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BRIEF COMMUNICATION

Endorsement of self-report neurovegetative items of depression is associated with multiple sclerosis disease symptoms

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Abstract

Some researchers have suggested that general self-report depression scales may be inadequate for assessing depression among individuals with Multiple Sclerosis (MS), because many of such items represent MS disease symptoms. However, research has been mixed on this issue: whereas some studies provide support for symptom overlap, others have found opposing evidence. We investigated this issue in two different MS samples with three different strategies. We (1) examined reliable change in depression symptom categories at two time points over three years, (2) assessed the relationship between variables associated with depression and different depression symptom subscales, and (3) assessed the relationship between symptom subscales and physical disability. In each instance we found significant evidence that items meant to assess vegetative symptoms of depression may be influenced by presence of MS disease symptoms or were not associated with other core elements or central correlates of depression. (*JINS*, 2008, *14*, 1057–1062.)

Keywords: Diagnosis, Mood disorders, Affective symptoms, Longitudinal studies, Central nervous system diseases, Demeyelinating disease

INTRODUCTION

The prevalence of depression is higher in multiple sclerosis (MS) than in the general population (e.g., Joffe et al., 1987), or other chronic illness and neurological patient groups (e.g., Minden et al., 1987). Despite this, depression often goes undetected and untreated in MS (Minden et al., 1987). Screening measures, such as the Beck Depression Inventory (BDI) or the Chicago Multiscale Depression Inventory (CMDI), are thus important for detecting mood disorders in individuals with MS because they are inexpensive, efficient means for alerting health professionals to possible mood disturbance.

Some researchers contend that assessment of depression in MS, particularly by self-report, is complicated by overlap between symptoms of depression and MS symptoms like fatigue, sleep disturbance, and sexual dysfunction (Mohr et al., 1997; Nyenhuis et al., 1995, 1998). Whereas it is known that some symptoms of MS are also symptoms of depression, and authors frequently discuss such overlap as a settled question (e.g., Goldman Consensus Group, 2005), there does not seem to be clear evidence of such overlap presenting a problem for assessment. Literature suggesting overlap has relied on cross-sectional studies, often examining the relative contribution of neurovegetative items to total depression score relative to non-MS controls (e.g., Mohr et al., 1997), which has been criticized elsewhere (Aikens et al., 1999). Whereas Nyenhuis and colleagues (1995) found little difference between an MS and non-MS group on the mood subscale of the CMDI, finding that vegetative depression items explained group differences between total BDI and CMDI scores, other authors have found little or no evidence of symptom overlap (Aikens et al., 1999; Moran & Mohr, 2005). Additionally, although measures exist, specifically designed to control for MS symptom overlap (e.g., BDI-Fast Screen; Benedict et al., 2003; CMDI, Nyen-

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huis & Luchetta, 1998) a panel of experts on MS and depression recently advocated for the use of the BDI, a measure with several neurovegetative items, suggesting simply a higher cutoff for depression (Goldman Consensus Group, 2005), a solution which misses 30% of MS patients with depression (Sullivan et al., 1995).

The current study seeks to find evidence of symptom overlap, which despite frequent assumptions of its existence appears to be somewhat elusive. To improve on existing research, our study uses a longitudinal design to examine the relationship of change among symptom categories and multiple time points and samples to verify the consistency of results. This multi-faceted strategy provides a more comprehensive analysis of this issue than has been reported. The question of symptom overlap has been assessed longitudinally in one study of change in BDI symptoms across a CBT treatment (Moran & Mohr, 2005). However, the study was limited in its generalizability because the sample consisted of participants with minimal disability, meaning few MS symptoms were present to overlap with depression symptoms. Also, subjects were selected for problems with depression. Thus, it is not surprising that the authors found significant improvement in all BDI items across treatment.

We used three strategies in the current study to investigate symptom overlap issues. First, we focused on the relationship of change among the three scales of the CMDI over two time points. Second, we used markers related to depression—depression history and depression proneness—and assessed the relationship between these markers and mood, evaluative and vegetative symptom items on the CMDI. Third, we assessed a marker of disease progression, physical disability, in order to assess differential correlations among depression symptom categories.

We had a number of a priori hypotheses. First, we predicted that change in CMDI mood and evaluative symptoms would be correlated, but that neither of these scales would be related to change in CMDI vegetative symptoms. We predicted this because we assumed that mood and evaluative items reliably assess depression symptoms, whereas vegetative symptoms are likely to be endorsed either when MS disease symptoms or true vegetative depression symptoms are present. Second, because vegetative depression items often pick up MS disease symptoms, we predicted that mood and evaluative symptoms would be associated with variables related to depression, but vegetative items would not. Finally, based on the same rationale, we hypothesized that vegetative items would be related to MS disease variables, but mood and evaluative items would not.

METHODS

Participants and Procedures

Two different MS participant groups were used in this study. For longitudinal analyses, the first sample consisted of 77 white MS patients. These patients were recruited from outpatient clinics and a regional National MS Society in Washington State. Of these original 77, 55 participants returned for follow-up testing 3 years later. Data analysis was performed using the 52 individuals participating in both testing sessions with data on all relevant variables. Participants were paid $75 for participation in the study at time 1; no monetary payment was made for participation in the follow-up. The study was approved by the Institutional Review Board at Washington State University (WSU). In the second group of analyses, participants were recruited from central Pennsylvania. Participants were paid $100 for participation in the study, which was approved by the Institutional Review Board at Penn State University (PSU). Participant characteristics are detailed in Table 1.

Exclusion criteria for all participant groups were as follows: (a) neurological disease other than MS; (b) drug or alcohol abuse history; (c) 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. For all participant groups, MS diagnosis and course type were assigned by board-certified neurologists according to accepted research protocols (Lublin & Reingold, 1996; Poser et al., 1983). Testing sessions involved assessing cognitive, physical, and emotional functioning. The human data in this manuscript were obtained in compliance with the standards of the Institutional Review Boards of WSU and PSU.

Measures

Chicago Multiscale Depression Inventory (CMDI; Nyenhuis et al., 1995)

The CMDI is a 42-item self-report measure consisting of three subscales. These 14-item scales measure mood, evaluative and vegetative symptoms. Participants rate how different adjectives or short phrases describe their experience (e.g., sad, easily awakened) over the past week using a 1 to 5 scale. All CMDI subscale scores were converted to *t*-scores using Nyenhuis et al.'s (1995) control sample as the reference group.

Beck Depression Inventory and Beck Depression Inventory-II (BDI; Beck & Steer, 1987; BDI-II; Beck et al., 1996)

The BDI is widely used as a self-report measure for screening depression symptoms in individuals with MS. It is a 21-item inventory asking participants to rate depressive symptoms over the past week. The BDI-II is similar but asks examinees to rate symptoms over the past two weeks. These scales were used only to describe the depression symptom levels in these samples.

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Table 1. Summary of participant characteristics

Sample 1 (n of 52)						
Variable	Mean T1	SD T1	Range	Mean T2	SD T2	Range
Age	46.57	(7.61)	30–64	49.33	(7.60)	32–66
Symptom Duration (yrs.)	14.04	(9.37)	1–48	16.87	(9.24)	4–50
Diagnosis Duration (yrs.)	7.57	(5.91)	0–34	10.40	(5.97)	3–37
EDSS Rating	4.55	(1.44)	0–7.5	4.71	(1.61)	0–8.0
CMDI mood scale t-scores	49.18	(7.61)	40–71	51.45	(11.85)	41–91
CMDI evaluative scale t-scores	51.54	(12.75)	42–107	49.59	(11.73)	42–92
CMDI vegetative scale t-scores	61.19	(13.77)	34–93	61.94	(13.87)	35–91
BDI	10.17	(7.39)	2–40	8.55	(5.63)	0–21
	n (T1)	% (T1)		n (T2)	% (T2)	
BDI depressed*	26	50		20	38%	
Clinical course						
Relapsing-remitting	30	58				
Secondary progressive	15	29				
Primary progressive	6	12				
Progressive relapsing	1	2				
Sample 2 (n of 96)						
Variable	Mean T1	SD T1	Range			
Age	47.41	(8.98)	23–65			
Symptom Duration (yrs.)	14.89	(8.75)	1–37			
Diagnosis Duration (yrs.)	10.89	(7.81)	1–37			
EDSS Rating	4.59	(1.56)	0–8.0			
CMDI mood Scale t-score	50.84	(10.42)	41–83			
CMDI evaluative scale t-score	52.18	(14.51)	42–111			
CMDI vegetative scale t-score	61.60	(12.20)	40–97			
BDI-II	11.91	(7.24)	0–32			
DPRS	50.01	(13.80)	13–79			
	n (T1)	% (T1)				
BDI-II depressed*	34	35				
Clinical Course						
Relapsing-remitting	73	58				
Secondary progressive	18	29				
Primary progressive	4	12				
Progressive relapsing	1	2				

Note. *Patients falling in the mild-moderate BDI and BDI-II depressed range or above.
BDI, Beck Depression; CMDI, Chicago Multiscale Depression Inventory; EDSS, Expanded Disability Status Scale.

Depression Proneness Rating Scale (DPRS; Zemore et al., 1990)

The DPRS measures an individual's general disposition towards depression and has been shown to be a better predictor of past depressive episodes than the BDI, and also predictive of future episodes of depression (Zemore et al., 1990). The DPRS was used in this study as a criterion variable against which different clusters of depression self-report items could be assessed.

The DPRS is a 13-item self-report inventory where participants respond to questions on a 7-point scale with the instructions to "summarize your feelings and attitudes over the past 2 years." The DPRS demonstrates adequate test-retest reliability and was supported as a unidimensional measure of depression proneness (Zemore et al., 1990).

Expanded Disability Status Scale (EDSS; Kurtzke, 1983)

Participant disability was assessed using a self-report version of the EDSS as described in Arnett et al. (2001). The EDSS is designed to assess MS disease progression and neurological impairment, in which participants are rated according to their functional abilities different domains. Solari et al. (1993) noted that self-administered versions of

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the EDSS were comparable to neurologists' independent ratings. The scale ranges from 0 to 10, with higher ratings indicating greater disability.

History of Depression

This study uses history of depression as a criterion variable to investigate symptom overlap. Depression in the general population has been found to be a highly recurrent disorder (e.g., Frank & Thase, 1999) and history of past depression has emerged as one of the best predictors of current depression (Coyne et al., 2001). Sixty-percent of individuals experiencing a single depressive episode will experience a second episode (American Psychiatric Association, 2000). Given this, in the present study, we used depression history as a standard against which categories of traditional depressive symptoms within an MS sample could be assessed.

Depression history was assessed by a single self-report item: "Do you currently have or have you ever had problems with depression?" Research has demonstrated that such assessment of past depression is suspect, because it is influenced by current depression (Coyne et al., 2001). Because of this, results involving this item should be viewed with caution and suggest directions for future research.

RESULTS

Key results from the analyses to follow are shown in Table 2. For longitudinal data, we used reliable change scores in an attempt to derive significant changes in depression symptoms above artifacts such as response bias and same-method variance. We calculated reliable change scores from time 1 to time 2 for all depression indices using an adaptation (Speer, 1992) of a reliable change index originally proposed by Jacobson and Truax (1991). Reliable change indices allow for the calculation of change in scores that are reliable, that is, not simply caused by the error inherent in the particular measure being examined. Following Speer's guidelines (1992), we also used estimated true scores at time 1 for all depression indices because of evidence for regression to the mean. We derived Cronbach's α from the current sample for the reliability indices used in calculating true score estimates. We calculated a threshold for reliable change in this sample, using a criterion of .05, and coded participants into one of three categories based on this threshold: depression improved, depression worsened and no change. Using these methods, on the CMDI mood scale, 11 participants reliably improved, 14 worsened, and 27 showed no change. On the evaluative scale, 7 improved, 7 worsened, and 38 showed no change. On the vegetative subscale, 5 improved, 8 worsened, and 39 showed no change.

We correlated these ordinal data using Spearman's rho, a correlational method intended for rank ordered data. Change in CMDI mood symptoms was highly correlated with change in evaluative symptoms, r (50) = .62, $p < .001$. However, vegetative subscale change was neither significantly associated with the mood, r (50) = .19, ns, nor evaluative scale, r (50) = −.20, ns.

Table 2. Study correlations

Correlations: Reliable change in depression subscales		
Sample 1, time 1 & 2	*r*	*p*
CMDI Evaluative and mood	.62	<.001
CMDI vegetative and mood	.19	ns
CMDI vegetative and evaluative	−.20	ns
Correlations: Depression categories and depression history		
Sample 2	*r*	*p*
CMDI Mood Subscale	.38	<.001
CMDI Evaluative Subscale	.31	<.001
CMDI Vegetative Subscale	.10	ns
Correlations: Depression categories and DPRS		
Sample 2	*r*	*p*
CMDI Mood Subscale	.53	<.001
CMDI Evaluative Subscale	.48	<.001
CMDI Vegetative Subscale	.15	ns
Correlations: Depression categories and EDSS		
Sample 1, Time 1	*r*	*p*
CMDI Mood Subscale	.13	ns
CMDI Evaluative Subscale	.09	ns
CMDI Vegetative Subscale	.31	<.05
Sample 1, Time 2		
CMDI Mood Subscale	.02	ns
CMDI Evaluative Subscale	.06	ns
CMDI Vegetative Subscale	.36	<.05
Sample 2		
CMDI Mood Subscale	.16	ns
CMDI Evaluative Subscale	.20	ns
CMDI Vegetative Subscale	.36	<.001

Next we assessed associations between categories of CMDI and variables related to depression. Depression History was only assessed among the Pennsylvania sample. CMDI Mood, r (94) = .38, $p < .001$, and Evaluative, r (94) = .31, $p < .001$, symptoms were significantly related to Depression History, but Vegetative symptoms were not, r (94) = .10, $p >$ ns.

Second, we examined the relationship between depression symptom scales and the DPRS in the Pennsylvania sample. Medium to large correlations were found between the DPRS and CMDI Mood, r (94) = .53, $p < .001$, and Evaluative, r (94) = .48, $p < .001$, subscales, while the Vegetative subscale, r (94) = .15, ns, was not significantly related to DPRS scores.

Finally, we examined correlations between CMDI scales and physical disability. At all three data points used in this study, EDSS ratings were related to CMDI vegetative symptoms, but not to mood or evaluative symptoms. Using the first sample at time one, EDSS ratings were related to CMDI vegetative symptoms, r (50) = .31, $p < .05$, but not to

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mood, r (50) = .13, ns, or evaluative symptoms, r (50) = .09, ns. This same pattern was evident at time two in this sample (vegetative, r (50) = .33, $p < .05$; mood, r (50) = .02, ns; evaluative, r (50) = .06, ns) and the second sample (vegetative, r (94) = .36 $p < .05$; mood, r (94) = .16, ns; evaluative, r (94) = .20, ns).

DISCUSSION

The aim of this study was to investigate overlap between items meant to assess neurovegetative symptoms of depression and MS disease related symptoms. Using a number of methods, we found consistent support for symptom overlap. We found that, although reliable change in CMDI Mood and Evaluative symptoms was highly correlated, vegetative items were not correlated with either subscale. This longitudinal approach is the first in the literature using a sample with a sufficient range of disease impairment in addressing the question of symptom overlap.

We also assessed the relationship between categories of depression symptoms and variables associated with depression, finding a pattern consistent with the above data. Depression history and depression proneness were both associated with CMDI Mood and Evaluative symptoms, but were not related to Vegetative symptoms. The lack of association between vegetative items and variables related to depression suggests that endorsement of these items reflects symptoms not related to depression.

Exploring what these symptoms might be related to, we examined the relationship between depression scales and EDSS scores. Consistent at three data points using two different samples with the CMDI, we found that MS physical disability was significantly associated with vegetative items but not mood or evaluative items. This relationship suggests that endorsement of vegetative items frequently reflects endorsement of disease rather than depression symptoms.

There were limitations to the present study. Comparing clinician assessment of depression items or depression history to self-report of depression symptoms would represent a more rigorous methodology than used here. Our methodology was also limited in that all of our analyses were correlational. Thus, alternative explanations are possible for each of our analyses. In addition, the use of a one-item depression history index may be insufficient. Also, examining a depressed, non-MS control group over time would allow for clearer conclusions to be drawn.

Despite the limitations of this study, the consistency of the results is of note. Each of the findings is consistent with the notion of MS and vegetative depression symptom overlap. The longitudinal approach used here is also of importance, in that reliable improvement or worsening in depression would be predicted to be uniform across depression symptom categories. In other words, if someone were to be depressed at time one, and not depressed at time two, it would not be expected that their neurovegetative symptoms would linger despite remission of mood and evaluative symptoms.

Only a small portion of those diagnosed with MS who are depressed receive treatment, making screening for depression essential. However, screening measures for depression are more useful if they accurately assess depression. Investigating the issue of neurovegetative item contamination caused by overlap with MS disease symptoms, we found consistent support for vegetative items measuring something other than depression, as well as finding a reliable relationship between only vegetative symptoms and MS disease progression. Our findings support the use of strategies to limit the inflation of depression scores among MS samples from vegetative depression items, steps that may provide more accuracy in screening for depression.

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