

Pain and affective memory biases interact to predict depressive symptoms in multiple sclerosis

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A large literature supports a direct relationship between pain and depressive symptoms among various patient populations. Patients with multiple sclerosis (MS) frequently experience both pain and depression. Despite this, no relationship between pain and depression has been found in MS. The present investigation explored the relationship between pain and depression in a sample of patients with MS. Consistent with cognitive theories of depression, results supported the hypothesis that pain would only contribute to depression when MS patients exhibited a concomitant cognitive vulnerability. Cognitive vulnerability to depression was measured using a performance based affective memory bias (AMB) task. Patients with high levels of pain and negative AMB reported more depressive symptoms compared to patients with pain and positive AMB. Implications for the identification and treatment of depression in MS are discussed. *Multiple Sclerosis* 2007; 13: 58–66. <http://msj.sagepub.com>

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Patients with multiple sclerosis (MS) frequently experience both pain and depression [1,2]. Point prevalence rates for depression among patients with MS have been estimated at between 14 and 57% [2]. Lifetime prevalence rates for depression are as many as 10 times higher than that of the general population [3]. Depression in MS is associated with overall quality of life, disease course, medication compliance, and cognitive functioning [4–7].

Between 65 and 86% of MS patients report pain at some time during the course of their MS [8,9]. Over 30% of patients report that pain is one of their worst MS symptoms. It is common for MS patients to experience trigeminal neuralgia, tonic seizures, optic neuritis, Lhermitte's sign, dysesthetic pain, back pain, and muscle spasms [10]. Numerous studies have found a link between pain and clinical depression in non-MS patient populations. Estimates of depression among patients with chronic pain range from 10 to 100% [11]. Fishbain *et al.*, reviewed 25 studies examining the relationship between depression and pain. All but two of these studies found a significant relationship [12]. De-

spite this, no relationship between depression and pain has been found in MS [8,13].

MS patients who experience pain may only become depressed if they also possess negative cognitive schemata. Fishbain *et al.*, outlined six studies which examined the role that negative cognitions may play in the development of depression among patients with chronic pain [12]. Five of these studies found evidence supporting the cognitive mediation model. For instance, one study administered a questionnaire that assessed patients' tendencies to use cognitive distortions [14]. Depressed lower back pain patients made more cognitive errors than both non-depressed patients and normal controls. This study concluded that how patients perceive their pain might partially determine whether they exhibit subsequent depression. Similarly, another study found that both pain and cognitive distortions correlate significantly with depression in lower back pain patients [15]. Pain no longer correlated with depression when variance associated with cognitive distortions was removed. Conversely,

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cognitive distortions continued to be correlated with depression when variance associated with pain was removed. These studies suggest that pain may only lead to depression if predisposing cognitive vulnerabilities exist. Tests of affective memory biases (AMBs) are one means of measuring vulnerability to depression.

AMB is defined as the tendency for people in negative moods to recall more negatively valenced information and less positively valenced information. Conversely, people in positive moods recall more positive information and less negative information. Numerous researchers have found evidence for the differential explicit recall of affectively laden words according to mood state [16]. Using an experimental paradigm, Bellew and Hill [17] administered an AMB test to a sample of undergraduates. Subsequently, participants engaged in a depressive mood induction procedure. Participants who recalled more negative words initially were also more likely to exhibit depressive symptoms following the mood induction. The authors concluded that negative cognitive schemata might increase one's vulnerability to depression.

Alloy *et al.* [18] used a high-risk design to test whether non-depressed people with negative AMB would develop subsequent depression. An AMB task was utilized in which participants were required to state 'me' or 'not me' when positive, negative, or neutral words appeared on a computer screen. Participants were then asked to recall as many of the words as they could from memory. Participants at high-risk for developing depression recalled significantly more positive words judged 'not me' and fewer positive words judged 'me' than low-risk participants. Over the course of the study, people in the high-risk group were twice as likely to experience a major or minor depressive episode. This study appears to support the notion that people with AMBs exhibit vulnerability toward depression.

In summary, MS and chronic pain patients are particularly susceptible to depression. Furthermore, MS patients commonly experience chronic pain. The present investigation examined the roles that AMB and pain play in the formation of depression in a sample of patients with MS. Previous findings in the MS literature found no relationship between depression and pain. In contrast, studies examining other patient populations have found a consistent relationship between depression and pain. Discrepant findings in the literature may suggest moderating variables. AMBs may moderate the relationship between pain and depression in MS. MS patients who experience a high degree of pain and exhibit negative recall biases may be more likely to endorse depressive symptoms. Conversely, MS patients with pain who exhibit positive recall

biases may be less likely to report symptoms of depression.

Method

Participants and procedure

A total of 101 patients with definite or probable MS were recruited from an advertisement placed in a newsletter distributed to individuals with MS in Western Pennsylvania, MS support groups in the Central Pennsylvania Region, and flyers distributed in the State College, Pennsylvania community. Patients who contacted the study team were subsequently administered a telephone screening interview to rule out exclusionary criteria (see below). Those participants not excluded were then scheduled for testing. Diagnoses and MS course types were assigned by board-certified neurologists based on established guidelines for research protocols in MS [19,20]. None of the patients included in the current study were experiencing a clinical exacerbation at the time of the evaluation. Participants were not included in the study if they had a history of: (a) neurological disease other than MS; (b) drug or alcohol abuse; (c) developmental learning disability; or (d) visual or motor impairments that would significantly alter test administration procedures. After establishing informed consent, graduate students trained by a licensed clinical neuropsychologist (PA), administered a variety of measures assessing physical, cognitive and emotional functioning. In return for their participation, patients with MS were given \$75 and a brief neuropsychological report outlining their cognitive functioning. Of the 101 patients assessed, three participants were not included in the current study: one had a history of electroconvulsive therapy, one reported a history of stroke after testing was completed, and one patient's diagnosis could not be confirmed. Furthermore, two participants had significant difficulty reading during the AMB test, and two were unable to recall any words at the delay. These patients were not included in analyses. Finally, five participants filled out the pain questionnaire improperly. Four of these participants were contacted by telephone to complete the questionnaire, however, a fifth could not be reached. In total, 64 patients with relapsing-remitting (RR), 27 patients with secondary progressive (SP), and two patients with primary progressive (PP) MS were included in the study. MS patients in this study were predominantly female (84%).

Measures

Chicago Multiscale Depression Inventory

As more traditional measures may overestimate depression in neurological samples [22], the Chicago Multiscale Depression Inventory (CMDI) [21], was used to assess depressive symptomatology in this study. The CMDI has been shown as a reliable and valid measure of depression [21]. The CMDI is a 42-item, five-point Likert-style, self-report measure, which includes 14 mood (sad, glum), evaluative (hated, useless), and vegetative (sluggish, unable to concentrate) items, which comprise each subscale. Consistent with the recommendation of Nyenhuis *et al.* [22], and the precedent set by our prior work [4,23–25], the vegetative scale was not included in analyses. Higher scores on the Mood and Evaluative scales of the CMDI indicated higher levels of depression.

Affective Reading Span Task

The Affective Reading Span Task (ARST) [25], is a modified version of the Daneman and Carpenter test of working memory [26]. The ARST was designed to tax working memory and assess AMB (Figure 1). Participants were instructed to orally read affectively laden sentences presented on a computer screen. Each sentence was followed by either a positive or negative word that matched the affective content of the sentence. Participants were instructed to remember the word after the sentence. After the participant read the affective word following the sentence, a new sentence and word combination was immediately presented. When participants saw a blank screen, they were instructed to recall the affective end words in the preceding block. As the test progressed, participants were asked to recall more end words. On completion of the task, participants were asked to recall as many of the end words as they could remember from all of the blocks. The positive and negative end words used in the ARST were matched for frequency of use in the English language and word length [27]. Moreover, positive and negative end words did not differ significantly by word type (eg, noun, verb, adjective). In total, 28 positive and 28 negative sentence/word combinations were presented. The presentation of positive and negative sentence/word combinations was alternated to reduce the potential influence of positional effects. Initial bias, delay bias, and retention bias indices were utilized as measures of AMB for this investigation. Previous research with this sample has demonstrated that depressed MS patients have

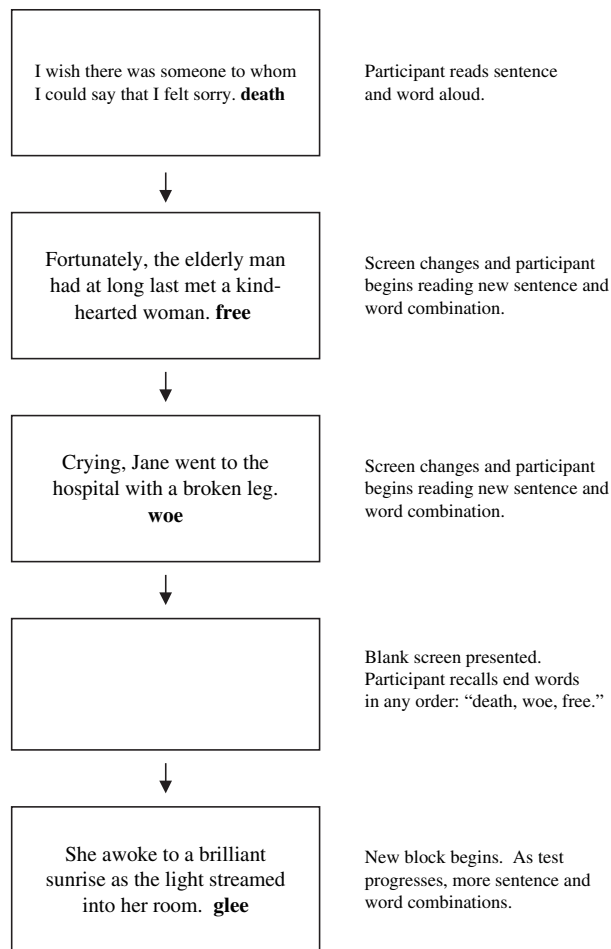


Figure 1 Schematic of the Affective Reading Span Task.

negative initial, delay, and retention biases when compared to non-depressed MS patients [25].

Initial bias

Initial recall bias was calculated by subtracting the number of negative words recalled during the task from the number of positive words recalled.

Delay bias

Delay recall bias was calculated by subtracting the number of negative words recalled at the delay from the number of positive words recalled at the delay.

Retention bias

This index was designed to measure the extent that positive or negative recall changes over time. Retention bias was calculated by dividing the number of positive words recalled at the delay by

the number of positive words recalled during the task. Similarly, the number of negative words recalled at the delay was divided by the number of negative words recalled during the task. Finally, the ratio of negative words retained was subtracted from the ratio of positive words retained.

Brief Pain Inventory

Using a 10-point Likert scale, the Brief Pain Inventory (BPI) assesses patients' pain intensity and pain-mediated interference with daily activities [28]. The BPI has been shown as reliable and valid in clinical populations [29]. Test-retest reliabilities for the instrument are adequate (>0.80) and the measure has good internal consistency (Cronbach's alpha >0.85). The BPI has been validated in pain treatment trials and among various patient populations [30]. For the present study, two BPI questions that assess life enjoyment and mood were excluded from statistical analyses *a priori*. The inclusion of questions assessing mood and enjoyment presented a potential confound because negative mood and lack of enjoyment are the cardinal symptoms of depression. As a result, BPI questions assessing life enjoyment and mood were removed to prevent construct and item overlap between the pain and depression measures administered in this study. Inter-item analysis conducted with this sample of MS patients showed that the remaining questions demonstrated good internal consistency (Cronbach's alpha >0.90). The variable of interest for this study was the total pain score on the BPI.

Expanded Disability Status Scale

The Expanded Disability Status Scale (EDSS) is a measure of MS disease progression and neurological impairment [31]. It is commonly used in both clinical practice and MS research. Participants were asked to rate their functional abilities in a number of different physical domains. Scores on the EDSS range from 0 (no neurological impairment) to 10 (death from MS). Self-report EDSS scales have been found to be highly correlated with neurologists' independent ratings [32].

Beck Depression Inventory

The Beck Depression Inventory (BDI) [33] is one of the most commonly used measures of self-reported depression. It consists of 21 items where participants rate themselves on a 0–3 scale. Higher scores reflect greater depression. The BDI was used as a descriptive adjunct to the CMDI. The BDI includes vegetative symptoms of depression that

overlap with neurological symptoms commonly experienced in MS. As a result, the BDI may overestimate depression in MS and was not included as the dependent variable in interaction analyses [22].

Current estimate of intellectual functioning

Current intellectual functioning [34], was estimated from the Vocabulary subscale of the Shipley Institute of Living Scale.

Data analysis

Pearson correlation was used to examine whether a direct relationship existed between pain and depressive symptoms. Consistent with previous research in MS, it was hypothesized that no direct relationship between pain and depression would be uncovered. Next, we constructed regression models to test the hypothesis that memory bias and pain interact to predict symptoms of depression in MS. First, Pearson correlations examining the relationship between CMDI and measures of age, diagnosis duration, and disability were conducted. Independent sample *t*-tests were conducted to determine the relationship between CMDI and the use of selective serotonin reuptake inhibitors (SSRI). We decided *a priori* that variables significantly related to CMDI would be used as covariates in regression models. CMDI Mood and Evaluative subscales were used as the dependent measures in regression models. Pain and AMB variables were placed in the first block. The interaction term was placed in the second block. It was hypothesized that the interaction would be significant and that follow-up analyses would reveal that pain would only correlate with depression when patients exhibited negative memory biases.

Regression interaction figures were constructed according to commonly accepted guidelines [35]. For each of the interaction figures depicted in this study, negative bias represents scores 1 standard deviation below the mean, and positive bias represents scores 1 standard deviation above the mean. Similarly, pain scores plotted on the *x*-axis represent *z*-score transformations of patients' scores on the BPI. Pain scores of -2 standard deviations were not plotted, as no patient scored 2 standard deviations below the mean. Finally, the *y*-axis, representing Mood or Evaluative subscales of the CMDI, begins at 14, the lowest obtainable score on the subscales.

Table 1 Descriptive statistics for independent, dependent, and demographic variables

Variable	Mean	SD	Minimum	Maximum	Skewness	Kurtosis
Age	7.70	8.84	23.00	65.00	-0.29	0.02
ARS initial bias	0.56	2.59	-6.00	7.00	-0.07	0.29
ARS delay bias	0.00	1.95	-4.00	5.00	0.26	0.19
ARS retention bias	-0.77	11.75	-31.87	33.33	0.40	0.88
BPI pain	25.37	22.39	0.00	78.00	0.62	-0.69
CMDI Mood	23.05	8.67	14.00	48.00	1.07	0.43
CMDI Evaluative	20.44	7.42	14.00	50.00	1.74	3.07
BDI	11.83	7.44	0.00	32.00	0.54	-0.29
Diagnosis duration	10.84	7.90	0.00	37.00	0.74	-0.05
Education	14.30	1.97	10.00	20.00	0.31	-0.48
EDSS	4.59	1.58	0.00	8.00	-0.35	0.36
ShIPLEY Vocabulary	54.18	7.62	23.00	69.00	-1.03	2.66

Positive ARS scores indicate positive recall bias.

Results

Preliminary analyses

Komogorov–Smirnov (K–S) testing revealed that the CMDI Mood and Evaluative subscales were not normally distributed ($P < 0.05$). CMDI Mood and CMDI Evaluative subscales were transformed using a negative inverse function to correct for positive skew and maintain directionality. Subsequent K–S testing with these transformed data revealed no significant normality violations. Table 1 shows means and standard deviations for independent, dependent, and demographic variables. Table 2 shows preliminary analyses that were conducted to determine whether bias, pain, age, disability, intellectual functioning, or diagnosis duration accounted for variance associated with depression in this sample of MS patients. Pearson correlation analyses revealed a significant relationship between the BDI and BPI. However, no significance was found when physical disability, as measured by EDSS, was partialled from the analysis ($r = 0.10$, $P = 0.35$). This suggests that the BDI and BPI both measure overlapping aspects of patients' neurological symptomatology. Consistent with previous reports in the MS literature, no significant relationship was found between pain and depression as measured by the CMDI.

No relationships were found between CMDI and measures of age, disability, intellectual functioning, and diagnosis duration. Independent samples t -tests revealed no significant differences in CMDI Mood ($t(91) = 0.78$, $P > 0.05$) or Evaluative ($t(91) = 1.15$, $P > 0.05$) subscales between patients currently using SSRIs ($n = 29$), and patients not currently using SSRIs ($n = 64$). Similarly, no differences in CMDI Mood ($t(91) = 0.39$, $P > 0.05$) or Evaluative subscales ($t(91) = 0.72$, $P > 0.05$) were found between male and female patients. Finally, we summed the positive and negative correct responses

on the initial portion of the ARS. Previous research has shown a significant relationship between total initial recall and common measures of information processing speed on a Reading Span Task that did not systematically manipulate the affective valence of the sentences and end words [23,24]. In contrast, no significant relationship was found between total initial recall and depression, as measured by the CMDI Mood and Evaluative scales in the present study (both r 's = 0.03). As a result, no covariates were used in subsequent regression models. It may be that including affectively negative sentences and words, as in the present ARS task, improves the overall recall of individuals with greater depressive symptoms to the level of non-depressed patients on this task because they more easily recall the negative words.

Regression interaction analyses

After entering the main effects at step 1 (see Table 3), the interaction of retention bias and pain significantly predicted variance in depression, as measured by the Mood and Evaluative subscales of the CMDI (R^2 change = 0.05, F change = 5.47, $P < 0.05$, and R^2 change = 0.08, F change = 8.74, $P < 0.01$, respectively). Similarly, the interaction of delay bias and pain significantly predicted variance in depression, as measured by the Mood and Evaluative subscales of the CMDI (R^2 change = 0.04, F change = 4.07, $P < 0.05$, and R^2 change = 0.06, F change = 6.17, $P = 0.01$, respectively).

In total, as much as 18% of the variance in depressive symptomatology was accounted for by AMB, pain, and the interaction of AMB and pain. As demonstrated in Figures 2 and 3, patients with negative AMB experienced more depressive symptoms as pain increased. Patients with positive AMB experienced fewer depressive symptoms as pain increased. These results appear to highlight both

Table 2 Correlation table of demographic, independent, and dependent variables

	ARS initial	ARS delay	ARS retention	Age	BPI pain	CMDI Mood	CMDI Evaluation	BDI	Diagnosis duration	Education	EDSS	Shipley Vocabulary
ARS initial	1.00											
ARS delay	0.20	1.00										
ARS retention	-0.05	0.95**	1.00									
Age	0.23*	0.11	0.03	1.00								
BPI pain	0.01	-0.11	-0.12	0.04	1.00							
CMDI Mood	-0.32**	-0.37**	-0.30**	0.06	-0.05	1.00						
CMDI Evaluation	-0.24*	-0.32**	-0.27**	-0.01	0.03	0.77**	1.00					
BDI	0.13	0.21*	0.16	0.42**	0.23*	0.69**	1.00					
Diagnosis duration	0.03	0.08	0.06	0.44**	0.07	0.69**	0.07	1.00				
Education	0.03	0.03	0.00	-0.08	0.00	0.06	0.02	0.19	1.00			
EDSS	-0.01	0.11	0.12	0.30**	0.35**	0.20	0.42**	0.31**	-0.25*	1.00		
Shipley Vocabulary	0.09	0.14	0.11	0.30**	-0.05	-0.10	-0.14	0.13	0.35**	-0.08	1.00	

* $P < 0.05$.

** $P < 0.01$.

ARS initial, delay, and retention bias indices from the Affective Reading Span Task. BPI pain, total pain from the Brief Pain Inventory. CMDI Mood, the Chicago Multiscale Depression Inventory Mood subscale. CMDI Evaluation, the Chicago Multiscale Depression Inventory Evaluative subscale. EDSS, Expanded Disability Status Scale.³¹ Shipley Vocabulary, vocabulary subtest t -scores from the Shipley Institute of Living Scale.³⁴

the potentially deleterious effects of negative AMB and protective effects of positive AMB.

The interaction of initial bias and pain revealed no significant results.

Discussion

Depression and pain are common among patients with MS [2,9]. Most research suggests that the experience of debilitating pain leads to depression [12]. Despite this, no direct relationship has been found between pain and depression in MS. Pain may only lead to depression among MS patients with a predisposing cognitive vulnerability [11]. Various researchers have posited that negative memory biases may represent a vulnerability marker for depression. The current investigation lends support to the hypothesis that pain and AMB interact to predict depressive symptoms in MS. As pain increased, patients with negative biases were more likely to experience depression than patients with positive biases. Specifically, patients with negative biases experienced more depressive symptoms as pain increased; patients with positive biases experienced fewer depressive symptoms with increasing pain. These results underscore the importance of both negative and positive AMB. As commonly posited in the AMB literature, negative biases may increase depressive vulnerability. In contrast, positive biases are rarely discussed in the literature and may play a protective role. Results from the present investigation suggest that MS patients who are able to maintain positive AMB when confronted with debilitating pain, may have exceptional depressive resilience. In short, these individuals may have affective/cognitive traits that highlight an uncanny ability to fend off depression.

Our findings were somewhat modest, therefore, highlighting that numerous other factors probably contribute to depression in MS, including psychosocial stressors, lesion location, and the interaction between cognitive deficits and coping strategies [36]. Nevertheless, we feel that the findings have important implications for the treatment of depression in MS. It may be possible to reduce depression by either successfully treating high levels of pain or addressing negative bias. Numerous studies have found that cognitive-behavioral therapy and/or pharmacological treatments can reduce depression associated with pain [37–40]. The results of this study point to one possible mechanism by which successful outcomes may occur. Both psychotherapy and anti-depressants have been shown to reduce negatively skewed AMB [41]. Cognitive-behavioral therapy and pharmacotherapy may decrease negative AMB, and therefore reduce the

Table 3 Regression analyses for AMB and pain interacting to predict self-reported depression

Variable	B	SEB	β	R^2	Adj R^2	Δr^2	ΔF	P-level
ARS delay bias and BPI predicting								
CMDI Mood scale								
Step 1								
ARS delay bias	8.9 E-3	1.4 E-3	0.11	0.14	0.12	0.14	7.13	<0.01
Pain	-8.0 E-6	6.7 E-5	-0.01					
Step 2								
ARS delay bias \times pain	7.1 E-5	3.5 E-5	0.32	0.18	0.15	0.04	4.07	<0.05
ARS delay bias and BPI predicting								
CMDI Evaluative scale								
Step 1								
ARS delay bias	-1.4 E-5	1.2 E-3	1.9 E-3	0.10	0.08	0.10	4.95	<0.01
Pain	6.7 E-6	6.4 E-5	1.0 E-3					
Step 2								
ARS delay bias \times pain	8.2 E-5	3.3 E-5	0.40					
ARS retention bias and BPI predicting								
CMDI Mood scale								
Step 1								
ARS retention bias	-4.2 E-5	2.2 E-4	-0.03	0.07	0.09	4.58	0.01	
Pain	7.2 E-6	6.9 E-5	0.01					
Step 2								
ARS retention bias \times pain	1.4 E-5	6.0 E-6	0.41	0.15	0.12	0.05	5.47	<0.05
ARS retention bias and BPI predicting								
CMDI Evaluative scale								
Step 1								
ARS retention bias	-1.8 E-4	2.1 E-4	-0.14	0.07	0.05	0.07	3.60	<0.05
Pain	2.7 E-5	6.4 E-5	0.04					
Step 2								
ARS retention bias \times pain	1.6 E-5	5.7 E-6	0.51	0.16	0.13	0.08	8.74	<0.01

B, beta value; SEB, standardized error beta; β , standardized beta; Adj R^2 , adjusted R^2 . K-S tests of the regressions' residuals revealed no violations of normality. No violations of multicollinearity were detected (tolerance >0.20, VIF <4).

likelihood that patients with high levels of pain will experience depression.

The interaction of AMB and pain was only significant with indices of delay and retention bias. Initial bias did not interact with any of the selected variables to account for additional variance in depression. It may be that delay and retention biases are more potent measures of vulnerability to depression. Physiological and behavioral evidence suggests that depressed individuals may process negative information for longer time periods than non-depressed individuals. Using a similar AMB

task, Siegle showed that depressed individuals who view negatively valenced words have longer amygdalar responses than non-depressed individuals [42]. Moreover, depressives' augmented amygdalar activation continued during neutral interference tasks. Unlike initial bias, delay and retention biases may encompass sustained and deeper levels of encoding, perhaps increasing vulnerability.

It is noteworthy that our effects were generally stronger for the CMDI Evaluative scale than for the Mood scale. It may be that because the CMDI

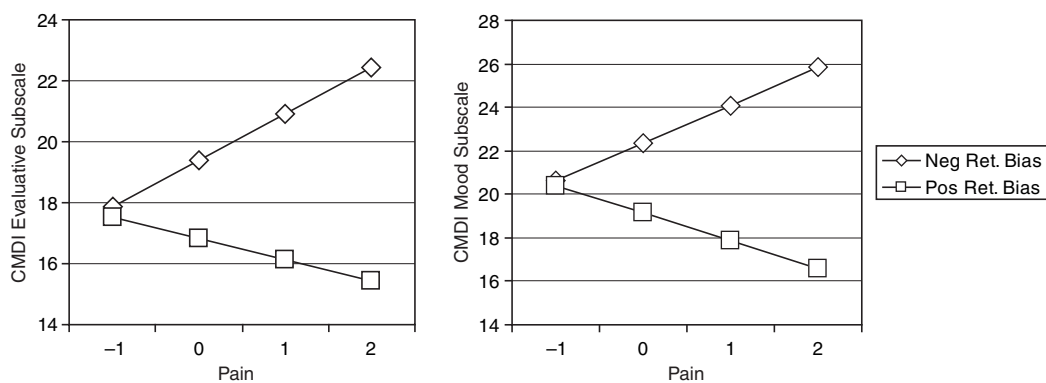


Figure 2 Pain and retention bias interact to predict mood and evaluative symptoms of depression.

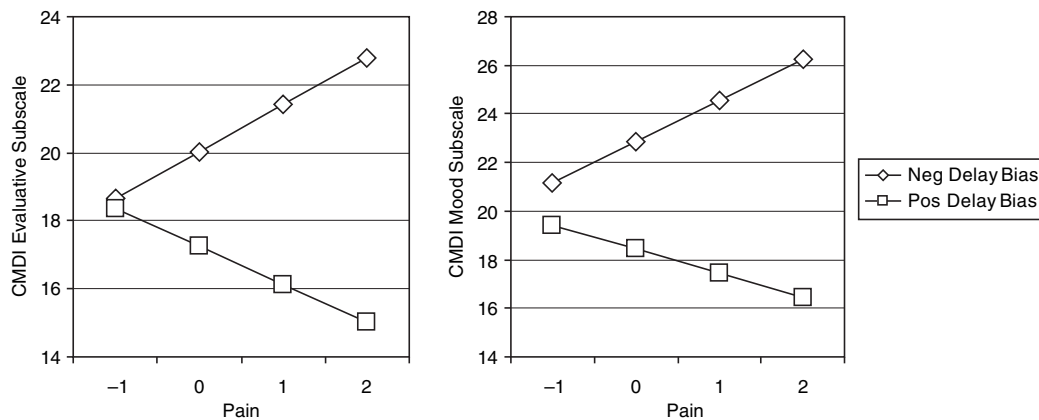


Figure 3 Pain and delay bias interact to predict mood and evaluative symptoms of depression.

Evaluative scale is also getting at a negative cognitive bias, albeit via self-report, it is more likely to be associated with AMB. A small, but significant, direct relationship was found between pain and the BDI. However, this relationship may have been driven by patients' physical disability. In the future, depression questionnaires that assess vegetative symptoms should be used with caution among patients with MS. Future studies would benefit from using longitudinal designs. Although correlational studies can inform future avenues of research, *causality and the temporal evolution of a phenomenon cannot be determined*. Among other things, this study was designed to investigate vulnerability to depression. AMB was measured to quantify this vulnerability. Given the correlational nature of this study's design, however, it is not possible to state with certainty that negative AMB predispose individuals to depression or that positive AMB protect individuals from depression. It is also plausible that depression causes AMB. Finally, AMB and depression may interact to create a self-sustaining positive feedback loop – AMB increasing depression, which increases AMB, which again increases depression, etc. Longitudinal designs that examine the expression of depression over time are more informative and can better address causality. For example, a study that assessed MS patients' AMB at the time of their diagnosis and before the onset of major depression would give a clear indication of whether AMB indicates a true vulnerability marker for depression. In addition, the onset of pain and depression could be examined. If pain typically occurred before the onset of depression, one could more accurately draw the conclusion that pain causes depression in MS and not vice versa. Future studies may also want to include depressed and non-depressed healthy control groups. Little is known about how neurological disease may affect AMB; one might speculatively posit that damage to frontal and/or limbic brain

regions could increase or altogether eliminate AMB. Whether AMB interacts with other MS symptoms should also be explored. In particular, AMB may be related to anosognosia, frontal lobe syndrome, and various other behaviors and physical ailments that require properly functioning frontal and limbic circuitry.

In summary, both depression and pain are common in MS. This is the first study to find a small to moderate relationship between depression and pain in MS. Results suggest that self-reported pain interacts with objective measures of AMB to predict depressive symptoms in MS. Patients with high levels of pain and negative AMB reported more depressive symptoms than patients with high levels of pain and positive AMB. Clinicians who treat MS patients who report high levels of pain may also want to screen for depression. Our results suggest that it may be possible to successfully treat depression in MS by reducing pain or decreasing negative memory biases.

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