ORIGINAL ARTICLE

Psychiatry and Clinical Psychopharmacology 2021;31(4):434-441
DOI:10.5152/pcp.2021.21039

Anxiety Sensitivity and Its Relation to Anxiety in Multiple Sclerosis

Menekşe Sıla Yazar[1], Kumru Şenyaşar Meterelliyoz[2]

[1]Department of Psychiatry, Altınbas University School of Medicine, Istanbul, Turkey; [2]Department of Psychiatry, Bakirkoy Prof. Dr. Mazhar Osman Research and Training Hospital for Neurology, Neurosurgery and Psychiatry, Istanbul, Turkey

ABSTRACT

Background: The role of anxiety sensitivity in the occurrence of clinical anxiety symptoms that accompany medical diseases is increasingly well understood. This study aimed to investigate the role of anxiety sensitivity in the occurrence of clinical anxiety symptoms in multiple sclerosis patients.

Methods: This cross-sectional research was conducted on 105 multiple sclerosis patients aged between 18 and 65 years. Hospital Anxiety Depression Scale and The Anxiety Sensitivity Index-3 (ASI-3) were used to assess depression, anxiety, and anxiety sensitivity. Participants with significant levels of anxiety were compared to those who were not anxious.

Results: Anxiety Sensitivity Index total and Anxiety Sensitivity Index cognitive, physical, and social concerns subdomains, Hospital Anxiety Depression Scale and Hospital Anxiety Depression total scores were significantly higher in the anxious group than the non-anxious group ($P < .05$). The correlation analysis revealed a positive and significant correlation between the scales that were used to assess anxiety, depression, and anxiety sensitivity ($P < .05$). Depression levels and Anxiety Sensitivity Index social concerns subdomain remained as the most significant variables in the prediction of anxiety levels (OR 1.37, 95% CI 1.17-1.61, $P < .001$ and OR 1.22, 95% CI 1.08-1.38, $P = .0009$, respectively).

Conclusion: Anxiety sensitivity is related to the occurrence of clinical anxiety symptoms in multiple sclerosis patients. Depression and Anxiety Sensitivity Index social concerns subdomain predict the occurrence of clinical anxiety symptoms.

ARTICLE HISTORY

Received: March 31, 2021
Accepted: August 30, 2021

KEYWORDS: Anxiety, anxiety sensitivity, depression, multiple sclerosis

INTRODUCTION

Anxiety is widely seen in multiple sclerosis (MS) patients, but in contrast to depression, the number of studies on the clinical characteristics and effects of anxiety is limited.[1] The presence of anxiety can affect the quality of life, treatment compliance, and disease symptoms remarkably if left untreated; therefore, the treatment of anxiety in the earliest possible period in MS patients has great importance in terms of the course of MS.[2] Surprisingly, there is no consensus on the anxiety experienced by MS patients, and the number of studies on the causes of anxiety and the factors that cause vulnerability in MS patients is limited.[3]

Beyond the disease-related factors, anxiety in MS patients is associated with several physical, cognitive, psychological, and social factors.[4] Depression is the principal factor that is reported to be associated with anxiety in MS.[5] Also, clinical factors such as disability level, social support level, quality of life, gender, and unhealthy behaviors such as alcohol and substance use were associated with anxiety in MS.[4,6] Although the demographic, physical, and social factors predicting anxiety in MS have been further investigated, information about the psychological components of anxiety in MS is limited.[7] Since anxiety is not always correlated with disease level and disability in MS, it is suggested that the occurrence of anxiety is associated with the psychological impact of the disease and disease-related factors.[8]

Anxiety sensitivity (AS) is a comparably stable cognitive-affective risk factor that includes an extreme fear about anxiety-related sensations and symptoms that has harmful physical and/or social consequences.[9] The presence of high AS level constitutes a higher risk for the reveal of anxiety symptoms and increases the risk of an anxiety disorder.[10-12] Although research on AS has initially focused on the role of AS in anxiety disorders, especially panic disorder, recent studies have shown that cognitive vulnerability factors such as AS may play a role in the occurrence of anxiety in medical disorders as well.[13] Increasing evidence that AS is associated with many medical diseases supports the view that AS may play a role as a transdiagnostic risk factor in medical disorders as well

Corresponding author: Menekşe Sıla Yazar, e-mail: meneksesila@gmail.com

Cite this article as: Yazar MS, Meterelliyoz KS. Anxiety sensitivity and its relation to anxiety in multiple sclerosis. *Psychiatr Clin Psychopharmacol*. 2021;31(4):434-441.

as psychiatric disorders.[14] Horenstein et al.[15] emphasize that in chronic medical diseases, increased sensitivity to symptoms and fear of symptoms is an interrelated process, and AS is a distal vulnerability factor for both.

Multiple sclerosis symptoms and attacks lead to emotional responses, such as anger and failure of self-control, and therefore physical independence is threatened by anger associated with it.[16] These factors may cause the MS patient to feel consistently sensitive to physical symptoms and somatic sensations. Asmundson et al.[14] stated that in medical conditions, AS may be indirectly intensifying fears specific to the medical condition. Thus, in MS patients with high AS levels, hypersensitivity to somatic symptoms and to interpret them fearfully may play a role in the occurrence of anxiety, as in other medical conditions.[15]

Concerns about the uncertainty and unpredictability of the disease's outcome and the severity of future episodes in MS are 2 of the major psychological factors leading to severe and persistent anxiety in this patient population.[17] Janssen et al.[8] declare that the uncertainty of unexplained symptoms is an element that triggers anxiety after diagnosis as well as before diagnosis. Considering that the high AS level is associated with intolerance of uncertainty,[18] uncertainty and unpredictable disease course and symptoms, which are disease-related factors specific to MS, may play a role as a disease-specific factor in individuals with high AS levels and may contribute to clinical anxiety.[15]

Treatment of anxiety and depression in MS patients is essential for the management and the prognosis of the disease.[19,20] Cognitive behavioral therapy interventions can also be effective in the treatment of comorbid anxiety symptoms accompanying medical conditions by targeting AS with a transdiagnostic approach as well as the anxiety disorders.[15,21] Therefore, identifying disease-specific factors that may play a role in the occurrence of anxiety and depression, such as AS, which is a modifiable factor by therapeutic intervention, can guide the treatment of comorbid anxiety and depression in MS patients.

MAIN POINTS

- Anxiety sensitivity, which is a relatively easy parameter to evaluate and detect with an easily applicable measure such as Anxiety Sensitivity Index and can be reduced by short psychotherapeutic interventions, may improve the prognosis by reducing the risk of psychopathology in MS patients.
- The findings of this study, which revealed that AS was associated with clinical anxiety symptoms and ASI social concerns subdomain predicted the occurrence of clinical anxiety symptoms in MS patients, extend prior empirical and theoretical work by examining these constructs in a patient population that has not previously been investigated.
- Clinical application of the findings of this study will contribute to the integration of physical and mental care and disease management for a good prognosis in this special patient population.

This study aims to investigate the role of AS in the occurrence of anxiety symptoms in MS patients. The presence of higher AS levels was hypothesized to be predictive in the occurrence of significant clinical anxiety in MS patients.

METHODS

Participants

A descriptive cross-sectional prospective study was conducted in the outpatient clinic of the Bakırköy Prof. Dr. Mazhar Osman Research and Training Hospital for Neurology, Neurosurgery and Psychiatry between June 2018 and January 2019. A total of 120 MS patients diagnosed with MS according to the 2010 McDonald's criteria who were aged between 18 and 65 years were included in the study by convenience sampling method.[22] This study approved by the Ethics Committee of Bakırköy Prof. Dr. Mazhar Osman Research and TRaining Hospital for Neurology, Neurosurgery and Psychiatry with 5.6.2018/183 decision number.

The sample size was calculated using power analysis G*Power 3.1.9.4 program and priority analysis method. A sample size of minimum 35 participants per group was determined based on a power of 95%, margin of error 0.05, and 0.80 effect size value ($d=0.80$). The study was conducted until to reach 35 participants for each group.

Twelve of the participants were not included in the study due to incomplete forms, and 3 refused to fulfill the informed consent and participate in the study. The participants were informed about the purpose and the procedures of the study, and their written consent was obtained. All of the patients had an Expanded Disability Status Scale (EDSS) score of 4 or below and had the relapsing-remitting clinical form of MS. The exclusion criteria were as follows: the presence of language problems, illiteracy, mental retardation, the patients who had an attack in the last month, and patients under corticosteroid treatment in the last week, and patients with psychotic and bipolar disorder diagnosis in the past and present. Depression and anxiety levels were evaluated using the Hospital Anxiety Depression Scale (HADS), and AS levels were evaluated using the Anxiety Sensitivity Index (ASI).

Instruments

Sociodemographic Data Collection Form: The participants' demographic data were collected using the Sociodemographic Data Collection Form, a structured questionnaire on sociodemographic characteristics which was created by the authors. The Sociodemographic Data Collection Form included the questions about age, education, marital status, economical status, employment status, alcohol and substance use, and past psychiatric history.

The Hospital Anxiety and Depression Scale: The HADS was used to measure the clinical anxiety and depression.

Hospital Anxiety Depression Scale is a scale of 14 items to assess anxiety and depression symptoms in a population with a medical disease.[23] Hospital Anxiety Depression Scale was preferred since the scale provides the possibility of measuring anxiety and depression separately, and also it is a validated scale in the group of patients with MS.[24] Reliability and validity study of the Turkish form was performed by Aydemir et al.,[25] and the cut-off points for the Turkish form were 10 (sensitivity 83.67%; specificity 81.60%) for the anxiety subscale and 7 (sensitivity 72.22%; specificity 68.29%) for the depression subscale, and these values were taken as reference values in our study.

Anxiety Sensitivity Index-3: The ASI-3 is a self-report questionnaire consisting of 18 items evaluating AS and consists of subscales of cognitive, physical, and social concerns. Both ASI and the subscales have powerful psychometric evaluation features.[12] Mantar et al.[26] reported the Turkish form's validity and reliability. The Turkish version has no cut-off score, and high scores indicate increased AS. The ASI-3 shows high internal consistency and has been found to have reasonably good re-test reliability ($r=0.64$, $P < .001$). On factor analysis, 61.72% of the total variance is attributable to physical, cognitive, and social factors.[26]

Statistical Analysis

All analyses were performed using SAS Studio 3.71 (SAS Institute, Cary, North Carolina). Descriptive analyses were performed for sociodemographic data and clinical characteristics. Categorical variables are presented as frequency and percentages, and continuous variables are presented as mean±standard deviation (SD). Shapiro–Wilk test was used to determine whether the variables had a normal distribution, and it was found that parametric hypothesis tests were not met ($W(105)=0.96$; $P=.005$).

Participants were grouped into 2 categories as those with and without clinical anxiety, the anxious group and the non-anxious group, according to HADS anxiety scores. In this study, HADS anxiety was taken as the primary outcome measure. The cut-off point was taken as 10 for both groups. Sociodemographic data and medical variables of the clinical anxious and non-anxious group were evaluated by chi-square test. When the expected frequencies were not met, Fisher's exact test was applied. Mann–Whitney *U*-test was used to determine the difference between the anxious and non-anxious groups according to the AS levels and HADS depression and total scores. Spearman's correlation analysis was performed to evaluate the relationship between the HADS anxiety subscale scores and ASI scores and HADS depression subscale scores in the anxious group. Binominal logistic regression analysis (stepwise variable selection method) was used to determine the predictors of anxiety. All statistical analyses were evaluated within a 95% CI ($P < .05$ significance level).

RESULTS

Of the 120 participants, 12 of the participants were excluded due to the incomplete forms, while 3 of them were excluded since they refused to give participation consent. Therefore, data of the 105 participants were analyzed.

Sociodemographic Characteristics of the Sample

Most of the patients in both groups were between 26 and 45 years of age (65.71% in the anxious group and 54.29% in the non-anxious group), and most of the patients were female (60% in the anxious group and 77.14% in the non-anxious group). Most of the patients in the non-anxious group were primary and high school educated (71.42%), while 65.71% were primary and high school educated in the anxious group. The marital status of the patients was as follows: 35% were single and 64.28% were married in the non-anxious group, and 25.71% were single and 74.29% were married in the anxious group. Most of the patients reported their economical status as middle in both groups (58.75% in the non-anxious group and 65.71% in the anxious group). In the non-anxious group, 51.34% were unemployed, while 54.29% were unemployed in the anxious group. Fort the non-anxious group, 85.71% patients have negative past psychiatric history, and 74.29% have negative past psychiatric history for the anxious group. The history of alcohol and substance use was as follows: in the non-anxious group, 80% of the patients has any alcohol and substance use history, 20% of them has the history of cigarette smoking, and in the anxious group, 71.43% of the patients has any alcohol and substance use history, 22.86% of them has the history of cigarette smoking, and 5.1% has the history of alcohol use.

Participants were divided into 2 groups according to the cut-off point of 10 based on the HADS anxiety subscale scores. Participants who had a score indicating clinically significant levels of anxiety (HADS anxiety score ≥10; n=35, 33.3%) were compared to those who scored under the clinically significant levels of anxiety (HADS anxiety score of 10 or less; n=70, 66.7%).

Shapiro–Wilk test was used to determine whether the variables had a normal distribution, and it was found that parametric hypothesis tests were not met. Chi-square and Fisher's exact test were used to determine the sociodemographic data and the clinical variables of the anxious and non-anxious group. We did not found significant difference between the groups according to the sociodemographic data such as age, gender, and marital status and clinical variables such as past psychiatric history. Anxious and non-anxious groups were matched regarding the sociodemographic data ($P > 0.05$). The results of the comparison of the groups are summarized in Table 1.

Mann–Whitney *U*-test was performed to determine the difference between the anxious and non-anxious groups

Table 1. Sociodemographic Characteristics of the Anxious and Non-anxious Groups

	Non-anxious		Anxious			
	N	%	N	%	χ^{2a}	*P*
Age						
18-25	14	20	4	11.43	1.60	.45
26-45	38	54.29	23	65.71		
45-65	18	25.71	8	22.86		
Education						
Literate	2	2.86	1	2.86	0.01	.86
Primary school	25	35.71	13	37.14		
High school	25	35.71	10	28.57		
University	18	25.71	11	31.43		
Gender						
Female	54	77.14	21	60	3.36	.07
Male	16	22.86	11	40		
Marital status						
Single	25	35.71	9	25.71	1.07	.31
Married	45	64.29	26	74.29		
Economical status						
Low	11	15.71	8	22.86	3.13	.21
Medium	41	58.75	23	65.71		
High	18	25.71	4	11.43		
Employement status						
Employed	34	48.57	16	45.71	0.08	.78
Unemployed	36	51.34	19	54.29		
Alcohol and substance use						
None	56	80	25	71.43	0.02	.14
Cigarette smoking	14	20	8	22.86		
Alcohol	0	0	2	5.71		
Past psychiatric history						
Positive	10	14.29	9	25.71	2.06	.15
Negative	60	85.71	26	74.29		

[a]Chi-square test.

according to the ASI total, subscale scores and HADS total, depression subscale scores. Post hoc power analysis was also performed with alpha level 0.05 to determine the effect size. Anxiety Sensitivity Index total was found significantly high in the anxious group than non-anxious group ($N_{anxious}$ = 35, $N_{non\text{-}anxious}$ = 70, U=542.000, Z=−4.647, effect size d_{cohen}=1.10, P < .001). Hospital Anxiety Depression Scale depression subscale scores were found significantly high in the anxious group ($N_{anxious}$=35, $N_{non\text{-}anxious}$ = 70, U=498.500, Z=−4.955, effect size d_{cohen}=2.32. P < .001). The comparison of the clinical scale scores of the groups is shown in Table 2.

Spearmen's correlation test was performed to determine the relationship between the HADS anxiety subscale scores and ASI total and subscale scores in the anxious group. We found significantly positive correlation with HADS total (r=0.91, P < 0.001) and ASI global (r=0.54, P < .001). The correlation matrix between the scales used to assess anxiety, depression, and anxiety sensitivity is shown in Table 3.

Gender, age, HADS depression scores, ASI physical, ASI social, and ASI cognitive concerns scores were taken in binominal logistic regression analysis (stepwise variable selection method) as independent variables sequentially.

At the first step of the model, the HADS depression score was included in the model and explained 35% of the model (b=0.34, P < .05). In the second step of the model, while the significance of HADS depression scores continues (b=0.32, P < .05), AS social concern (b=0.21, P < .05) was added to the model and has increased the overall disclosure percentage of the model up to 47%.

For the logistic regression analysis, the Hosmer-Lemeshow goodness-of-fit test showed that the logistic model was appropriate. One-unit increase in HADS depression score increases anxiety rate 1.376 times, 1-unit increase in AS social concern score increases anxiety rate 1.228 times (OR 1.37, 95% CI 1.17-1.61, P < .001 and OR 1.22, 95% CI 1.08-1.38, P=.0009, respectively). Logistic regression analysis results are summarized in Table 4.

DISCUSSION

This study examined the role of AS in the occurrence of significant clinical anxiety in MS patients. As hypothesized, a high AS level was found to be significantly associated with significant clinical anxiety in our sample of MS patients. Our findings revealed that depression and ASI-social concern is predictive for clinically significant anxiety with a variance higher than that calculated for age, gender, ASI cognitive, and physical concern.

In our study sample, the majority of the participants were between 26 and 45 years (58%, N=61) and females (71%, N=75), and our findings are consistent with the reports of the sociodemographic characteristics of MS patients.[27] In 105 participants whose data were analyzed, 33.3% showed clinically significant anxiety. The prevalence ratio is consistent with the literature studies that subject anxiety in MS and supports the finding that anxiety is a common, comorbid psychopathology in MS.[28]

In our sample, our findings (P < .05), which showed that AS total and subdomains were significantly higher in the anxious MS group compared to the non-anxious MS group, supports our hypothesis that AS plays a role in the occurrence of significant clinical anxiety symptoms in MS patients. Holas et al.[29] examined AS levels to evaluate cognitive anxiety vulnerability in sarcoidosis and found that ASI physical concerns subdomain was predictive for bodily vigilance in this patient group. McLeish et al.[30] reported

Table 2. Results of the Comparison of the Depression and Anxiety Sensitivity Levels of the Groups

	Non-anxious (n = 70)				Anxious (n = 35)					
	Min-Max	Mean±SD	Skewness	Kurtosis	Min-Max	Mean±SD	Skewness	Kurtosis	U^a	Z
ASI										
Physical	0-15	4.07±4.26	1.15	0.45	0-19	7.80±5.26	0.37	-0.85	678.00	-3.67**
Cognitive	0-20	4.84±4.25	1.18	1.34	0-24	9.86±6.35	0.37	-0.44	628.00	-4.00**
Social	0-13	2.81±4.68	1.40	0.95	0-16	7.00±4.51	0.12	-0.74	566.50	-4.48**
Global	0-42	11.56±10.63	1.35	1.08	0-52	24.66±14.14	0.21	-0.83	542.00	-4.65**
HADS										
Depression	0-14	4.59±3.57	0.61	-0.41	2-19	8.89±3.77	0.74	0.72	498.50	-4.96*
Total	0-23	9.33±5.28	0.36	-0.40	12-34	21.40±5.05	0.80	0.78	113.50	-7.56**

SD, standard deviation; **$P < .01$; [a]Mann–Whitney *U*-test.

Table 3. Correlations of the ASI Global and Subscale Scores With the HADS Anxiety, HADS Depression, and HADS Total

	HADS Anxiety	HADS Depression	HADS Total	ASI Physical Concerns	ASI Cognitive Concerns	ASI Social Concerns	ASI Global
HADS Anxiety	*						
HADS Depression	0.61**	*					
HADS Total	0.91**	0.89**	*				
ASI Physical Concerns	0.46**	0.32**	0.43**	*			
ASI Cognitive Concerns	0.50**	0.29**	0.47**	0.72**	*		
ASI Social Concerns	0.50**	0.31**	0.45**	0.61**	0.62**	*	
ASI Global	0.54**	0.32**	0.47**	0.88**	0.89**	0.83**	*

ASI, Anxiety Sensitivity Index; HADS, Hospital Anxiety Depression Scale; Spearman's correlation test; **$P < .01$.

Table 4. The Results of the Binary Logistic Regression Analysis

Variables	*B*	*P*	Odds Ratio *B*	%95 CI of Odds Ratio	
				Lower	Upper
Intercept	-3.79	**.0001**			
HADS depression	0.32	**.0001**	1.38	1.18	1.61
ASI social concerns	0.21	**.0009**	1.23	1.09	1.39

Cox and Snell $R^2 = 0.339$; Nagelkerke $R^2 = 0.601$; $\chi^2 = 2.652$; $P = .978$; $P < .05$.

that asthma-related physical sensations were perceived as a danger signal in asthmatic patients with high AS physical concerns; thus, patients experienced increased anxiety levels when faced with asthma symptoms. Multiple sclerosis has symptoms that may be associated with multiple arousal-related sensations such as fatigue, weakness, trembling, paresthesia, cognitive impairments, loss of balance, and there is also an emotional impact of symptoms which generates worry associated with the uncertainty and unpredictability of the subsequent relapses on MS patients.[16] The presence of elevated AS levels leads to increased bodily vigilance and appraisal of physical symptoms as fearful in MS patients; thus, it may stimulate the attack fear and cause anxiety symptoms in a disease like MS, whereas one of the most significant clinical features is the uncertain and unpredictable course.

Farris et al.[31] reported in their study investigating the relationship between AS and emotional disorders and migraine-related fear and avoidance behavior that patients with high AS levels react with fear and anxiety to migraine-related bodily sensations and that the resulting cognitive concerns are associated with behavioral problems such as painkiller abuses. Anxiety sensitivity cognitive concern subdomain was found to be significantly higher in the anxious MS group compared to the non-anxious group in our study ($P < .05$). Dennison and Moss-Morris[32] reported that dysfunctional beliefs about disease symptoms in early MS contributed to the psychological distress associated with the disease, leading to avoidance behaviors such as reducing social activities and over-resting. Jhonson et al.[33] state that fears in arousal-related sensations due to seizures in epilepsy patients limit the functionality of patients with the thought that it will trigger the seizure and that it led to avoiding activities, which increased the negative effect of the disease and decreased the quality of life. Multiple sclerosis patients with high AS levels may perceive physical symptoms and bodily sensations as a danger signal and tend to avoid avoidance behaviors such as decreasing social activities and over-resting, increasing the psychological distress associated with the disease due to fear of experiencing an attack. As a result, it may lead to the occurrence of anxiety by causing cognitive concerns for MS patients, such as the idea that they are approaching disability conditions, physical symptoms have

functional losses beyond the real impact. Further studies in which the relationship of "avoidance and interference with behaviors that promote physical well-being"[15] and AS cognitive concerns are revealed in MS patients are needed.

We found a significant positive correlation between depression and anxiety scores in our MS sample. This finding is parallel with studies that report the coexistence and association of anxiety and depression in MS.[4,27] When the predictive factors of anxiety symptoms were evaluated within the logistic regression model, we found that depression was a significant predictive factor of anxiety in MS patients (OR 1.376, 95% CI 1.175-1.610). Garfield and Lincoln[1] investigated the effects of psychological factors such as disability, depression, self-efficacy, locus of control, general and psychological distress on anxiety in MS patients, and they found depression as a significant predictor of anxiety consistent with our findings. The presence of depression is a predictive factor for anxiety in MS patients during the diagnostic period and long-term follow-up.[5,34] Although the strong correlation between depression and anxiety in MS was revealed, this relationship's nature is not precise. Hartoonian et al.[3] claimed that a common cognition that predisposes a person to a maladaptive thought pattern might reveal depression symptoms and anxiety symptoms at different times during the disease. Further research is needed to explore the role of AS in the occurrence of comorbid anxiety and depression in MS patients and to enlighten the mechanisms contributing to the interaction between AS and symptoms of depression and anxiety.

According to our findings, ASI social concerns subdomain (OR 1.22, 95% CI 1.08-1.38) was also a predictive factor in MS patients' anxiety symptoms. Dixon et al.[35] reported that AS social concerns moderated the association between stress and skin-related emotional and social functioning in adults with skin disease. They stated that this property plays a role in increasing the effect of skin disease on psychological symptoms in patients with high AS social concerns in this group because they care more about the physiological consequences related to stress and skin disease and fear more. In the study conducted by Poder et al.,[36] which reported that social anxiety symptoms were common in patients with MS, they stated that social anxiety is associated with the symptoms being anticipated or perceived unpredictability rather than the disability of symptoms. For example, neurological symptoms such as tremor, dysarthria, bowel, and bladder dysfunction in MS are specific neurological symptoms that may be associated with increased anxiety in social settings in MS patients.[36] According to our findings, the fact that AS social concern level is predictive of anxiety, MS patients with high AS social concerns take the physiological results of neurological symptoms that may be socially catastrophic into account[29] and having more fear of these may lead to an increase in anxiety levels in this patient group. Further studies are required for demonstrating how AS social concern levels and the impact of neurological symptoms on daily life interact with anxiety symptoms seen in MS.

Our study has many limitations. Small sample size and the cross-sectional design limit to make causal inferences from the results. Further prospective longitudinal studies in a heterogeneous patient sample with different disease levels and structured clinical evaluation using psychiatric comorbidities by objective measurement tools will contribute to a better understanding of the relationship between AS and anxiety in MS patients. On the other hand, according to our knowledge, this is the first study to examine the relationship between anxiety symptoms and AS in MS patients' population.

CONCLUSION

In conclusion, this article describes the association of the anxiety, depression, and anxiety sensitivity in a sample of patients with MS. This study's findings extend prior empirical and theoretical work by examining these constructs in a patient population that has not previously been investigated.

The fact of revealing a psychological vulnerability factor, which is a relatively easy parameter to evaluate and detect with an easily applicable measure such as ASI in MS patients, can be reduced by short psychotherapeutic interventions. Such management contributes to the integration of physical and mental care and will improve prognosis by reducing the risk of psychopathology.[37]

Ethics Committee Approval: Ethics committee approval was received from the Bakırköy Prof. Dr. Mazhar Osman Research and Training Hospital for Neurology, Neurosurgery and Psychiatry with 5.6.2018/183 decision number.

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer Review: Externally peer-reviewed.

Author Contributions: Concept – M.S.Y.; Design - M.S.Y., K.Ş.M. Supervision - M.S.Y.; Resource - M.S.Y., K.Ş.M.; Materials - M.S.Y.; Data Collection and/or Processing - M.S.Y., K.Ş.M.; Analysis and/or Interpretation - K.Ş.M.; Literature Search - M.S.Y., K.Ş.M.; Writing - M.S.Y., K.Ş.M.; Critical Reviews - M.S.Y.

Acknowledgments: We would like to express our special thanks of gratitude to the MS team of the Neurology Department of Istanbul Bakirkoy Professor Dr. Mazhar Osman Research and Training Hospital for Neurology, Neurosurgery, and Psychiatry for their facilitative support to our study.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Garfield AC, Lincoln NB. Factors affecting anxiety in multiple sclerosis. *Disabil Rehabil*. 2012;34(24):2047-2052. [CrossRef]
2. Korostil M, Feinstein A. Anxiety disorders and their clinical correlates in multiple sclerosis patients. *Mult Scler*. 2007;13(1):67-72. [CrossRef]
3. Hartoonian N, Terrill AL, Beier ML, et al. Predictors of anxiety in multiple sclerosis. *Rehabil Psychol*. 2015;60(1):91-98. [CrossRef]
4. Butler E, Matcham F, Chalder T. A systematic review of anxiety amongst people with multiple sclerosis. *Mult Scler Relat Disord*. 2016;10:145-168. [CrossRef]
5. Giordano A , Granella F , Lugaresi A, et al. Anxiety and depression in multiple sclerosis patients around diagnosis. *J Neurol Sci*. 2011;307(1-2):86-91. [CrossRef]
6. Pham T, Jetté N, Bulloch AGM, et al. The prevalence of anxiety and associated factors in persons with multiple sclerosis. *Mult Scler Relat Disord*. 2018;19:35-39. [CrossRef]
7. Butler E, Thomas R, Carolan A, Silber E, Chalder T. 'It's the unknown'-understanding anxiety: from the perspective of people with multiple sclerosis. *Psychol Health*. 2019;34(3):368-383. [CrossRef]
8. Janssens AC, van Doorn PA, de Boer JB, et al. Perception of prognostic risk in patients with multiple sclerosis: the relationship with anxiety, depression, and disease-related distress. *J Clin Epidemiol*. 2004;57(2):180-186. [CrossRef]
9. Reiss S, Peterson RA, Gursky DM. Anxiety sensitivity, injury sensitivity, and individual differences in fearfulness. *Behav Res Ther*. 1988;26(4):341-345. [CrossRef]
10. McNally RJ. Anxiety sensitivity and panic disorder. *Biol Psychiatry*. 2002;52(10):938-946. [CrossRef]
11. Schmidt NB, Zvolensky MJ, Maner JK. Anxiety sensitivity: prospective prediction of panic attacks and axis I pathology. *J Psychiatr Res*. 2006;40(8):691-699. [CrossRef]
12. Taylor S, Zvolensky MJ, Cox BJ, et al. Robust dimensions of anxiety sensitivity: development and initial validation of the Anxiety Sensitivity Index-3. *Psychol Assess*. 2007;19(2):176-188. [CrossRef]
13. Farris SG, Zvolensky MJ. Cognitive processes in anxiety and comorbid physical illness and health behavior: introduction to the special issue. *Cogn Ther Res*. 2019;43(1):1-5. [CrossRef]
14. Asmundson GJG, Wright KD, Hadjistavropoulos HD. Anxiety sensitivity and disabling chronic health conditions: state of the art and future directions. *Scand J Behav Ther*. 2000;29(3-4):100-117. [CrossRef]
15. Horenstein A, Potter CM, Heimberg RG. How does anxiety sensitivity increase risk of chronic medical conditions? *Clin Psychol Sci Pract*. 2018;25(3):e12248. [CrossRef]
16. Kalb R. The emotional and psychological impact of multiple sclerosis relapses. *J Neurol Sci*. 2007;256(suppl 1):29-33. [CrossRef]
17. Janssens AC, van Doorn PA, de Boer JB, et al. Impact of recently diagnosed multiple sclerosis on quality of life, anxiety, depression and distress of patients and partners. *Acta Neurol Scand*. 2003;108(6):389-395. [CrossRef]
18. Carleton RN, Sharpe D, Asmundson GJ. Anxiety sensitivity and intolerance of uncertainty: requisites of the fundamental fears? *Behav Res Ther*. 2007;45(10):2307-2316. [CrossRef]
19. Fiest KM, Walker JR, Bernstein CN, et al. Systematic review and meta-analysis of interventions for depression and anxiety in persons with multiple sclerosis. *Mult Scler Relat Disord*. 2016;5:12-26. [CrossRef]
20. Minden SL, Feinstein A, Kalb RC, et al. Evidence-based guideline: assessment and management of psychiatric disorders in individuals with MS: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2014;82(2):174-181. [CrossRef]
21. Olthuis JV, Watt MC, Mackinnon SP, Stewart SH. Telephone-delivered cognitive behavioral therapy for high anxiety sensitivity: a randomized controlled trial. *J Consult Clin Psychol*. 2014;82(6):1005-1022. [CrossRef]
22. Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol*. 2011;69(2):292-302. [CrossRef]
23. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361-370. [CrossRef]
24. Honarmand K, Feinstein A. Validation of the Hospital Anxiety and Depression Scale for use with multiple sclerosis patients. *Mult Scler*. 2009;15(12):1518-1524. [CrossRef]
25. Aydemir O, Güvenir T, Küey L, Kültür L. Reliability and validity of the Turkish version of Hospital Anxiety and Depression Scale. *Turk J Psychiatr*. 1997;8:280-287. [CrossRef]
26. Mantar A, Yemez B, Alkın T. The validity and reliability of the Turkish version of the Anxiety Sensitivity Index-3. *Turk Psikiyatri Derg*. 2010;21(3):225-234.
27. Dahl OP, Stordal E, Lydersen S, Midgard R. Anxiety and depression in multiple sclerosis: a comparative population-based study in Nord-Trøndelag County, Norway. *Mult Scler*. 2009;15(12):1495-1501. [CrossRef]
28. Boeschoten RE, Braamse AMJ, Beekman ATF, et al. Prevalence of depression and anxiety in multiple sclerosis: a systematic review and meta-analysis. *J Neurol Sci*. 2017;372:331-341. [CrossRef]
29. Holas P, Krejtz I, Urbankowski T, et al. Anxiety, its relation to symptoms severity and anxiety sensitivity in sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis*. 2013;30(4):282-288.
30. McLeish AC, Luberto CM, O'Bryan EM. Anxiety sensitivity and reactivity to asthma-like sensations among young adults with asthma. *Behav Modif*. 2016;40(1-2):164-177. [CrossRef]
31. Farris SG, Burr EK, Abrantes AM, et al. Anxiety sensitivity as a risk indicator for anxiety, depression, and headache severity in women with migraine. *Headache*. 2019;59(8):1212-1220. [CrossRef]
32. Dennison L, Moss-Morris R. Cognitive-behavioral therapy: what benefits can it offer people with multiple sclerosis? *Expert Rev Neurother*. 2010;10(9):1383-1390. [CrossRef]
33. Johnson AL, McLeish AC, Alsaid-Habia T, Shear PK, Privitera M. Anxiety sensitivity as a predictor of epilepsy-related quality of life and illness severity among adult epilepsy. *Cogn Ther Res*. 2019;43(1):6-13. [CrossRef]

34. Askari F, Ghajarzadeh M, Mohammadifar M, et al. Anxiety in patients with multiple sclerosis: association with disability, depression, disease type and sex. *Acta Med Iran*. 2014;52(12):889-892.

35. Dixon LJ, Witcraft SM, McCowan NK, Brodell RT. Stress and skin disease quality of life: the moderating role of anxiety sensitivity social concerns. *Br J Dermatol*. 2018;178(4):951-957. [CrossRef].

36. Poder K, Ghatavi K, Fisk JD, et al. Social anxiety in a multiple sclerosis clinic population. *Mult Scler*. 2009;15(3):393-398. [CrossRef]

37. Schmidt NB, Eggleston AM, Woolaway-Bickel K, et al. Anxiety Sensitivity Amelioration Training (ASAT): a longitudinal primary prevention program targeting the cognitive vulnerability. *J Anxiety Disord*. 2007;21(3):302-319. [CrossRef]