The influence of trait mindfulness on depression in multiple sclerosis: potential implications for treatment

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Abstract

Purpose This study seeks to add to existing literature on depression and illness intrusiveness in chronic disorders by examining, (1) how the perceived intrusiveness of multiple sclerosis (MS) leads to depression, (2) and the mediating role trait mindfulness plays in this relationship

Methods Participants ($N = 755$) were persons with MS (PwMS) recruited through the North American Research Committee on MS (NARCOMS) registry (a larger study). Participants completed the Illness Intrusiveness Ratings Scale, the Hospital Anxiety and Depression Scale and the Mindful Attention Awareness Scale. A mediation model assessed if trait mindfulness mediates the relationship between illness intrusiveness and depression

Results Illness intrusiveness predicted trait mindfulness ($a = -4.54$; $p < .001$), trait mindfulness predicted depression ($b = -.04$; $p < .001$); there was a *direct effect* of illness intrusiveness on depression ($c' = 2.53$; $p < .001$) and an *indirect effect* on depression ($ab = .17$, 95% BCa CI [.10, .25]) when trait mindfulness was in the model, which represented a medium size effect, $R^2_{med} = .10$ [95% CI .07, .14]

Conclusion Trait mindfulness mediates the relationship between illness intrusiveness and depression in PwMS. Providers could provide psychoeducation on the benefits of mindfulness and mindfulness-based interventions.

Keywords Multiple sclerosis · Depression · Illness intrusiveness · Trait mindfulness

Introduction

Multiple Sclerosis (MS) is a demyelinating disease of the central nervous system (CNS), which carries negative consequences for quality of life (QoL) by impacting multiple aspects of the lives of persons with MS (PwMS), including their physical, emotional, and cognitive functioning [1]. Although symptoms vary among patients, studies have shown significantly higher prevalence of psychiatric illness throughout the MS population [2]. Specifically, a systematic review of psychiatric disorders in PwMS has indicated that the prevalence rates for major depressive disorder and clinically significant anxiety are 54% and 22%, respectively, indicating significantly higher rates in PwMS compared to the general population [3]. Despite this, psychiatric illness is often under-assessed and inadequately treated in PwMS. Many patients remain undiagnosed and the appropriate treatment is frequently not prescribed and/or patients often do not follow treatment recommendations [4]. Therefore, there is a need for increased research and clinical care on determinants of depression to aid in improving treatment and outcomes [5].

Improvements in psychological symptom intervention is particularly important in PwMS because mood symptoms, such as depression, often lead to increased morbidity and mortality [6, 7]. One way in which MS symptoms lead to depression is by interfering with a patient's ability to engage in activities they once enjoyed [8]. This instrumental interference in lifestyle activities, relationships, and goals

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is known as illness intrusiveness [9]. MS in particular has been shown to be a highly intrusive disease when compared to other chronic conditions, such as rheumatoid arthritis and renal failure, likely due to the costly, time-consuming treatment regimens, as well as highly intrusive and debilitating motor and cognitive symptoms [10]. Higher levels of illness intrusiveness are associated with decreased involvement in positive experiences and general goal-oriented behaviors, in addition to reduced ability to adjust to chronic illnesses like MS. As such, there is often a detrimental impact on patients' mood and overall QoL, making it an important target for mental health and QoL research in PwMS [11].

Depression is highly correlated with illness intrusiveness, such that higher levels of illness intrusiveness often lead to higher levels of depressive symptoms [12, 13]. A previously proposed theoretical framework posits that consequences of disease (such as disability and pain) and barriers to treatment (such as disruptive treatment schedules or unpleasant side effects) increase patient perception of the intrusiveness of their disease, which in turn leads to depression [11]. One study found that a potential mechanism for this relationship is that patients who have low levels of trait resilience and low levels of social support may view their illness as more intrusive, which then leads to depression [14]. This shows that there is likely an intermediary appraisal mechanism that exists between illness intrusiveness and depression that drives this relationship.

Several interventions have been used to try and improve illness intrusiveness in chronic health conditions. For instance, brief cognitive behavioral therapy (bCBT) interventions have been successfully utilized in diseases such as chronic obstructive pulmonary disease (COPD) to reduce patient perception of illness intrusiveness. One study showed that bCBT was able to reduce perceived symptoms of illness intrusiveness significantly more than usual care, suggesting that altering the way patients view their illness can reduce illness intrusiveness [15].

Mindfulness-based interventions (MBI's), like the bCBT interventions, have been useful in improving QoL and other well-being factors in PwMS by altering appraisal mechanisms [1]. Some of those who respond the most favorably to MBI's are those with heightened trait mindfulness qualities [16]. Trait mindfulness, or the ability to attend to both the present moment and internal stimuli with intention, receptive awareness, and non-judgment [17], has been shown to protect against mental illness [18]. One study in PwMS demonstrated that patients with high levels of trait mindfulness had lower levels of mood symptoms, were more resilient, and had developed better coping strategies than people with lower levels of trait mindfulness that had MS [15].

Studies have established clear connections between illness intrusiveness and psychological outcomes in MS [19, 20]. However, little is known about potential mechanisms for

this relationship. Trait mindfulness may be a potential intermediary appraisal mechanism in the relationship between illness intrusiveness and depression in MS. Specifically, people who view their illness as less intrusive may have higher levels of trait mindfulness, which in turn leads to reductions in depressive symptoms.

Therefore, the primary goal of the current study is to evaluate the relationships among depression, illness intrusiveness, and trait mindfulness in PwMS. It was first hypothesized that illness intrusiveness and depression would be significantly related in PwMS, replicating findings from prior research [20, 21]. Second, it was hypothesized that higher levels of illness intrusiveness would be associated with lower levels of trait mindfulness in PwMS. Third, it was predicted that trait mindfulness and negative psychological outcomes, such as depression, would be inversely related in MS, as has been previously postulated [18, 22, 23]. Finally, it was predicted that trait mindfulness would mediate the relationship between illness intrusiveness and depression among PwMS.

Method

Participants

Participants were utilized as a secondary analysis from a larger study ($N = 932$) which recruited through the North American Research Committee on MS (NARCOMS) [24]. NARCOMS is a large, well-validated registry of PwMS who have consented to be contacted for research purposes. 3000 email notifications were sent to registry members to participate, with an electronic data collection process through a HIPAA-compliant version of Survey Monkey. From the total number of email notifications, 1038 PwMS signed an electronic consent form and 106 of these participants were removed due to significant amounts of missing data. From the remaining 932 individuals, 731 of these participants completed all the relevant demographic and study-related questionnaires. Thus, the sample size in the final analyses was $n = 731$. Data were collected prospectively for research purposes and the study was approved by the Institutional Review Board (IRB) of the Albert Einstein College of Medicine (IRB ethics # 2015-4777) in accordance with its ethical standards and with that of the 1964 Declaration of Helsinki [25].

The primary inclusion criteria in this study was a diagnosis of MS. In the present registry, over 98% of enrolled members had a definite diagnosis of MS according to medical records [26]. To further ensure all participants met the inclusion criteria, those who did not identify the type of MS they were diagnosed with, were excluded. Other exclusion criteria included the diagnosis of another major medical

condition other than MS [27]. For further details on collection procedures, see the previously published study [28].

Procedure

The study design was prospective and cross-sectional in nature; data utilized in the analyses were originally collected during a validation study of the MS Resiliency Scale [24]. In the original study, which focused on test development, a target sample size of 750 was used given the 75 items in the scale, with the goal of getting at least 10 respondents per item [24]. As response rates to NARCOMS surveys vary between 30 and 60% (Tuula M. Tyry, PhD, email communication, April 21, 2016), 3000 recruitment emails were sent.

Relapsing remitting multiple sclerosis (RRMS) is the most common disease course for MS, with approximately 80% of patients initially diagnosed with this form of the disease [29]. As such, MS phenotype was coded dichotomously as RRMS or as "other" MS phenotype. To ensure adequate sample sizes across demographic groups, race and education were coded dichotomously as Caucasian and non-Caucasian and as less than 12 years of education versus greater than or equal to 12 years of education, respectively.

Measures

The Illness Intrusiveness Rating Scale (IIRS) is a 13-item self-report questionnaire that asks participants to rate the degree to which their "illness and/or its treatments" interfere with a myriad of life domains. The IIRS was developed for people with chronic illness. It is a reliable and valid measure in MS with good internal consistency (Cronbach's $\alpha = .87$ for the total score) test–retest reliability [11, 30]. For the purposes of this study, a z-score of the IIRS total score was used, such that a lower z score reflects lower illness intrusiveness. The IIRS had good internal consistency in this sample (Cronbach's $\alpha = .89$) [11, 21, 31].

The Hospital Anxiety and Depression Scale (HADS) is a 14-item, 4-point self-report questionnaire made up of two subscales: HADS anxiety (HADS-A) and HADS depression (HADS-D). The scale has been validated in MS and is a reliable measure of depression and anxiety in the MS population [32]. The depression subscale has good internal consistency both in previous reports (Cronbach's $\alpha = .82$; Marrie et al. [33]) and in the current sample (Cronbach's $\alpha = .87$). For the purposes of this study, the total score of the HADS-D was used [34].

The Mindfulness Attention and Awareness Scales (MAAS) is a 15-item, 6-point, self-report questionnaire used to measure trait mindfulness, such as awareness and attention to the present moment [35]. The MAAS has been validated in prior studies of MS [36] with good internal consistency (Cronbach's $\alpha = .85$), construct validity, and

test retest reliability [37]. Internal consistency was good for this sample as well (Cronbach's $\alpha = .90$); the MAAS total score was used.

Statistical analysis

Statistical analyses were conducted using SPSS v.25. To assess the impact of missing data and to determine the number of participants to be included in the analyses, the original dataset, which utilized listwise deletion to account for missing data, was compared to a second database utilizing multiple imputation (MI). This function uses expectation maximization (EM)/maximum likelihood estimation to approximate missing values and create multiple versions of the same dataset (five, in this case). The parallel datasets were compared individually and no significant differences were found as compared to the original dataset [38]. Similarly, results of the model without covariates ($n = 755$) were comparable to a model with covariates ($n = 731$). Therefore, the simpler model, without covariates, is described.

Missing data were analyzed for the measurement tools as well as for demographic variables. Descriptive statistics were initially run to characterize the sample. Categorical demographic variables that did not have a sufficient size across groups were dichotomized, including race (Caucasian/non-Caucasian) and MS type (RRMS/other). To determine significant relationships among predictors and demographic variables, t tests were used to compare group means for dichotomized demographic variables, while Pearson correlations were used to assess continuous demographic variables (See Table 1). Pearson correlations were used to explore the first three hypotheses, that (1) illness intrusiveness and depression would be significantly related; (2) higher levels of illness intrusiveness would be related to lower levels of trait mindfulness; and (3) trait mindfulness and depression would be inversely related in MS.

For the primary hypothesis, that trait mindfulness mediates the relationship between illness intrusiveness and depression, a mediation model with 5000 bootstrap samples was run using Hayes' PROCESS macro [39]. IIRS

Table 1 Correlation matrix for continuous variables

Variable	1	2	3	4	5
1. HADS-d	–				
2. IIRS z score	.69**	–			
3. MAAS total score	− .34**	− .30**	–		
4. Age (years)	− .02	− .03**	.15**	–	

HADS-d hospital anxiety and depression scale, depression subscale, *IIRS* illness intrusiveness rating scale, *MAAS* mindful attention awareness scale

**$p \leq .01$

total score was entered as the predictor variable, MAAS total score was entered as the mediating variable, and the HADS-D score was entered as the outcome variable. Mediation effect size descriptors were used to characterize the effect size of the main analysis (R^2_{med}), namely .01 would be considered small, .09 would be considered medium, and .25 would be considered large [40].

Results

The majority of the study participants were white (94.8%*),* female (84%), in middle adulthood ($M = 56$ years, $SD = 9$ years), with at least twelve years of education (87.7%), relapsing remitting MS (62.7%) and had been diagnosed with MS several years before ($M = 18$ years, $SD = 9$ years) (See Table 2).

Males, those with less than 12 years of education, and those with RRMS were more likely to report high levels of depression and illness intrusiveness. Those with RRMS were also more likely to report higher levels of trait mindfulness (See Table 3). Significance was found for the *indirect*,

direct and *total effects* in both the original and imputed data sets using a 95% bias-corrected and accelerated (BCa) bootstrap confidence interval (CI). Results of the original dataset show that higher IIRS was significantly predictive of the lower MAAS total score ($a = -4.54$, $p < .001$). Both the IIRS (*direct effect, c' =* 2.53, $p < .001$) and the MAAS ($b = -.04$, $p < .001$) predicted HADS-D. Trait mindfulness was found to be a significant mediator between illness intrusiveness and depression, *indirect effect*, $ab = .17$, 95% BCa CI [.10, .25] (Fig. 1). This represented a medium, but meaningful, proportion of the total effect ($R^2_{med} = .10$ [95% CI .07, .14], $p < .001$).

Discussions and conclusions

This is the first study to date to investigate the relationship between illness intrusiveness and depression by examining trait mindfulness as a mediating factor. Results of this study first replicated prior research [20, 21], demonstrating a significant relationship between illness intrusiveness and depression. This study also found that higher levels of trait

Table 2 Descriptive statistics for demographic, predictor, and outcome variables

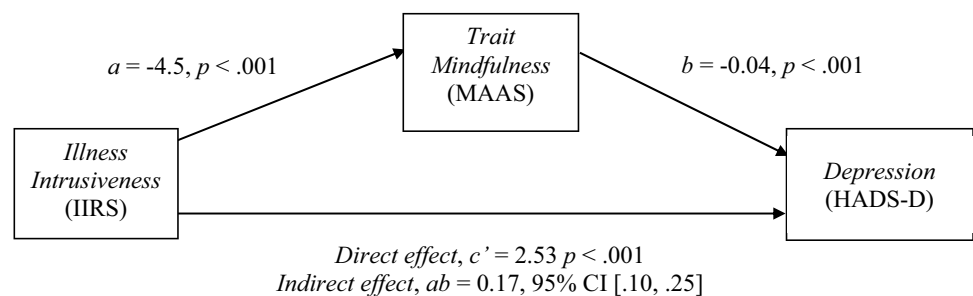| Variable	Total ($N = 755$)	
	n	%
Gender ($n = 699$)		
Female	587	84.0
Male	112	16.0
Education ($n = 751$)		
≥ 12 years	662	87.7
< 12 years	89	11.8
Race/ethnicity ($n = 696$)		
White	660	94.8
African American/Black	9	1.3
Asian/Alaska Native	1	0.1
Hispanic/Latino	19	2.7
American Indian	5	0.7
Other	2	0.3
Type of MS ($n = 703$)		
Relapsing remitting	441	62.7
Primary progressive	64	9.1
Secondary progressive	181	25.7
	M	SD
Age (years)	56	9
Years since diagnosis	18	9
MAAS total score	63.64	13.19
HADS depression subscale	5.17	3.28
IIRS z score	− 0.7	0.85

MAAS mindful attention awareness scale, *HADS* hospital anxiety and depression scale, *IIRS* illness intrusiveness rating scale

Table 3 Descriptive statistics and analysis of relationships between demographic and study variables

Variable	Total (N=755) M(SD)		t(df)	p
	Gender n=750			
	Male	Female		
Age	57.95 (10.33)	55.59 (9.23)	2.47 (737)	.014
HADS-d	5.52 (3.40)	4.76 (3.39)	2.25 (748)	.024
IIRS z score	.05 (.81)	− .17 (.88)	2.56 (748)	.011
MAAS	65.64 (11.63)	63.70 (13.24)	1.63 (178.57)	.106
	Education n=751			
	≥ 12 years	< 12 years		
Age	58.49 (8.99)	55.66 (9.45)	2.66 (739)	.008
HADS-d	5.7 (3.6)	5.99 (3.61)	3.31 (749)	.001
IIRS z score	− .16 (.87)	.05 (.87)	2.11 (749)	.035
MAAS	63.13(12.86)	62.97 (14.39)	−.787 (749)	.432
	Race n=747			
	Caucasian	Not-caucasian		
Age	48.45 (10.00)	56.36 (9.25)	− 5.11 (734)	<.001
HADS-d	4.85 (3.39)	5.42 (3.51)	1.04 (745)	.300
IIRS z score	− .15 (.87)	.00 (.97)	1.01 (745)	.313
MAAS	64.11 (12.95)	63.15 (14.67)	− .453 (745)	.651
	MS Type n=755			
	RRMS	Other		
Age	59.52 (7.93)	54.05 (9.62)	8.34 (633.36)	<.001
HADS-d	5.60 (3.25)	4.51 (3.45)	4.24 (753)	<.001
IIRS z score	.10 (.76)	− .26 (.91)	5.87 (641.86)	<.001
MAAS	66.64 (12.48)	62.52 (13.10)	4.21 (753)	<.001

HADS-d hospital anxiety and depression scale, depression subscale, *IIRS* illness intrusiveness rating scale, *MAAS* mindful attention awareness scale, *RRMS* relapse remitting multiple sclerosis

Fig. 1 Model of illness intrusiveness as a predictor of depression, mediated by trait mindfulness. The confidence interval for the indirect effect is a BCa bootstrapped CI based on 5000 samples

a = -4.5, p < .001 → Trait Mindfulness (MAAS) → *b = -0.04, p < .001* → Depression (HADS-D)

Illness Intrusiveness (IIRS)

Direct effect, c' = 2.53 p < .001
Indirect effect, ab = 0.17, 95% CI [.10, .25]

mindfulness were associated with lower levels of depression, and trait mindfulness mediated the relationship between illness intrusiveness and depression. Specifically, individuals with higher levels of illness intrusiveness are likely to show lower trait mindfulness, which in turn is associated with increased depressive symptomatology.

This finding is of critical importance for PwMS as well as other chronic conditions, because it has identified trait mindfulness as a modifiable treatment target that can reduce the burden and perceived intrusiveness of their disease. This can, in turn, reduce depressive symptoms in PwMS. Depression has been continually linked to morbidity and mortality, suicide [6, 7], reduced medication adherence [41], and lower quality of life [42]. Thus, much research has focused on determining potential treatment interventions for reducing depressive symptoms in MS.

The current study provides support for interventions that enhance mindfulness, which may be able to alter one's perception of the intrusiveness of their disease, and lead to a reduction in depressive symptoms in PwMS.

Given the myriad definitions of mindfulness, further research should investigate the nuances of trait mindfulness and how the varying components may individually predict depression. This will allow for targeted clinical interventions to focus not only on teaching practices of mindfulness, but also to understand which aspects of mindfulness may be the most useful in treating depression in PwMS. For example, it has been shown that one's level of trait mindfulness can be predictive of state mindfulness outcomes; that is, those with heightened trait mindfulness qualities may respond more favorably to MBI's [16]. Thus, it may eventually be possible to develop individualized MBI's for PwMS in addressing illness intrusiveness and depression. This is of utmost importance in light of the inverse relationship between trait mindfulness and depression [43], and its mediating effect on the relationship between perceived stress and QoL [44].

One limitation of this study is that it is a cross-sectional design, and therefore no direct statement can be made about causation. A prospective study would likely be required to infer causality, for example, by enrolling patients in MBI's while tracking illness intrusiveness and depression. A second limitation is that the studied relied on self-report of diagnoses and other inclusion criteria [24]. Also, in self-report participants do not always fill out all demographic criteria, leading to substantial amounts of missing data in this study on variables such as gender.

Future research is required to confirm the relationships found in this study and to better understand the specific mindfulness-based components that may contribute to this relationship. The electronic nature of the study design may have potentially excluded more impaired PwMS given the necessary access to a computer, smartphone, or tablet to complete the survey. This design also prevented direct contact with participants, along with external validation of the participant's self-reported information relevant to inclusion criteria. Finally, the demographics of this study (i.e., high percentage of Caucasians and women), may not be fully representative of the general MS population.

While illness intrusiveness was used as a predictor here, its utility as a mediator may also be examined in future studies. The authors chose not to look at this given that Andrew Hayes (author of the Process Macro) indicated that the primary goal of mediation is to determine important relationships among variables, not to establish direction of causality. Thus, with cross-sectional data used in this study, direction of causality cannot be established [39]. Therefore, switching the order of the variables should be done only if there is a strong theoretical reason to do so [39].

This study demonstrated the importance of trait mindfulness in reducing the perceived intrusiveness of MS. MS is one of the most highly intrusive chronic medical conditions [10], and it has a significant detrimental effect on most aspects of people's lives. This intrusiveness related to the disease, in turn, has a profound impact on the QoL of patients living with this disease, and often leads to depression. This study identified a potential mechanism for reduction of perceived intrusiveness related to MS, which may be an avenue through which depression may be reduced and QoL can be enhanced trait mindfulness. Treatments in MS that integrate mindfulness techniques may be an effective way to reduce illness intrusiveness, improve mood, and enhance quality of life in patients living with this chronic disease.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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