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COPING STYLE MODERATES THE EFFECT OF PAIN ON DEPRESSION IN MULTIPLE SCLEROSIS: A POSSIBLE TARGET FOR INTERVENTION

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Abstract

Objective. The present study examined coping style as a possible moderator in the relationship between pain and depression in persons with multiple sclerosis (PwMS).

Methods. Fifty-four PwMS completed a comprehensive neuropsychological test battery and psychosocial questionnaires that assessed physical, cognitive, and emotional functioning. Using four pain indices (i.e., average pain, current pain, pain intensity composite, and pain interference composite) from the Brief Pain Inventory (BPI), an overall pain index was created to capture a more comprehensive index of individuals' overall pain intensity and interference. The COPE questionnaire was used to derive three coping indices: active coping, avoidant coping, and a composite cope index that accounts for the relative contributions of both active and avoidant coping. The Beck Depression Inventory-Fast Screen (BDI-FS) was used to measure depression. A series of hierarchical linear regressions were conducted with depression as the outcome variable. Overall pain, each conceptualization of coping style, and their interactions were included as predictors. Disability status, measured with the Expanded Disability Status Scale (EDSS), and previous treatment for depression were included as covariates in the final analyses.

Results. Regression analyses revealed that the interactions between overall pain and each conceptualization of coping were significant (p = .001-.003). Simple effects tests revealed that overall pain only predicted depression in PwMS with low active coping (p < .001), high avoidant coping (p < .001), and low composite coping index (i.e., less adaptive coping; p < .001). Overall pain did not predict depression in PwMS who utilized more active coping, less avoidant coping, or a combination of the two represented by the composite cope index.

Conclusion. Coping style moderated the relationship between pain and depression in PwMS. More specifically, we found that pain predicted depression in PwMS who utilized more avoidant and less active coping strategies. Overall, these findings suggest that helping PwMS develop more active coping skills while relying less on avoidant coping may help limit the negative impact of pain on depression. Interventions aimed to improve coping style may be effective in enhancing the ability to manage pain and, subsequently, improve depression outcomes in MS.

Keywords: multiple sclerosis, pain, depression, coping

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Introduction

Multiple Sclerosis and Depression

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system that results in debilitating sequelae including cognitive impairment, physical disability, fatigue, pain, and, most notably, depression ((Arnett, Barwick, & Beeney, 2008). Depression is highly prevalent and affects up to 50% of persons with MS (PwMS) in their lifetime (Chwastiak et al., 2002; Feinstein, 2004; Sadovnick et al., 1996; Patten & Metz, 1997; Mohr, Hart, Julian, & Tasch, 2007), compared to the 10-15% lifetime prevalence in the general population (American Psychiatric Association, 1994). Comparable to the prevalence of cognitive sequelae observed in MS, depression also has significant negative implications for MS disease-related outcomes, including disease severity and progression, medication adherence (Bruce, Hancock, Arnett, & Lynch, 2010), and quality of life (Arnett & Strober, 2014; Arnett, Barwick, et al., 2008; Fruewald, Loeffler-Stastka, Eher, Saletu, & Baumhacki, 2001). Several studies found that cognitive impairment, physical disability, elevated perceived stress, and lack of social support were associated with an increased risk for depression in MS (Arnett, Barwick, et al., 2008; Arnett & Strober, 2014). However, previous studies investigating the association between pain, another common sequelae of MS, and depression are limited and findings less robust (Arnett, Barwick, et al., 2008). Accordingly, the present study aims to examine the association between pain and depression and the potential moderating role coping style plays in this relationship, given the limited research in this area.

Multiple Sclerosis and Pain

Similar to depression, pain is frequently endorsed by PwMS, ranging from acute (e., trigeminal neuralgia, Lhermitte's sign, painful tonic spasms, optic neuritis) to chronic (i.e., low back pain, dysesthesia, spasms, extremity pain and tension; Stenager, Knudsen, & Jensen, 1995; O'Connor, Schwid, Herrmann, Markman, & Dworkin, 2008). According to a study by Brichetto, Uccelli, Mancardi, & Solaro (2003) investigating the frequency of prescribed medications to treat major MS symptoms, pain was identified as the most commonly treated symptom in MS. Additionally, the estimated lifetime prevalence of pain in PwMS ranges from 29% to 86%, depending on the method used to define and assess pain (O'Connor et al., 2008; Solaro et al., 2004). More recent studies found that between 67% to 75% of PwMS experience pain in their lifetimes (Drulovic et al., 2015; Alschuler, Ehde, & Jensen, 2013b). Not only is pain extremely common in PwMS, but the pain that PwMS endorse is also fairly severe. For instance, Alschuler et al. (2013b) found that approximately 40% of a community sample of PwMS endorsed pain of moderate to severe intensity. Further, pain adversely affects MS-disease severity, quality of life, disability status (Goischke, 2019), functional ability in the workplace and completing household responsibilities, as well as level of fatigue and depression in PwMS (O'Connor et al., 2008; Ehde et al., 2003). However, pain remains infrequently addressed by healthcare providers (Ehde, Osborne, Hanley, Jensen, & Kraft, 2006; Newland, Naismith, & Ullione, 2009). Despite its prominence, severity, and interference in many facets of life, pain in MS is understudied, relative to other sequelae, such as depression or cognitive impairment.

Pain and Depression in Multiple Sclerosis

Pain and depression frequently co-occur in MS. Despite the comorbidity of pain and depression in chronic pain samples and the general population (Graham-Engeland, Zawadzki,

Slavish, & Smyth, 2016; Lumley et al., 2011), the prevalence of comorbid pain and depression in MS has been found to be relatively low, observed in 6-19% of the PwMS (Alschuler, Ehde, & Jensen, 2013a). However, the presence of pain in MS may exacerbate the presence and severity of depression, and vice versa, as observed in the chronic pain literature more broadly (Alschuler et al., 2013b, 2013a; Graham-Engeland et al., 2016; Lumley et al., 2011). In a study examining the biopsychosocial correlates of pain in a community-based sample of PwMS, Ehde and colleagues (2003) found that the risk (prevalence odds ratio = 2.03) for depression is doubled in PwMS who endorse pain, compared to PwMS with no pain. A more recent study revealed that PwMS who endorsed pain of at least moderate severity were approximately five times more likely to meet the criteria for a major depressive episode than PwMS without pain (Alschuler et al., 2013b). Further, depending upon the criteria used to define pain and depression, between 67% and 77% of PwMS who met criteria for depression also endorsed pain of moderate severity or worse (Alschuler et al., 2013a, 2013b). Given the debilitating nature of pain and depression separately, it is not surprising that PwMS with comorbid pain and depression experience an additive negative impact on mental health and quality of life. However, to address and alleviate the significant compounded risk of having MS, pain, and depression, these results underscore the need for continued exploration into this relationship, to ultimately identify potentially modifiable factors to target in interventions.

Factors Moderating Depression Outcomes in Multiple Sclerosis

Although pain has also been identified as a common and debilitating sequela of MS, the comorbid relationship observed between pain and depression has been shown to be less robust in MS samples (Alschuler et al., 2013a; Arnett et al., 2008). This weak finding is inconsistent

with the literature more broadly, which typically demonstrates a strong positive association between chronic pain and depression and emotional distress (Graham-Engeland et al., 2016; Lumley et al., 2011; Banks & Kerns, 1996). To explain this discrepancy, Arnett et al. (2008) suggested that there may be factors moderating the relationship between pain and depression in MS. Therefore, in a proposed model of depression in MS, Arnett, Barwick, and colleagues (2008) identified coping style (i.e., avoidant versus active) as one possible moderator between pain and depression in PwMS. Yet, little research has been done to investigate the role coping may play in moderating the relationship between pain and depression specifically in MS samples.

In response to stress, individuals engage in various coping strategies that can be adaptive or maladaptive to manage the psychological and behavioral effects of a stressor (Carver, Scheier, & Weintraub, 1989; Ukueberuwa & Arnett, 2014; Rabinowitz & Arnett, 2009). Generally, active coping has been shown to be more adaptive: individuals who, when faced with stress, take action, exercise restraint and plan responses, seek social support, and suppress attention or involvement in competing activities tend to be more effective in overcoming stress. Specifically, those who rely on active coping report having less depression (Aikens et al., 1997; Arnett et al., 2002; Mohr et al., 1997; Rabinowitz & Arnett, 2009), less cognitive impairment (Ukueberuwa & Arnett, 2014), better psychological well-being (Foley, Bedell, LaRocca, Scheinberg, & Reznikoff, 1987; Grech et al., 2018; Jean, Paul, & Beatty, 1999; Warren, Warren, & Cockerill, 1991), better adjustment to illness-related stressors (Pakenham, 1999; Pakenham, Stewart, & Rogers, 1997), and overall better quality of life (Goretti et al., 2009; Schwartz, 1999). In contrast, avoidant coping, which is comprised of denial, venting and

focusing on emotions, and disengagement from goal attainment, has been shown to be associated with worse psychosocial outcomes including depression, psychological distress, and poorer quality of life, especially in individuals with more chronic health conditions like MS (Aikens et al., 1997; Arnett et al., 2002; Rabinowitz & Arnett, 2009; Mohr et al., 1997; Ukueberuwa & Arnett, 2014; Grech et al., 2018; Goretti et al., 2009; Carver et al., 1989; Foley et al., 1987).

Given the association between active coping and positive psychosocial outcomes, it follows that a more adaptive, problem-focused approach coping style (i.e., high active coping and/or low avoidant coping) may reduce the effects of and protect against the stressful nature of MS sequela, including, but not limited to, pain, cognitive dysfunction, fatigue, disability, and anxiety, thus, improving overall quality of life (Ukueberuwa & Arnett, 2014; Rabinowitz & Arnett, 2009; Grech et al., 2018; Goretti et al., 2009; McCabe & McKern, 2002). Indeed, there is already some evidence to support the protective effects of active coping in PwMS. For example, in a longitudinal analysis of coping style as a moderator between cognitive dysfunction and depression in MS, researchers found that the relationship between cognitive dysfunction and depression was dependent upon coping style. Specifically, cognitive impairment was associated with depression when avoidant coping was utilized, while active coping was found to buffer against cognitive impairment and reduced risk for depression (Rabinowitz & Arnett, 2009). In another study investigating the potential moderating effect of coping style in the relationship between fatigue and cognitive performance in MS, Ukueberuwa and Arnett (2014) found that PwMS with greater fatigue who utilized less avoidant (adaptive) coping performed better on cognitive tasks, relative to PwMS who demonstrated high avoidant (maladaptive) coping. These

results provide evidence to support that active coping can protect against the burden associated with MS-related sequelae and lead to more positive functional and psychosocial outcomes. Taken together, it is possible that the protective nature of high active coping and low avoidant coping may extend to other physical consequences of MS, such as pain, which is a common source of stress (O'Connor et al., 2008; Solaro et al., 2004; Drulovic et al., 2015; Alschuler et al., 2013b) and contributes to depression symptomatology in MS and the population more generally (Alschuler et al., 2013a, 2013b; Ehde et al., 2003; Graham-Engeland et al., 2016; Lumley et al., 2011).

To date, the possible moderating effect of coping style on the relationship between pain and depression in MS has not been investigated. With the above considerations in mind, the present study examined whether coping style (active and avoidant) moderates the relationship between pain and depression in MS. Overall, the purpose of this study was to expand the literature on depression in MS, with a particular focus on pain and psychological moderators, given the lack of research in this area. Investigating the interaction between pain and coping style may aid in identifying possible targets (e.g., coping style) for future interventions to manage the physical and psychosocial burdens related to MS (Grech et al., 2018; Schwartz, 1999). This study also represents a test of a prediction outlined in Arnett, Barwick, and Beeney's (2008) model of depression in MS.

Hypotheses:

Hypothesis 1: PwMS with high pain will endorse more depression symptomatology, compared to PwMS with low pain.

Hypothesis 2: Coping style will moderate the relationship between pain and depression in PwMS.

H2a) The interaction of avoidant coping (maladaptive) and pain will explain significant variance in depression outcomes in PwMS, beyond the impact of the individual predictors. More specifically, PwMS with high pain levels and high avoidant coping will endorse *greater* depression symptomatology relative to those with high pain and less avoidant coping. It is hypothesized that the negative effects of pain and avoidant coping style will be additive and result in worse depression outcomes in PwMS.

H2b) The interaction of active coping (adaptive) and pain will explain significant variance in depression outcomes in PwMS, beyond the impact of the individual predictors, such that PwMS with high pain levels and high active coping will endorse significantly *less* depression symptomatology relative to those with high pain and less active coping. It is hypothesized that active coping will buffer and protect PwMS against the deleterious effects of pain on depression and result in better psychosocial outcomes.

H2c) The interaction of the Composite Coping Index and pain will explain significant variance in depression outcomes in PwMS, beyond the impact of the individual predictors, such that PwMS with high pain levels and a high Composite Coping Index, which is indicative of more adaptive coping, will endorse significantly *less* depression symptomatology, relative to those with high pain and a low Composite Coping Index (i.e., less adaptive coping).

Methods

Participants

Individuals diagnosed with MS by board-certified neurologists using the revised McDonald criteria set forth by Polman et al. (2011) were recruited from the greater Pennsylvania area to participate in a longitudinal study investigating the cognitive, emotional, and social sequelae related to MS. Exclusionary criteria included significant history of substance abuse; current or previous nervous system disorder other than MS; severe sensory impairment that could impede the testing procedures; (d) developmental history of Attention-Deficit/Hyperactivity Disorder (ADHD) or learning disability; (e) significant medical condition, other than MS that could interfere with cognition or motor function; (f) relapse or use of corticosteroids within 4 weeks of participating in the study; (g) or physical or neurological impairment that would not make the testing feasible. This study was approved by The Pennsylvania State University's Institutional Review Board, and testing procedures followed all relevant laws and institutional guidelines.

The data analyzed in the present study only included participants whose data were collected as part of the third phase of the longitudinal study. Individuals who completed less than 50% of any questionnaire items were excluded from analyses (N = 2), resulting in a final analytic sample size of N = 54.

Fifty-four PwMS (16 male; 38 female) were included in the final analyses of the current study. With a mean age of 52.57 (SD = 11.44), mean disease duration of 16.33 years (SD = 8.56), and Expanded Disability Status Scale (EDSS) score of 4.38 (SD = 1.66), this MS sample can be characterized as a chronic population with moderate disability. The most prominent course

type exhibited in this sample was relapsing-remitting (*N* = 39), followed by secondary progressive (*N* = 12) and primary progressive (*N* = 3) course types.

Approximately 81% (n = 44) of the PwMS endorsed experiencing some level of pain within twenty-four hours of testing. When compared to sample of healthy controls (HCs; see Arnett, Smith, Barwick, Benedict, & Ahlstrom, 2008 for sample characteristics), 44% (*n* = 24) of the PwMS reported significantly more pain (> 1.5 SD above the mean for HCs) than healthy controls. These prevalence rates are consistent with what previous studies have found when PwMS were screened for pain (Martinelli Boneschi et al., 2008; Solaro et al., 2004; Alschuler et al., 2013b; Stenager et al., 1995). Also comparable to previous studies that examined the prevalence of depression in MS (Sadovnick et al., 1996; Patel & Feinstein, 2017), approximately one-third of the sample (*n* = 15) met clinical criteria for depression (i.e., BDI-FS score $\geq$ 4; Strober & Arnett, 2015). Thirty-three PwMS (61% of the sample) reported receiving treatment for depression. See Table 1 for additional information on the demographic and disease-related variables examined.

[Insert Table 1 About Here]

Measures

Pain.

The Brief Pain Inventory-Short Form (BPI-SF; Cleeland, 1991) was administered to assess pain intensity and the degree to which the pain interferes with daily functioning in this study (Cleeland & Ryan, 1994). As one of the most widely used self-report clinical tools to assess pain and its impact, the BPI-SF is considered a standard for assessing pain in clinical and research settings (Cleeland, 2009). To assess pain intensity, PwMS rated their pain at its worst in the last

24 hours, at its least in the last 24 hours, on average, and current pain at the time of the assessment, using an 11-point visual analog scale (VAS) that ranged from 0 to 10 (0 = "*No Pain",* 10 = "*Pain as Bad as You Can Imagine"*). Average pain and current pain indices were created based on their respective single-item intensity ratings. Additionally, a pain intensity composite was derived by taking the average of the four aforementioned pain intensity ratings collected (Cleeland, 2009). The use of individual and combined pain intensity items to assess pain has been supported in recommendations by the Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials (IMMPACT; Turk et al., 2003, 2006; Dworkin et al., 2005, 2008) and the FDA Draft Guidance for Industry: Patient-Reported Outcome Measures (Food and Drug Administration, 2009).

The four pain intensity items have demonstrated good internal consistency with a Cronbach's alpha ranging from 0.80 to 0.87 in individuals with metastatic cancer (Cleeland & Ryan, 1994). Test-retest reliabilities of the pain intensity items have also been evaluated in a variety of pain populations (e.g., cancer, osteoarthritis, coronary artery bypass grafts, unspecified, etc.). Depending on the population examined, the pain intensity composite demonstrated sufficient test-retest reliability with intraclass correlation coefficients (ICC) falling greater than 0.72 (Mendoza, Mayne, Rublee, & Cleeland, 2006; Mendoza et al., 2004; Radbruch et al., 1999).

Participants were also asked to rate how much their pain has interfered with their daily functioning and feelings (e.g., general activity, walking, work, mood, enjoyment of life, relations with others, and sleep), on a 0-10 VAS scale where 0 = "*No Interference*" and 10 = "*Complete Interference*" (Cleeland, 2009). A pain interference composite was derived by calculating the

mean of the interference items, excluding the mood item to avoid any confounds given that the outcome variable of interest is depression. The pain interference composite, including all seven items, has been found to demonstrate excellent internal consistency in an MS population (Cronbach's alpha = 0.93; Ehde, Nitsch, & Smiley, 2015). When examining test-retest reliability in other pain populations, studies found that the pain interference composite demonstrated good test-retest reliability (ICCs > 0.81; Mendoza et al., 2004; Mendoza et al., 2006).

The four pain indices (i.e., average pain, current pain, pain intensity composite, and pain interference composite) were all highly intercorrelated, (r = 0.80-0.95, p < .001). Due to the multicollinearity of these indices, an "overall pain" composite was defined as the mean of z-scores of each pain index, to capture a more comprehensive index of individuals' overall pain intensity and interference. This composite is subsequently referred to as Overall Pain.

Coping Style.

The 52-item Coping Orientation to Problems Experience (COPE) Questionnaire (Carver et al., 1989) was administered to assess dispositional coping styles employed in response to stress (i.e., pain). In the current study, coping style was operationalized as either Active or Avoidant, based on six COPE scales. The individual subscales that comprised the Active Coping index were Active Coping, Planning, and Suppression of Competing Activities. Behavioral Disengagement, Mental Disengagement, and Denial subscales were included in the Avoidant Coping index. The Active and Avoidant Coping indices are not significantly correlated with each other, r = -.11, p = .42, which supports Rabinowitz and Arnett's (2009) claim that these indices are relatively not mutually exclusive (i.e., high on one index and low on the other). Therefore, it is possible for an individual to utilize a combination of both active and avoidant strategies,

resulting in high index scores on both indices (Rabinowitz & Arnett, 2009; Ukueberuwa & Arnett, 2014). Individuals may also utilize similar levels of avoidant coping, yet different levels of active coping, and vice versa, which yields different combinations of active and avoidant index scores (Rabinowitz & Arnett, 2009).

To account for the relative contributions of both active and avoidant coping indices, the Composite Coping Index was derived by taking the difference between the z-scores of an individual's active coping index and avoidant coping index (Rabinowitz & Arnett, 2009). Greater Coping Composite Index scores indicate more adaptive (i.e., more active, less avoidant) coping skills. The use of the Composite Coping Index was supported by Rabinowitz and Arnett (2009), who concluded that this coping composite predicted depression better than the active and avoidant coping indices individually.

Depression.

The Beck Depression Inventory-Fast Screen (BDI-FS) is a seven-item self-report questionnaire used to measure depressive symptoms, including dysphoria, anhedonia, negative cognitive-related symptoms, and suicidal ideation, in medical populations (Beck, Steer, & Brown, 2000). Unlike the full 21-item Beck-Depression Inventory-II (Beck, Steer, & Brown, 1996), the BDI-FS does not include the neurovegetative symptoms of depression (e.g., fatigue, sexual dysfunction, etc.), which often overlap with the clinical signs and symptoms experienced by PwMS (Benedict, Fishman, McClellan, Bakshi, & Weinstock-Guttman, 2003; Strober & Arnett, 2015). Therefore, the BDI-FS has been shown to be particularly useful and highly valid when assessing depression in PwMS (Benedict et al., 2003; Strober & Arnett, 2015). Using a four-point scale, where 0 indicates an absence of problems and 3 represents the most severe depressive

symptomatology, participants were asked to rate the degree to which each statement describes how they have been feeling in the past two weeks. The BDI-FS total score is the sum of all selected statements. A higher total score was indicative of greater depression levels.

Data analyses

The Statistical Package for Social Sciences (SPSS) version 27 was used for all data analyses (IMB SPSS Statistics for Macintosh, Version 27.0). To test the hypothesis that coping moderates the relationship between pain and depression, data were analyzed using hierarchical linear regression analyses. Missing data were accounted for by dividing the total number of survey items by the sum of the original items, multiplied by the sum of the missing data recoded as zero. A sample of healthy controls (Arnett, Smith, et al., 2008) was used as the normative reference group when calculating all *z*-scores. Additionally, all covariates and predictor variables were centered on their respective means for final analyses.

Covariates. Demographic and disease-related variables including age, sex, years of education, disease duration, and level of neurological disability (EDSS) were examined as potential covariates. Disability status was the only demographic variable significantly correlated with depression (BDI-FS) and was therefore retained as a covariate in the final analyses, $r(52) = .27$, $p = 0.05$. Prior depression treatment was also retained as a covariate in the final analyses, as it was found to be significantly correlated with depression (BDI-FS), $r(52) = -.32$, $p = .019$.

Analysis 1. The significant covariates (EDSS and prior depression treatment), Overall Pain, Active Coping, and their interaction were entered into a hierarchical linear regression analysis with depression (BDI-FS) as the dependent variable.

Analysis 2. The significant covariates (EDSS and prior depression treatment), Overall Pain, Avoidant Coping, and their interaction were entered into a hierarchical linear regression analysis with depression (BDI-FS) as the dependent variable.

Analysis 3. The significant covariates (EDSS and prior depression treatment), Overall Pain, Composite Coping Index, and their interaction were entered into a hierarchical linear regression analysis with depression (BDI-FS) as the dependent variable.

Simple Effects. Simple effect tests were used to clarify the pattern of any significant interactions. The effect of Overall Pain on depression was tested at high and low (1 SD above and below the mean) levels of Active Coping, Avoidant Coping, and the Composite Coping Index.

Results

Analysis 1

Controlling for disability burden (EDSS) and previous treatment for depression, a model that includes Overall Pain, Active Coping, and the product of Overall Pain and Active Coping significantly predicted depression, $F(5, 48) = 10.82$, $p < .001$. As illustrated in Table 2, there were significant main effects of both Overall Pain ($t(50) = 3.70$, $p = .001$, 95% CI [0.45, 1.50]) and Active Coping ($t(49) = -2.94$, $p = .005$, 95% CI [-0.29, -0.05] on depression (BDI-FS). Further, there was a significant interaction between Overall Pain and Active Coping, $t(48) = -3.15$, $p = .003$, 95% CI [-0.12, -0.03], accounting for approximately 10% of the variance in depression above and beyond the variance captured by the main effects of Overall Pain and Active Coping. Simple effects tests revealed that Overall Pain predicted depression in PwMS with low Active

Coping (1 *SD* below the mean), $t(48) = 5.01$, $p < .001$, $\eta_p^2 = .34$)[1], but not in those with high Active Coping (1 *SD* above the mean), $t(48) = 1.35$, $p = .18$, $\eta_p^2 = .04$. Therefore, results suggest that, after accounting for level of disability and prior depression treatment, pain predicts depression only in PwMS with low Active Coping. The nature of all interactions is illustrated in Figure 1.

Analysis 2

Controlling for disability burden and previous treatment for depression, a model that includes Overall Pain, Avoidant Coping, and the product of Overall Pain and Avoidant Coping significantly predicted depression, $F(5, 48) = 15.59$, $p < .001$. The main effects of both Overall Pain ($t(50) = 3.70$, $p = .001$, 95% CI [0.45, 1.50]) and Avoidant Coping ($t(49) = 4.71$, $p < .001$, 95% CI [0.22, 0.54]) were significant. Additionally, these main effects were qualified by a significant interaction between Overall Pain and Avoidant Coping, $t(50) = 3.14$, $p = .003$, 95% CI [0.04, 0.18], accounting for approximately 8% of the variance in depression above and beyond that accounted for by the main effects of Overall Pain and Avoidant Coping. Simple effects tests revealed that Overall Pain predicted depression in PwMS with high Avoidant Coping (1 *SD* above the mean), $t(48) = 4.92$, $p < .001$, $\eta_p^2 = .34$, but not in those with low Avoidant Coping (1 *SD* below the mean), $t(48) = 0.57$, $p = .57$, $\eta_p^2 = .007$. Overall, these results suggest that, when controlling for disability status and prior depression treatment, pain predicts depression only in PwMS with high Avoidant Coping.

Analysis 3

[1] η_p^2 = partial eta squared; small = .01, medium = .06, large = .14 (Field, 2013)

Controlling for disability burden and previous treatment for depression, a model that includes Overall Pain, the Composite Coping Index, and the product of Overall Pain and the Composite Coping Index significantly predicted depression, $F(5, 48) = 19.93$, $p < .001$. The main effects of Overall Pain ($t(50) = 3.70$, $p = .001$, 95% CI [0.45, 1.50]) and Composite Coping Index ($t(48) = -5.51$, $p < .001$, 95% CI [-1,44, -0.67) were significant. Additionally, the interaction between Overall Pain and Composite Coping Index was significant, $t(48) = -3.58$, $p = .001$, 95% CI [-0.44, -0.12], accounting for approximately 9% of the variance in depression above and beyond what was accounted for by the main effects of Overall Pain and Composite Coping Index. Simple effects tests revealed that Overall Pain predicted depression in PwMS with low Composite Coping Index scores (1 *SD* below the mean), $t(48) = 5.27$, $p < .001$, $\eta_p^2 = .37$, but not in those with high Composite Coping Index scores (1 *SD* above the mean), $t(48) = 0.92$, $p = .36$, $\eta_p^2 = .02$. Taken together, these results suggest that pain predicts depression only in PwMS with low Composite Coping Index scores (i.e., less adaptive coping strategies).

[Insert Table 2 About Here]

[Insert Figure 1 About Here]

Discussion

Pain and depression are both highly prevalent and often co-occur in PwMS, yet their relationship is poorly understood. Given the high prevalence of pain and depression, separately, in MS (Alschuler et al., 2013b; Chwastiak et al., 2002; Drulovic et al., 2015; Feinstein, 2004; Mohr et al., 2007; O'Connor et al., 2008; Patten & Metz, 1997; Sadovnick et al., 1996; Solaro et al., 2004), the purpose of the present study was two-fold. First, we examined the

relationship between pain and depression in a community sample of PwMS to determine if those with higher levels of pain are at an increased risk for depression than those with lower levels of pain. The results of the current study were consistent with this hypothesis, in that greater pain was associated with greater depression in our MS sample.

Secondly, this study examined how coping style can affect the functional outcomes in MS, by exploring how coping style interacts with pain to predict depression in MS. We predicted that our sample of PwMS with greater pain who utilize more active coping would report fewer depressive symptoms compared to those who utilize less active coping strategies. We also predicted that PwMS with greater pain who utilize more avoidant coping, relative to those who utilize less avoidant coping, would exhibit higher levels of depression in our sample. Further, we hypothesized that the use of more active coping and less avoidant coping would protect against the deleterious effects of pain on depression in MS. Consistent with these predictions, we found that pain predicted depression in PwMS who utilized more avoidant and less active coping strategies, whereas in those who utilized less avoidant and more active coping strategies, pain did not predict depression. These results suggest that helping PwMS develop more active coping skills, while relying less on avoidant coping, may help limit the negative impact of pain on depression. Therefore, coping style may be a useful target of intervention to ameliorate functional, psychosocial outcomes in MS.

Clinical Implications

Coping style may serve as a modifiable target of psychotherapeutic interventions that could have beneficial effects on both pain and depression to improve the quality of life and overall biopsychosocial functioning of PwMS. Typically, PwMS are prescribed multiple medications,

often accompanied by adverse effects, to help manage their pain with perceived effectiveness estimated to be around 50% (Archibald et al., 1994; Heckman-Stone & Stone, 2001; Hadjimichael, Kerns, Rizzo, Cutter, & Vollmer, 2007; Aboud & Schuster, 2019; Claudio Solaro & Messmer Uccelli, 2011). The present study demonstrates that helping individuals to modify the way they cope, with an emphasis on maximizing active coping skills, while decreasing avoidant coping, could serve as a less invasive alternative to manage pain and improve prognosis in MS (Mohr & Goodkin, 1999; Rabinowitz & Arnett, 2009; Ukueberuwa & Arnett, 2014). There is evidence to support that manual-driven psychotherapeutic interventions, such as stress management therapy for MS (SMT-MS; Mohr, 2010a; Mohr, 2010b) and stress inoculation training (Foley et al., 1987), aimed at teaching PwMS problem-focused, active coping skills, are effective in enhancing the ability to manage stress and treat depression in MS (Mohr & Goodkin, 1999; Siegert & Abernethy, 2005).

Given the high prevalence of depression in MS (around 50% over the lifetime), identifying effective interventions that target risk factors for depression is imperative. The present study highlights that one possible way to manage depression is through effective pain management. The SMS-MS program developed by Mohr (2010a, 2010b) that is specifically tailored to PwMS includes an optional pain management module. Thus, this guide may be optimal in targeting coping style and pain, in tandem, which, ideally, will improve depression outcomes, beyond what those observe when coping or pain are addressed in treatment alone. Additional interventions found to effectively reduce pain and improve mood and physical outcomes in individuals with chronic pain conditions include mindfulness-based stress reduction (MBSR; Burns et al., 2021) and emotional awareness and expression therapy (EAET;

Lumley et al., 2021; Lumley & Schubiner, 2019). Future work exploring the effectiveness of these alternative interventions in reducing pain and improving psychosocial outcomes specifically in PwMS with pain is warranted.

Limitations

One limitation of the present study is that the sample was comprised of only White or European Americans with MS. Therefore, the generalizability and intervention implications of these findings are limited to White PwMS, necessitating further exploration into coping style as a moderator in the relationship between pain and depression in more diverse samples of PwMS. Another possible limitation of this study is the use of depression as a continuous outcome variable, instead of using a diagnostic interview or a validated cutoff score for depression on the BDI-FS (Strober & Arnett, 2015) to differentiate PwMS meeting criteria for major depressive disorder from those with subclinical depressive symptoms (Rabinowitz & Arnett, 2009). Although examining depression continuously allows us to evaluate PwMS who experience subthreshold, but still significant, depressive symptoms and better understand the implications of these symptoms, these findings may not apply to PwMS formally diagnosed with major depression. Still, as Figure 1 shows, PwMS high in overall pain who showed low active coping, high avoidant coping, and a low coping composite index had BDI-FS scores that exceeded the typical clinical cutoff (≥ 4) that is highly diagnostic of major depression. Additionally, the cross-sectional, correlational design of this study is a practical limitation that needs to be considered. Longitudinal research examining the role of coping style as a moderator between pain and depression with a larger sample is a necessary first step in addressing the casual nature of this relationship.

Conclusions

The results of this study support that coping style moderates the impact of pain on depression in MS. Overall, greater pain was associated with greater depression in PwMS. Additionally, PwMS who reported a higher level of overall pain had higher levels of depression if they also relied more on avoidant coping and less active coping, while those who used less avoidant coping and more active coping showed lower depression levels, regardless of pain level. These results may inform future research and clinical interventions identifying and targeting modifiable factors, such coping, to reduce pain and depression and improve quality of life in persons with MS.

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APPENDIX

TABLES AND FIGURES

Table 1

Table 2

Figure 1

Table 1. Descriptive statistics for demographic, disease-related characteristics, and predictor variables (N = 54)

	Mean	SD	Range
Sex (% Female, *N*)	70.40 (38)	--	--
Age (years)	52.57	11.44	27-76
Education (years)	14.80	1.97	12-19
EDSS	4.38	1.66	0-8
Course Type (% relapsing-remitting, *N*)	72.22 (39)	--	--
Disease duration (years)	16.33	8.56	1.42-38.17
BPI			
Pain experienced within 24 hours (% yes)	53.70	--	--
Current pain	2.33	2.56	0-8
Average pain within 24 hours	2.85	2.52	0-8
Pain intensity composite within 24 hours	2.56	2.37	0-8
Pain interference composite (no mood) within 24 hours	2.40	2.63	0-8.83
Overall Pain Index (z-scores)	1.46	1.98	-0.6-5.75
Coping			
Active Coping	32.44	7.54	13-46
Avoidant Coping	20.78	4.71	13-35
Coping Composite Index (z-scores)	-0.84	1.85	-5.59-2.27
BDI-FS	3.02	3.78	0-19

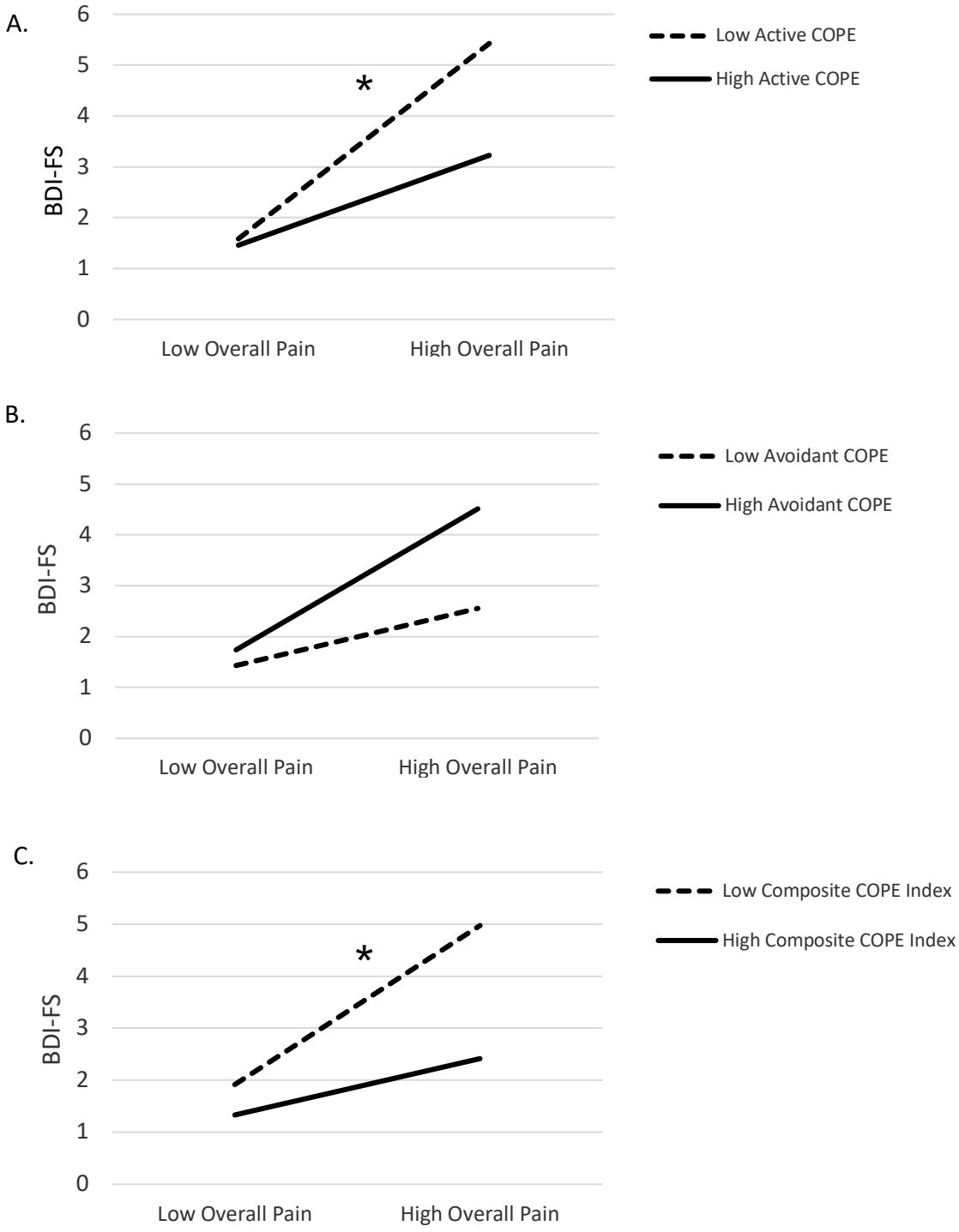
Note. EDSS = Expanded Disability Status Scale. BPI = Brief Pain Inventory. BDI-FS = Beck Depression Inventory-Fast Screen.

Table 2. Summary of Hierarchical Regression Analyses for Overall Pain and Coping Indices Predicting Depression

	Variables entered	*B*	*SEB*	β	R^2	ΔR^2	ΔF	*p*
Active COPE Analysis:								
Step 1	EDSS	0.51	0.30	0.22	0.15	0.15	4.50	n.s.
	Previous Depression Treatment	-2.17	1.01	-0.28	-	-	-	.04
Step 2	Overall Pain Composite	0.97	0.26	0.51	0.33	0.18	13.72	.001
Step 3	Active COPE	-0.17	0.06	-0.34	0.43	0.10	8.63	.005
Step 4	Overall Pain Composite*Active COPE	-0.08	0.02	-0.32	0.53	0.10	9.91	.003
Avoidant COPE Analysis:								
Step 1	EDSS	0.51	0.30	0.22	0.15	0.15	4.50	n.s.
	Previous Depression Treatment	-2.17	1.01	-0.28	-	-	-	.04
Step 2	Overall Pain Composite	0.97	0.26	0.51	0.33	0.18	13.72	.001
Step 3	Avoidant COPE	0.38	0.08	0.47	0.54	0.21	22.18	<.001
Step 4	Overall Pain Composite*Avoidant COPE	0.11	0.04	0.34	0.62	0.08	9.84	.003
Composite COPE Index Analysis:								
Step 1	EDSS	0.51	0.30	0.22	0.15	0.15	4.50	n.s.
	Previous Depression Treatment	-2.17	1.01	-0.28	-	-	-	0.04
Step 2	Overall Pain Composite	0.97	0.26	0.51	0.33	0.18	13.72	.001
Step 3	Coping Style Index	-1.06	0.19	-0.52	0.59	0.26	30.37	<.001
Step 4	Overall Pain Composite*Composite COPE Index	-0.28	0.08	-0.35	0.68	0.09	12.82	.001

Note. The dependent variable for all analyses was the BDI-FS; n.s. = not significant.

Figure 1. Moderation of the relationship between overall pain and depression (BDI-FS) by Active Coping (A), Avoidant Coping (B), and Composite COPE Index (C)



Note. Low and high coping represents the first and third quartiles of the sample distribution respectively. * indicates slope of designated line is significantly different from zero. Relative to their disability status and previous treatment for depression, only PwMS with high overall pain who relied more on avoidant coping or less on active

coping strategies (or the combination of the two represented by the Composite Cope index) exhibited greater levels of depression.