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# THE ROLE OF COPING STYLE AND COGNITIVE RESERVE IN DEPRESSION AND COGNITIVE FUNCTIONING IN MULTIPLE SCLEROSIS

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# ABSTRACT

*Introduction*: Cognitive impairment and depression are extremely prevalent in persons with MS, and both are exceptionally detrimental to the quality of life for these individuals. Previous research has shown that cognitive reserve and coping can moderate and/or mediate the relationship between cognitive impairment and depression; however, researchers have yet to consider how cognitive reserve and coping relate to each other, and the relationship that might exist among cognitive reserve, coping, cognitive functioning, and depression. The purpose of this study was to explore a mediating and/or moderating relationship, where coping mediated/moderated the relationship between cognitive reserve and cognitive functioning/depression.

*Methods*: The sample consisted of 54 individuals with MS who were brought in for neuropsychological testing. For mediation, Baron and Kenny's (1986) method of analysis was used. A 95% confidence interval for the indirect effect was tested using a bootstrapping analysis. For moderation, a series of regression analyses were used, controlling for disease severity at step 1, cognitive reserve at step 2, coping at step 3, and the interaction at step 4.

*Results*: Coping was found to be a significant mediator, but not a significant moderator, of the relationship between cognitive reserve and depression. Additionally, coping was not found to be a significant mediator or moderator of the relationship between cognitive reserve and cognitive functioning.

*Discussion*: Results suggest that high cognitive reserve protects against cognitive impairment and allows for the recruitment of mental resources necessary to engage in high adaptive coping. Further, coping may serve as a viable source of clinical intervention to treat depression in patients with MS.

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# Introduction

## Overview of Multiple Sclerosis

Multiple sclerosis (MS) is an autoimmune disease marked by the chronic degradation of the central nervous system (CNS). Among similar diseases affecting the CNS, MS is the most prevalent. Original estimates reported that MS impacts approximately 400,000 individuals in the United States and more than 2,000,000 around the world (Reich, Lucchinetti, & Calabresi, 2018); however, more recent evidence suggests these numbers may be much higher (National Multiple Sclerosis Society, 2017). The reason for this variation is, at least in part, due to the difficulty in diagnosing MS (Solomon et al. 2016). Currently, the McDonald criteria represent the standard diagnostic tool in the field. Diagnoses are made based on a pattern of lesions in the CNS and the presentation of clinical attacks/progressive neurological decline. Above all, the McDonald criteria also require careful consideration of other diagnoses that may explain the observed symptoms (Thompson et al., 2018).

Deterioration of the CNS due to MS is characterized by the presence of lesions throughout the brain and spinal cord. Lesions are most notably observed in white matter at locations of demyelination and inflammation (Reich et al., 2018).

MS is primarily defined by periods of disability, the effects of which may or may not be wholly or partially reversible (Reich et al., 2018). Presentations of MS can be divided into one of three subtypes: relapsing-remitting, primary progressive, or secondary progressive. Relapsing-remitting MS represents the most common subtype, and is characterized by alternating periods of symptom onset (relapse) and stable conditions with little change (remittance). The effects of relapses are highly variable, as is the degree of recovery afterwards (Lublin & Reingold, 1996).

Secondary progressive MS can develop gradually from relapsing-remitting MS in some cases. In secondary progressive MS, symptoms continue to worsen after an initial relapse and no significant periods of remittance are observed (Lublin et al., 2014). Finally, primary progressive MS is defined by steady decline from the onset of the disease, without periods of distinct relapses (Lublin & Reingold, 1996).

The variability in the presentation of MS and the difficulty in simply acquiring a correct diagnosis has clouded research aimed at identifying a cause. To date, it is unclear what triggers the onset of MS, and whether it is due to any specific event (Reich et al., 2018); however, certain risk factors have been identified. Through reasons yet unknown, women make up nearly three quarters of the MS population. There is also evidence for a genetic component to MS, though having an affected first-degree relative only increases the risk to 2-4% (compared to 0.1% in the general population) (Ascherio & Munger, 2016). Environmental factors such as exposure to tobacco and obesity have also been implicated in increased risk for developing MS.

In line with the lack of a known cause, there is currently no known cure for MS. At present, medications and treatments promoted to individuals with MS focus on maintaining their quality of life through reducing or managing debilitating symptoms (Cree et al., 2016). The symptoms experienced by patients with MS vary greatly among individuals; however, some common features include muscle weakness, mental and physical fatigue, pain, problems with vision, depression, and cognitive impairment (Arnett, Barwick, & Beeney, 2008; McIntosh-Michaelis et al., 1991).

MS is unique in that, compared to other conditions affecting the CNS, it has a relatively early onset (Calabrese, 2006). This means that patients diagnosed with MS can live with the disease for many years, despite the fact that it can be extremely debilitating. The cognitive deficits experienced can be particularly impactful, and are sometimes considered to be greater hinderances

to daily life than any physical disability (Elsass & Zeeberg, 1983). It has also been reported that during the course of the disease, 50-80% of patients with MS will become unemployed (Grant, McDonald, Trimble, Smith, & Reed, 1984; Strober & Arnett, 2016).

## Cognitive Function and Depression in Multiple Sclerosis

Cognitive impairment is a general term used to describe a range of neuropsychological deficits. Patients with MS have been found to have significant deficits in areas such as processing speed (Matthews, Cleeland, & Hopper, 1970), working memory (Rao et al., 1993), and cognitive flexibility – including planning and problem solving (Vowels & Gates, 1984). Cognitive impairment, generally, has been observed in 45% to 65% of patients with MS, and is often viewed as more debilitating than the physical effects of MS (Brassington & Marsh, 1998; Rao, 1995). This may be because the physical effects are more readily treated and managed compared to the cognitive effects. However, as noted above, not all patients with MS experience a decrease in cognitive function, and those who do experience varying levels of impairment. Thus, it is vitally important to determine factors that may serve to maintain the cognitive function of patients with MS.

Another symptom of note is depression. In order to meet the clinical requirements for depression, the American Psychiatric Association (2013) specifies that the individual must experience multiple specific symptoms for at least two weeks, which may include a depressed mood, apathy, fatigue, and cognitive difficulties. However, it is important to consider that a patient with MS may experience fatigue, cognitive difficulties, and other depressive symptoms as a result of the MS. Even when controlling for this, estimates place the lifetime risk for a person with MS having depression at 50%, which is significantly higher than the lifetime risk of 17% associated

with the general population (Cadden, Meyer, & Arnett, 2017). Depression in patients with MS is somewhat unique, in that it does not appear to be a simple response to the physical disabilities caused by MS (Rabinowitz & Arnett, 2009). Cognitive impairment may play a role in the development of depression or it may be a source of stress that increases the risk of depression in patients with MS. These relationships are not mutually exclusive and research surrounding this topic is mixed (Arnett, Barwick, & Beeney, 2008). As is the case with cognitive function, not all patients with MS experience depression. Therefore, investigating the different characteristics of patients with MS who are not depressed compared to patients with MS who are depressed is a significant area of inquiry.

## Cognitive Reserve and Coping in Multiple Sclerosis

Two characteristics of patients with MS that may have an impact in the maintenance of cognitive function or the prevention of depression are cognitive reserve and coping ability.

Cognitive reserve is best defined as the mental resources an individual possesses that help separate disease burden from cognitive impairment (Sumowski & Leavitt, 2013). Importantly, in the context of MS, cognitive reserve has been defined as the moderator between the measurable damage caused by the disease and the functional outcome of the damage (Cadden, Guty, & Arnett, 2018). In other words, two individuals with similar brain pathology and disease course could have noticeably different levels of functioning, and it is theorized that this is due to cognitive reserve. An individual with higher cognitive reserve can resist greater neurological impairments (i.e. brain atrophy) and show less cognitive impairment than might otherwise be predicted.

As of yet there is no standard measure for cognitive reserve. Common operationalization techniques include using measures of intelligence and/or vocabulary, education, and occupational

attainment (Benedict, Morrow, Guttman, Cookfair, & Schretlen, 2010; Ghaffar, Fiati, & Feinstein, 2012). More recently, however, some researchers have shifted away from using these measures as they tend to be either relatively fixed by adulthood or highly related to factors outside the individual's control. Instead, measures focusing on cognitively enriching lifestyle choices such as engagement in cognitively stimulating activities and time spent socializing have been used (Patel, Walker, & Feinstein, 2017). Cognitive reserve has been found to moderate the relationship between disease burden and cognitive function in patients with MS (Amato et al., 2013; Benedict et al., 2010). Cadden and colleagues (2018) found that higher disability predicts depression only in individuals with low cognitive reserve, while disability did not predict depression in individuals with high cognitive reserve.

Coping has been classically defined by Lazarus (1966) as the process of executing a response to a perceived threat. Broadly, coping strategies were divided into one of two camps: problem-focused coping or emotion-focused coping. Problem-focused strategies seek to alter the source of the stress, while emotion-focused strategies seek to simply reduce the stress itself (Lazarus, 1993). Carver, Scheier, and Weintraub (1989) set out to explain their novel conceptual approach to coping, including the articulation of specific dimensions of coping. Of these dimensions, the most widely utilized are active coping (i.e. active coping, planning) and avoidant coping (i.e. behavioral disengagement, denial), and they provide another beneficial classification for coping strategies. Researchers consider active and adaptive coping, and avoidant and maladaptive coping, as equivalents, respectively (Arnett, Higginson, Voss, Randolph, & Grandey, 2002).

In patients with MS, coping has been associated with the relationship between certain symptoms and disease outcomes. Ukueberuwa and Arnett (2014) found that coping style

moderated the relationship between fatigue and cognitive performance. Coping was also found to moderate the relationship between cognitive impairment and depression (Arnett et al., 2002; Rabinowitz & Arnett, 2009). Mediating relationships have also been supported. In the same study that supported a moderating relationship between cognitive impairment and depression, Rabinowitz and Arnett (2009) found that cognitive impairment had a negative effect on coping, contributing to the development of depression. Specifically, these investigators suggested that cognitive impairment reduced individuals' ability to use adaptive coping strategies, leading to them to using maladaptive strategies less reliant on intact cognitive functioning.

The mechanisms that connect cognitive function, depression, cognitive reserve, and coping is extremely complex and not well articulated. On the surface, it would seem that cognitive reserve would relate to cognitive function outcomes, while coping would relate to depression outcomes. There is a dearth of research examining the relationship between these concepts, but not in populations with MS. In patients with MS, there is a noted lack of research regarding how they might interact with each other. In other words, researchers have yet to consider the possibility that cognitive reserve and coping might interact with each other to influence cognitive function and/or depression.

**Study Goals**

With these considerations in mind, the present study will explore the relationship between coping and cognitive reserve, and whether this relationship predicts cognitive function and/or depression outcomes in an MS sample. The intended outcome of the project would be to explore the mediating or moderating relationship between cognitive reserve, coping abilities, and depression/cognitive function. The guiding inquiries of this type of research, including this study,

is to investigate the features that distinguish a person with MS who is depressed from a person with MS who is not depressed. Finding how these two groups differ will contribute to the long-term goal of being to acquire enough knowledge to make depression preventable, or at least treatable, in patients with MS. Broadly, this project will contribute to the growing knowledge base surrounding depression and quality of potentially malleable characteristics (i.e., cognitive reserve and coping) in individuals with MS.

**Hypotheses**

Two hypotheses are outlined: (1) *it is hypothesized that a mediating relationship will exist in which cognitive reserve predicts cognitive function/depression status, mediated by adaptive coping*; (2) *it is hypothesized that a moderating relationship will exist in which cognitive reserve's prediction of cognitive function/depression status will be moderated by adaptive coping*. In a mediating relationship, high cognitive reserve is expected to predict high adaptive coping, which in turn will predict low depression/high cognitive function outcomes. In a moderating relationship hypothesis, it is predicted that cognitive reserve will interact significantly with adaptive coping to predict depression/cognitive function outcomes. Specifically, high cognitive reserve combined with high adaptive coping will predict low depression/high cognitive function outcomes, while low cognitive reserve combined with poor adaptive coping will predict high depression/low cognitive function outcomes. It is possible that both mediating and moderating relationships will be found, as they are not mutually exclusive hypotheses.

# Methods

The current study involves a secondary analysis of data collected as part of a longitudinal study examining various physical, cognitive, emotional, and social factors related to MS.

## Participants

Participants were recruited from in and around the State College, Pennsylvania area. Inclusion criteria for the study required only a positive MS diagnosis by a board-certified neurologist. Individuals were excluded for any of the following: (a) significant history of drug or alcohol abuse; (b) nervous system disorder other than MS; (c) sensory impairment that could significantly interfere with testing; (d) history of learning disorder or attention deficit hyperactivity disorder; (e) significant medical condition, other than MS, that could interfere with cognitive or motor function; (f) relapse or corticosteroid use within four weeks of participation in the study; (g) physical or neurological impairment that would make testing impossible. Once they were deemed eligible, participants were brought in for testing.

## Description of Measures

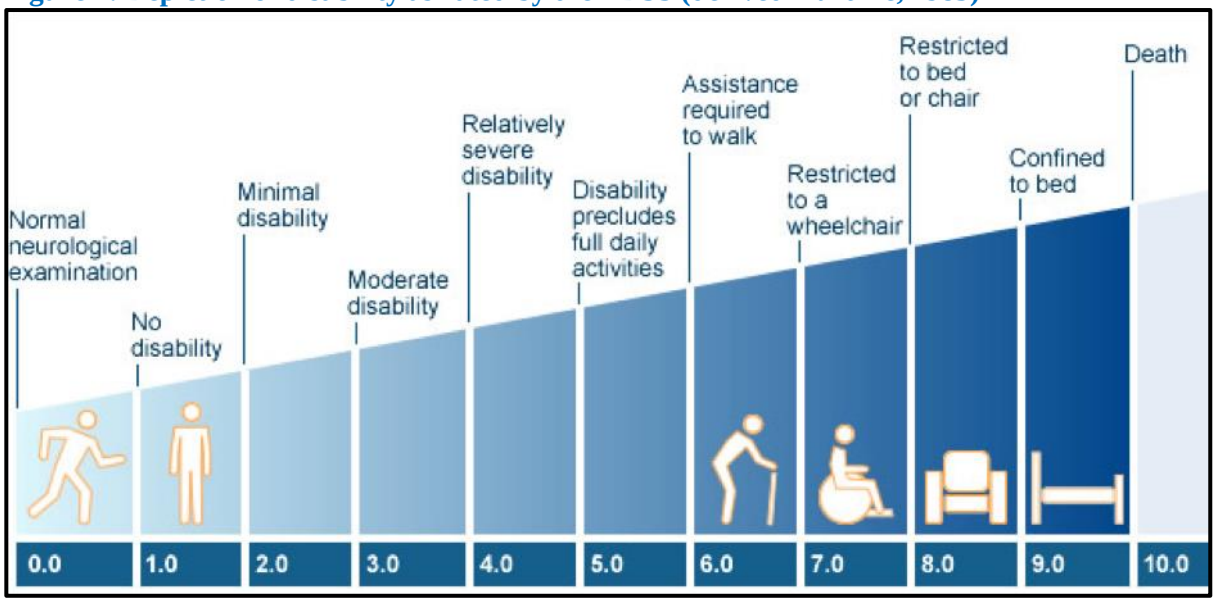
Participants were administered a structured battery of neuropsychological tests and interviews, which yielded the measures reported in this study.

### *Disease Severity*

Disease severity was measured using Kurtzke's (1983) Expanded Disability Status Scale (EDSS). The EDSS is administered by clinicians, and measures disability of the various systems of the CNS. The scale ranges from 0 (normal functioning) to 10 (death due to MS), and increases

in increments of 0.5 – after reaching a score of 1 (Meyer-Moock, Feng, Maeurer, Dippel, & Kohlmann, 2014). The EDSS gives a rough metric of the progression of MS, but is generally interpreted according to **Figure 1**. It should be noted that the EDSS heavily weights ambulation. as it is centered around walking. The EDSS has been found to be valid and is the most widely used tool for measuring disease outcome (Meyer-Moock et al., 2014).

**Figure 1: Depiction of disability as rated by the EDSS (derived Kurtzke, 1983)**




*Cognitive Functioning*

Cognitive functioning was measured using a composite variable, combining measures from multiple cognitive tests. The composite was comprised of the Digit Span subtest from the WAIS-IV, Symbol-Digit Modalities Test-Oral (SDMT), Controlled Oral Word Association Test (COWAT), Animal Naming Test, Paced Auditory Serial Addition Test (PASAT), Brief Visuospatial Memory Test-Revised (BVMT-R), and the California Verbal Learning Test-II (CVLT-II). In all cases, higher scores indicate better cognitive functioning.

The Digit Span Test is widely considered a reliable test of attention (Leung, Lee, Lam, Chan, & Wu, 2011). It requires participants to listen to and repeat (in order, verbally) a series of

numbers read by the examiner. The test starts with two digits, and increases by one digit with each successive round. If participants fail a trial, they are given another trial with the same number of digits. The test stops after two consecutive fails at the same trial. The test is also given in reverse, where the procedure is the same except participants must repeat the series in reverse order. For the present study, the forward, reverse, and combined scores were used for the cognitive functioning composite.

The SDMT is a complex task involving attention and visual tracking, but it is chiefly aimed at measuring processing speed (Arnett et al., 1999; Charvet, Beekman, Amadiume, Belman, & Krupp, 2014). To account for the motor deficits potentially experienced by patients with MS, an oral version was administered for this study (Rao, Leo, Bernardin, Unverzagt, 1991). The SDMT requires participants to match a series of symbols to their corresponding numbers. The form consists of eight rows of two boxes stacked on top of each other. The top box contains one of nine unique symbols, and the bottom box is blank. There is a key located at the top of the form, and it is also made up of two boxes stacked on top of each other. The top boxes in the key contain the nine unique symbols, and the bottom boxes contain their corresponding digit (1-9). Participants are tasked with matching the symbols with their corresponding digits, according to the key at the top of the form, and saying the digit aloud. They are given 90 seconds to complete as many symbol-digit pairings as possible. For the present study, the total number of correct symbol-digit pairings in the 90-second limit was used for the cognitive functioning composite.

The COWAT is a widely used test for measuring verbal fluency, requiring participants to spontaneously produce words (orally) in a given time limit (Ross et al., 2007). More commonly, a starting letter is given as a parameter for the test – for this study, the letters “F”, “A”, and “S” were used. Participants are given 60 seconds to say as many words as possible starting with the

designated letter, excluding all proper nouns, numbers, and the same word with a different ending (e.g. fast and faster). The COWAT has been shown to be both a reliable and valid, while sensitive measure of verbal fluency (Ross et al., 2007). For the present study, the total number of correct words generated between all three letter-trials was used for the cognitive functioning composite.

The Animal Naming also measures verbal fluency, but specifically focuses on semantic fluency (Ross et al., 2007). For this task, one trial is conducted where participants are instructed to name as many animals as they can think of in a 60 seconds time limit. Much like the COWAT, the Animal Naming Test was also found to be both reliable and valid (Ross et al., 2007). For the present study, the total number of correct animal names generated was used for the cognitive functioning composite.

The PASAT is considered a reliable tool for measuring working memory and sustained, divided attention (Cortés-Martínez et al., 2019). Participants are asked to listen to an audio recording, which presents 61 digits at a rate of one digit every three seconds (for a total of 60 possible responses). Participants are tasked with adding each newly presented digit to the digit announced immediately prior to it, and orally responding with this sum. For example, if the recording presented the sequence "9-1-3-5-2-6," the correct responses would be "10-4-8-7-8." For the present study, the total number of correct responses was used for the cognitive functioning composite.

The BVMT-R is a common test for measuring visuospatial learning and memory (Tam & Schmitter-Edgecombe, 2013). Participants are given pencil and booklet for this test. The test consists of three trials, where participants are presented with a 2 X 3 matrix of simple figures for 10 seconds. After each presentation period, participants flip to a separate page and are tasked with drawing as many of the figures as accurately as they can in the exact locations they were presented

on the original page. After a 25-minute delay – with interference tasks – participants are again asked to reproduce as many of the figures as accurately as possible in their correct locations. Though optional, a copy trial was given upon completion of the test. In this trial, participants were tasked with copying the figures as accurately as possible, while looking at them. This helps raters to identify how motor or visuoconstructive impairments may impact performance, and this information was considered during scoring. Participants can earn up to two points per figure, based on the accuracy of the drawing and the location, for a total of 12 points per trial. The BVMT-R was found to be highly reliable and valid (Tam & Schmitter-Edgecombe, 2013). For the present study, the combined score across the three initial trials, as well as the delayed trial score were used for the cognitive functioning composite.

The CVLT-II is a verbal word-learning task that assesses list-learning and memory (Beier, Hughes, Williams, & Gromisch, 2019). Participants are read aloud Word List A, which consists of 16 words that can be grouped evenly into four semantic categories – though they are not presented this way – and asked to recall the list for five trials (these are immediate recall trials 1-5). While not instructed to, participants are expected to group the words by semantic category as a learning and memory strategy. Participants are first instructed to recall as many words as possible in any order. They are then read aloud Word List B, which consists of 16 words from four semantic categories – two overlapping and two non-overlapping for the purpose of interference, and tasked with recalling this list. After this, participants are tasked with freely recalling Word List A (this is the short delay free recall trial). They are then presented with the four semantic categories and asked to recall Word List A again (this is the short delay cued recall trial). After a 20-minute delay, long delay free recall and long delay cued recall trials are administered using Word List A. Finally, a "yes/no" recognition trial is administered. In the recognition trial, participants are presented with

48 words consisting of those from List A, List B, and some unrelated words. After being read aloud each word, they are tasked with responding "yes" if the word is from List A, and "no" if it is not. The CVLT-II has been shown to be both a highly reliable and valid measure of verbal learning and memory, and other related tests are often compared to it for tests of validity (Beier et al., 2019). For the present study, the total summation of scores from immediate recall trials 1-5, the short delay free recall score, and the long delay free recall score were used for the cognitive functioning composite.

To create the cognitive functioning composite, standard scores were calculated for each of the 12 aforementioned scores on cognitive tests. The standard scores were then combined to create the final mean composite variable, with a mean of 100 and standard deviation of 15.

*Depression.*

Current depression status was measured using the Beck Depression Inventory – Fast Screen (BDI-FS), derived from scores on the Beck Depression Inventory – II (BDI-II). The BDI-II is a 21-item, self-report questionnaire. Participants respond to each item by choosing one of four statements (assigned values 0 to 3, with 3 indicating higher depression symptomology) that best describe the way they have been feeling over the previous two weeks. Scores from each question are summed to create a total score. The BDI-II has been validated with many populations and has been shown to be reliable as well (Arnau, Meagher, Norris, & Bramson, 2001; Osman, Kopper, Barrios, Gutierrez, & Bagge, 2004; Steer, Ball, Ranieri, & Beck, 1999). Thus, the BDI-II was used to measure depression at the time of data collection.

However, while the BDI-II was validated with many populations, it contains certain items that may be invalid in a population of patients with MS. Namely, it includes questions about the neurovegetative symptoms of depression, the answers to which may be confounded by the physical

manifestations of MS (Benedict, Fishman, McClellan, Bakshi, & Weinstock-Guttman, 2003). The BDI-FS was developed to be used in medical populations due to the belief that it is unconfounded by medical illnesses. It is a 7-item, self-report questionnaire that focuses on items such as dysphoria, anhedonia, various cognitive symptoms, and suicidal ideation in patients (Benedict et al., 2003). In the same manner as the BDI-II, participants read questions and respond by choosing one of four statements, assigned values 0 to 3. A total score is calculated by summing the total of each question. A score of four or more on the BDI-FS constitutes a diagnosis of clinical depression; however, the test also allows for a continuum of depression severity. The BDI-FS has been found to be highly valid in MS and other clinical populations (see Strober & Arnett, 2015), which is why BDI-II scores were converted to BDI-FS scores for this study.

*Adaptive Coping*

Adaptive coping was also measured using a composite variable. Coping was measured using the Coping Orientation to Problems Experienced (COPE) Inventory (Carver, Scheier, & Weintraub, 1989). Participants were presented with a set of 60 statements targeting various aspects of their coping strategies in response to a stressful situation, and asked to respond to each one regarding how likely they were to engage in that behavior in response to the stress. Ratings ranged from 1 ("I wouldn't do this at all") to 4 ("I would do this a lot"). The 60 questions could be grouped evenly into 15 scales for the different aspects of coping, but only 6 scales were considered for the present study – 3 for creating an active coping index and 3 for creating an avoidant coping index. Active coping, planning, and suppression of competing activities comprised the active coping scale, while mental disengagement, behavioral disengagement, and denial comprised the avoidant coping scale. Since each index consisted of 3 scales, and each scale consisted of 4 statements, the max score for active or avoidant coping was 48.

Active and avoidant coping were considered because they represent rich areas for potential clinical intervention. Planning, for example, could easily be targeted for improvement in a therapeutic setting, whereas a different area, such as social support is less easily targeted within an individual. Targeted clinical interventions to increase active coping behaviors and decrease avoidant coping behaviors in this manner would, ideally, lead to better outcomes. An individual can use strategies from both active and avoidant coping, and the scores on each will not necessarily be inversely related (Rabinowitz & Arnett, 2009). The coping composite variable took the avoidant coping index score and subtracted it from the active coping index score (active coping – avoidant coping) to provide an accurate representation of adaptive coping. Positive values reflect the use of more active coping strategies, while negative values reflect the use of more avoidant coping strategies. High levels of adaptive coping are preferable (i.e. someone who uses active coping strategies more and avoidant coping strategies less); therefore, this composite is theoretically sound because higher active coping and lower avoidant coping lead to higher adaptive coping.

*Fixed Cognitive Reserve*

This study uses Cadden, Guty, and Arnett's (2018) conceptualization of fixed cognitive reserve. In their study, the researchers also defined malleable cognitive reserve (not discussed here) as novel way to conceptualize cognitive reserve that may better serve as a source for clinical intervention. Fixed cognitive reserve, however, is still a valid measure and is defined as the aspect of cognitive reserve that is less easily changed over an individual's life course. Fixed cognitive reserve was operationalized as the mean of the standard score of years of education and the Wechsler Test of Adult Reading (WTAR) standardized score.

The WTAR aims to measure premorbid intellectual functioning in individuals, after the onset of a neurological illness or trauma (Steward et al., 2017). Intelligence, as measured by the

WTAR, is thought to be relatively unaffected by most types of neuropathological change, and can therefore be estimated using tests such as this one. Premorbid functioning is important for giving clinicians a better understanding of the relative level of cognitive impairments a person is experiencing due to their neurological illness. For example, two individuals may have the same level of current cognitive function in the domain of, say, memory; however, if one started at a higher level of premorbid functioning, they would be experiencing greater relative decline in memory.

When administering the WTAR, participants are asked to read aloud 50 words with increasingly irregular pronunciations. For example, the first word is "again" (pronounced "uh-GEHN" or "uh-GAIN"), and the forty-sixth word is "vertiginous" (pronounced "vur-TI-jin-us" or "vur-TIJ-uh-nus). Correct pronunciations are scored "1" and incorrect pronunciations are scored "0," and participants are not told whether or not they were correct. The test ends after 12 consecutive incorrect attempts. The raw score (max of 50) is then standardized by comparing it to normative sample to determine the Demographic Predicted Full-Scale IQ. The WTAR has been shown to be a reliable and valid test of premorbid intelligence in a United States sample (The Psychological corporation, 2001).

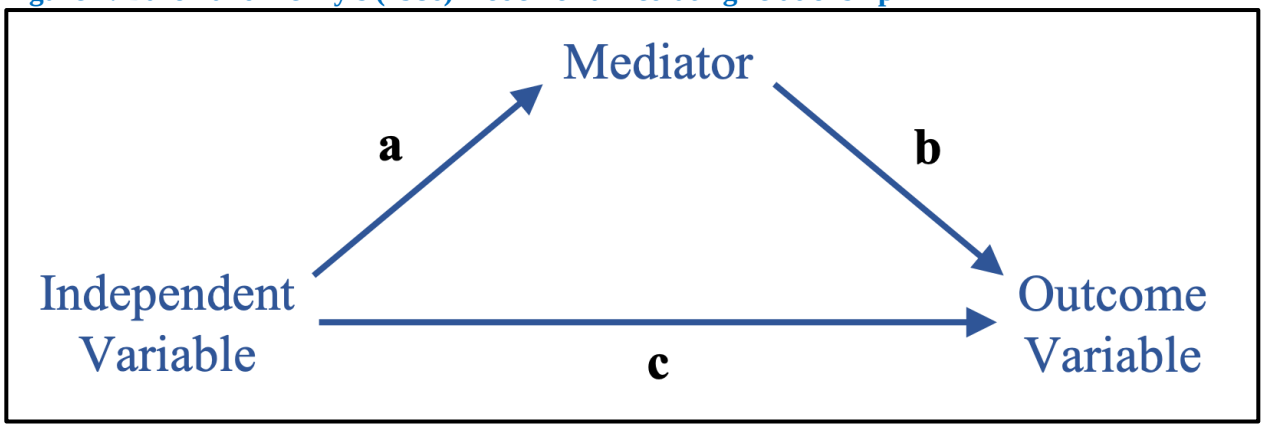
**Description of Analyses**

A bivariate correlation was run between participant characteristics and the outcome variables (cognitive functioning/depression) to account for any potentially significant confounds. Disease severity was found to be a significant covariate of the outcome variables and was controlled for during hypothesis testing (see **Table 2**).

*Test for Mediation*

To evaluate the first hypothesis, that adaptive coping mediates the relationship between cognitive reserve and disease outcome (cognitive functioning/depression), Baron and Kenny's (1986) method of analysis was used. Their depiction of a mediating relationship is shown **Figure 2**:

**Figure 2: Baron and Kenny's (1986) model for a mediating relationship**




In this depiction, there are two variables that have a causal relationship with the outcome variable. To test for a significant mediating relationship, the independent variable must first be established as a significant predictor of the outcome variable (i.e. Path *c* must be significant). After this, Baron and Kenny (1986) denote three conditions for mediation: (1) the independent variable must be a significant predictor of the mediator, such that variations in the independent variable are accounted for by variations in the mediator (Path *a*); (2) the mediator is a significant predictor of the outcome variable (Path *b*); and (3) when a regression analysis is performed on Path *c*, controlling for both Path *a* and Path *b*, the relationship between the independent variable and the outcome variable is no longer significant. If all of these conditions are met, there is significant mediation.

If the predictive power of Path *c* in the final step is reduced to zero, there is evidence for a significant full mediation with one, dominant mediator; however, this is often not the case in

psychology. If, in the final step, Path *c* is no longer significant but its predicting power is not reduced to zero, there is evidence for a partial mediation with multiple mediators.

To test for the indirect effect of adaptive coping as a mediator between cognitive reserve and disease outcome (depression/cognitive functioning), a bootstrapping analysis with 5,000 bootstrap samples was performed. A 95% confidence interval (CI) was calculated and used to determine the significance – if zero is in the interval the indirect effect was non-significant, if zero was not in the interval the indirect effect was significant.

*Test for Moderation*

To evaluate the second hypothesis, that adaptive coping moderates the relationship between cognitive reserve and disease outcome (cognitive functioning/depression), a regression analysis was conducted. Disease severity was controlled for at step 1, the main effects of adaptive coping and cognitive reserve were entered at steps 2 and 3, and the interaction of these two were entered at step 4 (adaptive coping X fixed cognitive reserve).

# Results

## Participant Data

The sample consisted of 54 participants who had completed the battery of tests. The majority of those 54 participants were women (38, 16 men), which agrees with previous research regarding sex and MS (Reich et al., 2018). The average age of the sample was 52.57 (± 11.44) years, with 14.80 (± 1.97) years of education. Thirty-nine participants were diagnosed with relapsing-remitting MS, 12 were diagnosed with secondary progressive MS, and 3 were diagnosed with primary progressive MS. One participant was diagnosed with progressive-relapsing MS, an older classification that would now be classified as primary progressive MS under the 2013 McDonald Criteria Revisions (Lublin et al., 2014). On average, the sample had experienced the symptoms of MS for 18.01 (±11.18) years, but had only been formally diagnosed with MS for 12.61 (± 7.11) years. The sample also had an average EDSS score of 5.38 (± 1.66).

**Table 1: Demographic and study-related information about the sample**

| | N | Mean | Min | Max | Std. Dev. |
|---|---|---|---|---|---|
| **Age** | 54 | 52.57 | 27 | 76 | 11.44 |
| **% Female** | 54 | 70.37 | — | — | — |
| **Symptom Duration** | 30 | 18.01 | 2.17 | 44.42 | 11.18 |
| **Diagnosis Duration** | 30 | 12.61 | 1.25 | 26.33 | 7.11 |
| **Disease Severity** | 54 | 4.38 | 0 | 8 | 1.66 |
| **Education** | 54 | 14.80 | 12 | 19 | 1.97 |
| **Depression** | 54 | 3.02 | 0 | 19 | 3.78 |
| **Cog. Functioning** | 49 | 1205.17 | 886.24 | 1397.12 | 115.15 |
| **Adaptive Coping** | 51 | 11.59 | -11 | 27 | 9.29 |
| **Fixed Cog. Reserve** | 54 | 104.02 | 73.17 | 124.76 | 11.45 |

**Pre-Analysis Data**

Two tailed correlation analyses were performed on both outcome variables and participant characteristics that could be potential covariates. Disease severity (EDSS score) was found to be a significant covariate of depression ($r(54) = .27$, $p = .050$) and cognitive functioning ($r(49) = -.36$, $p < 0.05$) and was controlled for during subsequent analyses. The correlations are reported in **Table 2**. Raw scores for individual components of the cognitive functioning composite are reported in **Table 3**.

**Table 2: Bivariate correlations of outcome variables and participant characteristics**

| | Age (years) | Diagnosis Duration (years) | Disease Severity (EDSS) | Depression (BDI-FS) | Cognitive Functioning (composite) |
|---|---|---|---|---|---|
| **Age (years)** | — | .66*** | .38** | -.07 | -.08 |
| **Diagnosis Duration (years)** | | — | .03 | -.18 | .05 |
| **Disease Severity (EDSS)** | | | — | **.27*** | **-.36*** |
| **Depression (BDI-FS)** | | | | — | -.28 |
| **Cognitive Functioning (composite)** | | | | | — |

*Significant at the 0.05 level, **Significant at the 0.01 level, ***Significant at the 0.005 level

**Table 3: Raw scores for cognitive functioning composite variable**

| | N | Mean | Min | Max | Std. Dev. |
|---|---|---|---|---|---|
| **Digit Span Forward** | 53 | 10.83 | 5 | 27 | 3.03 |
| **Digit Span Backward** | 53 | 7.00 | 1 | 12 | 2.63 |
| **Digit Span Combined** | 53 | 17.83 | 7 | 36 | 4.94 |
| **SDMT Total Correct** | 53 | 48.92 | 17 | 69 | 10.80 |
| **COWAT Total** | 54 | 40.59 | 12 | 70 | 12.32 |
| **Animal Total** | 54 | 20.33 | 8 | 30 | 5.53 |
| **PASAT Total Correct** | 52 | 42.75 | 2 | 60 | 13.36 |
| **BVMT-R Trials 1-3** | 53 | 24.60 | 1 | 34 | 6.19 |
| **BVMT-R Delay** | 53 | 9.64 | 0 | 12 | 2.42 |
| **CVLT-II Trials 1-5** | 53 | 49.04 | 22 | 69 | 12.34 |
| **CVLT-II Short Free Delay** | 53 | 10.36 | 2 | 16 | 3.72 |
| **CVLT-II Long Free Delay** | 53 | 10.92 | 2 | 16 | 3.57 |

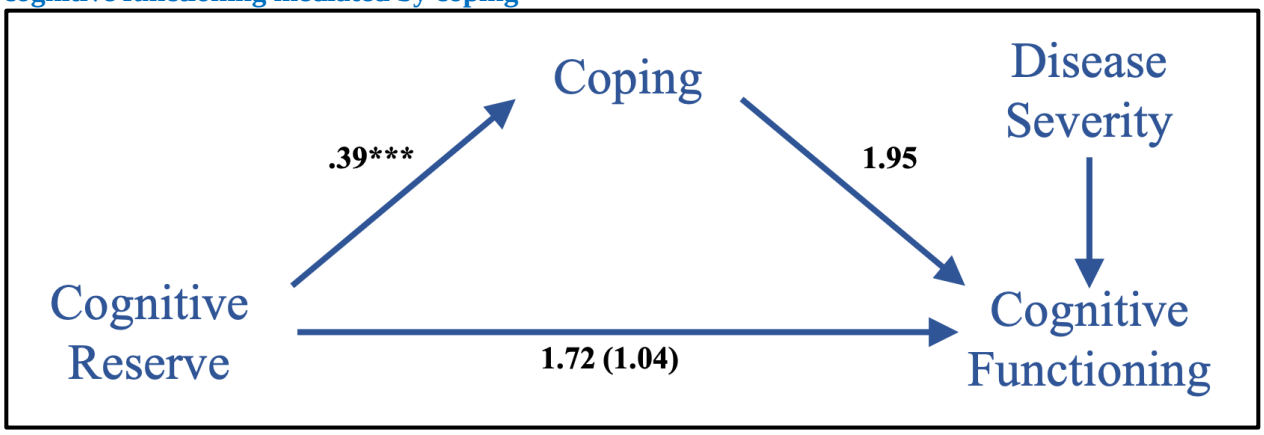
## Mediation Results

In the tests of mediation, following Baron and Kenny's (1986) approach, fixed cognitive reserve was the independent variable, cognitive functioning/depression was the outcome variable, disease severity as measured using EDSS was included as a covariate, and adaptive coping was the mediator. Disease severity was included as a covariate based on a significant correlation between EDSS scores and both outcome variables (see **Table 2**).

*Cognitive Functioning*

Fixed cognitive reserve predicted adaptive coping ($\beta$ = .39, $p$ < .001), but was not a significant predictor of cognitive functioning ($\beta$ = 1.72, $p$ = .29). Adaptive coping also did not predict cognitive functioning ($\beta$ = 1.95, $p$ = .28). When controlling for adaptive coping, the relationship between fixed cognitive reserve and cognitive functioning remained nonsignificant ($\beta$ = 1.04, $p$ = .50); however, the significance decreased even further. **Figure 3** illustrates the mediating relationship. The results do not support the hypothesis that adaptive coping mediates the relationship between fixed cognitive reserve and cognitive functioning.

**Figure 3: Standardized regression coefficients ($\beta$) for the relationship between cognitive reserve and cognitive functioning mediated by coping**



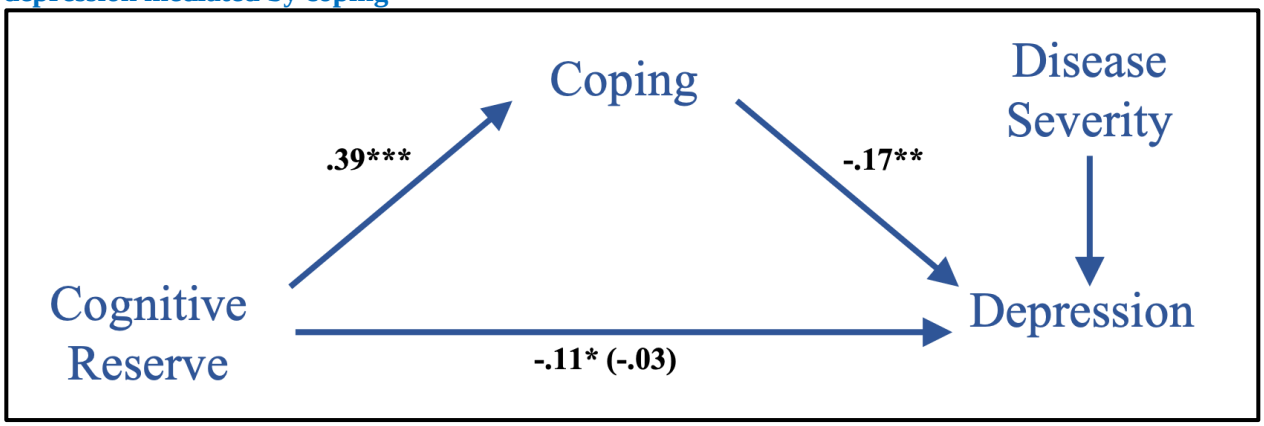

The coefficient in parenthesis is the effect of cognitive reserve on cognitive functioning controlling for coping. *Significant at the 0.05 level, **Significant at the 0.01 level, ***Significant at the 0.005 level

*Depression*

Fixed cognitive reserve significantly predicted both adaptive coping ($\beta$ = .39, $p$ < .001) and depression ($\beta$ = -.11, $p$ < .05). Adaptive coping also predicted depression ($\beta$ = -.17, $p$ < .01). Further, when controlling for adaptive coping, the predictive power of fixed cognitive reserve became nonsignificant ($\beta$ = -.03, $p$ = .50).

To test the indirect effect of fixed cognitive reserve on depression through adaptive coping, a bootstrapping analysis was conducted using the SPSS PROCESS macro published by Preacher and Hayes (2004). Results of the mediation analysis using 5,000 bootstrap samples indicate that adaptive coping significantly mediated the relationship between cognitive reserve and depression, indirect effect = -.08, 95% CI [-1.67, -.01]. After controlling for adaptive coping, the effect of cognitive reserve on depression became nonsignificant ($p$ = .68). Through this, the bootstrapping estimates suggest a significant mediating relationship of adaptive coping on the relationship between fixed cognitive reserve and depression. **Figure 4** illustrates the mediation relationship. The results support the hypothesis that adaptive coping mediates the relationship between fixed cognitive reserve and depression.

**Figure 4: Standardized regression coefficients ($\beta$) for the relationship between cognitive reserve and depression mediated by coping**




The coefficient in parenthesis is the effect of cognitive reserve on depression controlling for coping.
*Significant at 0.05 level, **Significant at 0.01 level, ***Significant at 0.005 level

## Moderation Results

*Cognitive Functioning*

A linear regression was performed to determine the relationship between fixed cognitive reserve, adaptive coping, and cognitive functioning, controlling for disease severity as measured using the EDSS. This analysis showed no support for a moderating relationship. No main effect was observed for fixed cognitive reserve ($\Delta F$ = 1.49, $p$ = .23) or adaptive coping ($\Delta F$ = 2.27, $p$ = .14). Further, the interaction between fixed cognitive reserve and adaptive coping was nonsignificant ($\Delta F$ = .01, $p$ = .91). This model is illustrated in **Figure 5**. High and low fixed cognitive reserve/adaptive coping represents one standard deviation above and below the sample mean, respectively.

**Table 4: Linear regression analysis for cognitive reserve and coping predicting cognitive functioning**

| | $R^2$ | $\Delta R^2$ | $\Delta F$ | Sig. |
|---|---|---|---|---|
| **Step 1: Demographics** | .08 | .08 | 3.61 | .06* |
| **Disease Severity** | | | | |
| **Step 2: Cognitive Reserve** | .11 | .03 | 1.49 | .23 |
| **Fixed Cognitive Reserve** | | | | |
| **Step 3: Adaptive Coping** | .15 | .05 | 2.27 | .14 |
| **Composite Variable** | | | | |
| **Step 4: Interaction** | .15 | .001 | .01 | .91 |

*Approached significance at $p < .10$

*Depression*

A linear regression was performed to determine the relationship between fixed cognitive reserve, adaptive coping, and depression, controlling for disease as measured using EDSS. This analysis also showed no support for a moderating relationship, with the interaction between fixed cognitive reserve and adaptive coping being non-significant ($\Delta F$ = 2.53, $p$ = .12); however, main effects were observed for both fixed cognitive reserve ($\Delta F$ = 5.17, $p < .05$) and adaptive coping ($\Delta F$ = 13.07, $p < .005$). In this model, fixed cognitive reserve accounted for 8.9% of the variance

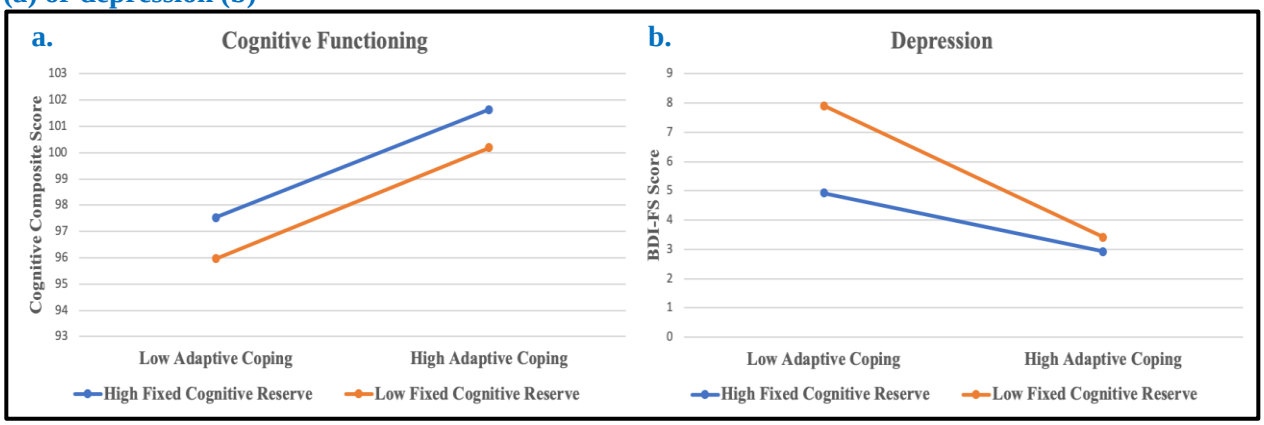
in depression scores, and adaptive coping accounted for 18.1% of the variance in depression scores. This model is illustrated in **Figure 5**. High and low fixed cognitive reserve/adaptive coping represents one standard deviation above and below the sample mean, respectively.

**Table 5: Linear regression analysis for cognitive reserve and coping predicting depression**

| | $R^2$ | $\Delta R^2$ | $\Delta F$ | Sig. |
|---|---|---|---|---|
| **Step 1: Demographics** | .08 | .08 | 4.23 | .05* |
| **Disease Severity** | | | | |
| **Step 2: Cognitive Reserve** | .17 | .09 | 5.17 | .03* |
| **Fixed Cognitive Reserve** | | | | |
| **Step 3: Coping** | .35 | .18 | 13.07 | .001*** |
| **Composite Variable** | | | | |
| **Step 4: Interaction** | .38 | .03 | 2.53 | .12 |

*Significant at 0.05 level, **Significant at 0.01 level, ***Significant at 0.005 level

**Figure 5: Moderation models for fixed cognitive reserve and active coping, and cognitive functioning (a) or depression (b)**



# Discussion

## Discussion of Findings

The goal of the present study was to investigate how cognitive reserve and coping abilities related to the outcomes of cognitive functioning and depression in a sample of individuals with MS. Namely, coping was evaluated as both a mediator and moderator of the relationship between cognitive reserve and cognitive functioning/depression. These roles were not mutually exclusive, and, indeed, it was hypothesized that analysis would support coping as both a mediator and a moderator.

Coping as a mediator indicates that cognitive reserve's effect on cognitive functioning or depression may be indirect. Instead, cognitive reserve's effect on coping would better explain variation in cognitive functioning or depression status. In this scenario, cognitive reserve would act to help or hinder and individual's coping abilities. High cognitive reserve may protect against cognitive impairment, thereby increasing the mental resources available for individuals to recruit in order to use adaptive coping strategies. This would be consistent with Rabinowitz and Arnett's (2009) conclusion that cognitive impairment reduces individuals' ability to use adaptive coping strategies, leading to them to using maladaptive strategies less reliant on intact cognitive functioning. Adaptive coping strategies may then be used to retain better cognitive functioning and/or reduce the risk of developing depression.

The results of the study support that coping is a significant mediator of the relationship between cognitive reserve and depression, but not as a significant mediator of the relationship between cognitive reserve and cognitive functioning. These findings are consistent with previous studies that have shown an association between better coping abilities and positive disease

outcomes in MS populations (Arnett et al., 2002; Rabinowitz & Arnett, 2009; Ukueberuwa & Arnett, 2014). The current study also builds on previous work through the incorporation of cognitive reserve. Cognitive reserve has been an area of major focus in recent research, but much of this has conceptualized cognitive reserve in a mediator/moderator role (Amati et al., 2013; Benedict et al., 2010; Cadden et al., 2018). Further, in these studies it has often been concluded that cognitive reserve attenuates the effects of undesirable outcomes (i.e. disability). Due to this, the mechanism through which cognitive reserve acts has not been well studied. In examining cognitive reserve as the independent variable (see **Figure 2**) with coping as the mediator, the present study has illuminated a potential mechanism through which cognitive reserve acts and identified a potential source for future clinical intervention.

Coping as a moderator indicates that the relationship between cognitive reserve and cognitive functioning or depression may be different depending on use of adaptive coping strategies. In this scenario, the interaction of both cognitive reserve and adaptive coping would better explain individuals' level of cognitive functioning or depression status than either variable, individually. It was hypothesized that high cognitive reserve combined with high adaptive coping would predict low depression/high cognitive function outcomes, while low cognitive reserve combined with poor adaptive coping would predict high depression/low cognitive function outcomes. High use of adaptive coping may protect individuals from deficits experienced with low cognitive reserve. Namely, it may protect them from experiencing depression that may be due to poor cognitive functioning, as suggested by Arnett, Barwick, & Beeney (2008). Conversely, low use of adaptive coping (i.e. high use of maladaptive coping), may not protect individuals from deficits experienced with low cognitive reserve, and may be put at risk for depression due to poor cognitive functioning.

The results of the study do not support that coping is a significant moderator of the relationship between cognitive reserve and cognitive functioning, nor do they support that coping is a significant moderator of the relationship between cognitive reserve and depression. A possible explanation for this may be as simple as the fact that one cannot improve cognitive functioning through coping. From a theoretical standpoint, coping, by nature, focuses on stress and emotions. As defined by Lazarus (1966), coping is the process of executing a response to a perceived threat. In other words, it is a means to an end. As demonstrated in the present study, it may be that those behaviors outlined in the adaptive coping index – derived from Carver, Scheier, and Weintraub's (1989) conceptualization of coping – are enough to protect an individual from depression; however, these behaviors may not be enough to protect an individual from cognitive impairments. This is likely because depression is more directly related to stress and emotions, therefore placing it in the same domain as coping. Cognitive functioning may better be studied as a symptom *to be coped with* rather than an outcome that coping can protect against (Brassington & Marsh, 1998). Many researchers have already studied cognitive functioning in this way (see Rabinowitz & Arnett, 2009).

The present study helped to illuminate the impact of cognitive reserve and coping on cognitive functioning and depression in a population with MS, but it is not without limitations. As is the case with much research focusing on MS, the sample size was relatively small ($N = 54$). This limits the statistical power of the findings presented, and may have prevented the identification of small-to-moderate sized effects. Small statistical power may explain why the interaction between fixed cognitive reserve and adaptive coping did not significantly predict depression status. Additionally, the way in which depression was measured may be a limitation of this study. While found to be valid, the BDI-FS is a self-report measure and thus incurs the potential for skewed

evaluations compared to clinical diagnoses. Further, the BDI-FS is a continuous scale that cannot wholly replace a clinician diagnosis for Major Depressive Disorder (MDD). Therefore, comparisons between depressed individuals in this study and those with a diagnosis of MDD are not exact; however, it should be noted that the BDI-FS offers the potential benefit of accounting for subthreshold depressive symptoms that may greatly impact quality of life.

A significant limitation of this study is that it is correlational in nature. Thus, causality and the direction of the described relationships cannot be absolutely concluded. Additionally, the current study operationalized cognitive reserve through characteristics thought to be fixed by adulthood or outside of the individual's control (i.e. reading skills and education). There is a growing body of research that suggests conceptualizing cognitive reserve using more fluid measures that may be more easily impacted through clinical intervention. Therefore, it suggested that future studies use Cadden et al.'s (2018) so called "malleable" cognitive reserve, as this may offer better insight for clinical research.

A final suggestion for future research may be found in Cadden et al.'s (2017) method of evaluating depression in 3 MS groups – currently depressed, remitted (i.e. formerly) depressed, and never depressed. Whereas remitted depressed and never depressed are usually included in the same group (not depressed), these researchers found that studying them separately yielded unique advantages. Namely, these researchers found that never depressed individuals must possess protective factors that prevented them from developing depression, while remitted depressed individuals must possess some compensatory factors that allowed them to overcome their depression. Protective factors would be important for implementation before the development of depression, whereas compensatory factors may help identify additional sources for clinical intervention. It is possible that these factors are distinct from one another. These potential benefits

help contribute to the overarching goal of this research, investigating the features that distinguish a person with MS who is depressed from a person with MS who is not depressed, and it is therefore suggested that future studies incorporate a 3-group method for examining depression.

## Conclusion

In sum, the results of the present study support that adaptive coping is a mediator of the relationship between fixed cognitive reserve and depression. The findings of this study have important clinical implications that should be investigated in future work. They suggest that clinical interventions intended to reduce depression in MS may benefit from targeting coping strategies. This study and others (Arnett et al., 2002, Schwartz, 1999) have shown that coping is a malleable characteristic primed for interventions aimed at increasing use of active coping and decreasing use of avoidant coping. This study also contributes to the growing body of knowledge regarding depression and the quality of potentially malleable characteristics in individuals with MS. Through identification and examination in future research, these characteristics may potentially be used to prevent or treat depression in MS populations.

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## EDUCATION

**The Pennsylvania State University | Schreyer Honors College** **University Park, PA**
*College of the Liberal Arts*
*Class of 2020*
Bachelor of Science in Psychology (Neuroscience Option)
Biology Minor
Thesis Title: *The Role of Coping Style and Cognitive Reserve in Depression and Cognitive Functioning in Multiple Sclerosis*
Thesis Supervisor: Peter A. Arnett, Ph.D.

## RESEARCH EXPERIENCE

**Penn State Neuropsychology of Multiple Sclerosis Program** **University Park, PA**
*Research Assistant* *January 2018-Present*

- Score neuropsychological tests for Phase 3 clinical trial investigating efficacy of online treatment for depression in persons with MS
- Worked with and maintained large clinical datasets
- Analyze data in SPSS

**Poster/Abstract Presentations**

- **Hochberg, A.R.,** Riegler, K.E., Guty, E.T., Cadden, M.H., & Arnett, P.A. (2020, April). The role of coping style and cognitive reserve in depression and cognitive functioning in multiple sclerosis. Poster presented at Penn State's Psi Chi Undergraduate Research Exhibition, University Park, PA. (Conference cancelled).

## PROFESSIONAL EXPERIENCE

**Hospital Elder Life Program at Abington Hospital- Jefferson Health** **Abington, PA**
*Volunteer* *May 2017-August 2018*

- Contributed 8 hours a week with a focus on geriatric patients admitted to Abington Hospital-Jefferson Health
- Interacted with patients and performed various social/physical activities to mitigate loss of cognitive and physical functions that could arise during hospitalization
- Assisted hospital staff as requested and worked with them to pursue common patient-related goals

**Shadowed Timothy Witham, M.D.** **Baltimore, MD**
*Neurosurgeon at The Johns Hopkins Hospital* *June, 2017/June, 2019*

- Shadowed for 20 hours over 2 days (on both occasions)
- Observed clinical assessments and postoperative follow-up appointments
- Viewed 3 surgeries (2 variations of spinal fusion, and part of a brain surgery procedure)
- Gained deeper understanding of role of a surgeon and valuable experience in a large hospital setting

**Shadowed Joshua Rabinowitz, D.O.** **Paoli, PA**
*General Pediatrician at Paoli Hospital* *July, 2017*

- Shadowed for 7 hours
- Observed routine examinations over a variety of patients
- Learned more about primary care and general practices

## LEADERSHIP, AND ACTIVITIES

**The Pennsylvania State University Marching Blue Band** **University Park, PA**
*Guide, trombonist* *August 2016-Present*

- With team of four, responsible for leading 33 other trombonists in understanding expectations and traditions of the Blue Band
- Maintained high standards of musicality, memorization, and uniformity
- Acted as liaison between staff and section
- Performed before 100,000 people each week and represented Penn State on multiple trips

**Jewish Relief Agency** **Philadelphia, PA**
*Volunteer* *May 2019-August 2019*

- Contributed 4 hours on one Sunday each month
- Packed and delivered boxes of food to struggling families in the Philadelphia and Greater Philadelphia Area

**Penn State IFC/ Panhellenic Dance Marathon (THON)** **University Park, PA**
*Operations Committee Member* *October 2017-Present*

- THON is a student-run philanthropy, committed to enhancing the lives of children and families impacted by childhood cancer. Its yearlong fundraising efforts culminate in a 46-hour dance marathon.
- Worked with over 30 committee members to clean and maintain facilities in Bryce Jordan Center during dance marathon
- Assisted in other events to ensure smooth execution of THON weekend activities (e.g. cleaning dancer mats and preparing and cleaning Bryce Jordan Center)

## AWARDS:

- The Schreyer Honors College- Academic Excellence Scholarship *Fall 2016-Present*
- Dean's List *Fall 2016-Present*
- Blue Band Academic Achievement Award *Fall 2017*