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The role of disease activity as a determinant of body awareness and central sensitization in patients with axial spondyloarthritis: a cross-sectional study

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ABSTRACT

Aims: The aim of this study was to investigate the effects of disease activity on body awareness and central sensitization in patients with axial spondyloarthritis (axSpA).

Methods: This cross-sectional study included patients diagnosed with axSpA. Disease activity was evaluated using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and a score of four or higher was considered high disease activity. Patients were divided into two groups according to BASDAI: high disease activity (BASDAI ≥ 4) group (HG) and the low disease activity (BASDAI<4) group (LG). Body awareness levels were assessed with the Body Awareness Questionnaire (BAQ). The Central Sensitization Inventory (CSI) was used for central sensitivity. Simple linear regression analyses were performed to investigate which of the independent variables could explain the disease activity.

Results: Sixty-two patients with a mean disease duration of 10.8 years were included. The mean BASDAI, CSI-A, and BAQ were 4.2, 38.5, and 73 points, respectively. Demographics and clinical characteristics were comparable between the groups (p>0.05). The CSI-A score was higher in HG compared to LG (44 (31-54) vs. 31 (21-41), p=0.008). The HG had poorer BAQ scores than the LG (61 (52-85) vs. 85 (64-96), p=0.017). BASDAI was moderately associated with CSI-A (r=0.145, R2=0.172, p=0.001). No significant correlation was found between BASDAI and BAQ (p=0.167). The results of the simple linear regression analysis suggested that CSI-A explained 17.2% of the disease activity. BASDAI (β = 0.415, p=0.001) significantly predicted central sensitization. BASDAI was strongly correlated with VAS (r=0.665, R2= 0.442, p<0.001). The VAS explained 44.2% of the disease activity, and BASDAI (r=0.665, p<0.001) significantly predicted pain severity.

Conclusion: High disease activity adversely affects central sensitization and body awareness in patients with axSpA. Physicians should also consider a multimodal biopsychosocial perspective in the management of patients with high disease activity.

Keywords: Central sensitization, spondyloarthritis, awareness, pain

INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease characterized by sacroiliitis, enthesopathy, and spondyloarthropathy, with variable peripheral joint involvement.[1] Chronic pain, stiffness, fatigue, sleep disturbance, and functional impairment are common symptoms of axSpA, and these symptoms limit activity and worsen quality of life during the active phase of the disease.[2] At present, the most widely used patient-based outcome measure to assess disease activity in patients with axSpA is the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). This scale assesses parameters such as fatigue, peripheral joint pain, spinal pain, attachment point inflammation and duration and severity of morning stiffness.[3] The assessment of disease activity in axSpA is crucial in the management of the disease, follow-up of patients, and prediction of prognosis.

Different medical approaches utilized in controlling the disease and disease activity provide significant gains to the patient in patients with axSpA, however, sometimes they may not adequately treat disease-related pain, fatigue, sleep disturbance, anxiety, and depression.[4] Chronic inflammation in axSpA may trigger both peripheral and central modifications of pain pathways, and lead to central sensitization (CS). CS is described as an increased sensitivity of nociceptive neurons in the central nervous system to usual or subthreshold peripheral stimuli,[5] and the high prevalence of CS in patients with axSpA despite biologic therapy suggests that inflammation may not be the sole cause of pain and that additional pain mechanisms, such as

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perception and interpretation of pain, may play a role in the persistence of pain.[6,7] Recently, CS has been recognized as a possible underlying pathophysiological mechanism of the chronic pain associated with axSpA. In addition, previous studies suggested chronic musculoskeletal pain, cognitive impairment and emotional state related to body awareness.[8,9] However, little is known about body awareness in patients with axSpA and its association with disease activity.

Body awareness is defined as the ability to focus attentively on and be aware of internal body sensations or to recognize nuances in body cues.[10,11] Body awareness occurs through the integration of many sensory inputs such as interoceptive, proprioceptive, exteroceptive, vestibular, and it is involved sensory, physical and physiological mechanisms.[12] Many cortical areas are interconnected to help the perception of body position, the relationship between body segments and the body itself, and body awareness, which is the ability to recognize one's own body, is formed.[13] Previous studies have suggested a negative relationship between body awareness, pain and emotional mood in healthy individuals[14] and that cognitive impairment and chronic musculoskeletal pain reduce body awareness in older adults.[8] Shifting the focus of attention from pain sensations to different mental tasks may be beneficial in reducing pain, indeed, previous studies on experimental pain or other models of acute pain show such benefits.[15,16] Preliminary evidence suggests that body awareness may have significant benefits in the management of chronic painful diseases and improving health-related quality of life.[17,18] Our knowledge about body awareness in axSpA characterized by chronic musculoskeletal pain, fatigue, systemic inflammation, and other complaints are limited. Furthermore, disease activity, which is commonly assessed in the clinical setting, may affect both body perception and central sensitivity. The aim of this study was investigating the effects of disease activity on body awareness and CS in patients with axSpA. The primary hypothesis suggests that high disease activity is associated with impaired body awareness. The secondary hypothesis suggests that disease activity is a determinant factor of the body awareness and CS.

METHODS

Study Design

The study was carried out with the permission of Ankara Medipol University Non-interventional Clinical Researches Ethics Committee (Date: 11.04.2023, Decision No: 44). Informed consent was obtained from all patients, and all procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The data was obtained in the Ankara Etlik City Hospital Department of Rheumatology between April 2023 and July 2023.

Participants

Inclusion criteria were age ranged from 18 to 65 years, diagnosed with axSpA by criteria of Assessment of Spondyloarthritis International Society classification criteria for axial spondyloarthritis[19] for at least 1 year, had chronic musculoskeletal pain for more than 3 months. Patients with any cardiovascular disease (history of acute myocardial infarction, heart failure, etc.), neurological diseases (Parkinson, multiple sclerosis, stroke, dementia), the presence of active malignancy, neuropsychiatric medical treatment, locomotor disorders (fractures and prostheses) and/or osteoporosis, history of lower extremity and spine surgery, visual and hearing problems, chronic addiction to alcohol, and pregnancy were excluded from the study. All patients included in the study were divided into two groups according to BASDAI: high disease activity (BASDAI ≥ 4) group (HG) and the low disease activity (BASDAI<4) group (LG).

Instruments

Information about disease duration, comorbidities and medications were recorded. Smoking history and regular exercise habits were questioned. Regular exercise habits were considered to be at least 2-3 days a week for at least 30 minutes. Routine laboratory findings such as erythrocyte sedimentation rate (ESR) (mm/h), C-reactive protein (CRP) (mg/L), creatine kinase (U/L), vitamin D3 (nmol/L), folic acid (ng/ml), vitamin B12 (ng/L), ferritin (µg/L), and TSH (mIU/L) were obtained on the day of the assessment.

Pain Severity

The severity of the pain was assessed with the Visual Analogue Scale (VAS). The 10-cm horizontal line was defined as 0 "no pain" and 10 "very severe pain", and the patients were asked to mark a line indicating their musculoskeletal pain, and then the line was measured in centimeters.[20]

Disease Activity

Disease activity was determined using BASDAI, which is a patient reported outcome measure. BASDAI includes six questions related to fatigue, spinal pain, peripheral joint pain, attachment point inflammation, and duration and severity of morning stiffness. A total score ranges from 0 to 10, and a higher score indicates more severe disease activity. A BASDAI score ≥4 is a threshold, which indicate considered as active of disease.[3]

Central Sensitization

Central Sensitization Inventory (CSI) is used to assess the presence and severity of CS. The CSI is a self-reported tool and is consists of two parts: the first part (CSI-A) contains 25 items investigating emotional and somatic disorders associated with CS. Each response is scored

between 0 and 4, and the total score is obtained as 0-100. High scores indicate CS symptoms of increasing severity. The second part of the scale (CSI-B) investigates disorders diagnosed by a physician that may be related to CS, such as restless leg syndrome, chronic fatigue syndrome, fibromyalgia syndrome, temporomandibular joint problems, migraine, irritable bowel syndrome, anxiety, and depression.[21] The cut-off point of the CSI is 40 points. The Turkish validity and reliability study of the scale was conducted by Düzce et al.[22]

Body Awareness

The Body Awareness Questionnaire (BAQ) is determined whether the body's level of sensitivity is normal or abnormal. The BAQ includes 18 items. Each item is rated by the patients on a scale of 1 to 7 (1=not true for me at all, 7 = completely true for me). The questionnaire uses the total score for the rating. The maximum total score that can be obtained from the questionnaire is 126 and the minimum score is 18 points. Higher scores indicate a better level of body awareness.[23] The Turkish validity and reliability study of the scale was conducted by Karaca et al.[23]

Statistical Analysis

A priori sample size analysis was performed with G Power software (Version 3.1.9.2, Franz Faul, University of Kiel, Kiel, Germany). The sample size of at least 58 individuals was found to have a power of 0.80, an effect size of 0.31 (medium effect d≥0.3), correlation test r^2= 0.10, and an alpha value of 0.05 (one-tailed). BM SPSS (Statistical Package for the Social Sciences, ver. 22.0) was used for statistical analyses. Descriptive data were given as mean (standard deviation) or median (IQR) and minimum to maximum for numerical data, and number (n) and percentage (%) values were calculated for non-numerical data. Kolmogorov-Smirnov tests were performed to determine whether variables were normally distributed. The relationship among disease activity, body awareness, and CS was evaluated with Pearson's correlation analysis due to parametric conditions. The size of the correlation coefficient was considered to be very high (0.90 to 1.00), high (0.70 to 0.89), moderate (0.50 to 0.69), low (0.30 to 0.49), and negligible (0 to 0.29).[24] Simple linear regression analyses were performed to investigate which of the independent variables (VAS, CS) could explain the dependent variables (BASDAI) in presence of the significant correlations. Each analysis is performed only one independent variable. p value <0.05 was considered for statistical significance.

RESULTS

Sixty-two patients (38 male, 24 female, mean age: 43.9 (9.7) years, mean disease duration: 10.8 (4.8) years) were included. The demographic and clinical features of patients with axSpA are shown in Table 1. The groups had similar characteristics in terms of clinical and demographic characteristics (p>0.05). CRP is higher in HG compared to LG (p<0.001). The mean BASDAI score of all patients was 4.2 (1.4) points. The CS is positive in 48.4% of all patients. CS presence is more common in HG than LG (20 (60.6) vs 10 (34.5), p=0.036).

A comparison of CS and body awareness between the groups is presented in Table 2. There were significant among-group differences in the CSI-A scores (p=0.008), BAQ scores (p=0.017), and VAS (p<0.001). HG had higher CSI-A (44 (31-54) vs 31 (21-41)), poorer BAQ (61 (52-85) vs 85 (64-96)), and more severity pain (7 (6-8) vs 5 (4-6)) compared to LG.

BASDAI is moderately correlated with the CSI-A scores (r=0.415, R2= 0.172, p=0.001) and is highly correlated with VAS (r=0.665, R2= 0.442, p<0.001). No significant correlation was found between BASDAI and BAQ (p=0.167). The results of the simple linear regression analysis suggested that disease activity explained 17.2% of the variance. BASDAI (r= 0.415, p=0.001) significantly predicted CS. The VAS score is explained 44.2% of the variance and BASDAI (r=0.665, p<0.001) significantly predicted pain severity (Figure 1). The relationship between the disease activity, CS and pain severity of axSpA patients are shown in Table 3.

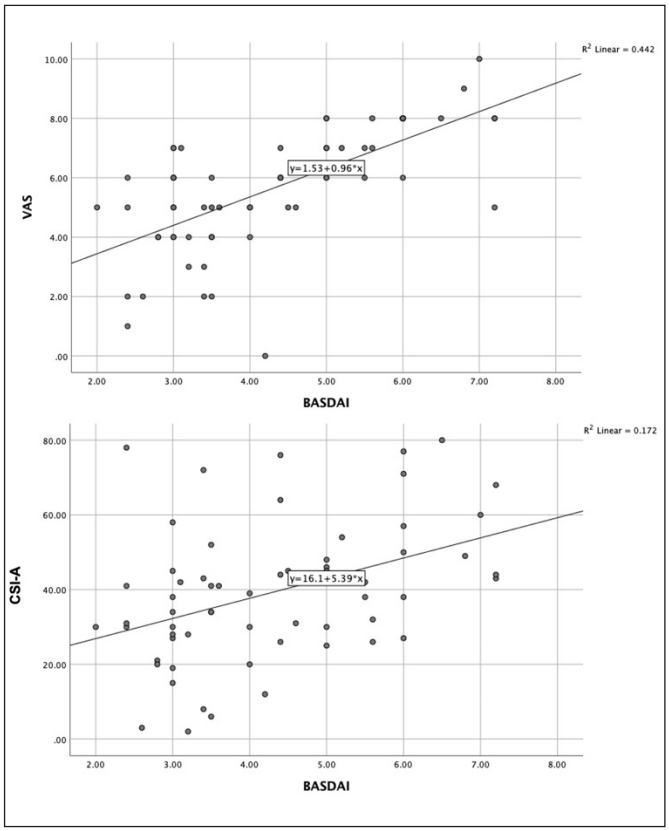

Figure 1. Scatter plots of disease activity, central sensitization, and pain severity

Tablo 1. The demographic and clinical features of patients with axial spondyloarthritis

	AxSpA (All patients) (n=62)	HG (BASDAI ≥ 4) (n=33)	LG (BASDAI<4) (n=29)	p value*
Age (year), mean (SD), min-max	43.9 (9.7) (25-63)	44 (10.2)	43.8 (9.3)	0.947
Male, n (%)	38 (61.3)	24 (72.7)	14 (48.3)	0.049
BMI (kg/m²), mean (SD)	28.0 (3.46)	27.8 (3.2)	28.1 (3.7)	0.778
Disease duration (year), mean (SD), min-max	10.8 (4.8) (2-20)	10.5 (5.2)	11.4 (4)	0.632
History of smoking, n (%)				
None	45 (72.6)	24 (72.7)	21 (72.4)	
Active	17 (27.4)	9 (27.3)	8 (27.6)	0.978
Pack-year, median (IQR)	10 (7.5-16)	10 (10-16)	8 (5-15)	0.340
Regular exercise habits n (%)	13 (21)	6 (18.2)	7 (24.1)	0.565
Comorbidity n (%)				
Diabetes mellitus	6 (9.7)	5 (15.2)	1 (3.4)	0.201
Hypertension	8 (12.9)	5 (15.2)	3 (10.3)	0.430
Coronary artery disease	2 (3.2)	1 (3)	1 (3.4)	0.721
Thyroid disorder	2 (3.2)	0 (0)	2 (6.9)	0.215
Chronic renal failure	1 (1.6)	1 (3)	0 (0)	0.541
COPD-asthma	7 (11.3)	4 (12.1)	3 (10.3)	0.574
Depression	1 (1.6)	0 (0)	1 (3.4)	0.468
Laboratory findings, median (IQR)				
ESR (mm/h)	18 (9-27)	18 (12-26)	15 (9-30)	0.553
CRP (mg/L)	7.8 (4-20)	14 (7-21.5)	5 (1-8)	<0.001
Creatine kinase (U/L)	69.5 (59.5-103)	92 (66.5-117)	63.5 (58.5-77)	0.094
Vitamin D3 (nmol/L)	39 (27-78)	39 (33-66.5)	30 (17-78)	0.635
Folic acid (ng/ml)	7 (6-10)	6.6 (6.1-10.5)	8.4 (6-10)	0.831
Vitamin B12 (ng/L)	360 (275-447)	403 (317-463)	360 (235-432)	0.472
Ferritin (µg/L)	57.5 (30-88)	71.5 (30-95)	54 (31.5-74)	0.241
TSH (mIU/L)	1.86 (1.14- 2.45)	1.98 (1.5-2.3)	1.76 (1.08 2.80)	0.910
Active medications, n (%)				
Methotrexate	3 (4.8)	2 (6.1)	1 (3.4)	0.549
Sulfasalazine	20 (32.3)	13 (39.4)	7 (24.1)	0.200
Biological DMARDs	34 (54.8)	18 (54.5)	16 (55.2)	0.961
Anti-TNF alpha drug	33 (53.2)	19 (57.6)	14 (48.3)	0.633
NSAIDs	21 (33.9)	12 (36.4)	9 (31)	0.658
BASDAI, mean (SD)	4.2 (1.4)	5.4 (0.9)	3.02 (0.4)	-
CS positive, n (%)	30 (48.4)	20 (60.6)	10 (34.5)	0.036

AxSpA, axial spondyloarthritis; HG, high disease activity group; LG, low disease activity group; TNF, Tumor Necrosis Factor; DMARDs, disease-modifying antirheumatic drugs; BMI, Body mass index; COPD, chronic obstructive pulmonary disease; IQR, interquartile range, ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; TSH, thyroid stimulating hormone; NSAIDs, non-steroidal anti-inflammatory drugs; CS, central sensitization. * p value indicates comparison of HG and LG. *x^2 test or Fisher exact test **Independent t test or Mann-Whitney U test.

Table 2. Comparison of central sensitization and body awareness between the groups

	AxSpA (All patients) (n=62)	HG (BASDAI ≥ 4) (n=33)	LG (BASDAI<4) (n=29)	z	p value
CSI-A (point), median (IQR)	38.5 (28-48)	44 (31-54)	31 (21-41)	-2.640	0.008
CSI-B (point), median (IQR)	0 (0-1)	0 (0-0)	0 (0-1)	-0.649	0.517
BAQ (point), median (IQR)	73 (53-90)	61 (52-85)	85 (64-96)	-2.379	0.017
VAS (cm), median (IQR)	6 (4-7)	7 (6-8)	5 (4-6)	-4.659	<0.001

AxSpA, axial spondyloarthritis; HG, high disease activity group; LG, low disease activity group; CSI-A, Central Sensitization Inventory Part A; CSI-B, Central Sensitization Inventory Part B; BAQ, Body Awareness Questionnaire; VAS, Visual Analogue Scale. * p value indicates comparison of HG and LG. * Mann-Whitney U test.

Table 3. Relationship between the disease activity, central sensitization and pain severity of axial spondyloarthritis patients

					CSI-A				
	r	R^2	P	F	B coefficient	Std. error	β	t	p
Constant					-3.035	0.391	-	7.753	<0.001
Disease activity	0.415	0.172	0.001	12.480	0.032	0.009	0.415	3.533	.001
					VAS				
Constant					1.688	0.401	-	4.211	<0.001
Disease activity	0.665	0.442	<0.001	47.501	0.462	0.067	0.665	6.892	<0.001

CSI-A, Central Sensitization Inventory Part A; VAS, Visual Analogue Scale. * Linear regression analysis.

DISCUSSION

The present study aimed to investigate the effects of disease activity on body awareness and CS in patients with axSpA. This study's results showed that high disease activity adversely affected body awareness and CS. As well as, disease activity is an important determinant of CS in patients with axSpA. As the disease activity increased, CS and pain severity deteriorated.

A study involving healthy individuals reported an inverse association between body awareness and pain intensity and emotional state.[14] In older adults, chronic musculoskeletal pain and cognitive impairment are reduced body awareness.[8] Hider et al.[25] reported that body totality was associated with disease acceptance in patients with ankylosing spondylitis and that body image, including body totality and body self-consciousness, was inversely related to depression. Another study examining the relationship of physical activity level with body awareness and balance showed that physical activity level is associated with body awareness in patients with ankylosing spondylitis.[26] About 50% of ankylosing spondylitis patients reported discomfort about their appearance by Ward et al.[27] study. A brief report showed high disease activity negatively affected catastrophic thoughts, body awareness, and kinesiophobia in patients with ankylosing spondylitis.[28] The present study showed that patients with high disease activity have poorer body awareness compared to low disease activity, which is consistent with Karaca et al.[28] study. In addition, in present study, CRP level of HG is higher compared to LG. The BASDAI scores ≥ 4 with high CRP levels may indicate poor body awareness. In the few studies conducted on patients with axSpA related to body awareness, the present study would improve our knowledge of body awareness in treatment and management of AS.

Previous studies in which the prevalence of CS for axSpA was reported ranged from 45% to %57.[4,6,29-32] Another study reported that CS rates were 45.1% for axSpA and that the frequency of severe forms of CS was higher in patients with axSpA than in healthy individuals.[30] In a study including different rheumatic diseases, authors reported that CS syndromes were present in almost half the patients: 45% of axSpA, 41% of rheumatoid arthritis, 62% of osteoarthritis, and 94% of fibromyalgia patients.[29] The present study detected clinical CS in 48.4% of patients with axSpA, which is consistent with the literature. In addition, the study determined that patients having high disease activity (also high CRP levels) showed two times more common clinical CS compared to low disease activity. Clinical CS is a common condition in patients with axSpA and should be considered in treatment management and patient follow-up.

Kieskamp et al.[6] showed that CS, specific illness perceptions and obesity were all independently associated with BASDAI. Another study reported that CS adversely affects disease activity in axSpA.[30] Sariyildiz et al.[31] confirmed that worse disease activity, more enthesal involvement, and anxiety independently predict the development of CS in axSpA. Unlike these studies, Guler et al.[29] did not find a relationship between CSI score and disease activity in patients with axSpA. The present study found patients with axSpA with high disease activity have higher CS scores than those with low disease activity. In addition, the results of the regression analysis performed in the present study showed that CS and disease activity were moderately associated. The disease activity may predict the presence and severity of CS in patients with axSpA, which is consistent with the previous studies. As the disease activity increases, the severity of CS is also increased.

Study Limitations

The study has some limitations. Firstly, patients' psychological states weren't evaluated in this study, but body awareness and CS may be affected by psychological factors. Secondly, we did not evaluate neuropathic pain profiles of patients, which may be involve the CS. An important strength of our study is that body awareness is assessed in detail and to investigate relationship of disease activity with body awareness and CS in patients with axSpA. Future studies may assess the effects of body awareness therapies on disease activity, health-related quality of life, psychological and emotional status, and CS.

CONCLUCION

Our study provides comprehensive evidence of the relationship between disease activity, body awareness, and CS in patients with axSpA. This study is focused on body awareness and disease activity in patients with axSpA, which are missing in the literature. Early detection of impaired body awareness and CS would help in planning treatment and management of axSpA. In addition to pharmacological treatments, nonpharmacologic treatments such as exercises therapy, pain-coping strategies, and cognitive behavioral therapies, body awareness therapy may reduce pain and CS, and increase the body awareness. Physicians should also consider a multimodal biopsychosocial perspective in patients with high disease activity.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Medipol University Non-interventional Clinical Researches Ethics Committee (Date: 11.04.2023, Decision No: 44).

Informed Consent: Written consent was obtained from the patient participating in this study.

Referee Evaluation Process: Externally peer reviewed.

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

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Author Contributions: All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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