

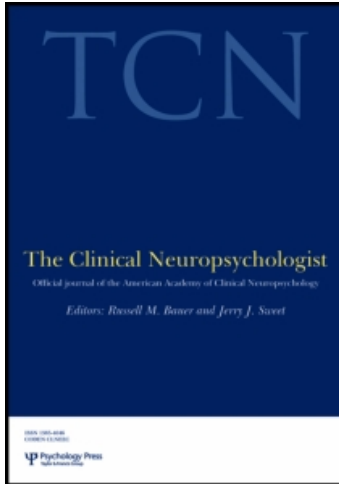
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### Assessment Of Depression In Multiple Sclerosis: Development Of A “Trunk And Branch” Model

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## **CE** ASSESSMENT OF DEPRESSION IN MULTIPLE SCLEROSIS: DEVELOPMENT OF A “TRUNK AND BRANCH” MODEL

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*The objective of the present investigation was to improve the detection of depression in multiple sclerosis (MS). It has been hypothesized that the overlap of MS symptomatology and neurovegetative depression symptoms may lead to an over-diagnosis of depression in MS. Discerning what is depression and what is more attributable to the disease renders a complicated picture when assessing depression in medically ill people. Given this, “trunk and branch” models have been proposed. In such models “trunk” symptoms are purported to be the symptoms common to the medical condition and less likely reflective of depression. “Branch” items are those symptoms that are independent of the medical condition and likely reflect depression. In the present investigation we compared depressed individuals with MS, non-depressed individuals with MS, and non-depressed controls, to devise a “trunk and branch” model for use with individuals with MS. By identifying which symptoms are typical in MS, which exceed what is typical in MS, and which symptoms are independent of MS, but more often present in depressed individuals with MS, we hoped to present a better understanding of the nature of depression in MS.*

**Keywords:** Multiple sclerosis; Depression; Assessment.

### INTRODUCTION

Disentangling symptoms of depression and medical illness is a significant hurdle and often an etiological conundrum. Symptoms such as fatigue, sleep disturbance, and sexual dysfunction, among others, plague individuals suffering from depression and medical illness. Depression may also precipitate an illness and amplify medical conditions while medical illnesses are also more common in the mentally ill population, particularly depression (Katon, 1984). Moreover, reactive hypotheses of depression in medically ill people render it difficult to determine what reflects depression and what reflects a normal adjustment to being diagnosed with a chronic medical disorder. Given this difficulty of separating medical and psychological symptoms, depression in medically ill people has been conceptualized differently than in the general population.

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Clark, Cook, and Snow (1998) present a concise discussion of the theories and approaches in assessing depression in medically ill people. For instance, some view cognitive symptoms as the best indicators of depression, including symptoms of self-accusation, suicidal ideation, hopelessness, sense of guilt, sense of failure, and indecisiveness (Cavanaugh, Clark, & Gibbons, 1983; Goldberg, Bridges, Duncan-Jones, & Grayson, 1988). In fact, when conducting a latent trait analysis of the Beck Depression Inventory (BDI), Clark, Cavanaugh, and Gibbons (1983) found that among medically ill inpatients (e.g., individuals with diabetes, cancer, renal insufficiency, cardiovascular disease, respiratory disorder, neurological disorder, gastrointestinal disease, and bone or connective tissue disease), six symptoms best depicted depression in a medical sample. These included sense of failure, suicidal ideation, feelings of punishment, loss of interest, dissatisfaction, and indecisiveness. Others view somatic symptoms as indicators of depression, especially if symptoms are above the expected severity of the medical disorder (Arnau, Meagher, Norris, & Bramson, 2001; Katon, 1982). Similarly, Cavanaugh (1986) suggested that when assessing for depression in medically ill people, somatic complaints should be used in conjunction with affective-cognitive symptoms of depression. In particular, when examining the severity and frequency of affective-cognitive and vegetative symptoms of the BDI, Cavanaugh determined that the *frequency* of vegetative items increased minimally as depression worsened. However, the *severity* of the vegetative symptoms increased linearly as the severity of depression increased. She asserted that, if somatic complaints were not proportionate to the medical illness, and were related to the affective-cognitive symptoms of depression, they might be more representative of depression. Similarly, Rodin and Voshart (1986) speak to the importance of identifying "masked depression" in which pain and other physical complaints are presenting features of depression. Together they suggest that attention be given to all physical complaints, especially if the severity exceeds what is typical for the medical condition. Finally, some investigators have examined the extent to which motivation and behavioral changes are indicative of underlying depression in medically ill people (Emmons, Fetting, & Zonderman, 1987; Van Hemert, Hawton, Bolk, & Fagg, 1993). Such aspects of depression include loss of energy, social withdrawal, lack of interest, and dissatisfaction. In review of these theories it may appear that no domain of depressive symptomatology is less relevant to the diagnosis in a medical population. What appears more pertinent is the extent to which these symptoms *exceed* what is caused by or expected in the disease.

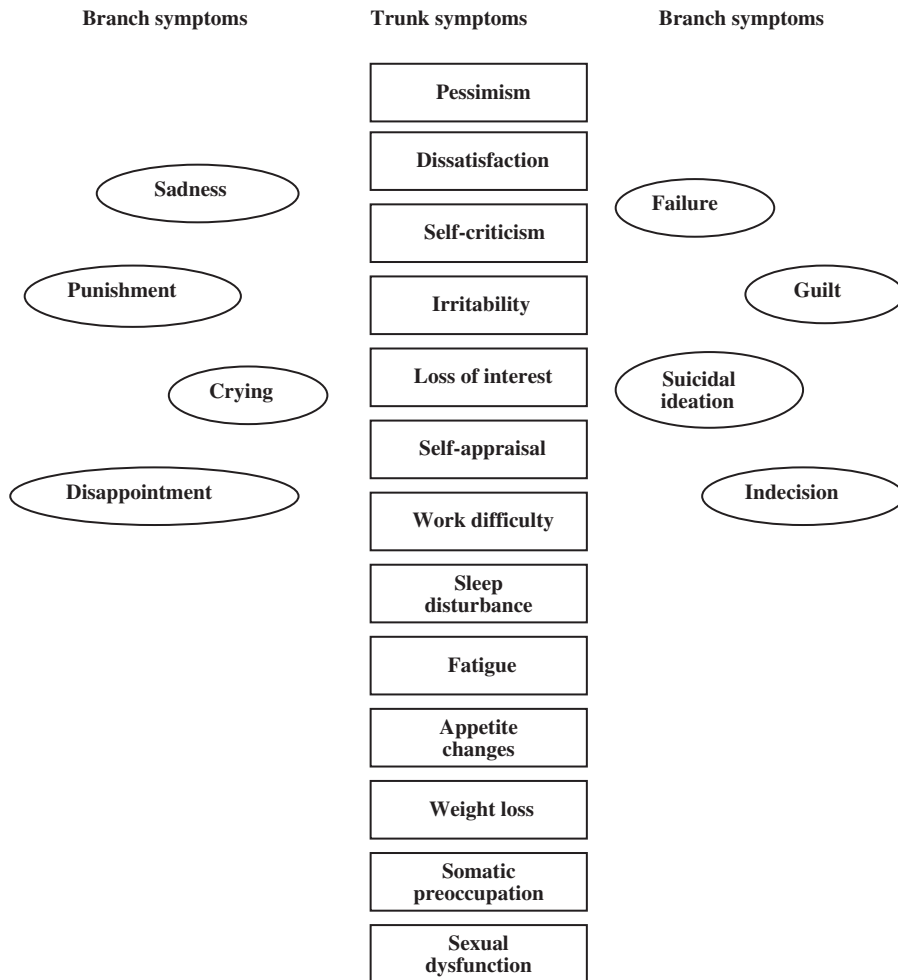
### **Possible model for detection of depression in medically ill populations**

Given the aforementioned theories, inclusion of all items of depression appears warranted in medical populations. However, a reconceptualization of our assessment models is needed. Parker, Hilton, Hadzi-Pavlovic, and Bains (2001) present a "trunk and branch" model of depression in a medical sample. In such a model the "trunk" items are thought to be the items commonly found in both depressed and non-depressed individuals with the illness of interest. These items are ones impacted more by the disease than depression per se. The "branch" items are those less impacted by the illness, and as such are thought to be endorsed by

depressed individuals in this model. However, what Parker et al. found was that depressed individuals reported higher levels of all items, both trunk and branch. Such findings may be consistent with Cavanaugh's (1986) and Rodin and Voshart's (1986) suggestions that not only are the extraneous depressive symptoms endorsed, but that medically related complaints may be disproportionate to the particular medical condition among those that are depressed. Thus when attempting to utilize such models it is necessary to not only determine what the "trunk" symptoms are, but whether the endorsement of the "trunk" symptoms is above the norm for the particular disorder and/or related to symptoms more indicative of depression in the disorder. The present investigation involves the adoption of this model for use with a multiple sclerosis (MS) sample, including first identifying which symptoms are common to MS and then exploring their severity and relationship to other more "depressive" symptoms. See our proposed model in Figure 1. To date, exploration of which symptoms are purported to be common to MS and which are most indicative of depression in MS among depressed and non-depressed individuals with MS and controls has not been investigated.

## MULTIPLE SCLEROSIS AND DEPRESSION

Depression is common in MS. Point prevalence rates reported in the literature range from 27% to 54% (for a full review, see Arnett, Barwick, & Beeney, 2008). However, lower prevalence rates (approximately 17% to 26%) have been found when stringent criteria such as clinical interviews or diagnostic codes are used (Mohr, Hart, Fonareva, & Tasch, 2006; Nyenhuis et al., 1995; Patten, Svenson, & Metz, 2005). Detection of depression in MS is difficult given the nature of the disease, the demographics of the people afflicted and, most importantly, the overlap with physical complaints. Many of the cardinal symptoms of depression are also hallmarks of the disease (e.g., fatigue, sleep disturbance), rendering accurate assessment difficult. To meet criteria for a mood disorder, according to the *Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition [DSM-IV]* (American Psychiatric Association, 1994), an individual must endorse at least five of the nine following symptoms: depressed mood, loss of interest or pleasure, weight/appetite changes, sleep disturbance, loss of energy/fatigue, psychomotor retardation or agitation, feelings of worthlessness/guilt, diminished concentration, or recurrent thoughts of death. Individuals with MS, depressed or not, may easily endorse six of these items (sleep disturbance, fatigue, appetite changes, concentration difficulties, psychomotor slowing, and loss of interest/pleasure) because they are also disease symptoms of MS (Mohr et al., 1997). Given this, MS is recognized in the *DSM-IV* as a common medical disorder associated with depression. The *DSM-IV* criteria allow for an individual with "low mood", who does not meet the full criteria listed above, to be diagnosed as depressed. Despite such leniency in the *DSM-IV*, evaluation based solely on mood may not create an accurate picture of depression for all suffering from MS. Care providers and researchers cannot deny the importance of taking the vegetative, cognitive/evaluative, and mood components of depression into consideration when making a diagnosis. Again, if such an approach is taken, an understanding of what symptoms are common, excessive, or independent of the disease must be developed.



**Figure 1** Proposed trunk and branch model of depression in MS based on Parker et al.'s (2001) model and relevant clinical and research findings in MS.

**Vegetative complaints: Depression or MS?**

Frequent physical symptoms of MS include a variety of somatic complaints as well as chronic pain and numerous neuropsychological difficulties (Shnek, Foley, LaRocca, Smith, & Halper, 1995). In addition, individuals with MS experience secondary symptoms such as fatigue and sleep disturbance at strikingly high rates (Clark et al., 1992; Saunders, Whitman, & Schaumann, 1991). Appetite changes may also be found in MS due to medications or difficulty swallowing. Finally, sexual dysfunction in MS occurs quite frequently (McCabe, McKern, McDonald, & Vowels, 2003). Despite the high prevalence of sexual dysfunction and the potential contribution of the MS disease process to it, Randolph, Arnett, Higginson, and Voss (2000) contend that lack of interest in sex may be a good indicator of

depression in an MS sample and given even more weight than other neurovegetative symptoms. In particular, using structural equation modeling encompassing neurovegetative symptoms of depression (sleep disturbance, tiredness, disinterest in sex, appetite changes, and decision difficulties) disease severity, depression and fatigue, these investigators showed that lack of interest in sex was most related to depressed mood and independent of disease severity and fatigue. Taken together, such findings show that while fatigue, sleep disturbance, appetite changes, and sexual dysfunction are common MS symptoms, a distinction must be made regarding whether these symptoms exceed what is expected for the disease or relate to underlying depression.

### **Beyond the physical: How are evaluative depression symptoms influenced by MS?**

Given the high level of functional disability of some patients and the exuberant age at which the disease occurs, individuals with MS may evaluate themselves differently relative to others. Furthermore, not being able to do what one once enjoyed, or as well as one once did, may lead to a negative self-appraisal or withdrawal of activities. This sense of anhedonia or negative appraisal would typically present as depression. However, in MS it may at times simply be a reflection of one's disability (Nyenhuis et al., 1995). Alternatively, when asked about sense of self-appraisal, individuals with MS may truthfully report that they are less capable or feel more self-critical.

**Coming full circle: Are we left only with mood?** It may appear that mood is the only domain that unambiguously reflects depression in MS. In fact, Nyenhuis et al. (1995) suggested that the mood scale on the Chicago Multiscale Depression Inventory (CMDI) was the best indicator of depression in MS. These investigators found lower rates of depression when only the mood scale was used to diagnose depression compared to the full scale that included mood, evaluative, and vegetative symptoms of depression (17.7% vs 26.6%). When matched with healthy controls based on BDI scores, individuals with MS did not differ on mood, but displayed significantly higher vegetative and evaluative scales, suggesting that these scales may be the cause of inflated prevalence rates of depression in MS. Similarly, Feinstein and Feinstein (2001) showed that, although 73% of their sample endorsed some degree of emotional dyscontrol—namely reports of irritability, crying, and sadness as measured by the BDI—only 17% met criteria for depression when more stringent criteria (*DSM-IV*) were used (Feinstein & Feinstein, 2001). Such findings suggest that if attention is only given to reports of mood/affective symptoms on self-report measures such as in Nyenhuis et al.'s study or if structured clinical interviews are used we may find lower and more accurate prevalence rates of depression in MS. That said, 48% of Feinstein and Feinstein's sample—which is closer to the higher prevalence estimates of depression in MS—had some sort of emotional difficulty. Feinstein and Feinstein caution that only employing the "low mood" criterion of the *DSM-IV* may result in overlooking the nearly 50% reporting significant distress with no formal syndromal diagnosis.

In summary, past approaches to rectifying the problem of MS symptom/vegetative depression symptom overlap have involved the removal of somatic items, or given heightened priority to a few mood or evaluative items hypothesized to be relatively independent of MS. It is here proposed that, rather than allocating greater relative importance to the few remaining depression items, or eliminating potentially crucial somatic items, further exploration of all symptom clusters of depression in MS is necessary.

With these considerations in mind, the purpose of the present investigation was to gain a better understanding of what symptoms are most indicative of depression in MS in hopes of improving its assessment and developing a “trunk and branch” model for MS. By disentangling which symptoms are common to MS and which are common to depression, a better appreciation of how to best conceptualize and assess depression in MS can be obtained. To accomplish these aims, comparisons between non-depressed healthy controls, non-depressed individuals with MS, and depressed individuals with MS on a modified self-report depression measure (modified BDI) were conducted, as described below.

## RESEARCH DESIGN AND METHODS

### Participants

**Individuals with multiple sclerosis.** Multiple sclerosis participants were recruited through the Western Pennsylvania chapter of the Multiple Sclerosis Society and local support group meetings for MS. Exclusion criteria for MS participants included history of alcohol/drug abuse; history or current diagnosis of a neurological disorder besides MS; severe visual or motor impairment that may impede cognitive testing that was conducted for purposes outside the scope of the present investigation; evidence of a premorbid learning disability; and severe physical or neurological impairment that would have made evaluation impractical.

**Healthy controls.** Recruitment of healthy controls was conducted through the MS chapter and referrals by our MS participants. MS participants were asked if they had a friend of similar age and education who would want to participate. Exclusion criteria for healthy controls included the same relevant criteria as those used for the MS sample.

**Significant others.** All MS participants and healthy controls were asked to identify a significant other (e.g., spouse, child, partner) to complete questionnaires pertaining to the participant’s mood, coping skills and other psychosocial variables approximately 1 week prior to the evaluation.

### Procedures

Participants underwent a neuropsychological evaluation as part of an ongoing study examining the contributors to and consequences of depression in MS. A psychosocial interview was conducted on the same day and prior to testing. The battery consisted of cognitive tests interspersed with self-report measures of depression, anxiety, fatigue, and psychosocial factors. Participants completed most

measures assessing present depression and anxiety (see below) on the day of testing. Administration of these measures was always in the following order: BDI-II, CMDI, STAI, MBDI, but these questionnaires were distributed throughout the overall test battery. Participants and significant others of the participants also completed additional self-report questionnaires the week prior to testing. In particular, significant others completed measures rating participants' depression (the Chicago Multiscale Depression Inventory [CMDI]) and participants also completed a measure of their proneness and past experience of depression (the Depression Proneness Rating Scale [DPRS]). Finally, the Structured Clinical Interview for DSM-IV Axis I Disorders – Patient Edition (SCID) for major depressive episode was conducted at the completion of the testing session.

For the purposes of the present study certain inclusion and exclusion criteria were applied to identify the three respective groups of the present investigation: depressed MS, non-depressed MS, and healthy controls. Group selection was based on the following:

**Depressed MS group.** The identification of depressed individuals was based on the following: (1) a diagnosis of a major depressive episode on the SCID interview, (2) a score above the median on the DPRS, and/or (3) a score of one and a half standard deviations or more above the mean of the significant others' report of participants on the CMDI mood subscale, per Nyenhuis et al.'s (1995) recommendation. Additionally, we chose this one and a half standard deviation criterion because this is a common approach taken to identifying clinically significant levels of symptomatology on self-report measures, including the MMPI-2. Individuals who met at least two out of these three criteria were labeled as suffering from clinically significant depressive symptoms. We reasoned that utilizing our two out of three criteria would allow us to capture individuals likely to be experiencing significant depression who may not necessarily have endorsed all DSM-IV criteria. The mean for the significant other's CMDI was derived from the healthy control sample (Mean = 22.73,  $SD = 9.20$ ). A median split of the DPRS (Median = 51) was conducted with the MS sample to separate the groups.

**Non-depressed MS group.** For the purpose of removing any confounding effects of psychological distress among our non-depressed MS group, we excluded any individual with MS whose self-reported anxiety was one-and-a-half standard deviations or more above the mean on the State Trait Anxiety Inventory (STAI) state or trait scale per standardization norms. Again, we chose a cutoff of one and a half standard deviations above the mean because this is a common approach taken to identifying clinically significant levels on self-report measures.

**Healthy controls.** Healthy controls were excluded if (1) they met criteria for depression on the SCID and/or met two of the other criteria for depression (proneness and significant other's report); and (2) their reported anxiety was one and a half standard deviations or more above the mean on the STAI state or trait scale.

## Measures

**Structured Clinical Interview for DSM-IV Axis I Disorders – Patient Edition (SCID).** The SCID (First, Spitzer, Gibbon, & Williams, 1995) was conducted by the same clinician who administered the testing battery. The clinician conducted the interview following the neuropsychological battery and was kept blind to participants' self-report data. For the purposes of this investigation the SCID interview included only the Major Depressive Episode (MDE) component of the mood disorders module.

**Depression Proneness Rating Scale (DPRS).** The DPRS (Zemore, Fisher, Garratt, & Miller, 1990) examines an individual's susceptibility to depression and tendency to experience long-lasting depression. It has been shown to be a valid predictor of past (measured by prior treatment, antidepressant prescriptions, suicide attempts, and hospitalizations) and future (as measured by the BDI) depression in the general population. The DPRS asks participants about the frequency, severity, and duration of depressive episodes. It also includes depressive symptoms; that is, sense of failure, discouragement, isolation, etc. Participants are asked to rate themselves on a 7-point Likert scale on these depressive features they have experienced over the past 2 years in comparison to other people. The DPRS was chosen as a measure of one's propensity and past experience of depression in hopes of capturing participants who may suffer from depression but who were not experiencing a depressive episode at the time of evaluation as per the SCID.

**Chicago Multiscale Depression Inventory (CMDI).** The CMDI (Nyenhuis et al., 1998) is a 42-item inventory consisting of three subscales: mood, evaluative, and vegetative. Each subscale contains 14 items. These subscales can be used separately or in combination with one another. Significant others of the participant completed the CMDI. Other investigators have suggested that reports from significant others be obtained (Aikens et al., 1999), as patients may not be most accurate in their perceptions of depression. Significant others of participants are asked to rate on a scale of 1 to 5 the extent to which each word/phrase describes the patient during the past week, including today with "1" being "Not at All" and "5" being "Extremely." For the purpose of identifying depressed participants by other's reports, only the mood subscale was used. The decision to utilize only the mood scale of the CMDI was based on previous suggestions that the mood scale may be the least confounded by disease symptomatology. Again, a cutoff of one and half standard deviations above the mean of controls was also used to differentiate depressed from non-depressed as recommended by Nyenhuis et al. (1995).

**Modified BDI (MBDI).** The modified BDI takes into account research in MS and clinical observations in adding follow-up questions to certain BDI (Beck & Steer, 1987) items thought to be confounded with MS symptomatology. These questions are intended to ascertain if and how much one's endorsement of particular BDI items is due to MS or depression, per se. This modified BDI was designed by the present authors, but the follow-up questions were not explored in the present study. Only participants' responses to the original 21 BDI items were included in the present study. Participants rate themselves on a 4-point Likert scale ranging

from 0 to 3 the extent that they have experienced the symptom in the past week yielding a total score in the range of 0 to 63.

**Beck Depression Inventory-II (BDI-II).** The BDI-II (Beck, Steer, & Brown, 1996) is a self-report inventory consisting of 21 items. The BDI-II is a revision of the BDI-I. Modifications included allowing for responses indicating both increase and decrease in sleep and appetite as well as the removal of four items (body image, work difficulty, somatic preoccupation, and work difficulty). These items were replaced with items assessing agitation, worthlessness, loss of energy, and concentration difficulty. Participants rate themselves on a 4-point Likert scale ranging from 0 to 3 the extent that they have experienced the symptom in the past 2 weeks, yielding a total score in the range of 0 to 63.

**State Trait Anxiety Inventory (STAI).** The STAI (Spielberger & Gorsuch, 1983) is a 40-item measure divided into two 20-item scales to assess both present (state) and longstanding (trait) anxiety. Ratings are based on a 4-point Likert scale. Participants are asked to describe how they feel at the present moment (state) as well as how they generally feel (trait).

**Expanded Disability Status Scale (EDSS).** The EDSS (Kurtzke, 1983) measures disability based on ambulation and neurologic symptoms. Scores range from "0" to "10", with "0" being no impairment or disability and "10" being death due to MS. Scores ranging from 1.0 to 4.5 refer to individuals with MS who are fully ambulatory. Scores between 5.0 and 7.5 are indicative of some impairment in ambulation that requires some aid (cane, walker, wheelchair). Scores above 7.5 indicate that the individual can only be propelled by others in a wheelchair or are essentially restricted to a bed or chair. A self-report measure used in other studies (e.g., Arnett, Higinson, & Randolph, 2001) was administered. Self-report measures have been found to have an intraclass correlation with independent ratings made by neurologists (.84; Solari et al., 1993). An experienced neuropsychologist with expertise in MS (P.A.) made the EDSS ratings based on the self-report of participants on a questionnaire after receiving instruction from a neurologist specializing in MS.

## RESULTS

A total of 97 individuals with MS and 27 healthy controls participated in a larger, ongoing investigation examining the contributions and consequences of depression in MS. Of these, 17 individuals with MS were found to meet two out of the three criteria for depression. In particular, all 17 depressed individuals met criteria based on the DPRS; 11 met criteria for depression based on the SCID interview and 10 met criteria based on significant others' report. Thus, six depressed participants did not meet full criteria for a present depressive episode, but reported a proneness to depression and were rated as depressed by their significant others. Of the remaining sample of 80 individuals with MS who did not meet criteria for depression, 13 were excluded from the study because their self-reported anxiety was one and a half standard deviations or more above the mean on the State Trait Anxiety Inventory (STAI) state or trait scale per standardization norms. This resulted in a total of 67 individuals in our non-depressed MS group.

**Table 1** Participant demographics and comparisons of depressed and non-depressed multiple sclerosis (MS) groups on illness variables, depression, and anxiety

Variable	Depressed MS ( <i>N</i> = 17)	Non-Depressed MS ( <i>N</i> = 67)	Controls ( <i>N</i> = 22)
Age	45.24 (8.39)	47.93 (9.30)	46.18 (13.36)
Education	13.76 (1.89)	14.42 (1.99)	15.00 (1.93)
WAIS-R IQ	99.76 (9.86)	106.09 (9.23)	106.04 (12.17)
Estimate			
Gender (F/M)	14F(82%)/3M	56F(84%)/11M	18F(82%)/4M
Variable	Depressed ( <i>N</i> = 17)	Non-Depressed ( <i>N</i> = 67)	<i>t</i> -test, <i>p</i>
	Mean ( <i>SD</i> )	Mean ( <i>SD</i> )	
EDSS	5.18 (1.50)	4.32 (1.54)	<i>t</i> (82) = -2.06, .043
Symptom			
Duration	15.71 (8.34)	14.82 (9.22)	<i>t</i> (82) = -.360, <i>ns</i>
Diagnosis			
Duration	10.59 (6.42)	11.15 (8.66)	<i>t</i> (82) = .250, <i>ns</i>
DPRS	62.06 (7.67)	44.58 (13.23)	<i>t</i> (82) = -7.09, <.001
CMDI Mood	32.47 (9.23)	18.63 (5.16)	<i>t</i> (82) = -5.95, <.001
CMDI Eval	26.53 (10.24)	16.45 (3.56)	<i>t</i> (82) = -4.00, .001
CMDI Veg	40.35 (7.50)	33.21 (8.89)	<i>t</i> (82) = 3.05, .003
CMDI Total	99.35 (22.81)	68.28 (12.86)	<i>t</i> (82) = -5.40, <.001
MBDI	16.06 (5.96)	7.88 (3.82)	<i>t</i> (82) = -5.38, <.001
BDI-II	20.35 (6.49)	8.61 (4.80)	<i>t</i> (82) = -8.36, <.001
STAI Trait	50.88 (6.31)	36.03 (6.99)	<i>t</i> (82) = -7.96, <.001
STAI State	34.94 (9.59)	31.13 (7.16)	<i>t</i> (82) = -1.82, .072

WAIS-R = Wechsler Adult Intelligence Scales-Revised; EDSS = Expanded Disability Status Scale; DPRS = Depression Proneness Rating Scale; CMDI Mood, Eval, Veg, Total = Chicago Multiscale Depression Inventory Mood, Evaluative, Vegetative subscales, and Total raw score; MBDI = Modified Beck Depression Inventory; BDI-II = Beck Depression Inventory-Second Edition; STAI Trait = State Trait Anxiety Inventory Trait Scale; STAI State = State Trait Anxiety Inventory State Scale.

Similarly, 5 healthy controls were removed from the original sample for the same reason, leaving a control group of 22 participants.

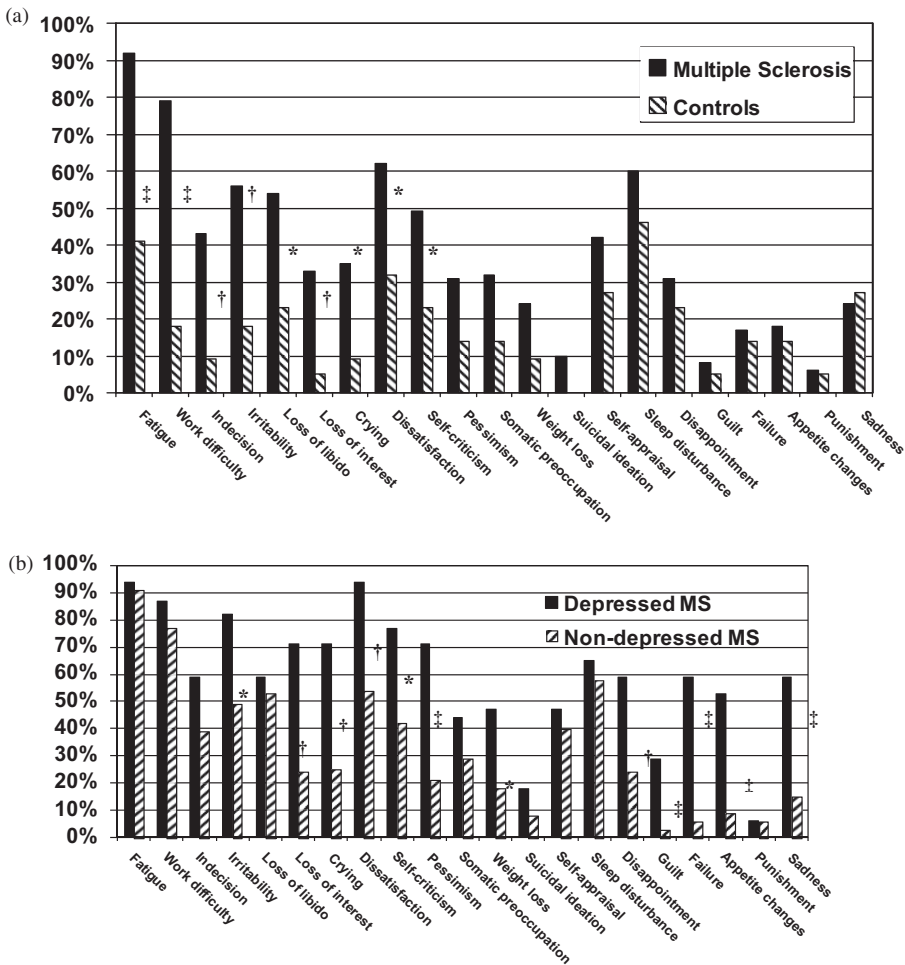
Comparisons of depression and anxiety measures between the depressed and non-depressed MS groups were conducted (see Table 1). Reports of depression and trait anxiety were greater for the depressed MS group than the non-depressed MS group. There were no significant between-group differences for current anxiety (STAI state scale). It should be noted that individuals in the depressed MS group were not excluded if their anxiety exceeded the cutoff on the STAI given the high comorbidity of depression and anxiety. The reports of 10 out of the 17 depressed MS group were one and half standard deviations above the mean.

Demographics of the three samples can be found in Table 1. There were no significant differences between the three groups on age, education, or estimated IQ. No significant differences were found between the depressed and non-depressed MS groups on symptom duration and diagnosis duration, while they were significantly different on their level of disease severity as measured by the EDSS (see Table 1).

All statistical analyses were conducted using SPSS 14.0 computer software. Initial examination of the relationship between the depression screening measures

(MBDI and CMDI), and depression proneness (DPRS) was established using Pearson correlation coefficients. The MBDI was found to be moderately correlated with the DPRS and the CMDI. The correlation between the MBDI and DPRS ( $r = .52, p < .01$ ) was consistent with correlations found for the CMDI and the DPRS ( $r = .48, p < .01$ ). The correlation between the MBDI and CMDI ( $r = .76, p < .01$ ) also suggests that this measure had concurrent validity with other validated self-report depression measures.

Chi-square analyses were next conducted between MS (non-depressed and depressed) and healthy controls to identify which symptoms (as measured by the MBDI) were more prevalent in MS (see Figure 2a). We found that the



**Figure 2** (a) Differences in endorsement of modified Beck Depression Inventory items between healthy controls and depressed and non-depressed multiple sclerosis patients. (b) Differences in endorsement of modified Beck Depression Inventory items between depressed and non-depressed multiple sclerosis patients.

Note: \* =  $p < .05$ , † =  $p < .01$ , ‡ =  $p < .001$

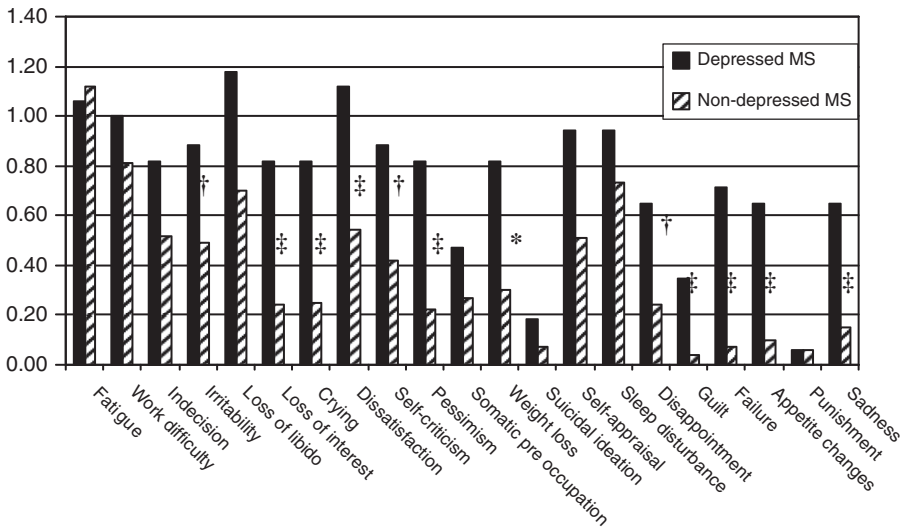
non-depressed and depressed MS group endorsed (i.e., had a score of 1 or more) the following items more often than healthy controls: fatigue, work difficulty, indecision, irritability, loss of libido, loss of interest, crying, dissatisfaction, and self-criticism. It should be noted that the non-depressed and depressed MS groups and controls did not differ in their endorsement of sleep disturbance, but both reported high rates.

Next we examined which symptoms were more indicative of depression in MS. To accomplish this, we examined the endorsement patterns of the non-depressed and depressed MS groups using chi-square analyses. As Figure 2b illustrates, we found that depressed individuals with MS endorsed the following MBDI items significantly more often than non-depressed individuals with MS: sense of failure, appetite changes, pessimism, loss of interest, sadness, crying, feelings of guilt, less satisfaction, disappointment, irritability, weight loss, and self-criticism. As noted above, compared with controls, both the depressed and non-depressed MS groups differentially endorsed indecision, work difficulty, and loss of libido. Fatigue was also found to be the most prevalent symptom with 91% of the non-depressed MS group and 94% of the depressed MS group endorsing this symptom. Finally, although not found to be “trunk” symptoms in the previous analysis, both depressed and non-depressed MS groups frequently reported experiencing somatic preoccupation (44% and 29%, respectively), negative self-appraisal (47% and 40%), and sleep disturbance (65% and 58%).

Another set of analyses were conducted to determine (1) which symptoms were more severe in the depressed MS group and (2) which common MS symptoms were also associated with depression. To determine whether or not endorsement of depressive symptoms was more severe in the depressed MS group, Mann-Whitney *U* tests were conducted between depressed and non-depressed MS groups.

As shown in Figure 3, symptoms that were common to MS, regardless of depression, but more severe in depressed individuals with MS consisted of loss of interest, less satisfaction, crying, irritability, and self-criticism. Other symptoms commonly reported by individuals with MS (fatigue, indecision, work difficulty, and loss of libido) were not found to be more severe in the depressed MS group compared with the non-depressed MS group. Finally, to determine whether certain somatic symptoms were reflective of depression if associated with symptoms more indicative of depression, Spearman Rho correlations were conducted to examine the associations between common MS symptoms and symptoms indicative of depression within both the depressed and non-depressed MS groups (see Table 2).

Symptoms common to MS, but that had associations with more “depressive symptoms” among the depressed MS group, included crying, work difficulty, loss of interest, self-criticism, irritability, and dissatisfaction. Symptoms common to MS that were found to be related to more “depressive symptoms” in the non-depressed MS group included loss of interest and self-criticism; both were found to be related to feelings of disappointment while self-criticism was found to be related to feelings of pessimism as well. Although sleep disturbance was not an overtly discriminating symptom, it was found to be related to other significant symptoms of depression (sadness, sense of failure, disappointment) in the depressed MS group, while showing no association with such symptoms in the non-depressed MS group. Finally, fatigue, which was found to be extremely common in MS showed no



**Figure 3** Differences in severity of depressive symptoms between depressed and non-depressed multiple sclerosis patients.  
 Note: \* =  $p < .05$ , † =  $p < .01$ , ‡ =  $p < .001$

**Table 2** Spearman's rho correlation of common symptoms of multiple sclerosis and common symptoms of depression in depressed and non-depressed multiple sclerosis

	Symptoms common to depression						
	Sadness	Pessimism	Failure	Guilt	Disappointment	Appetite Change	Weight Change
<i>Depressed MS group (N = 17)</i>							
Dissatisfaction	-.05	-.12	.49*	-.18	.40	.16	.30
Self-criticism	.18	.09	.50*	-.08	.62**	.06	.17
Crying	.61**	-.18	.50*	-.06	.51*	.03	.10
Irritability	.42	-.35	.50*	.41	.53*	.15	-.11
Loss of Interest	.23	-.64**	.30	.18	.21	-.12	.06
Indecision	-.15	-.13	.01	.40	.26	.24	-.01
Work Difficulty	-.05	.50*	-.06	.59*	.20	.33	-.10
Fatigue	-.07	.14	-.16	.15	-.14	.41	.17
Loss of Libido	.10	-.10	-.12	-.01	-.19	.04	.39
Sleep Disturbance	.57*	.01	.58*	.23	.54*	.31	-.31
<i>Non-depressed MS group (N = 67)</i>							
Dissatisfaction	.05	.11	.15	.16	.24	.08	.06
Self-criticism	.07	.39**	.19	.21	.38**	-.06	-.10
Crying	.05	-.05	.16	-.10	.08	.17	.19
Irritability	.01	.00	-.05	.01	.22	.10	.07
Loss of Interest	.16	.14	.03	.10	.34**	-.06	.00
Indecision	-.15	-.15	.01	.08	.13	-.15	.03
Work Difficulty	-.32**	.02	-.06	-.09	.12	-.09	.02
Fatigue	.05	.20	.26*	.28*	.30*	.02	-.05
Loss of Libido	-.09	-.00	-.10	-.03	.04	.22	.12
Sleep Disturbance	-.07	-.09	-.10	-.19	-.05	-.00	.22

\*Significant at the .05 level. \*\* Significant at the .01 level.

**Table 3** Delineation of symptom clusters found to be (1) common to multiple sclerosis (MS); (2) common to depression, (3) more severe in depressed multiple sclerosis group; and (4) associated with depression

Symptom	Common to MS to Depression	Common Depressed MS	Excessive in
Fatigue‡	Fatigue	-----	-----
Indecision	Indecision	-----	-----
Loss of Libido	Loss of Libido	-----	-----
Work Difficulty†	Work Difficulty	-----	-----
Irritability†‡	Irritability	Irritability	Irritability
Loss of Interest‡	Loss of Interest	Loss of Interest	Loss of Interest
Crying†	Crying	Crying	Crying
Dissatisfaction†	Dissatisfaction	Dissatisfaction	Dissatisfaction
Self-Criticism†‡	Self-Criticism	Self-Criticism	Self-Criticism
Sadness	-----	Sadness	-----
Pessimism	-----	Pessimism	-----
Failure	-----	Failure	-----
Guilt	-----	Guilt	-----
Appetite Changes	-----	Appetite	-----
Disappointment	-----	Disappointment	-----
Weight Loss	-----	Weight Loss	-----
Punishment	-----	-----	-----
Self-Appraisal	-----	-----	-----
Somatic Preoccupation	-----	-----	-----
Sleep Disturbance†	-----	-----	-----
Suicidal Ideation	-----	-----	-----

†Related to depressive symptoms in depressed multiple sclerosis group. ‡Related to depressive symptoms in non-depressed multiple sclerosis group.

association with “depressive symptoms” in the depressed MS group, but was related to feelings of failure, guilt, and disappointment in the non-depressed MS group. (Please refer to Table 2.)

Based on our findings, two sets of symptom clusters were revealed: (1) items endorsed by MS regardless of depression, so called “common” symptoms of MS; and (2) items commonly endorsed by depressed individuals with MS but not non-depressed individuals with MS. Moreover, an appreciation of which common MS symptoms are more severe and/or associated with depression in the depressed MS group was obtained (see Table 3).

## DISCUSSION

The intent of the present investigation was to develop a better understanding and appreciation of the intricacies involved in assessing depression in MS. More specifically, we sought to determine which symptoms best differentiated depressed from non-depressed individuals with MS on self-report depression measures in hopes of developing a “trunk and branch” model for use with MS. The conceptualization of a “trunk and branch” model is that certain “trunk” symptoms (e.g., fatigue), which are common in MS, may not be the most representative

of depression, while certain “branch” symptoms (e.g., sadness) may be more indicative. However, these “trunk” symptoms *may* be reflective of depression if the endorsement of the symptom exceeds what is typical for the disorder or if the symptom is related to other identified “branch” symptoms of depression.

In order to develop such a model, this investigation examined the symptom endorsement of depressed individuals with MS, non-depressed individuals with MS, and non-depressed healthy controls. These comparisons distinguished symptoms into the following four categories: “branch” symptoms indicative of depression in MS, “trunk” symptoms common in MS, symptoms that exceed what is common in MS, and common MS symptoms associated with “depressive” symptoms in MS (see Figure 4).

### **“Branch” symptoms indicative of depression in MS**

Previously, Clark et al. (1983) found that sense of failure, suicidal ideation, sense of punishment, loss of social interest, dissatisfaction, and indecisiveness were the best indicators of depression in a medically ill sample. In the present investigation, symptoms most indicative of depression in MS were sadness, pessimism, sense of failure, guilt, disappointment, and changes in appetite and/or weight as seen in Figure 4.

Consistent with Clark et al.’s (1983) findings, feelings of failure and pessimism continued to reign as significant symptoms of depression. Moreover, findings confirmed the hypothesis of this study that sadness, disappointment, and guilt are important in assessing depression in MS. Surprisingly, dissatisfaction, suicidal ideation, and feelings of punishment, symptoms purported by Clark et al. to be indicative of depression, were not. The finding that dissatisfaction was prevalent in MS and perhaps not best at differentiating depression is consistent with Cavanaugh’s contention that dissatisfaction is common in medically ill people. Punishment, a symptom found by Clark et al. to be indicative of depression, was neither common to MS nor depression and was reported at a seemingly low rate (6%) in both groups. This is a positive finding and may suggest adequate coping in which individuals with MS, depressed or not, refrain from potentially viewing their disease as a punishment.

### **“Trunk” symptoms common to MS**

Based on endorsement patterns on the modified BDI, we found that symptoms of fatigue, work difficulty, indecision, irritability, loss of interest, loss of libido, crying, dissatisfaction, and self-criticism are common symptoms in MS. Consistent with previous findings (Mohr et al., 1997), fatigue and work difficulty were found to be common in MS and may demonstrate little utility in identifying depression. Given the high prevalence of sexual dysfunction it was not surprising that loss of libido was found to be common in MS. However, based on previous results, the finding that loss of interest, dissatisfaction, crying, self-criticism, indecision, and irritability were considered to be common in MS was, in part, surprising. In previous investigations (Clark et al., 1983) it has been found that loss of social interest, dissatisfaction, and indecision were among the six discriminating

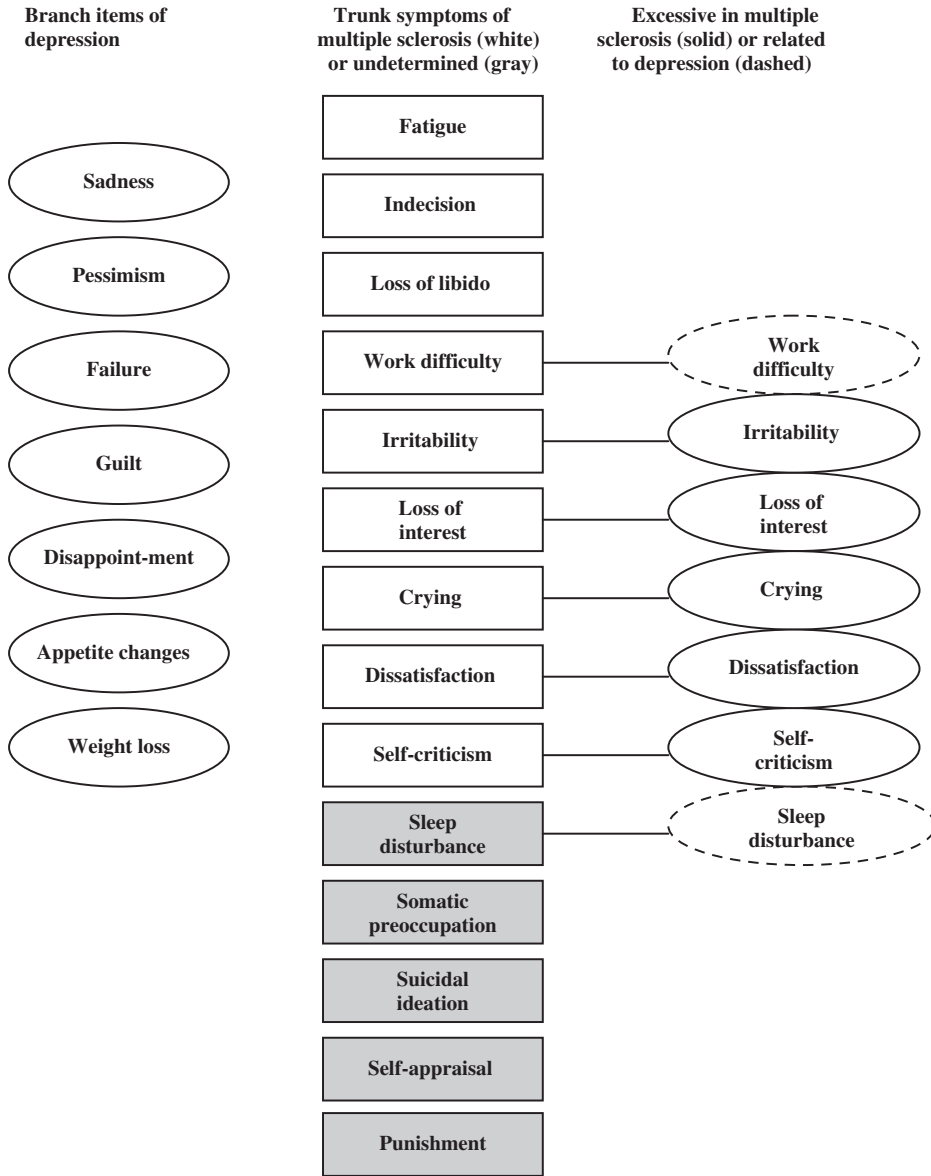


Figure 4 Modified “trunk and branch” model for use in multiple sclerosis.

symptoms of depression in a medically ill sample. The fact that they were not discriminating in our MS sample suggests that something different is occurring in those suffering from MS. One can suppose that indecision may be related to the high prevalence of cognitive impairment in MS while irritability and crying may be more related to the emotional lability commonly observed (Feinstein & Feinstein, 2001). Similarly, dissatisfaction is thought to be common in medically ill people and,

as stated before, was common to MS. Loss of interest may be a result of limited physical ability in a population that is typically more active. It is possible that these symptoms are experienced differently in MS than other medical conditions. However, further exploration of these symptoms is warranted in order to determine if the presence of the symptom exceeds what is common to MS and if it is related to other symptoms more indicative of depression.

### **Symptoms that exceed what is common in MS**

Cavanaugh (1986) suggested that “trunk” symptoms might be more indicative of depression if the symptoms are disproportionate to the medical illness. In the present investigation it was found that, although reports of irritability, loss of interest, crying, dissatisfaction, and self-criticism were common in MS, their endorsement was greater in those who were depressed. In contrast, reports of fatigue, work difficulty, loss of libido, and indecision were not found to be more severe in depressed MS, suggesting that these symptoms may have little utility in differentiating depressed from non-depressed MS.

### **Common MS symptoms associated with “depressive” symptoms in MS**

Symptoms common to MS that were found to be related to identified depressive symptoms included dissatisfaction, self-criticism, crying, irritability, and work difficulty. With the exception of work difficulty, these symptoms were also found to be more severe in depressed individuals with MS. It is suggested that these symptoms be considered as potential predictors of depression, despite being common to the disease, particularly if they are found in conjunction with other depressive “branch” symptoms. Similarly, sleep disturbance was found to be related to other significant symptoms of depression in the depressed MS group, while showing no association with such symptoms in the non-depressed MS group. The relevance of these symptoms as indicators of depression is supported by the finding that other common symptoms of MS; namely fatigue, loss of libido, and indecision were not related to other depressive symptoms. Finally, fatigue, though regarded as an extremely frequent symptom of MS, was found to be related to feelings of failure, guilt, and disappointment in the non-depressed MS group, suggesting that fatigue may have a more detrimental impact overall on a patient’s appraisal of self, even in the absence of clinical depression.

In sum, our findings suggest a sort of hierarchy in assessing depression in MS. Reports of sadness, guilt, disappointment, feelings of failure, and pessimism, accompanied with appetite or weight changes should be given top priority. Second, if loss of interest, crying, dissatisfaction, irritability, and self-criticism are present, further exploration should be conducted to determine whether these symptoms exceed what one may expect in MS. Similarly, consideration should be given to the presence of all of these symptoms, with the inclusion of work difficulty (denoted by a dotted eclipse), when other depressive symptoms are apparent, as they were found to be associated with such symptoms. Finally, given these findings, the least amount

of merit should be given to reports of fatigue, loss of libido, and indecision when determining the presence of depression in MS.

There were no conclusive findings regarding the importance of suicidal ideation, somatic preoccupation, punishment, self-appraisal, or sleep disturbance (highlighted in gray in Figure 4). These symptoms did not prove to be either common to MS or depression, but it should be noted that negative self-appraisal, somatic preoccupation, and sleep disturbance were highly prevalent in both non-depressed and depressed individuals with MS. Moreover, sleep disturbance was related to depressive symptoms in the depressed MS group (as denoted by a dotted eclipse) and is likely to be indicative of depression in the presence of such symptoms. Additionally, suicidal ideation should always be given top priority in the assessment of depression in MS, especially as it was present in both depressed and non-depressed individuals with MS.

It is worth noting that the depressed MS group was slightly more disabled than the non-depressed MS group based on the EDSS score (Cohen's  $d = .57$ ). There are mixed findings regarding the relationship between depression and disease severity in the literature, with some studies finding a direct relationship, and others showing no association (Arnett et al., 2008). It has also been questioned whether it is the difference in duration of illness that has a greater impact on the development of depression in MS (e.g., shorter duration being associated with greater depression); this was not found in this sample as the mean duration for both groups was around 10 years, a time at which the risk of depression is lower than earlier in the disease course (Chwastiak et al., 2002). It may be that participants in our sample reacted to higher levels of disability with greater depression. Alternatively, greater levels of disability may implicate greater MS CNS involvement which, in turn, may result in greater organic risk for depression. Additionally, the fact that we used a self-report measure of EDSS may have played some role in these differences; more depressed individuals with MS may have *perceived* themselves as having more disability because of a negative cognitive schema associated with depression that might have resulted in them rating themselves worse on anything asked of them, including rating their own disability. Future work will be needed to explore the validity of these possibilities.

Finally, while we did conduct a structured clinical interview to assess for current major depressive episode (MDE), we did not explicitly assess for the full spectrum of past depression and relied on self-reported proneness of depression for such. Additionally, given the contention that depressed individuals with MS may not always accurately report their present depression we also relied on significant others' reports to substantiate our selection of the depressed sample. This best two out three approach resulted in approximately 35% of our depressed sample not meeting formal criteria for a MDE at the time of testing. However, in comparing those who met criteria for a present MDE and those who did not among the depressed sample, there were no significant differences on the BDI-II, an additional measure that was administered as part of this study, with means of 22 and 18, respectively. These findings suggest that we did in fact capture those who were experiencing a significant degree of depression utilizing our selection criteria. Moreover, the derived prevalence rate of 20% found in this sample is consistent with previous findings when more stringent criteria such as clinical interviews and others (physician and psychiatrists' diagnoses) are used, with rates of 17% to 26%

typically reported. If we had included only those who self-reported a MDE, our prevalence would have been only 13%, a particularly low estimate in MS and likely an inaccurate reflection of our sample.

There were several limitations of this investigation. First, the omission of a structured clinical assessment of comorbid anxiety disorders may have affected our results. In particular, the high rate of self-reported trait anxiety among the depressed group may have resulted in an “over reporting” of symptoms. Future investigations may need to examine the influence of anxiety more systematically, and ways in which it may pervade reports of depression and MS symptoms in individuals with MS. Another limitation of this investigation was the absence of a depressed control sample. Comparisons between depressed MS and depressed controls would have enhanced our ability to substantiate the findings that certain symptoms are more representative of depression. Finally, given the relatively small sample of depressed individuals with MS, future investigations are warranted, which employ a larger, overall sample size.

In sum, it is hoped that the proposed investigation provides clinicians and researchers a better understanding and appreciation of the intricacies involved in assessing depression in MS. The creation and support of a “trunk and branch” model for use with MS has been outlined and will hopefully guide further research in developing and applying such models in MS. Such clarity and specificity may enhance our detection of depression in MS, improve our treatment, and guide theoretical conceptualizations of depression in medically ill people in general. However, first and foremost, the aim of this investigation was to improve the lives and care of individuals with MS. It is hoped that the knowledge gained through this investigation will make a significant contribution to both research and practice in attaining this goal.

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