that there were no major violations of assumptions. Analyses were conducted under the assumption that all assessments were administered in a standardized manner and that participants answered truthfully.

Although initially intended, demographic variables (e.g., age, sex, race, marital status, handedness, marital status, age at diagnosis, education) were not included in the regression analysis due to small sample size and potential model instability associated with too many predictor variables. Including such variables would have resulted in approximately 13 predictor variables, well over the theoretical limit for regression analyses with 86 participants. However, *t*-tests were conducted to explore how the estimation of memory function might differ by sex, marital status, education, age at diagnosis, or MS duration. Although any significant differences may not remain in the presence of other predictors, the results could be suggestive of differences to be explored with a larger sample. Sex was categorized by males and females. Marital status was categorized into married and not married. There was no distinction within the not married group between divorced, widowed, separated or never married. Making distinctions at such a level would have resulted in multiple groups with too few participants. Education was categorized into those who had any education beyond high school and those who completed high school or had fewer than 12 years of education. Again, making further distinction would have resulted in groups with exceedingly small sample sizes. Age at diagnosis was categorized into those younger than 36 years and those older than 36 years. The age of 36 years was chosen because it was the mean age of MS diagnosis. MS duration was categorized into those who had MS for 10 years or fewer and those who had been diagnosed for more than 10 years. Ten years was chosen because there was a natural break in the data and group sizes were satisfactory. Race and handedness were not analyzed because the sample was overwhelmingly white and right handed.

CHAPTER IV: RESULTS

Participants

Retrospective data were collected for 119 individuals with MS. However, due to missing data and exclusion criteria, the final sample consisted of 86 participants. Disease course was unspecified for 80 participants (see Future Study section). All participants were diagnosed with MS and completed neuropsychological testing at Aurora St. Luke's Medical Center in Milwaukee, WI from 2006 – 2014. The sample was primarily composed of Caucasian females, with an average age of 47 years (See Table 1). Participants scored in the average range for the cognitive index, somatization, PIM, and NIM variables. Anxiety and depression were endorsed at the mild level (See Table 2).

Table I. *Participant Characteristics*

	<i>MS Patients (n = 86)</i>
<i>Mean Age</i>	47 (<i>sd</i> = 9)
<i>Mean Age of MS Diagnosis</i>	36 (<i>sd</i> = 11)
<i>Mean Years of Education</i>	14 (<i>sd</i> = 3)
<i>Sex (M/F)(n)</i>	20/66
<i>Right Handed (n)</i>	74
<i>Race (n)</i>	
<i>Caucasian</i>	75
<i>African American</i>	5
<i>Latino</i>	6
<i>Disease Course (n)</i>	
<i>Relapsing remitting</i>	2
<i>Secondary progressive</i>	3
<i>Primary progressive</i>	1
<i>Progressive relapsing</i>	
<i>Unspecified</i>	80
<i>Marital Status (n)</i>	
<i>Married</i>	58
<i>Divorced</i>	16
<i>Never Married</i>	10
<i>Widowed</i>	1
<i>Separated</i>	1

Correlations

There were significant correlations between MS patients' estimations of memory function and predictor variables, as well as between the predictor variables themselves. Anxiety was most strongly associated with estimation of memory function ($r = -0.44, p < .001$), followed closely by depression ($r = -0.43, p < .001$), NIM ($r = -0.41, p < .001$), somatization ($r = -0.39, p < .001$), and PIM ($r = 0.27, p < .01$). The correlation between the cognitive ability index and estimation of memory was non-significant (See Table 2).

Additionally, significant correlations were noted between predictor variables. Anxiety scores were correlated with depression ($r = .75, p < .001$), somatization ($r = .49, p < .001$), positive impression management ($r = -.58, p < .001$), and negative impression management ($r = .61, p < .001$). Depression scores were correlated with somatization ($r = .48, p < .001$), positive impression management ($r = -.60, p < .001$), and negative impression management ($r = .69, p < .001$). Somatization scores were correlated with positive impression management ($r = -.32, p < .01$), and negative impression management ($r = .43, p < .001$). Cognitive index scores were only correlated negative impression management ($r = -.32, p < .01$).

Table II. Means, Standard Deviations, and Correlations Among Variables

	<i>Estimation</i>	<i>Anxiety</i>	<i>Depress.</i>	<i>CogIndx</i>	<i>Somatiz.</i>	<i>PIM</i>	<i>NIM</i>
<i>Estimation</i>	1	-0.44***	-0.43***	-0.18	-0.39***	0.27**	-0.41***
<i>Anxiety</i>		1	0.75***	-0.17	0.49***	-0.58***	0.61***
<i>Depression</i>			1	-0.16	0.48***	-0.60***	0.69***
<i>Cog Indx</i>				1	-0.09	-0.02	-0.32**
<i>Somatization</i>					1	-0.32**	0.43***
<i>PIM</i>						1	-0.37
<i>NIM</i>							1
<i>M</i>	0.0002	14.3	19.1	0.0002	8.7 (61T)	13.9 (47T)	3.4 (56T)
<i>SD</i>	1.1	10.9	11.8	0.6	4.7 (13T)	5.4 (12T)	3.3 (12T)

** $p < .01$; *** $p < .001$

Predictors

Hierarchical linear regression was utilized to investigate predictors of patient estimations of memory function. Anxiety scores were entered into the model first and accounted for 18% of the variance in estimation of patient reported memory function ($R^2 = .18$, $F_{1,84} = 19.77$, $p < .001$). Depression scores were added in the second step, ($R^2 = .20$, $F_{2,83} = 19.39$, $p < .001$) but did not significantly increase the explanation of variance ($\Delta R^2 = .03$, $F_{1,83} = 2.63$, ns). The cognitive index scores were added next and resulted in additional explanation of variance ($\Delta R^2 = .07$, $F_{1,82} = 7.67$, $p < .01$), accounting for 26% of the variance ($R^2 = .26$, $F_{3,82} = 10.76$, $p < .001$). The personality variables were added in the final step and resulted in additional explanation of variance in the estimation of memory function ($\Delta R^2 = .07$, $F_{3,79} = 2.74$, $p < .05$). The fully saturated model accounted for 30% of the variance in the criterion variable ($R^2 = .30$, $F_{6,79} = 7.09$, $p < .001$). The final regression model was significant only for the cognitive index variable ($B = -.57$, $t = -3.36$, $p = .001$, 95% CI [-.932, -.234]). Anxiety, depression, somatization, positive impression management, and negative impression management were not significant in the final regression model (See Table 3). Effect sizes for anxiety ($B = -0.02$), depression ($B = -0.01$), somatization ($B = -0.04$), positive impression management ($B = -0.01$), and negative impression management ($B = -0.09$) were exceedingly small with no discernable meaning.

Table III. Hierarchical Regression Analysis Predicting Patient Estimations of Memory Function

<i>Predictors</i>	<i>B</i>	<i>SE B</i>	β	<i>t</i>	<i>R</i> ²	<i>Adj R</i> ²	<i>F</i>	ΔR^2	ΔF
Step 1:					0.19	0.18***	19.77	0.19***	19.77
<i>Anxiety</i>	-0.04***	0.01	-0.44	-4.45					
Step 2:					0.22	0.20***	11.39	0.03	2.63
<i>Anxiety</i>	-0.03	0.02	-0.26	-1.72					
<i>Depression</i>	-0.02	0.01	-0.24	-1.62					
Step 3:					0.28	0.26***	10.76	0.07**	7.67
<i>Anxiety</i>	-0.03	0.01	-0.28	-1.98					
<i>Depression</i>	-0.02	0.01	-0.26	-1.83					
<i>Cognitive Index</i>	-0.46**	0.17	-0.26	-2.77					
Step 4:					0.35	0.30***	7.09	0.07*	2.74
<i>Anxiety</i>	-0.02	0.02	-0.20	-1.38					
<i>Depression</i>	-0.01	0.02	-0.11	-0.64					
<i>Cognitive Index</i>	-0.57**	0.17	-0.33	-3.36					
<i>Somatization</i>	-0.04	0.03	-0.19	-1.75					
<i>PIM</i>	-0.01	0.02	-0.07	-0.59					
<i>NIM</i>	-0.09	0.05	-0.26	-1.90					

* $p < .05$; ** $p < .01$; *** $p < .001$

Demographic Variables

T-tests were conducted to determine how the estimation of memory function differed by sex, marital status, education, age at diagnosis, or MS duration. Homogeneity of variance was tested and taken into account. No group differences reached statistical significance (See Table 4). However, the effect size for marital status was notable, suggesting that there might be a relationship between marital status and the estimation of memory function in the population. Additional research should investigate marital status and estimation of memory with a larger sample size to further examine such relationships.

Table IV. *T*-test Results Comparing Demographic Groups on Estimates of Memory Function

<i>Variable</i>	<i>N</i>	<i>M</i>	<i>SD</i>	<i>t</i>	<i>p</i>	<i>d</i>	<i>Decision</i>
<i>Sex</i>							
<i>Male</i>	20	.09	1.31	.443	.666	.10	n/s
<i>Female</i>	66	-.03	1.03				
<i>Education</i>							
≤ <i>High School</i>	38	.08	0.92	.615	.54	.13	n/s
> <i>High School</i>	48	-.06	1.22				
<i>Marital Status</i>							
<i>Married</i>	58	.14	1.08	1.69	.095	.37	n/s
<i>Not Married</i>	28	-.28	1.10				
<i>Age at Diagnosis</i>							
< <i>36 years</i>	39	.13	1.18	.972	.334	.21	n/s
≥ <i>36 years</i>	47	-.10	1.02				
<i>MS Duration</i>							
≤ <i>10 years</i>	54	-0.12	.98	-1.37	.174	0.30	n/s
> <i>10 years</i>	32	.20	1.25				

CHAPTER V: DISCUSSION

The present study examined the relationship between cognitive impairment, depression, anxiety, and personality function among MS patients, and determined how such variables related to MS patient estimations of memory function. Memory function was the primary cognitive domain of interest because memory difficulties are common and often clinically reported as a domain of cognitive difficulty by MS patients (Rao et al., 1993). Overall, findings suggested that nearly all variables examined were associated with the estimation of MS patient-reported memory function, though cognitive function emerged as the only unique predictor in the regression analysis. Individual findings and implications are discussed below.

The present study also sought to examine the associations between race/ethnicity, sex, educational level, age, and MS patient estimations of memory function. Unfortunately, because a significant number of participants were excluded from the study due to incomplete data, it was not possible to include demographics in the prediction equation. However, analyses were conducted to determine if estimation of memory function differed based on sex, education, marital status, age, or MS duration without including the predictor variables.

Prior to a discussion of study's findings and implications, it is worth noting how the chosen analyses and construction of the dependent variable affect the inferences that can be made. The present study was unique in that it used an estimation variable created from MS patient perceived memory difficulty relative to actual memory performance, as measured with neuropsychological testing. This method is in contrast to other studies (e.g. Carone et al., 2005) that constructed accuracy scores using informant reports. As

Randolph et al. (2001) noted, informant reports are not necessarily more accurate than patient reports and should not be considered the standard measure of accuracy. The present dependent variable, estimation of patient-reported memory function, was initially constructed as an accuracy score. It theoretically ranged from -4 to 4, with 0 indicating complete accuracy between patient reports of memory function and actual memory function, as measured by neuropsychological testing. More negative scores were designed to indicate the degree to which patients underestimated their memory performance, while more positive scores were designed to represent the degree to which patients overestimated their memory performance. However, because the dependent variable is on a linear scale from under- to over-estimating, decreases in the dependent variable simply represent a decrease in the estimation of patient-reported memory function. The linear dependent variable does not allow for differentiation between decreases from overestimation to more accurate or from accurate to underestimation. Similarly, increases in the estimation variable simply represent an increase in the estimation of patient-reported memory function. Differentiation of increases from underestimation to accurate or from accurate to overestimation are not possible with this choice of methodology. As such, conclusions from the present study can only be made regarding patient estimations of memory performance, not accuracy.

Additionally, the present study is unique in that it used a memory index composed of multiple memory tests, rather than a memory screening test, as has been done previously. Utilizing a memory index score ensures that the present study is actually measuring the construct of memory. It should also be noted that the cognitive function index was composed of tests that measure language abilities, visuospatial skills, and

executive functions. As such, implications drawn from the findings regarding the cognitive function index reflect these specific cognitive domains, rather than a global cognitive domain represented by all areas of cognitive function.

Participants

Participants in the present study are representative of the general MS population. Most participants were Caucasian females who were, on average, approximately 47 years old. Although diagnosed at about 36 years of age, many participants reported experiencing symptoms well before actual diagnosis. However, data were not collected regarding this discrepancy. The majority of participants were right handed and married. Participants averaged 14 years of education. The sample's similarity to the general MS population supports the external validity of the present study. Participants scored in the average range for the cognitive index, somatization, PIM, and NIM variables. Anxiety and depression were endorsed at the mild level. See Table 2. Although the present sample was relatively benign in presentation, MS can be an episodic and progressive disease. As such, participants may present with mild anxiety or intact cognitive function at one point, though dramatically decline in function at a later time.

Bivariate Correlations

Depression. The present study found that depression was related to the estimation of patient-reported memory function, such that increased depression was associated with a decrease in patient-estimations of memory performance. This finding is similar to others (Christodoulou et al., 2005; Goverover, Kalmar et al., 2005; Lovera et al., 2006; Maor et al., 2001; Middleton et al., 2006) who found that depression was positively correlated with patient reports of cognitive impairment (i.e., decreased estimation of

function). However, rather than examining general complaints of cognitive impairment as previous studies have done, the present study is unique in that it utilized a dependent variable representing the difference between neuropsychological test scores and perceived memory function. Constructing the dependent variable in such a manner would have characterized individuals reporting a high number of symptoms, who also had poor performance, as accurately perceiving their memory function. In previous studies, individuals reporting a high number of symptoms were characterized simply as reporting a high number of symptoms. Although initially intended to represent accuracy, the construction of the dependent variable only allows for discussion regarding general estimation without differentiation between over and under estimation of function. Nonetheless, the consistency of the findings is notable and provides additional support regarding the robust association between increased depression and distorted perceptions of memory function.

Overall, the present study indicates that depression is significantly related to the manner in which patients perceive their own cognitive function when other predictors are excluded from the model, a finding consistent with multiple studies (Bruce & Arnett, 2004; Fischer, LaRocca, Miller, Rivto, Andrews, & Paty, 1999; Gold, Schulz, Monch, Schulz, & Heesen, 2003). In fact, in previous studies depression was consistently more correlated with self-reports of cognitive functioning than actual neuropsychological performance, a finding consistent with the present study. The strength of the association between depressive symptoms and cognitive symptom reporting is further highlighted by Kinsinger et al. (2010) and Julian et al. (2007). Both authors found that after receiving successful treatment for depression, MS patients reported fewer symptoms of cognitive

dysfunction, suggesting that treating depression may result in more accurate self-reports, and supporting the theory that depressive symptoms may be associated with distorted perceptions of cognitive and functional abilities. While the present study does not address such findings, the association between depression and cognitive symptom reporting is nonetheless supported. Overwhelmingly, greater levels of depression among MS patients were associated with a decrease in estimations of memory function, absent other predictors.

Although depression is the most studied psychological aspect of MS and the direction of the relationship appears well established, it should be noted that other factors may also influence the expression of depressive symptoms and one's subsequent perception of cognitive impairment. For example, Beier, Amtmann, and Ehde (2015) recently found that fatigue was a stronger predictor of general cognitive and executive function concerns than depression. The results from Beier et al. (2015) highlight the fact that the relationship between depression and cognitive symptom reporting in MS is, although well established, complicated by multiple factors likely influencing both the expression of depressive symptoms as well as patients' reports of cognitive symptoms. Additional study is certainly needed to map the complexity of the relationship between depression and patient perceptions of function.

It should be noted that the level of depression endorsed by the participants in the present study was in the mild range. If patients were experiencing more clinically significant depression, one might expect stronger correlations. Interestingly, Christodoulou et al. (2005) and Lovera et al. (2006) intentionally excluded patients with moderate to severe depression from their studies. However, their depression inventory

scores were still significantly correlated with patient-reported cognitive difficulty. The present study supports the robustness of this association, especially given the mild level of depression endorsed by participants.

Anxiety. As noted earlier, relative to depression, anxiety has been far less studied in its relation to both MS and cognitive symptom reporting. However, multiple studies (i.e. Akbar et al., 2011; Middleton et al., 2006) have suggested that anxiety is likely related to cognitive symptom reporting in a manner similar to depression. Indeed, the present study supports the minimal, albeit consistent, body of research on the topic. Notably, the correlation identified in the present study suggests that an increase in anxiety is associated with a decrease in the estimation of memory function, when other predictors are excluded. In fact, of all variables analyzed, anxiety was most strongly related to the estimation of memory function. Although the relationship between anxiety and estimation was only slightly stronger than the relationship between depression and estimation, the trend is nonetheless consistent with Akbar et al. (2011) and Middleton et al. (2006), who found that anxiety was more strongly associated with patient-reported cognitive impairment than depression.

The strength of the association between anxiety and cognitive symptom reporting should not necessarily be a surprise, especially when one considers the potential difficulties associated with managing a chronic and debilitating illness. Jones and Amtmann (2015) recently found that more MS-specific worry was related to more depressive symptoms, anxiety, fatigue, sleep disturbance, pain interference, worse social function, and perceived cognitive function. MS-specific worry, similar to health care worry, could include concerns about obtaining medication, high health care costs, being a

burden to family, or uncertainly regarding disease progression. The work of Jones and Amtmann (2015) supports the need to both identify and treat anxiety-related issues with MS patients, as doing so could be related to functional patient improvements.

Similar to depression, it should be noted that participants, on average, endorsed a mild level of anxiety. Higher levels of anxiety could produce stronger correlations between anxiety and the dependent variable. The fact that such a correlation exists, despite the mild level of anxiety, again supports the robustness of the association.

Personality. The available literature investigating the role of personality function in the accuracy of self-reported cognitive function is notably limited. The three available studies (i.e. Akbar et al., 2011; Bruce & Lynch, 2011; & Carone et al., 2005) suggest that cognitive impairment, depression, anxiety, and personality function influence cognitive symptom reporting. Although each study used the NEO Five Factor Inventory (NEO-FFI), comparisons between studies must be made with caution due to varied methods and foci. However, they were consistent in finding that a higher reported level of cognitive difficulty was associated with less conscientiousness, while reporting fewer cognitive difficulties was associated with higher conscientiousness.

The present study did not utilize the NEO-FFI, making direct comparisons difficult. Rather the personality variables used in the present study included somatization, positive impression management, and negative impression management. Somatization could include the manifestation of vague physical symptoms in response to psychological distress, as well as general complaintiveness and dissatisfaction. Positive impression management is the degree to which one presents her-/himself in an overly positive light,

denying common shortcomings. Negative impression management is the degree to which one presents her-/himself in an overly negative light, denying common positive attributes.

Findings from the present study indicated that there is, indeed, a relationship between such variables and the estimation of memory function. Both the somatization and NIM variables were negatively correlated with estimation, such that increases in somatization or NIM were associated with decreases in the estimation of memory function. Conceptually, NIM and somatization are similar, a fact that was further evidenced by the significant correlation between them. However, NIM implies a more deliberate effort to present oneself in a negative light while somatization is, by definition, not intentional. Nonetheless, an increase in either variable is likely to manifest similarly with an increased complaints and denial of positive attributes, and may further distort one's perception of function. There were also significant positive correlations between somatization, NIM, depression, and anxiety. While the correlations do not allow for statements about causation, the significance certainly highlights the role of psychological variables in the expression of personality, and *visa versa*. For example, there may be a compounding effect regarding one's perception of function for individuals suffering from a somatization disorder who are also experiencing severe symptoms of depression. Alternatively, it is theoretically possible that an individual who tends to present her-/himself negatively may have more accurate perceptions of her/his function in the absence of mood disturbances or anxiety.

While separating such aspects of the psyche may be difficult, clinicians should consider that the implications for treatment are quite different.

Alternatively, PIM was significantly positively correlated with the estimation memory function in the bivariate correlation. An increase in PIM, or one's effort to present her-/himself in a favorable light, was associated with an increase in the estimation of one's memory function. Similar to depression and anxiety, it should be noted that participants were, on average, within normal ranges on the PAI scales utilized.

The finding that PIM was positively correlated with estimation is not surprising, though it is unique, as other studies have not examined such constructs. It represents one of the few examinations of a variable that directly relates to one's attempt to present her-/himself favorably, rather than solely focusing on more negative (i.e. pathological) variables such as depression or anxiety. While one's attempt to present favorably can certainly be characterized as pathological (e.g., narcissism), the present study suggests there may be more positive aspects of personality that contribute to one's perception and estimation of cognitive difficulty. For example, Schmitt, Goverover, DeLuca, and Chiaravalloti (2014) recently found that self-efficacy, or the belief of an individual in her/his ability to effectively cope with challenging situations, is a primary factor in facilitating psychological adjustment to MS. They found that MS patients who reported higher levels of self-efficacy also reported better quality of life, fewer depressive symptoms, and had better physical functioning. Notably, the information provided in Schmitt et al.'s study regarding quality of life and self-efficacy was self-reported, with no informant reports or other measures for validation. As such, the results could be influenced by unaccounted-for variables. Despite this limitation, the study suggests that there are variables that may offset the potential effects of more pathological variables

such as anxiety, depression, or even maladaptive personality styles in coping with a diagnosis of MS.

Cognitive function. It was expected that cognitive function would be significantly associated with the estimation of MS patients self-reported memory function. In fact, numerous previous studies (i.e. Carone et al., 2005; Goverover, Chiaravalloti et al., 2005; Marrie et al., 2005) suggested that as cognitive impairment becomes more severe, patients also tend to lack awareness and underestimate their own cognitive difficulty (i.e. overestimate their cognitive function). However, the analysis excluding other predictors, did not find such a correlation. Cognitive function, as measured by the cognitive index, was not significantly correlated with the estimation of memory function. The lack of significant correlation could be due to the relatively mild level of cognitive impairment demonstrated by the sample. Most participants were functioning within the average range, and a higher level of impairment may have resulted in stronger correlations. Indeed, Marrie et al. (2005) had a larger and more cognitively impaired sample, with 56% of participants scoring below the 5th percentile, and found that the relationship was curvilinear. Extant research suggests that the relationship between cognitive impairment and patient reported function is dependent on the level of cognitive impairment. That is, mildly impaired individuals are often aware of their deficits, while severely cognitively impaired individuals tend to claim that they are free of deficits. Such a relationship would not be exhibited in a linear regression analysis, though could be examined using scatterplots and curvilinear regression. Unfortunately, the examination of both yielded non-significant results. While the lack of a curvilinear relationship may appear to contradict previous findings, such assertions should be made with caution. Both

a small sample size and limited sample variability likely prohibited the observation of the relationship. Nearly all participants in the present study scored within one standard deviation of the mean, with none scoring in the lower 5th percentile. As such, conclusions regarding this finding should be made with caution.

Cognitive function was, however, significantly negatively correlated with NIM, suggesting that as cognitive function increases, one's tendency to present her-/himself negatively decreases. This may be due to increased confidence or self-efficacy that may accompany more intact cognitive capacities and possible accomplishments. However, such suggestions are purely speculative at this point, as other inquiries into the topic are non-existent.

Overall, the estimation of memory function was significantly correlated with nearly all predictor variables. Anxiety scores were most strongly correlated with the estimation of memory function, followed closely by depression scores. Psychological and personality factors were individually more strongly correlated with estimation than cognitive function. In fact, the correlation between cognitive function and estimation was non-significant when other predictors were excluded. With the exception of the cognitive function scores, all correlational findings support previous research and highlight the robust associations between psychological variables, personality variables, and MS patients' perceptions and subsequent estimations of memory function.

Prediction Model

A linear regression model was built to explore the independent and collective contributions of anxiety, depression, cognitive function, and personality to the estimation of memory function. Each step of the hierarchical analysis revealed that the predictors

accounted for significant variance in MS patients' estimations of memory function. Anxiety, when entered alone, accounted for 18% of the variance in estimation scores. There was no effect for depression scores beyond that of anxiety scores, though the overall model with both variables accounted for 20% of the variance in estimation. The fact that depression scores did not contribute beyond the variance explained by anxiety scores is a relatively novel finding. Most research regarding MS patients and self-report of cognitive function has focused on depression, and only recently have others (Akbar et al., 2011; Middleton et al., 2006) suggested that anxiety may contribute. Indeed, the present study highlights the significant role that anxiety may play in MS patients lives, and suggests the need for clinicians to attend very carefully to patients' anxiety. However, the fact that anxiety and depression were significantly correlated likely explains the suppression effect on the depression variable. While depression and anxiety were not significant in the regression model, they are relatively common phenomena among the MS population and should be carefully considered in the care of MS patients. Clinicians should also consider variables such as MS-specific worry noted by Jones and Amtmann (2015), as addressing health-care specific worry may have a beneficial impact on patients' symptom presentation and adaptive functioning.

The addition of the cognitive function index was significant, indicating that cognitive function scores contributed to the explanation of variance beyond the variance explained by anxiety and depression scores. The unique contribution of cognitive function beyond depression and anxiety is consistent with others (e.g., Matotek et al., 2001; Smith & Arnett, 2010). The model with the cognitive function index included accounted for 26% of variance in estimation scores.

Finally, the personality scores were entered into the model and contributed to the explanation of variance beyond the other variables entered. The fully saturated model was significant and accounted for 30% of the variance in estimation scores, which is comparable to other studies (e.g., Akbar et al., 2011; Julian et al., 2007; & Maor et al., 2001). However, the present study examined a unique combination of predictor variables that has not been previously studied. The total variance accounted for represents a meaningful contribution to the literature, though the explained variance could likely be increased with the inclusion of additional unrelated predictor variables. While the personality variables used in the present study were not the same as those used in previous studies (e.g. Akbar et al., 2011), they accounted for a similar 7% of variance in the criterion variable, suggesting that personality is likely related to patient symptom reporting in a related, yet different, manner than depression, anxiety, and cognitive function. Although the personality variables used in the present study were highly correlated with other variables (i.e. depression, anxiety), they represent unique aspects of personality function. Notably, the current variables denote the manner in which one presents her-/himself to others and the degree that one manifests psychological turmoil as physical symptoms. While the present personality variables accounted for unique variance in the estimation of memory function, they were not significant predictors in the final regression model. Similar to the relationship between anxiety and depression, the personality variables were highly correlated with each other, which may have suppressed their predictive contribution. The personality variables were also significantly correlated with other variables (i.e. depression, anxiety), which may have additionally suppressed the predictive effect of any of the related variables.

Furthermore, the small difference between R^2 and the adjusted R^2 (i.e., 0.35 vs. 0.30, respectively) in the present study suggests that the sample was sufficiently large for the number of predictors used and that R^2 was not overly biased. If the model were over saturated, either via too many predictors or too few participants, one could expect a more inflated R^2 and larger discrepancy between R^2 and the adjusted R^2 . Nonetheless, the adjusted R^2 value was used in the present analyses, as is common practice, because it accounts for the number of variables in the model and only increases when a predictor enhances the model beyond what would be expected by chance.

Cognitive function emerged as the only unique predictor of MS patients' estimation of memory function in the final step of the hierarchical regression analysis. For every 1 standard deviation unit increase in cognitive function, one can expect a .57 standard deviation unit decrease in the estimation variable, when other variables are held constant. In other words, increases in cognitive function predict a decrease in the estimation of memory function when the depression, anxiety, and personality variables are fixed. However, it is important to note that the true slope of the regression line is best represented as a confidence interval. The estimated rate of change of estimation of memory function with respect to cognitive function, when the depression, anxiety, and personality variables are fixed, is between -.932 and -.234. Similar to others (e.g., Carone et al., 2005; Marrie et al. 2005), the present study may support the conclusion that relatively intact cognition is needed to maintain awareness of one's cognitive function. It is important to remember that a decrease in estimation could mean more accurate or more underestimation of memory function, a differentiation that cannot be made at this time. The consistency of the findings in the present study is notable due to the creation of the

estimation score from patient reports and patient testing performance, rather than using informant reports. Arguably, using patient reports of function and neuropsychological test data to determine patient estimations is more valid than using informant reports as the baseline. Consistent with the present study, Goverover, Chiaravalloti et al. (2005) found that executive function was predictive of perceptions of function after accounting for affective factors. These authors also suggested that clinicians could rely on MS patients' self-reports of cognitive function when cognition was intact, despite the presence of depression or anxiety. However, given the very limited number of variables and participants in their study, such a statement may be overgeneralizing. Additionally, such a statement risks minimizing the potential impact of psychological factors on patient reports of cognitive symptoms and minimizes the potential need for treatment. It may be that intact cognitive function is needed to maintain accurate perceptions, but the methodological challenges of the present study and Goverover, Chiaravalloti et al. (2005) do not necessarily negate the impact of other factors such as depression, anxiety, and personality. In fact, the present study highlights the inter-related nature of such variables and suggests that anxiety, mood, and personality dysfunction are relatively common among MS patients. Readers should consider the present findings as evidence that intact cognitive abilities are likely necessary for accurate estimations of memory function, though other variables are still likely contributory to perceptions of function. Minimally, clinicians should consider the presence of such factors in the MS patients they treat.

Although cognitive function emerged as the only unique predictor of MS patient estimations of memory function, the linear and curvilinear correlations between cognitive function and estimation of memory were notably non-significant. Although the remaining

predictor variables were all significantly correlated with the estimation of memory function in the absence of the other predictors, none were significant predictors in the final regression model. Such a trend was unexpected and the most likely explanation is model misspecification. The inclusion of the anxiety, depression, and personality variables, all highly related, likely suppressed variance irrelevant to the prediction of estimation of memory function, while potentially enhanced the effects of other predictor variables. Unfortunately, determining which of the predictor variables may have contributed suppression or inflation effects is not possible. Doing so would require analyses with fewer predictor variables to isolate the manner in which individual variable contributions change as specific predictors are included.

Demographic Variables

Demographic variables were assessed to determine if estimations of memory function differed by sex, education level, marital status, age of MS diagnosis, or MS duration. Unfortunately, none of the analyses produced significant results, indicating males and females, individuals with more than a high school education and individuals with less than a high school education, married and not married individuals, those older than 36 years and younger than 36 years old at MS diagnosis, and individuals who had been diagnosed for 10 or fewer years and individuals who had been diagnosed for 10 or more years did not differ in their estimations of memory function. However, the effect size for marital status was notable. Although small, it suggests that there might be a relationship between marital status and the estimation of memory function within the population. The present study was the first to examine such relationships. Due to necessarily categorizing the marital status, age at diagnosis, MS duration, and education

variables, some degree of variability was lost. Additional research would be able to examine subgroups (e.g., divorced vs. never married or smaller duration intervals) with larger sample sizes. It is important to note that the non-significant findings regarding these demographic variables are distinct from the regression analyses. It is possible that such demographic variables are predictors of the estimation of memory function, though this could not be determined in the present study.

Conclusion

In conclusion, the present study highlights the multiple correlations that exist between depression, anxiety, personality, cognitive function, and the estimation of memory function among MS patients. Increases in anxiety, depression, somatization, and negative impression management were all associated with a decrease in the estimation of memory function. Alternatively, an increase in positive impression management was associated with an increase in estimation of memory function. Cognitive function was not significantly correlated with estimation in the absence of other predictors, though emerged as the only significant predictor in the regression analysis. The fact that cognitive function emerged as the only unique predictor may indicate that cognitive function is the only variable clinicians need to consider when assessing patient reported information, as Goverover, Chiaravalloti et al. (2005) suggested. However, as noted above, it is more likely that other predictive relationships were suppressed due to the high level of multicollinearity among anxiety, depression, negative impression management, and somatization. Nonetheless, the findings regarding cognitive function suggest that it plays an important role in self-awareness and perceptions of function. Additionally,

estimation of memory function did not differ by sex, education level, marital status, age of MS diagnosis, or MS duration.

Limitations. The primary limitation in the present study was the construction of the dependent variable, which did not allow for examination of under- versus over-reporting of memory function, as was originally intended. Unfortunately, inferences can only be made regarding increases or decreases in MS patients' estimations of memory function. While interesting, estimations of memory performance likely have less clinical utility than the accuracy of MS patient predictions of function.

Due to the relatively small sample size, the present study was not able to assess the association of demographic/cultural factors with the estimation of patient memory function. As such, the external validity of the present study is potentially limited. A larger sample size would have allowed for the inclusion of more variables in the regression analysis and greater generalizability of results.

As mentioned earlier, nearly all predictor variables were significantly correlated with each other. While this fact likely reflects the manner in which such symptoms or characteristics are experienced in the real world, the relationships may have produced a suppression or inflation effect in the regression analysis. A larger sample size may have made the regression analysis more resistant to the impact of related predictor variables.

The personality variables were unique to the present study. Unfortunately, this did not allow for overt comparison to other research. The research regarding MS cognitive symptom reporting, and personality is notably limited, and the present study suggests that personality likely plays an important role in cognitive symptom reporting. However,

broader statements cannot be made due to the specificity of the personality variables used in the present study.

Finally, the level of psychological and cognitive impairment endorsed by participants was minimal, which likely resulted in less variability and weaker correlations and regression coefficients. Depression- and anxiety-related symptoms were generally endorsed at the mild level. Most personality scores were also within the average range, and most patients tested within the average range on cognitive testing. Notably, the limited variability may have prevented the observation of the curvilinear relationship that has been previously demonstrated between cognitive function and estimation of memory function.

Clinical implications. Clinicians treating individuals with MS should assess cognitive function regularly, as deficits are both common and influential in MS patient reports of memory function. However, they should interpret subjective complaints of cognitive dysfunction with caution. Both the present study and extant literature suggest that patient reports of symptoms may vary depending on level of cognitive impairment. It is also likely that factors such as mood, fatigue, and implemented coping strategies may be related to the information patients disclose. Unfortunately, the design of the present study does not allow for further interpretation of the predictive role of level of cognitive function. Extant research suggests that greater cognitive function is associated with more accurate perceptions of cognitive function, though further investigation and analyses are needed to determine if the present study fully supports such a trend.

Anxiety and depression are notably common among MS patients, a fact clinicians should consider carefully. While the present study does not support the predictive role of

such variables in MS patient estimations of memory function, it does support their relatively common presence. Although anxiety and depression were both reported at a mild level, on average, it is important to consider the episodic and progressive nature of MS and the potential for worsening function at times, and related increases in anxiety and depression. As such, dismissing the potential role of anxiety and depression would be a disservice to patients. MS patients with relatively intact cognitive capacities may be correctly reporting their memory function, while also suffering from psychological disturbances. As such, clinicians should regularly assess for symptoms of mood disturbances and anxiety with MS patients. Doing so could be done in a cost effective and rapid manner with self-administered screening assessments, and would allow for the proper comprehensive treatment of MS patients. In fact, previous studies (e.g. Kinsinger et al., 2010; Julian et al., 2007) suggested that the successful treatment of depression could lead to reduced cognitive complaints among MS patients. Personality disturbance should also be considered by clinicians, as it is also likely common among MS patients (Rintell, 2012) and likely related to MS patient-reported cognitive symptoms. However, it would be more difficult to assess personality patterns in a rapid manner, and may need to be assessed by clinicians in more extreme cases of misreporting. Additionally, more research is needed to establish the prevalence and types of personality alterations that occur in MS patients.

Finally, clinicians should facilitate protective factors such as self-efficacy, or patients' beliefs that they can manage challenging situations, when possible. Recent research (Schmitt et al., 2014) found that self-efficacy was a significant predictor of increased physical functioning, subjective cognitive functioning, and social functioning

in MS patients. Increasing self-efficacy could be accomplished with the implementation of self-management interventions (Rae-Grant et al., 2011), which could include patients' increasing their knowledge of MS, sharing in medical decision making; adopting a lifestyle that addresses risk factors; focusing on prevention and early intervention; actively monitoring symptoms; and managing the physical, emotional, social, and occupational consequences of the condition. Such interventions may increase self-efficacy and help produce functional changes in patients. It is important for treating providers to promote patient function as much as possible, and facilitating protective factors such as self-efficacy is one way to do so.

The treatment of MS thus should be approached in a multifactorial fashion, as MS is truly a multifaceted disease. Managing cognitive decline, pain, and physical dysfunction represent the more tangible aspects of MS. However, equally deserving of treatment, though not necessarily as observable, are aspects of chronic illness such as excessive worry, depression, fatigue, social isolation, occupational impairment, and alterations of personality, which are likely related to the expression of physical symptoms. MS is a complicated chronic illness, and the variables examined in the present study likely represent a small fraction of those that are actually related to cognitive symptom reporting. Identifying and treating the wide range of symptoms associated with MS and fostering protective factors may impact patient self-reports of cognitive symptoms and, perhaps more significantly, could impact quality of life for patients suffering from the chronic and debilitating effects of a devastating disease.

Research implications. Patient perceptions, estimations, and subsequent reports of symptoms remain one of the most common ways providers receive information. The

need to understand the factors related to patient symptom reporting is significant, as identifying and treating such factors may have profound effects on lives of patients with MS.

Future research should analyze a larger sample and a dependent variable that can be separated into underestimating, accurate, and overestimating performance, and then analyze the associations with psychological variables. Doing so would be possible with a procedure such as discriminant function analysis or multinomial logistic regression, and could allow for more clinically applicable findings. It is likely that MS patients who over report vs. under report cognitive difficulty are characteristically different, and understanding such differences remains necessary for the appropriate treatment of MS patients. Additionally, structural equation modeling could be utilized to more accurately map the complex relationships between predictor and criterion variables.

Future study should also increase sample size, sample variability, and continue to investigate the relationship between psychological variables and cognitive symptom reporting. Related predictor variables, such as those in the present study, may be combined using statistical procedures such as Principle Component Analysis to create non-related predictors. An increased sample size would allow for the inclusion of demographic and other psychosocial variables in the analyses, as was originally intended with the present study. For example, recent research (i.e., Beier et al., 2015) suggests that fatigue is predictive of cognitive symptom reporting. Research should continue to identify important variables that are related to cognitive symptom reporting, as doing so would allow treating providers to target interventions with the greatest chance of clinical impact. In this regard, researchers should also continue to investigate protective factors,

such as self-efficacy. Identifying and facilitating protective factors may affect the accuracy of patient self-report, but could also lead to improved patient functioning.

When possible, future study should account for the varied types of MS. There were very few MS types specified in patient charts for the present study. Although this lack of specificity does not alter the current analyses, there can be no differentiation between types of MS, which differ in multiple ways, as noted previously. It is possible that patients with different types of MS experience varying degrees of depression, anxiety, cognitive impairment, and personality disturbance. Finally, although the duration of MS was not used in the present analysis, data collection revealed an interesting trend that should be integrated into future research: There was a notably varied report of when patients were diagnosed with MS and when they first experienced symptoms. Some patients experienced their first symptoms and almost immediately sought consultation with a physician, resulting in their MS diagnosis. However, others noted experiencing symptoms of MS and not receiving a diagnosis for up to 17 years later. Such a discrepancy is worthy of investigation, as multiple factors could have been contributory. It is possible that individuals had different types of MS, resulting in varied symptom presentation and severity. It is also possible that individuals had varying levels of knowledge of MS symptoms, access to care, social support, personality characteristics, or psychological symptoms.

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