Neuropsychology
2008, Vol. 22, No. 1, 118–126

0894-4105/08/$12.00 DOI: 10.1037/0894-4105.22.1.118

Stress and Memory Bias Interact to Predict Depression in Multiple Sclerosis

Joe Beeney and Peter A. Arnett
Pennsylvania State University

This study is an investigation of the moderating effect of cognitive schema on the relationship between stress and depression in individuals with multiple sclerosis (MS). In the study, the authors employed a performance-based measure of affective memory bias and a self-report measure of everyday stress to assess both direct and interactive effects of cognitive schema and stress on depression in individuals with MS. The specific hypotheses were that high stress would be more highly associated with depression if an individual also demonstrated a bias for negative information, but that a bias for positive information may buffer against the effects of stress on depression. Results supported the hypotheses, demonstrating a significant effect of the interaction and differential effects of stress based on the direction of memory bias. Implications for understanding depression in MS are discussed, as well as dominant theories of adult depression in the general population. The results are also discussed as a potential contradiction to A. T. Beck's (1967, 1976) developmental hypothesis of cognitive schemas.

Keywords: emotional content, human information storage, major depression, stress, memory

In the normal brain, myelin sheaths insulate axonal fibers, enabling fluid electrical conduction along the axon between gaps in the myelin. In the brains of those with multiple sclerosis (MS), this process is disrupted (Arnett, 2003; Brassington & Marsh, 1998; Compston et al., 2005). Discrete plaques form, partly caused by proliferating astrocytes, resulting in the destruction, swelling, or fragmentation of myelin. Such plaques can form anywhere in the brain and spinal cord, interrupting saltatory conduction and resulting in highly variable physical and cognitive impairments. Although about three fourths of plaques are found in the white matter, some affect the gray matter and junctions between gray and white matter (Pittock & Lucchinetti, 2007). Common symptoms of this process include muscle weakness, visual disturbances, urinary disturbance, balance problems, and significant problems in any domain of cognition (Arnett, 2003).

Depression is much more common among individuals with MS than the general population (Joffe, Lippert, Gray, Sawa, & Horvath, 1987; Minden & Schiffer, 1990; Sadovnick et al., 1996), and research suggests depression is more common in individuals with MS than other chronic illnesses, including other neurological disorders (Minden, Orav, & Reich, 1987; Schiffer & Babigan, 1984). Before onset of the disease, individuals are no more at risk for depression than the general population. However, after onset of the disease, risk for depression is highly elevated, with lifetime prevalence estimated at around 50% (Joffe et al., 1987; Siegert & Abernethy, 2005). Understanding what changes are related to this inflation in the prevalence of depression is essential for understanding the disorder and targeting possibilities for treatment.

In the current study, we attempt to assess the importance of the moderating effect of memory bias on the relationship between stress and depressive symptoms in MS. A central goal is to further limited research on the importance of these variables, essential to numerous cognitive models of depression for the general population, within an MS sample. Various cognitive models have attempted to explain the onset and maintenance of depression in the general population (e.g., Abramson, Metalsky, & Alloy, 1989; Abramson, Seligman, & Teasdale, 1978; Beck, 1967, 1976). Vulnerability to depression in cognitive models (henceforth called *cognitive vulnerability*) occurs when an individual possesses depressogenic cognitive schemas—structures for "screening, coding, and evaluating the stimuli that impinge on the organism" (Beck, 1967, p. 283). According to Beck (1967), these schemas remain latent until activated by stressful life events. When activated, such representations allow greater access to negative themes, shape expectations, evaluations, and perceptions, and they interact with stimuli to guide attention, memory, and cognition (Segal, 1988; Williams, Watts, MacLeod, & Mathews, 1997). Because schemas are thought to interact with information to guide attention and memory, many researchers have used information processing paradigms to examine negative information processing biases in those with unipolar depression (e.g., Ingram, Bernet, & McLaughlin, 1994; Teasdale & Dent, 1987; Timbremont & Braet, 2004). These paradigms are performance-based procedures for measuring cog-

Joe Beeney and Peter A. Arnett, Department of Psychology, Pennsylvania State University.

This work was presented (in part) at the 35th Annual Meeting of the International Neuropsychological Society in Portland, Oregon, February 2007. It was also part of a master's thesis from the Pennsylvania State University granted to Joe Beeney. Special thanks to the many neurologists in Pennsylvania, particularly Brian Ahlstrom, who contributed their time to verifying multiple sclerosis diagnoses and ratings of course for the participants with multiple sclerosis in the project. We would also like to thank Dawn Polen, Lauren Strober, Jared Bruce, Fiona Barwick, Stephanie Pantalone (Marshall), Molly Riley, Luciano Tristan, Martin Pankiewicz, Jess Clark, Karisa Cortellini, Kate Caddick, Lisa Martin, Alfred Bagamasbad, Jennifer Leer (Cromer), Kristin King, La Riena Ralph, Maya Ramirez, Elizabeth Ranft, Hannah Roggenkamp, Megan Wagner, Pinar Miski, Michelle Olson, Erin Stover, and Andrae Laws for their help with various aspects of the project.

Correspondence concerning this article should be addressed to Peter A. Arnett, Department of Psychology, Pennsylvania State University, 522 Moore Building, University Park, PA 16802-3105. E-mail: paa6@psu.edu

nitive schema. Such procedures are in contrast to self-report paradigms of dysfunctional attitudes in that, rather than asking a participant about certain cognitions, the variable of interest is actually output on a certain task. This output is thought to be influenced by cognitive schemas. Some examples include asking participants to remember emotionally valenced words, track a story in a dichotic listening task while positive and negative distracter stimuli are presented, or take a modified Stroop task with positive and negative stimuli.

Cognitive theories have been criticized because of early research that consistently found that information processing biases and negative or dysfunctional cognitions were found when individuals were depressed but were not apparent when depressive symptoms remitted (e.g., Coyne & Gotlib, 1983). If this were correct, it would provide evidence against the influence of cognitive schemas in depression and suggest that memory bias and dysfunctional attitudes found in depression are simply concomitant symptoms. However, in response to these criticisms, subsequent researchers have called attention to the diathesis-stress nature of Beck's (1967, 1976) cognitive theory (Segal & Ingram, 1994). Proponents of schema theories have argued that Beck's theory proposes that such schemas remain latent until they are activated by stress. Importantly, studies that make attempts to activate such schemas through mood induction and other means are largely supportive of the presence of depressogenic cognitive schemas, both measured as dysfunctional attitudes and as information processing biases among those with current as well as remitted depression (see Scher, Ingram, & Segal, 2005).

The nature of the stress that activates cognitive schemas is not well defined, and conceptualizations of stress differ within the stress literature. Whereas some stress inventories focus on major life events, the Hassles and Uplifts Scale (DeLongis, 1985; DeLongis, Folkman, & Lazarus, 1988; Lazarus & Folkman, 1989), used in this study, conceptualizes stress as both the minor stressors that occur every day (hassles) and the positive compensatory experiences (uplifts) that may balance these stressors (Kanner, Coyne, Schaefer, & Lazarus, 1981). Further, the authors of the scale place importance on both the significance of the stressful and positive events for an individual as well as his or her perceived ability to meet the demands of these stressors. Thus, the Hassles and Uplifts Scale is a measure of stress appraisal.

In the current study, we used a performance-based measure of cognitive schema, and we examined the moderating effect of cognitive schema on the relationship between stress and depression, which is a common and central interaction to many models of depression (Abramson et al., 1978, 1989; Beck, 1967, 1976). For instance, Abramson et al. (1989) have posited with their hopelessness theory that stress leads to depression when a negative life event interacts with the distal influence of depressogenic inferential styles about the self and the cause and consequence of the stressor, coupled with the proximal influence of maladaptive attributions about the negative event. Similarly, in Beck's (1967, 1976) theory, negative self-schemas are hypothesized to provide a cognitive vulnerability to depression through effects on information processing and appraisals of life experiences.

The relationship between cognitive schemas and depression among individuals with MS has not been extensively studied. Additionally, the bulk of inquiry has been research employing both self-report measures of schema and depression, which is problematic because of same-method overlap and potential response bias influencing associations. However, research to date suggests the importance of the influence of cognitive factors on depression in MS. Shnek, Foley, LaRocca, Smith, and Halper (1995) found learned helplessness, cognitive distortions, and self-efficacy each held significant zero-order correlations with depression in an MS sample. Kneebone and Dunmore (2004) found that stable and global attributional styles to hypothetical negative events were positively correlated with Center for Epidemiological Studies Depression scale scores. Another study (Barrett, 1992) did not support the relationship between attributional style and depression but has been criticized for using an insufficient sample size ($n = 55$) to detect an effect (Kneebone & Dunmore, 2004). Johnson, Lange, Tiersky, DeLuca, and Natelson (2001) found that—compared with healthy, sedentary control participants—individuals with MS demonstrated a depressive attributional style that was characterized by beliefs that good events are isolated, whereas causes for bad events are omnipresent. Despite this interesting finding, this study was limited by the fact that no measure of depression was used.

The use of performance-based measures of cognitive schema reduces the possibility that the relationship between self-report measures of negative response bias and depression may be inflated by shared method variance. The proposed study involves a sentence reading working memory measure called the Affective Reading Span Task (ARST; Bruce & Arnett, 2005), which allows for a performance-based assessment of memory bias. Using this task (described later), Bruce and Arnett (2005) found that mildly and moderately depressed participants demonstrated a recall bias for affectively negative words relative to the nondepressed MS group. The study is the first in the MS literature to demonstrate that individuals with depression evidence a memory bias for negative information.

Despite this evidence of the importance of cognitive factors in depression in individuals with MS, a feature of Beck's (1967, 1976) theory of depression appears to make it an improper fit for depression in individuals with MS. Beck posits that depressogenic schemas are developed in childhood or early adolescence. However, research has found that before onset of MS, patients experience depression at rates similar to the general population (Joffe et al., 1987; Minden et al., 1987), and after disease onset, individuals with MS experience depression at much higher rates. It would appear then, that cognitive vulnerability to depression would have to be acquired after disease onset. Because disease onset is typically in the late 20s and early 30s, findings that schema-related variables are associated with depression in individuals with MS (e.g., Bruce & Arnett, 2005; Kneebone & Dunmore, 2004) seem inconsistent with Beck's developmental hypothesis and appear to argue that depressogenic cognitive representations can be formed in adulthood. An alternative hypothesis is simply that those with MS possess these cognitive schemas but that the individual has yet to meet adequate levels of stress. MS, in turn, provides the significant stress to activate these schemas that are otherwise buried representations about the self.

In addition to a number of studies that link life stress to onset of first MS symptoms (Grant et al., 1989; Warren, Greenhill, & Warren, 1982), clinical exacerbations (Ackerman et al., 2000; Franklin, Nelson, Heaton, Burkes, & Thompson, 1988; Mohr, Goodkin, Nelson, Cox, & Weiner, 2002), and poorer general health (Fisk, Pontefract, Ritvo, Archibald, & Murray, 1994), research has consistently supported a relationship between stress and depression in MS samples (Pakenham, 1999; Patten, Metz, & Reimer, 2000) and among the general population (see Hammen, 2005; Kessler, 1997; Mazure, 1998). In the MS literature, Aikens et al. (1999) found life stress at Time 1 to be a strong predictor of depression at two time points, even after controlling for physical disability and cognitive status. Gilchrist and Creed (1994) reported that a group of individuals with MS and depression had higher stress than a nondepressed MS group. Prior work has also supported a relationship between stress in the form of economic pressure and depression among individuals with MS (McCabe & de Judicibus, 2005).

One study (Kneebone & Dunmore, 2004) in the MS literature has tested whether attributional style, one conceptualization of cognitive schema, moderates the relationship between life stress and depression. The authors assessed life stress via a self-report measure of recent life changes, as well as time since last MS exacerbation. They found significant relationships between both measures of stress and depression, and a significant relationship between global and stable negative attributional styles and depression. These investigators also found a significant interaction between stress and attributional style, but only for global negative attributions. The present study and Kneebone and Dunmore's (2004) study are similar in their attention to the interaction between stress and cognitive schema. However, in the current study we employ different conceptualizations of both stress and cognitive schema, and different methods of assessment, using a performance-based measure of memory bias and a scale of appraisal of daily life stressors.

With these considerations in mind, we hypothesized that memory bias will moderate the effect of stress in predicting depression in individuals with MS. More specifically, we predicted that as report of stress increases, MS patients who demonstrate relatively better recall of negative information will evidence higher ratings of depression, whereas better recall for positive information, even in the context of higher stress, will be associated with lower report of depressive symptomology.

Method

Participants and Procedure

Participants were 93 individuals recruited by a number of means: advertising in a newsletter, recruitment from MS support groups in the central Pennsylvania area, and flyers distributed in the State College (PA) community. All participants included in the study had definite or probable MS. MS diagnosis and course type were assigned by board-certified neurologists according to accepted research protocols (Lublin & Reingold, 1996; Poser et al., 1983). Exclusion criteria for the study were as follows: (a) history of neurological disease other than MS, (b) history of drug or alcohol abuse, (c) history of developmental learning disability, (d) visual or motor disturbances that would prohibit testing without significant alteration of testing procedures, or (e) currently experiencing a clinical exacerbation. Participants were given 75 dollars for their participation in the study. Informed consent was obtained for all participants, and the study was approved by the Behavioral Committee of the University Institutional Review Board at the Pennsylvania State University.

Measures

Chicago Multiscale Depression Inventory (CMDI). Researchers have argued that most traditional measures of depression tend to overestimate depression in chronic illness populations because of inclusion of items that overlap with disease symptoms (Arnett & Randolph, 2006; Mohr et al., 1997; Nyenhuis et al., 1998). The CMDI, which has been found to be a valid and reliable measure of depression (Nyenhuis et al., 1998), is a 42-item self-report measure, consisting of three subscales. These scales measure mood, evaluative, and vegetative symptoms—an approach meant to control for possible confounds between MS disease symptoms and vegetative depressive symptoms. Consistent with Nyenhuis et al.'s (1995) recommendation, only the Mood and Evaluative subscales are included in analyses.

ARST. The ARST (Bruce & Arnett, 2005) is a modification of a test for working memory originally developed by Daneman and Carpenter (1980). The task is a computer-based measure meant to tax working memory, limit use of complex encoding schemes, and assess memory bias for affective words. As such, the task also represents a performance-based measure of cognitive schema. Participants begin the task by reading aloud negatively or positively valenced sentences on a computer screen. Following each sentence is a target word of the same affective valence, also read aloud. Participants are asked to remember just the target words as they read through a series of sentences. Each screen contains only one sentence and target word combination. Participants are instructed to read sentences until they are confronted with a blank screen. At that time, they say aloud all target words that appeared in the previous testing block (since the last blank screen appeared). Initially, testing blocks are two sentence/target word combinations. However, as the task progresses, testing blocks incrementally increase to five sentence/target word combinations. After completion of the task, participants are also asked to recall as many words as they can remember from all of the testing blocks. An example of the task is presented in Figure 1.

The test includes 28 positive and 28 negative sentence/target word combinations. Affective valence is alternated throughout the task (e.g., negative then positive then negative) to control for potential positional effects. The ARST has been used in two published studies to date (Bruce & Arnett, 2005; Bruce, Polen, & Arnett, 2007). In the initial study using the ARST (Bruce & Arnett, 2005) the authors found that a nondepressed MS group tended to demonstrate a positive memory bias across all memory indices, whereas both mildly and moderately depressed MS groups tended to demonstrate negative memory biases. This is a similar pattern of results found for other memory bias measures (see Matt, Vazquez, & Campbell, 1992, for review). No normative data exist, as of yet, for the ARST. However, as an experimental task, it resembles other performance-based memory bias tasks that have been used in the literature, is modeled after a widely used working memory test (Daneman & Carpenter, 1980), and demonstrates patterns of memory recall for valenced material among depressed and nondepressed individuals comparable with other studies.

The memory bias variable used in the study was derived by converting both the memory bias during the task (initial bias) and during free recall (delayed bias) to z scores and summing these (total bias). The z scores were constructed with the values of the current MS sample as the reference group, as in Bruce and Arnett's

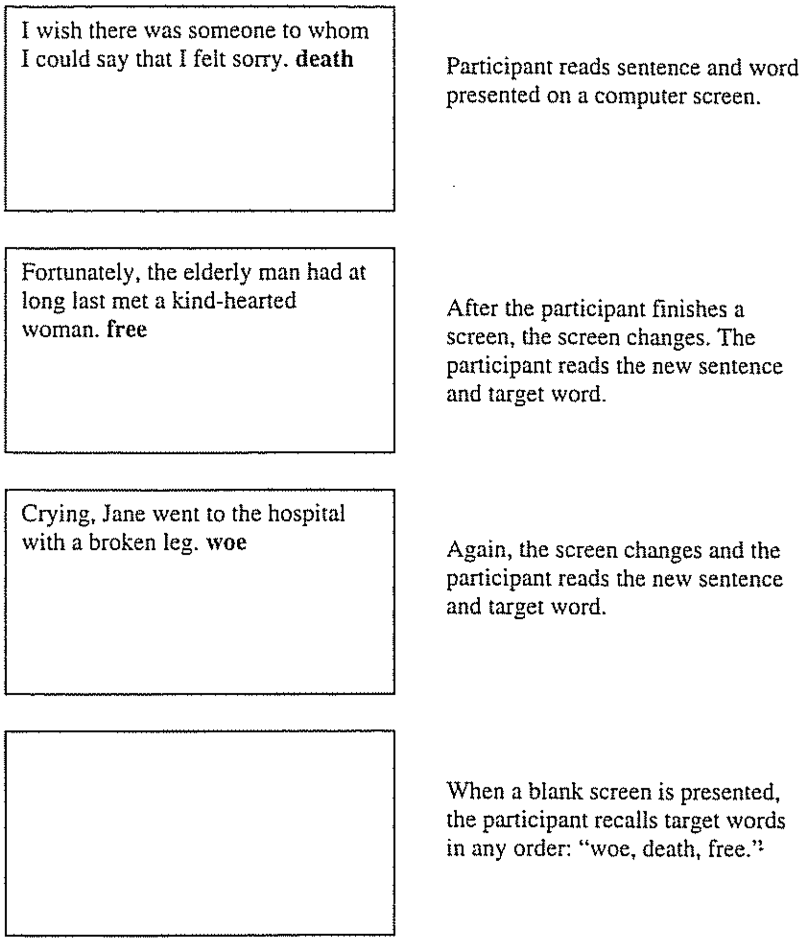

Figure 1. Illustration of the Affective Reading Span Task.

(2005) study. This was done to maintain the relative distance from the mean in relation to the sample for both positive and negative words, simply putting each on a common metric. Both the initial and delayed indices were obtained by subtracting negative from positive words recalled. The total bias index is used because it is meant to capture additive effects of initial and delayed bias and is the index most highly associated with depression in prior research (Bruce & Arnett, 2005).

Because differences between positive and negative target words and positive and negative sentences not related to affective valence could create rival hypotheses for any memory bias observed using the ARST, such differences were assessed. Analyses were used to assess whether positive or negative target words significantly differed in terms of frequency of use in the English language and word type (i.e., noun, verb, adjective). Positive and negative sentences were also assessed for possible differences in number of syllables.

Hassles and Uplifts Scale. The Hassles and Uplifts Scale (DeLongis, 1985; DeLongis et al., 1988) is a measure of everyday life stress. Participants are instructed to rate 53 items on a 4-point scale ranging from 0 (*none* or *not applicable*) to 3 (*a great deal*) on the basis of the past month. Participants make a rating of each item on the degree to which it is a hassle, and they make another rating of each item on the degree to which it is an uplift. Items are drawn from a wide variety of life domains. Researchers have supported that the scale demonstrates adequate reliability and validity (DeLongis, 1985).

Expanded Disability Status Scale (EDSS). Participant disability was assessed with the EDSS (Kurtzke, 1983). The EDSS is a commonly used measure in clinical and research settings for assessing MS disease progression and neurological impairment, in which participants are rated according to their functional abilities in a number of different physical domains. The scale ranges from 0 to 10. Higher ratings indicate greater disability, with a 0 rating meaning no physical disability/disturbance in functional systems, 9.5 meaning extreme functional system disturbance (inability to communicate or eat), and 10 meaning death due to MS.

Data Analysis

Depressive symptomology was measured with the mean of the CMDI Mood and Evaluative subscales, which were converted to *t* scores with Nyenhuis et al.'s (1995) healthy controls as the reference point. Relative stress appraisal was assessed with the Hassles and Uplifts Scale and more specifically was computed as uplifts minus hassles. Some published studies have used this approach (e.g., Madu & De Jong, 2002; Weller & Avinir, 1993). Memory bias was assessed with the ARST, using the total bias index outlined above. Relationships among demographic and disease-related variables and depression were assessed, including age, gender, disease course, disease duration, symptom duration, and EDSS rating. If any factors were significantly associated with the CMDI Mood and Evaluative depression scores, we planned to enter them into the first step of the regression equation to control for variance associated with these factors.

Regression interaction analyses were performed according to accepted methods as outlined by Baron and Kenny (1986). The stress variable was entered after any demographic variables, the memory bias score followed, and the interaction between stress and memory bias was entered into the final step of the model. All regression assumptions for the analysis were met, except for a violation of normality, which was corrected (see below). There was no evidence of violations of linearity, homoscedasticity, or multicollinearity.

Results

Preliminary Analyses

A violation of normality was detected with a Kolmogorov–Smirnov test and was corrected by transforming the CMDI Mood and Evaluative subscales' variable with a negative inverse function (to correct for positive skew while maintaining directionality). Table 1 displays means and standard deviations for all independent, dependent, and demographic variables. Table 2 displays zero-order correlations between all variables. These correlations were conducted to assess for a relationship among the CMDI, demographic variables, and independent variables. Because there were no significant relationships between the CMDI and demographic or illness variables, these latter variables were excluded from subsequent analyses.

We assessed differences between positive and negative target words in terms of word frequency and word type. Positive and negative target words did not differ in terms of relative frequency of use in the English language, $t(54) = 1.06, p > .29$, nor did they differ in terms of word type $\chi^2(2, N = 60) = 0.46, p > .70$. Likewise, positive and negative sentences did not differ in terms of number of syllables, $t(54) = 1.4, p > .17$.

Regression Analyses

Regression analyses are displayed in Table 3. Uplifts minus hassles was entered at Step 1 of the regression model. This variable explained around 12% of the variance in depression scores, supporting a relationship in which report of greater stress appraisal was associated with higher CMDI scores, $R^2 = .12, p < .01, \beta = .35$. The ARST total bias index was entered at Step 2 of the model and significantly accounted for additional variance, $\Delta R^2 = .06$, $p = .01, \beta = .29$. Bias toward remembering positive words was associated with report of lower CMDI scores. The interaction between hassles minus uplifts and the ARST total bias index was entered at Step 3 of the regression model. The interaction significantly explained variance in depression scores beyond that already accounted for by main effects, R^2 model $= .26, p < .01$, $\Delta R^2 = .09, p < .01, \beta = -.30$.

A graph of the interaction was plotted by creating three regression lines with three data points each. Because the stress variable was calculated as uplifts minus hassles, the regression lines represented one standard deviation above the mean in terms of uplifts minus hassles (low stress), the mean (no stress), and one standard deviation below the mean (high stress). The three data points for each regression line represented one standard deviation above the mean (positive bias), the mean (no bias), and one standard deviation below the mean (negative bias) for the memory bias variable. A graph of the interaction is presented in Figure 2. As demonstrated by the graph and consistent with the hypotheses, reports of high amounts of hassles relative to uplifts were related to higher CMDI scores if individuals also demonstrated a bias on the ARST. Interestingly, report of more hassles relative to uplifts, coupled with demonstration of a bias for remembering positive words on the ARST, was associated with lower CMDI scores.

Discussion

The importance of cognitive factors in relation to depression in individuals with MS is not well understood. A handful of studies

Table 1
Participant Characteristics

Variable	*M*	*SD*	Minimum	Maximum	Skewness	Kurtosis
Age	47.59	8.87	23	65	−.25	−.04
Memory bias	0.02	1.55	−4.09	4.04	.26	.19
CMDI Mood and Evaluative *t* score	51.25	11.35	41.20	92.87	1.67	2.59
BDI	11.67	7.05	0.00	28.00	.49	−.43
Diagnosis duration (years)	10.87	7.87	0.00	37.00	.75	.07
Symptom duration (years)	14.89	8.75	1.00	37.00	.36	−.63
Education	14.32	1.96	10.00	20.00	.32	−.52
EDSS	4.59	1.58	0.00	8.00	−.35	.36
Hassles	42.00	19.71	6.00	96.00	.67	.02
Uplifts	60.20	22.22	23.00	133.00	.59	.10
Uplifts minus hassles	18.20	26.91	−38.00	91.00	.36	.13

Note. CMDI = Chicago Multiscale Depression Inventory Mood and Evaluative subscales; BDI = Beck Depression Inventory; EDSS = Expanded Disability Status Scale.

Table 2
Correlations Among Variables

Variable	Age	CMDI	Diagnosis duration	Education	EDSS	Gender	Memory bias	Hassles and uplifts	Symptom duration
Age	1.00	−.04	.45**	−.10	.29**	.12	.22*	−.04	.51**
CMDI Mood and Evaluative		1.00	.13	.03	.19	.01	−.27*	−.32**	.06
Diagnosis duration			1.00	−.10	.32**	.10	.06	.05	.77**
Education				1.00	−.24*	−.12	.05	.03	−.10
EDSS					1.00	.11	.08	−.15	.39**
Gender						1.00	.07	.00	.17
Memory bias							1.00	.21*	.14
Hassles and uplifts								1.00	.02
Symptom duration									1.00

Note. CMDI = Chicago Multiscale Depression Inventory Mood and Evaluative subscales; EDSS = Expanded Disability Status Scale.
* $p < .05$. ** $p < .01$.

has assessed variables related to cognitive schema, but only one study (Bruce & Arnett, 2005) has employed a performance-based measure of cognitive schema—a more rigorous, objective test of the construct. Furthermore, only one study (Kneebone & Dunmore, 2004) has examined the possible interaction of stress and schema factors as proposed by cognitive theories of depression. The purpose of the current study was to examine the moderating effect of cognitive schema, which was assessed using a performance-based construct of memory bias, on the relationship between stress and depression in individuals with MS.

The current study supports the importance of the interaction between stress and cognitive schema in relation to depression in individuals with MS. After entering two factors into the regression equation explaining close to 18% of the variance in depression scores, the interaction variable explained an additional 9% of the variance. The nature of the interaction was essentially as predicted. More negative memory bias and relatively high stress appraisal were associated with higher depression scores. More positive memory bias, even when individuals endorsed relatively more stressors, was associated with lower depression scores. Although we have conceptualized that schema moderates the relationship between stress and depression symptoms, because the data are correlational, other models cannot be ruled out. For instance, stress may lead to depression, which may lead to a negative memory bias. Such a hypothesis is a serious rival to the conceptualization that cognitive schemas are activated by stress and lead to depression. Although this latter hypothesis has support in the general population, the current study or previous research has not clearly supported such a model in an MS sample.

Importantly, tests of several aspects of the memory bias measure were used in the current study to rule out potential rival hypotheses. Tests comparing the relative word frequency in the English language and word type between positive and negative sentences on the ARST revealed no significant differences. Syllables per sentence between the two types of sentences also were not significantly different.

Generally, the results of the current study can be counted as support for a number of theories of depression. Specifically, the study appears to support Beck's (1967, 1976) theory of depression, which suggests that negative experiences activate depressogenic cognitive schemas, within an MS sample. The current data appear to support the importance of cognitive factors and the interaction between stress and schema within an MS sample, although more research is needed to better clarify the association of memory bias as a measure of cognitive schema in an MS population.

In addition to clarifying the understanding of depression in the context of MS, this study, and others focused on cognitive variables in MS samples, may help refine understanding of the nature of such variables. Beck (1967) hypothesized that depressogenic cognitive schemas are developed in childhood or early adolescence as a result of negative experiences. However, attending to findings that suggest (a) people who have MS become depressed at rates no greater than the general population before disease onset, (b) risk for depression is highly elevated following disease onset, and (c) support is accumulating for the importance of schema-related variables in depression among those with MS, it appears that the cognitive schemas would necessarily develop after disease onset. This would suggest that depressogenic schemas can develop in response to a chronic disease with an onset typically in adulthood. As mentioned, an alternative hypothesis is simply that those with MS have not been confronted with adequate levels of stress required to activate such schemas. Although plausible, such a conceptualization may be less likely than our previous suggestion. Because of a high prevalence of depression in individuals with MS, often estimated at around 50%, this hypothesis would imply that a large number of individuals have early experiences that

Table 3
Regression Examining the Interaction Between Stress and Memory Bias on Depression Symptoms

Step	B	β	R^2	ΔR^2	ΔF	p
Step 1: Relative stress (uplifts minus hassles)	0.00	0.35	.12	.12	12.12	<.01
Step 2: Memory bias (Affective Reading Span Task total bias)	0.00	.29	.18	.06	6.82	.01
Step 3: Stress × Memory Bias	−0.00	−.30	.26	.09	10.23	<.01

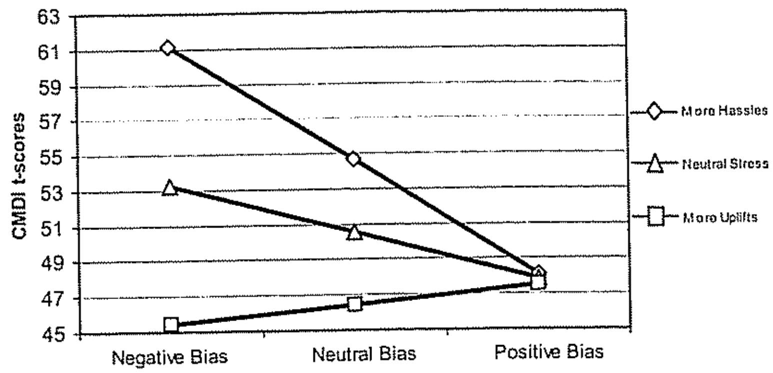

Figure 2. Graph of the interaction. Negative memory bias and relatively high stress is associated with higher depression scores, whereas positive memory bias is associated with lower depression scores, even when combined with high stress. CMDI = Chicago Multiscale Depression Inventory.

make them vulnerable to depression. However, whereas remitted-depressed patients in the general population have tended to show evidence of depressogenic schemas, never-depressed individuals do not typically demonstrate such cognitive structures (Scher et al., 2005). Still, the current methodology does not allow us to eliminate such a possibility in our MS sample. Our findings thus argue for investigating the potential need for refinement in understanding of the development of depressogenic cognitive schemas, at least in patients who develop chronic neurological illnesses, such as MS.

Our data are consistent with a study that found that disease representations are related to depression in individuals with MS (Jopson & Moss-Morris, 2003). Jopson and Moss-Morris (2003) found that facets of disease representations—such as beliefs in serious consequences of the disease, low appraisal of personal control over the disease, and making psychological attributions for the disease—were all related to depression. Their study appears to suggest that cognitive representations of the disease itself impact depression.

There are a number of limitations of the current study. First, as a correlational analysis, the results rule out making firm attributions of the causal direction between variables. Second, the study employed a self-report measure of depression, better understood as a measure of depressive symptomology rather than clinical depression. Third, our study employed a self-report measure of stress that combines the assessment of stress with stress appraisal. Although this conceptualization is an explicit feature of the scale used, it could be argued that this stress scale is overly influenced by cognitive schema in a manner similar to the way memory bias is affected by such representations. However, although the memory bias index and the stress inventory were significantly associated, the magnitude of the relationship was small, with one scale only explaining 4% of the variance in the other. This suggests that the overlap between the stress measure and cognitive schema was not large.

Although the current study further supports the influence of cognitive factors in depression in the context of individuals with MS, more research is needed. A primary question still to be answered is whether evidence of the presence of cognitive schemas in individuals with MS is apparent after depressive symptoms remit or can be activated by stress as has been found in the general depression literature. It could be that memory bias among those with depression and MS is simply a concomitant of depression, even though this does not appear to be true in the general population.

The current study adds to a growing but limited literature that supports the significance of cognitive factors in depression among those with MS. Specifically assessed in the current research was a hypothesized interaction between stress and a performance-based measure of memory bias. The results of the study support the interaction, a moderating effect consistent with a number of cognitive diathesis–stress models of adult depression, suggesting such models may be important in understanding depression amongst those with MS.

References

Abramson, L. Y., Metalsky, G. I., & Alloy, L. B. (1989). Hopelessness depression: A theory based sub-type of depression. *Psychological Review, 96,* 358–372.

Abramson, L. Y., Seligman, M. E. P., & Teasdale, J. (1978). Learned helplessness in humans: Critique and reformulation. *Journal of Abnormal Psychology, 87,* 49–74.

Ackerman, K. D., Rabin, B., Heyman, R., Anderson, B. P., Houch, P. R., & Frank, E. (2000). Stressful life events preceded multiple sclerosis disease exacerbations. *Psychosomatic Medicine, 62,* 147.

Aikens, J. E., Reinecke, M. A., Pliskin, N. H., Fischer, J. S., Wiebe, J. S., McCracken, L. N., & Taylor, J. L. (1999). Assessing depressive symptoms in multiple sclerosis: Is it necessary to omit items from the original Beck Depression Inventory? *Journal of Behavioral Medicine, 22*(2), 127–142.

Arnett, P. A. (2003). Neuropsychological presentation and treatment of demyelinating disorders. In P. Halligan, U. Kischka, & J. Marshall (Eds.), *Handbook of clinical neuropsychology* (pp. 528–543). Oxford, England: Oxford University Press.

Arnett, P. A., & Randolph, J. J. (2006). Longitudinal course of depression symptoms in MS. *Journal of Neurology, Neurosurgery & Psychiatry, 77,* 606–610.

Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*(6), 1173–1182.

Barrett, L. (1992). The hopelessness theory of depression: A test of the diathesis-stress component in a multiple sclerosis sample. *Dissertation Abstracts International, 53,* 2535B.

Beck, A. T. (1967). *Depression: Clinical, experimental, and theoretical aspects*. New York: Harper & Row.

Beck, A. T. (1976). *Cognitive therapy and the emotional disorders*. New York: International Universities Press.

Brassington, J. C., & Marsh, N. V. (1998). Neuropsychological aspects of multiple sclerosis. *Neuropsychology Review, 8*, 43–77.

Bruce, J. M., & Arnett, P. A. (2005). Depressed MS patients exhibit affective memory biases during and after a list learning task that suppresses higher-order encoding strategies. *Journal of the International Neuropsychological Society, 11*, 514–521.

Bruce, J. M., Polen, D. M., & Arnett, P. A. (2007). Pain and affective memory biases interact to predict depressive symptoms in multiple sclerosis. *Multiple Sclerosis, 13*(1), 58–66.

Compston, A., McDonald, I. R., Noseworthy, J., Lassmann, H., Miller, D. H., Smith, K. J., et al. (2005). *McAlpine's multiple sclerosis* (4th ed.). London: Churchill Livingstone.

Coyne, J. C., & Gotlib, I. H. (1983). The role of cognition in depression: A critical appraisal. *Psychological Bulletin, 94*(3), 472–505.

Daneman, M., & Carpenter, P. A. (1980). Individual differences in working memory and reading. *Journal of Verbal Learning and Verbal Behavior, 19*, 450–466.

DeLongis, A. (1985). *The relationship of everyday stress to health and well-being: Inter- and intraindividual approaches*. Berkeley, CA: University of California, Berkeley.

DeLongis, A., Folkman, S., & Lazarus, R. S. (1988). The impact of daily stress on health and mood: Psychological and social resources as mediators. *Journal of Personality and Social Psychology, 54*, 486–495.

Fisk, J. D., Pontefract, A., Ritvo, P. G., Archibald, C. J., & Murray, T. J. (1994). The impact of fatigue on patients with multiple sclerosis. *Canadian Journal of Neurological Sciences, 21*, 9–14.

Franklin, G. M., Nelson, L. M., Heaton, R. K., Burkes, J. S., & Thompson, D. S. (1988). Stress and its relationship to acute exacerbations of multiple sclerosis. *The Journal of Neurological Rehabilitation, 2*, 7–11.

Gilchrist, A. C., & Creed, F. H. (1994). Depression, cognitive impairment, and social stress in multiple sclerosis. *Journal of Psychosomatic Research, 38*, 193–201.

Grant, I., Brown, G. W., Harris, T., McDonald, W. I., Patterson, T., & Trimble, M. R. (1989). Severely threatening events and marked life difficulties preceding the onset or exacerbation of multiple sclerosis. *Journal of Neurology, Neurosurgery & Psychiatry, 52*, 8–13.

Hammen, C. (2005). Stress and depression. *Annual Review of Clinical Psychology, 1*, 293–319.

Ingram, R. E., Bernet, C. Z. & McLaughlin, S. C. (1994). Attentional allocation processes in individuals at risk for depression. *Cognitive Therapy and Research, 18*(4), 317–332.

Joffe, R. T., Lippert, G. P., Gray, T. A., Sawa, G., & Horvath, Z. (1987). Mood disorder and multiple sclerosis. *Archives of Neurology, 44*, 376–378.

Johnson, S. K., Lange, G., Tiersky, L., DeLuca, J., & Natelson, B. H. (2001). Health-related personality variables in chronic fatigue syndrome and multiple sclerosis. In R. Patarca-Montero (Ed.), *Innovations in chronic fatigue syndrome research and clinical practice*. Binghamton, NY: Haworth Medical Press.

Jopson, N. M., & Moss-Morris, R. (2003). The role of illness severity and illness representations in adjusting to multiple sclerosis. *Journal of Psychosomatic Research, 54*, 503–511.

Kanner, A. D., Coyne, J. C., Schaefer, C., & Lazarus, R. S. (1981). Comparison of two modes of stress measurement: Daily hassles and uplifts versus major life events. *Journal of Behavioral Medicine, 4*(1), 1–39.

Kessler, R. C. (1997). The effects of stressful life events on depression. *Annual Review of Psychology, 48*, 191–214.

Kneebone, I., & Dunmore, E. (2004). Attributional style and symptoms of depression in persons with multiple sclerosis. *International Journal of Behavioral Medicine, 11*, 110–115.

Kurtzke, J. F. (1983). Rating neurologic impairment in multiple sclerosis: An Expanded Disability Status Scale (EDSS). *Neurology, 33*, 1444–1452.

Lazarus, R. S., & Folkman, S. (1989). *Manual for the Hassles and Uplifts Scales: Research edition*. Palo Alto, CA: Consulting Psychologists Press.

Lublin, F. D., & Reingold, S. C. (1996). Defining the clinical course of multiple sclerosis: Results of an international survey. *Neurology, 46*, 907–911.

Madu, S. N., & De Jong, E. S. (2002). Changing stress levels through gaining information on stress. *Curationis, 25*(1), 28–34.

Matt, G. E., Vazquez, C., & Campbell, W. K. (1992) Mood-congruent recall of affectively toned stimuli: A meta-analytic review. *Clinical Psychology Review, 12*(2), 227–255.

Mazure, C. M. (1998). Life stressors as risk factors in depression. *Clinical Psychology: Science and Practice, 5*, 291–313.

McCabe, M. P., & de Judicibus, M. (2005). The effects of economic disadvantage on psychological well-being and quality of life among people with multiple sclerosis. *Journal of Health Psychology, 10*, 163–173.

Minden, S. L., Orav, J., & Reich, P. (1987). Depression in multiple sclerosis. *General Hospital Psychiatry, 9*, 426–434.

Minden, S. L., & Schiffer, R. B. (1990). Affective disorders in multiple sclerosis. *Archives of Neurology, 47*, 98–104.

Mohr, D. C., Goodkin, D. E., Likosky, W., Beutler, L., Gatto, N., & Langan, M. K. (1997). Identification of Beck Depression Inventory items related to multiple sclerosis. *Journal of Behavioral Medicine, 20*, 407–414.

Mohr, D. C., Goodkin, D. E., Nelson, S., Cox, D., & Weiner, M. (2002). Moderating effects of coping on the relationship between stress and the development of new brain lesions in multiple sclerosis. *Psychosomatic Medicine, 64*, 803–809.

Nyenhuis, D. L., Luchetta, T., Yamamoto, C., Terrien, A., Bernardin, L., Rao, S. M., et al. (1998). The development, standardization, and initial validation of the Chicago Multiscale Depression Inventory. *Journal of Personality Assessment, 70*, 386–401.

Nyenhuis, D. L., Rao, S. M., Zajecka, J., Luchetta, T., Bernardin, L., & Garron, D. (1995). Mood disturbance versus other symptoms of depression in multiple sclerosis. *Journal of the International Neuropsychological Society, 1*, 291–296.

Pakenham, K. I. (1999). Adjustment to multiple sclerosis: Application of a stress and coping model. *Health Psychology, 18*, 383–392.

Patten, S. B., Metz, L. M., & Reimer, M. A. (2000). Biopsychosocial correlates of lifetime major depression in a multiple sclerosis population. *Multiple Sclerosis, 6*, 115–120.

Pittock, S. J., & Lucchinetti, C. F. (2007). The pathology of MS: New insights and potential clinical applications. *The Neurologist, 13*, 45–56.

Poser, C. M., Paty, D. W., Scheinberg, L., McDonald, I. W., Davis, F. A., Ebers, G. C., et al. (1983). New diagnostic criteria for multiple sclerosis: Guidelines for research protocols. *Annals of Neurology, 13*, 227–231.

Sadovnick, A. D., Remick, R. A., Allen, J., Swartz, E., Yee, I. M., Eisen, K., et al. (1996). Depression and multiple sclerosis. *Neurology, 46*, 628–632.

Scher, C. D., Ingram, R. E., & Segal, Z. V. (2005). Cognitive reactivity and vulnerability: Empirical evaluation of construct activation and cognitive diatheses in unipolar depression. *Clinical Psychology Review, 25*, 487–510.

Schiffer, R. B., & Babigan, H. M. (1984). Behavioral disorders in multiple sclerosis, temporal lobe epilepsy, and amyotrophic lateral sclerosis. *Archives of Neurology, 41*, 1067–1069.

Segal, Z. V. (1988). Appraisal of the self-schema construct in cognitive models of depression. *Psychological Bulletin, 103*(2), 147–162.

Segal, Z. V., & Ingram, R. E. (1994). Mood priming and construct activation in tests of cognitive vulnerability to unipolar depression. *Clinical Psychology Review, 14*(7), 663–695.

Shnek, Z. M., Foley, F. W., LaRocca, N. G., Smith, C. R., & Halper, M. S. N. (1995). Psychological predictors of depression in multiple sclerosis. *Journal of Neurologic Rehabilitation, 9*(1), 15–23.

Siegert, R. J., & Abernethy, D. A. (2005). Depression in multiple sclerosis: A review. *Journal of Neurology, Neurosurgery & Psychiatry, 76*, 449–475.

Teasdale, J. D. & Dent, J. (1987). Cognitive vulnerability to depression: An investigation of two hypotheses. *British Journal of Clinical Psychology, 26*(2), 113–126.

Timbremont, B., & Braet, C. (2004) Cognitive vulnerability in remitted depressed children and adolescents. *Behaviour Research and Therapy, 42*(4), 423–437.

Warren, S., Greenhill, S., & Warren, K. G. (1982). Emotional stress and the development of multiple sclerosis: Case-control evidence of a relationship. *Journal of Chronic Diseases, 35*(11), 821–831.

Weller, L., & Avinir, O. (1993). Hassles, uplifts, and quality of sleep. *Perceptual and Motor Skills, 76*(2), 571–576.

Williams, J. M. G., Watts, F. N., MacLeod, C., & Mathews, A. (Eds.). (1997). *Cognitive psychology and emotional disorders* (2nd ed.). Chichester, England: Wiley.

Received January 29, 2007
Revision received June 19, 2007
Accepted July 9, 2007 ■