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ORIGINAL ARTICLE

Case Control Study

Effects of illness perception on negative emotions and fatigue in chronic rheumatic diseases: Rumination as a possible mediator

Yanxia Lu, Xia Jin, Li-Wei Feng, CSK Tang, Michelle Neo, Roger C Ho

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Abstract

BACKGROUND

Illness perception has long been hypothesized to be linked to psychological well-b eing in patients with rheumatic diseases, although substantial evidence is lacking, and the contribution of ruminative coping style to this relationship is unclear.

AIM

To investigate the roles of illness perception and rumination in predicting fatigue and negative emotions in patients with chronic rheumatic diseases.

METHODS

Illness perception, rumination, fatigue and negative emotions (*i.e.* depression, anxiety and stress) were assessed by the Illness Perception Questionnaire-Revised, Stress Reactive Rumination Scale, Multidimensional Assessment of Fatigue, and the Depression, Anxiety and Stress Scale respectively. Multivariate regression analysis, the Sobel test, and the bootstrap were used to identify the mediating effect of rumination.

RESULTS

All five subscales of illness perception, including perceived illness identity, chronicity, cyclical nature, consequences and coherence of illness, were significantly

associated with fatigue and negative emotions. In mediational analysis, rumination was found to mediate three components of illness perception (the identity, cyclical nature and consequences of illness) and negative emotions/fatigue.

CONCLUSION

Perceived identity, cyclical nature, and consequences of illness are significantly associated with fatigue and negative emotions in patients with chronic rheumatic diseases and these associations are mediated by rumination. Our findings suggest that psychological intervention should target rumination to improve physical and emotional well-being of patients with chronic rheumatic diseases.

Key Words: Fatigue; Illness perception; Negative emotions; Rheumatoid arthritis; Rumination; Systemic lupus erythematosus

Core Tip: The present study investigated the association of multiple components of illness perception and psychological outcomes (fatigue and negative emotions) in patients with chronic rheumatic diseases, as well as the potential mediating role of rumination in this relationship. The results showed that perceived identity, chronicity and consequences of illness were significantly associated with fatigue and negative emotions, and these associations were mediated by rumination. Identification of the mediating role of rumination has important implications clinically for developing cognitive interventions for patients with rheumatoid arthritis and systemic lupus erythematosus.

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INTRODUCTION

Rheumatic diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), are autoimmune inflammatory conditions that result not only in poor physical health but also in unfavorable mental well-being, including fatigue[1] and negative emotions[2,3]. In previous research, RA has often been evaluated together with SLE because these two conditions are similar in female predominance, pathology and treatment[4-6]. In a literature review of Eastern and Western studies[7-9], British patients with RA were four times more likely to be anxious and twice as likely to develop depressive symptoms than the general population[9]. In the United States, depression, anxiety, stress and anger in patients with SLE were associated with the exacerbation of lupus symptoms[10]. In Asia, approximately 26% of patients with RA had anxiety, 15% had depression and 11% had mixed depression and anxiety according to a study conducted in Singapore[8]. Fatigue is defined as extreme and persistent tiredness, weakness or exhaustion experienced in the absence of any excessive expenditure of effort[11]. Fatigue is a physical health outcome commonly reported by patients with RA and SLE; 53% to 81% of patients with SLE experience fatigue[12-14] and 42% to 98% of patients with RA experience fatigue[15-17]. Fatigue has been considered the most severe symptom experienced by patients with SLE[12] and is second to pain as the most severe symptom in patients with RA[17]. The above findings prompted liaison psychiatrists to explore psychological mechanisms that may be associated with negative emotions and physical fatigue in RA and SLE. Based on the Common-Sense Model of Self-Regulation (CSM)[18,19], illness perception may be one potent underlying factor. Ruminative copying style is proposed to be a potential mediator of the association between illness perception and physical and mental health status[20,21], although substantial evidence is lacking regarding this relationship in rheumatic diseases. The present study thus focuses on the roles of illness perception and rumination in negative emotions and fatigue in RA and SLE patients.

Negative emotions

Negative emotions such as depression, anxiety, and stress are common among patients with rheumatic diseases. Among them, depression is considered the leading cause of disease-related disability around the world[22]. The symptoms of depression involve depressed mood (feeling sad, irritable, empty), a

loss of pleasure or interest in activities, feelings of excessive guilt or low self-worth, hopelessness about the future, thoughts about dying or suicide, disrupted sleep, changes in appetite or weight, feeling especially tired or low in energy, poor concentration, and cognitive impairment. Especially when frequently recurrent or with moderate to severe intensity, depression may become a serious health condition leading to disabilities in work, school and family functions and even suicide which is the 4th leading cause of death among 15-29-year-old individuals. The onset of depression is a result of the complex interaction of biological, psychological, social, and environmental factors. The core brain regions involved are the prefrontal cortex (PFC) and subcortical limbic brain regions such as hippocampus, amygdala, and nucleus accumbens. Clinical and basic studies have shown that the synergistic effects of genetic factors, environmental factors, and developmental stages lead to disturbances in the activities of the abovementioned brain regions and brain networks, including the stress response system dominated by the hypothalamic-pituitary-adrenal axis; the glutamate/gamma-aminobutyric acid neurotransmitter system; microglia and inflammatory factors, promoting neurotrophic and nerve regeneration; and abnormality in the brain-gut axis and other multsystem molecular network activities. In addition, epigenetic modification alterations are important mechanisms for translating the influence of environmental factors into specific gene expression patterns and may be important biological pathways by which depression exerts persistent effects on psychological development and neurodevelopment. A prominent role of the ventromedial prefrontal cortex (vmPFC) in emotion is achieved by inhibiting amygdalar output[23]. Patients with damage to the vmPFC are less likely to develop depression[24]. Consistently, temporary inactivation of the rat vmPFC reduces depression-like symptoms[25]. In patients with depression, decreased volume and altered activity patterns of the vmPFC have been observed, highlighting how frontal lobe dysfunction affects these patients' memory and emotional learning capacity. Studies suggest that the vmPFC is also fundamental to the pathophysiology of anxiety disorders[26] and posttraumatic stress disorder[27]. Due to these biological mechanisms, rumination intensifies in patients with depression, especially among those who possess the notion of low self-worth.

Illness perception

Moss-Morris *et al*[59] categorized illness perception into nine dimensions: perceived illness identity, illness chronicity, cyclical nature of illness, consequences of illness, personal control over illness, treatment control of illness, illness coherence, emotional representation, and causes of illness. Specific to rheumatic diseases, it is consistently evident that illness perception has emerged as an important contributor to physical and mental health[28-30]. For example, illness perception in RA patients is associated with disease severity including long disease duration, more disability, and higher disease activity[30]. Illness perception outweighs the impact of the actual disease status in predicting psychological adjustment in patients with RA[31]. Furthermore, the perceived consequences of illness consistently predicted depression in patients with RA[32]. Similarly, patients with SLE who have little understanding of their illness tend to perceive that their illness can result in negative life consequences, and they report higher levels of depression[33]. Hawro *et al*[34] speculated that inadequate perception of the symptoms and disease course of SLE and required treatment may lead to psychological consequences such as maladaptive coping and anxiety disorder.

Rumination

The impact of rumination on the well-being of patients with rheumatic diseases has received little attention. Rumination has been defined as the tendency to think repetitively and passively about negative emotions, focusing simultaneously on symptoms of distress[35-37]. Rumination or repetitive negative thinking is a transdiagnostic process in psychiatric disorders because more rumination on experienced traumas or negative emotions is associated with longer-term and more severe psychiatric symptoms and emotional problems[38-40]. Consequently, the link between rumination and negative emotions in psychiatric patients is well established. In rheumatic diseases, rumination is one of the most important predictors of psychological maladjustment in adolescents with juvenile idiopathic arthritis [41]. Patients with SLE were found to ruminate more frequently than healthy persons but less frequently than patients with depression[42-46]. Furthermore, mindfulness mediation-based intervention, which prevents excessive rumination and facilitates acceptance, is suggested to improve psychological distress in RA and SLE patients[47-49]. A potential mediator of negative emotions and fatigue: Rumination. The psychological mechanisms that link rumination to illness perception and well-being have been examined in medically ill patients. Soo *et al*[50] proposed that chronic illnesses may trigger rumination by activating the individual's illness schema and perception. Previous studies have confirmed that rumination is associated with negative illness perception and negative emotions[2,7,17,20,31,33,35,40,41,51-53]. A recent review demonstrated that rumination is a mediator of poor physical health through intensified perception of somatic symptoms in medical patients[21]. Recently, various models have been proposed to explain the interaction between these variables in other chronic medical illnesses. In one such model, Closa *et al*[20] purported that perceived stress mediated the relationship between anger rumination and cardiac symptoms in patients undergoing angiography. They argued that intervention should reduce perceived stress and advocated a reappraisal and support-seeking approach to avoid a ruminative coping style. Similarly, another study suggested that rumination may result in higher

perceived pain levels in patients with low back pain and fibromyalgia[54]. It is not clear how much of the variance in negative emotions and fatigue may be explained by rumination and illness perception in patients with RA and SLE. Understanding the psychological mechanisms that link rumination, illness perception and well-being has important implications for developing psychological interventions for patients with RA and SLE.

Aims of the present study

The current study aims to assess the relationship between illness perception, rumination, and negative emotions and fatigue in patients with chronic rheumatic diseases, particularly RA and SLE. Specifically, the role of rumination in explaining the potential associations between illness perception, negative emotions and fatigue was investigated. Rumination was assessed by the Stress Reactive Rumination Scale (SRRS), which was developed to rapidly assess rumination in clinical settings and can assess rumination that is not confounded by depressive symptoms. Additionally, we examined the association between negative emotions and fatigue and specific domains of illness perception by Pearson correlation analyses. Distinguishing between different components of illness perception is important because we can identify specific components that are associated with negative emotions/fatigue and become future therapeutic targets in psychotherapy for patients with chronic rheumatic diseases.

Hypotheses of this study. First, it was hypothesized that illness perception (including identity, chronicity, cyclical nature, and consequences of illness) and rumination are associated with a greater severity of negative emotions and fatigue in patients with chronic rheumatic diseases. Second, we hypothesized that rumination may mediate the relationship between illness perception and negative emotions or between illness perception and fatigue.

MATERIALS AND METHODS

Characteristics of participants

The participants were adult outpatients with RA or SLE who were followed up at the Rheumatology Clinic, National University Hospital, Singapore. Patients who fulfilled the American College of Rheumatology classification criteria for RA[55] or SLE[56] and were older than 21 years of age were eligible for the study. The inclusion criteria were as follows: (1) 21 years old and above; (2) Able to understand and respond to questions in English and/or Mandarin; (3) Having RA or SLE with any severity or pharmacotherapy duration; and (4) Routinely followed up at the Rheumatology Clinic of National University Hospital, Singapore. The exclusion criteria were severe cognitive deficits (*e.g.*, intellectual disability or dementia) and major psychiatric illnesses, such as schizophrenia, substance use disorder or bipolar disorder. Consecutive patients were approached and those who met the inclusion criteria were recruited. The response rate was 85%. No eligible participants had severe cognitive deficits or major psychiatric illnesses. The study was approved by the National Healthcare Group Ethics Committee (reference number: DSRB E/10/228) and written informed consent was obtained from all participants.

Demographic questionnaire

The demographic questionnaire included the participants' gender, age, ethnicity, education level, marital status, and occupation. Their medical records were referred to for information about the duration of the disease, use of medications and hospitalization of the patients.

Illness Perception Questionnaire-Revised (IPQ-R)

The Illness Perception Questionnaire-Revised (IPQ-R) scale has three sections and assesses total nine domains of illness perception as perceived by patients. The 70-item IPQ-R has already been validated in rheumatic diseases[57,58] and other medical illnesses[59,60]. Section one is the identity subscale (14 items, score range: 0-14), in which patients responded using a binomial scale of 0 (no) and 1 (yes). Patients were asked whether they experienced a list of specific symptoms, including pain, sore throat, nausea, breathlessness, weight loss, fatigue, stiff joints, sore eyes, wheeziness, headaches, upset stomach, sleep difficulties, dizziness, and loss of strength. If patients responded yes to a symptom, they were asked whether they thought this symptom was related to RA or SLE. In section two, patients responded using a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). This section assesses patients' beliefs according to seven subscales: (1) The chronicity of illness (6 items, score range: 6-30); (2) The cyclical nature of illness (4 items, score range: 4-20); (3) The consequences of illness (6 items, score range: 6-30); (4) Personal control over illness (6 items, score range: 6-30); (5) Treatment control over illness (5 items, score range: 5-25); (6) Coherence of illness (*i.e.*, consistency of symptoms and easy understanding of illness; 5 items, score range: 5-25)); and (7) Emotional representation (perception of negative emotions generated by the illness; 6 items, score range: 6-30). Higher scores on the chronicity and consequences subscales indicate a stronger belief that the illness is chronic and has greater consequences on the patients' quality of life[60]. Higher scores on the personal control and

treatment control subscales indicate that patients believe they have a greater degree of control over their illness and that the treatment is more effective. Illness coherence measures how well the patients understand their illness, with higher scores denoting greater understanding[60]. As the subscale of emotional representations contained items that overlapped with the Depression, Anxiety and Stress Scale-21 which was administered specifically to the participants to assess their emotional status, this subscale was not included in the assessment of this study. The third section consists of items on perceived causes of illness. This section was omitted as suggested for studies on rheumatic diseases[57], considering that the etiology for RA and SLE is currently still unknown. This scale was established to have good internal reliability in previous studies[59]. The internal reliability of the subscales in our study is listed as follows: Identity of illness (Cronbach's α = 0.73), chronicity of illness (α = 0.83), cyclical nature of illness (α = 0.82), consequences of illness (α = 0.77), and illness coherence (α = 0.79). Two subscales with Cronbach's α less than 0.7, personal control over illness (α = 0.580) and treatment control over illness (α = 0.557), were removed from the analyses. Thus, we included five components of illness perception in the analyses.

Stress Reactive Rumination Scale (SRRS)

The development and initial validation of the SRRS in psychological and medical settings has been described elsewhere[61,62]. The SRRS was developed by Robinson and Alloy (2003) to rapidly assess rumination in clinical settings. In addition to assessing the cognitive tendency to focus on negative attributions and inferences that comprise the negative inferential style in response to major life stressors [62], the SRRS can assess rumination that is not confounded by depressive symptoms, which is a limitation of many other self-report rumination scales[61]. In this scale, 25 items assess an individual's rumination in response to a stressful event in the previous week. The participants were instructed that the "stressful event" referred to their rheumatic disease (*i.e.*, RA or SLE). The participants responded by giving a score between 0 (never) to 100 (always). The total extent of rumination was obtained by summting all of the scores (score range: 0-2500), with higher scores indicating more frequent rumination. The internal reliability of the scale was adequate (α = 0.89) in our study, and it was demonstrated to possess a one-month test-retest reliability of 0.71[63].

Multidimensional Assessment of Fatigue (MAF)

Fatigue can be measured by observers or self-reported by patients with chronic diseases[64-67]. Self-assessment of fatigue is important because the evaluation of fatigue by an observer may not correlate with the patients' self-assessment of fatigue[67]. The MAF is a 16-item measure that assesses 4 dimensions of fatigue including severity, distress, degree of interference in daily activities and duration of fatigue. Using the previous week as a time frame[68], the participants responded using an 8-point Likert scale ranging from 1 (not at all) to 8 (a great deal) for in the first fourteen items, with the last 2 items requiring multiple-choice responses. The Global Fatigue Index was obtained by the summation of all of the scores (scores range: 1 (no fatigue) to 50 (severe fatigue)), with greater scores indicating higher levels of fatigue. The MAF questionnaire demonstrated excellent internal reliability (α = 0.93) in this study.

Depression, Anxiety and Stress Scale-21

The DASS-21 measures three types of negative emotions including depression, anxiety, and stress[69]. The depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest, anhedonia, and inertia. The anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The stress scale assesses difficulty relaxing, nervous arousal, and state of being easily agitated, overreactive and impatient. A total score for negative emotions was obtained by the summation of all of the scores (score range: 0-126), with greater scores denoting higher levels of negative emotions. This scale demonstrated good to excellent internal reliability (depression subscale, α = 0.88; anxiety subscale, α = 0.82; stress subscale, α = 0.90; total scale, α = 0.93) in this study.

Statistical analyses

The data analysis was performed using Predictive Analytics Software Statistics version 18. All continuous variables met the assumptions of normality based on the Shapiro-Wilk test and linearity for path analysis. Continuous variables were compared using the independent sample t-test and are presented as the mean ± SD values. Discrete variables were compared using the chi-squared test and are presented as numbers and percentages. Pearson correlation analyses and univariate and multivariate linear regressions were conducted to examine the associations among illness perception, rumination, fatigue, and negative emotions. A 2-tailed $P < 0.05$ was defined as statistically significant. In our study, we applied the hypotheses of the mediation model published in the literature[70-73]. In Figure 1 Model A, the "c path" refers to a significant relationship between the predictor (X, illness perception) and the outcome (Y, negative emotions/fatigue), when indirect effects were not considered[72]. In Model B, the "a path" and "b path" refer to the relationship between X and Y, respectively, and the mediator (M)[31]. When M is included in the model, the relationship between illness perception and negative emotions/fatigue is mediated by M (rumination) and is assumed by the "c path".

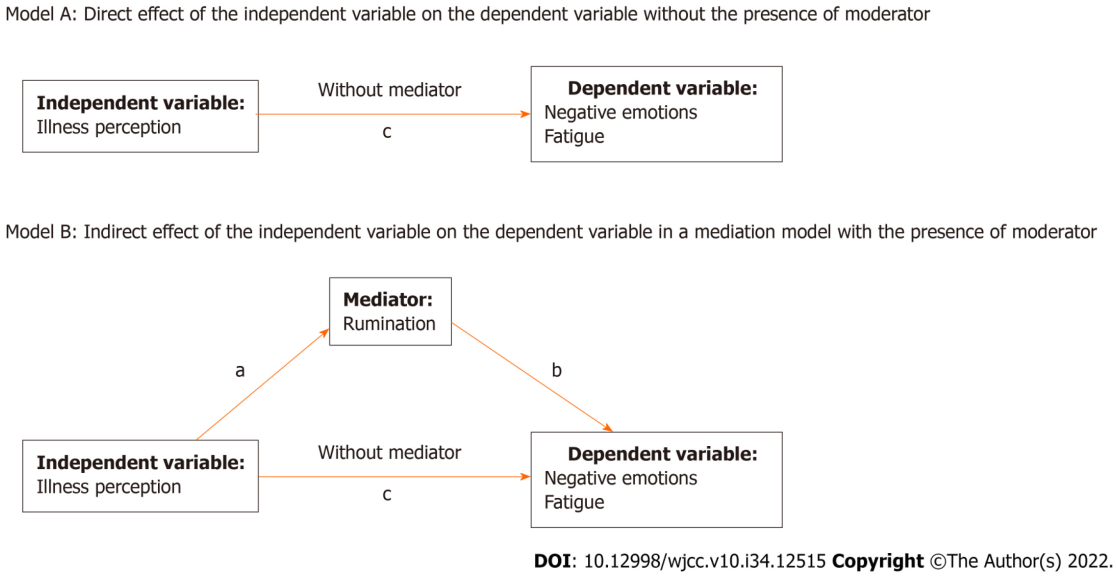

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Figure 1 Direct and indirect models of the relationship between illness perception and negative emotions/fatigue. In Model A, a relationship between illness perception and negative emotions/fatigue is assumed by "c". The "c path" refers to a significant relationship between the predictor (X) and the outcome (Y) when indirect effects were not considered. In Model B, the "a path" refers to the relationship between the predictor (X) and the mediator (M). The "b path" refers to the relationship between the mediator (M) and the outcome variable (Y). When M is included in the model, the relationship between illness perception and negative emotions/fatigue is mediated by M and is assumed by "c".

The Sobel test, which is one of the most well-known modern approaches to infer intervening variable effects [74-76], was performed to test this hypothesis. The Sobel test determines whether the reduction in the effect of illness perception, after including rumination in the model is statistically significant. A significant reduction implies that rumination exerts a mediating effect in the model. Then, the two-tailed z-test of the hypothesis that the mediated effect of rumination equals zero in the study population was performed [Z value = a × b/SQRT (b2 × sa2 + a2 × sb2)]. Despite the wide usage of the Sobel test, some researchers propose that it should be frequently used as a supplement to the Baron and Kenny approach rather than instead of it, and simulation research shows that bootstrapping, which is highly recommended for small sample sizes, as in the current study, may be more powerful than the Sobel test and the causal steps approach to testing intervening variable effects[77,78]. A series of bootstrapping procedures were performed using the SPSS INDIRECT script to verify the results of the Sobel test, although no requirements were made to report the results of both methods[74]. A bootstrap sample size of 5000 was used for this study.

RESULTS

Demographics and clinical symptomatology of chronic rheumatic diseases

Fifty-three adult patients diagnosed with RA (n = 33, 62.3%) or SLE (n = 20, 37.7%) were recruited for this study. The sociodemographic and disease characteristics of these patients are shown in Table 1. No differences were observed in terms of gender proportions (P = 0.292), ethnicity (P = 0.116), marital status (P = 0.085), financial status (P = 0.445), duration of illness (P = 0.343) and hospitalization as a result of RA or SLE in the previous year (P = 0.141). Patients with SLE were significantly younger (P < 0.001), more educated (P = 0.046), and more likely to be employed (P = 0.007). Among all of the subjects, the most common complaints were stiff joints (83.3%), pain (79.6%) and fatigue (51.9%). The mean disease durations of patients with RA or SLE were 4.24 (SD: 4.30) and 4.87 (SD: 5.51) years. Almost all patients received long-term medication (93.9% for RA and 95.0% for SLE), and 21.2% of RA patients and 40.0% of SLE patients were hospitalized due to RA or SLE in the past year. Slightly more than half (52.8%) of the patients indicated moderate to extremely severe fatigue, and 50.9% of the patients indicated that concurrent fatigue caused moderate to extreme levels of distress. For negative emotions, the subscale scores were used to characterize the degree of severity relative to the population spanning mild, moderate, severe, and extremely severe categories. There were 30.2% patients who had moderate to extremely severe anxiety (anxiety subscale score ≥ 6). Approximately 24.5% and 13.2% of the patients reported moderate to extremely severe depressive symptoms (depression subscale score ≥ 7) and stress (stress subscale score ≥ 10), respectively.

Table 1 Sociodemographic and disease characteristics of patients with chronic rheumatic diseases

	RA	SLE	*t*-test or chi-squared test	*P* value
Overall *n* (%)	33 (62.3)	20 (37.7)		
Gender				
Male	7 (21.2)	2 (10.0)	χ^2 = 1.110, 1 df	0.292
Female	26 (78.8)	18 (90.0)		
mean age (SD)	61.12 ± 15.00	37.10 ± 13.52	*t* = 5.860	< 0.001
Ethnicity				
Chinese	26 (78.8)	11 (55.0)	χ^2 = 5.915	0.116
Malay	2 (6.1)	6 (30.0)		
Indian	4 (12.1)	2 (10.0)		
Others	1 (3.0)	1 (5.0)		
Education				
Primary school	14 (43.8)	3 (15.0)	χ^2 = 6.150	0.046
Secondary school	10 (31.3)	6 (30.0)		
Tertiary and university	8 (25.0)	11 (55.0)		
Marital status				
Married	24 (72.7)	10 (50.0)	χ^2 = 0.140	0.085
Single	9 (27.3)	10 (50.0)		
Employment				
Employed	19 (57.6)	16 (80.0)	χ^2 = 7.158	0.007
Unemployed	14 (42.4)	4 (20.0)		
Financial status				
Poor	3 (9.1)	1 (5.0)	χ^2 = 1.620	0.445
Average	26 (78.8)	14 (70.0)		
Good	4 (12.1)	5 (25.0)		
Duration of illness	4.24 ± 4.30	4.87 ± 5.51	*t* = 0.454	0.343
Receiving long-term medication				
Yes	31 (93.9)	19 (95.0)	χ^2 = 0.026	0.871
No	2 (6.1)	1 (5.0)		
Hospitalisation in the previous year as a result of RA or SLE				
Yes	7 (21.2)	8 (40.0)	χ^2 = 2.166	0.141
No	26 (78.8)	12 (60.0)		

Discrete variables (gender) were compared using the chi-squared test and df and χ^2 are presented in the table. Continuous variables were compared with independent sample t test and t values are presented. SLE: Systemic lupus erythematosus; RA: Rheumatoid arthritis.

Illness perception, fatigue, rumination and negative emotions

The levels of illness perception, rumination and negative emotions were compared in patients with RA and those with SLE using a 2-tailed t test, as shown in Table 2. Patients with RA and SLE reported comparable scores for perceived identity (P = 0.292), cyclical nature (P = 0.855), consequences (P = 0.188), and coherence of illness (P = 0.998); global fatigue index (P = 0.081); and depression (P = 0.416) and stress (P = 0.053). Patients with SLE had higher levels of perceived chronicity of illness (P = 0.008), rumination (P = 0.006) and anxiety (P = 0.041) than those with RA. As such, the RA and SLE groups were collapsed into one group for subsequent analyses.

Table 2 Components of illness perception, rumination and negative emotions in patients with chronic rheumatic diseases

	RA	SLE	*t*	*P* value
Various components of illness perception				
Perceived identity of illness	4.24 ± 2.24	4.40 ± 2.96	-0.220	0.827
Perceived chronicity of illness	17.21 ± 4.25	20.50 ± 4.05	-2.780	0.008
Perceived cyclical nature of illness	12.18 ± 3.25	12.35 ± 3.17	-0.184	0.855
Perceived consequences of illness	17.58 ± 4.14	19.15 ± 4.20	-1.335	0.188
Perceived illness coherence	15.30 ± 3.82	15.30 ± 3.10	0.003	0.998
Rumination	832.52 ± 470.09	1181.25 ± 355.13	-2.856	0.006
Global fatigue index	18.31 ± 9.71	23.02 ± 8.62	-1.781	0.081
Total DASS score	20.61 ± 19.81	32.20 ± 27.35	-1.785	0.080
Depression score	6.48 ± 7.50	8.30 ± 8.32	-0.820	0.416
Anxiety score	5.94 ± 5.93	10.40 ± 9.64	-2.092	0.041
Stress score	8.18 ± 8.51	13.50 ± 10.89	-1.983	0.053

SLE: Systemic lupus erythematosus; RA: Rheumatoid arthritis; DASS: Depression, anxiety and stress scale-21.

Correlation analysis between illness perception, rumination, and negative emotions and fatigue

Table 3 shows the positive correlations of the perceived identity of illness (fatigue: $P < 0.001$, negative emotions: $P < 0.001$), chronicity of illness (fatigue: $P = 0.046$, negative emotions: $P = 0.031$), cyclical nature of illness (fatigue: $P < 0.001$, negative emotions: $P < 0.001$), consequences of illness (fatigue: $P = 0.001$, negative emotions: $P < 0.001$), and rumination (fatigue: $P < 0.001$, negative emotions: $P < 0.001$) with fatigue and negative emotions. Coherence of illness was negatively correlated with fatigue ($P = 0.045$) and borderline correlated negative emotions ($P = 0.063$). Rumination was positively correlated with fatigue ($P < 0.001$), negative emotions ($P < 0.001$), illness identity ($P = 0.002$), chronicity ($P = 0.043$), cyclical nature ($P = 0.002$), and consequences ($P = 0.001$) and negatively correlated with coherence of illness ($P = 0.048$).

Mediating effect of rumination on the association between illness perception and negative emotions and fatigue by regression models

The mediation model in Figure 2 shows that the explanatory variables are the various components of illness perception, the mediating variable is rumination, and the outcome variable is fatigue. Three steps of the regression analysis were taken to analyze the mediating effect of rumination on the relationship between illness perception and fatigue. The first step showed that the three components of illness perception (identity of illness: $\beta = 0.422$, $P = 0.002$, cyclical nature of illness: $\beta = 0.416$, $P = 0.002$, and consequences of illness: $\beta = 0.443$, $P = 0.001$) significantly explained rumination. Two components of illness perception (chronicity of illness and illness coherence) failed to explain rumination ($P > 0.05$). The second step showed that rumination significantly affected fatigue ($\beta = 0.703$, $P < 0.001$). Finally, three components of illness perception (identity of illness: $\beta = 0.226$, $P = 0.039$, cyclical nature of illness: $\beta = 0.223$, $P = 0.040$, consequences of illness: $\beta = 0.174$, $P = 0.018$) were found to explain fatigue. After introducing rumination to the model, the regression coefficients of the three components of illness perception on fatigue were reduced but remained statistically significant (identity of illness, cyclical nature of illness, consequences of illness). The Sobel test demonstrated that there was a statistically significant mediating effect of rumination on the relationship between the three components of illness perception and fatigue (identity of illness: $Z = 2.96$, $P = 0.003$; cyclical nature of illness: $Z = 2.92$, $P = 0.003$; consequences of illness: $Z = 3.10$, $P = 0.002$).

The mediation model in Figure 3 shows that the explanatory variables are the various components of illness perception, the mediating variable is rumination, and the outcome variable is negative emotions. Three steps of the regression analysis were taken to analyze the mediating effect of rumination on the relationship between illness perception and negative emotions. The first step showed that the three components of illness perception (identity of illness: $\beta = 0.422$, $P = 0.002$, cyclical nature of illness: $\beta = 0.416$, $P = 0.002$, and consequences of illness: $\beta = 0.443$, $P = 0.001$) significantly explained rumination. The second step showed that rumination significantly affected negative emotions ($\beta = 0.626$, $P < 0.001$). Finally, the three components of illness perception (identity of illness: $\beta = 0.295$, $P = 0.013$, cyclical nature of illness: $\beta = 0.266$, $P = 0.025$, consequences of illness: $\beta = 0.264$, $P = 0.029$) explained negative emotions. After introducing rumination to the model, the regression coefficients of the three compo-

Table 3 Correlations among various components of illness perception, rumination, fatigue, and negative emotions among patients with chronic rheumatic diseases

Illness perception	Fatigue		Negative emotions		Rumination	
	r	*P* value	r	*P* value	r	*P* value
Identity of illness	0.482	< 0.001	0.507	< 0.001	0.422	0.002
Chronicity of illness	0.264	0.046	0.296	0.031	0.24	0.043
Cyclical nature of illness	0.477	< 0.001	0.48	< 0.001	0.416	0.002
Consequences of illness	0.451	0.001	0.489	< 0.001	0.443	0.001
Coherence of illness	-0.265	0.045	-0.257	0.063	-0.21	0.048
Rumination	0.703	< 0.001	0.626	< 0.001		

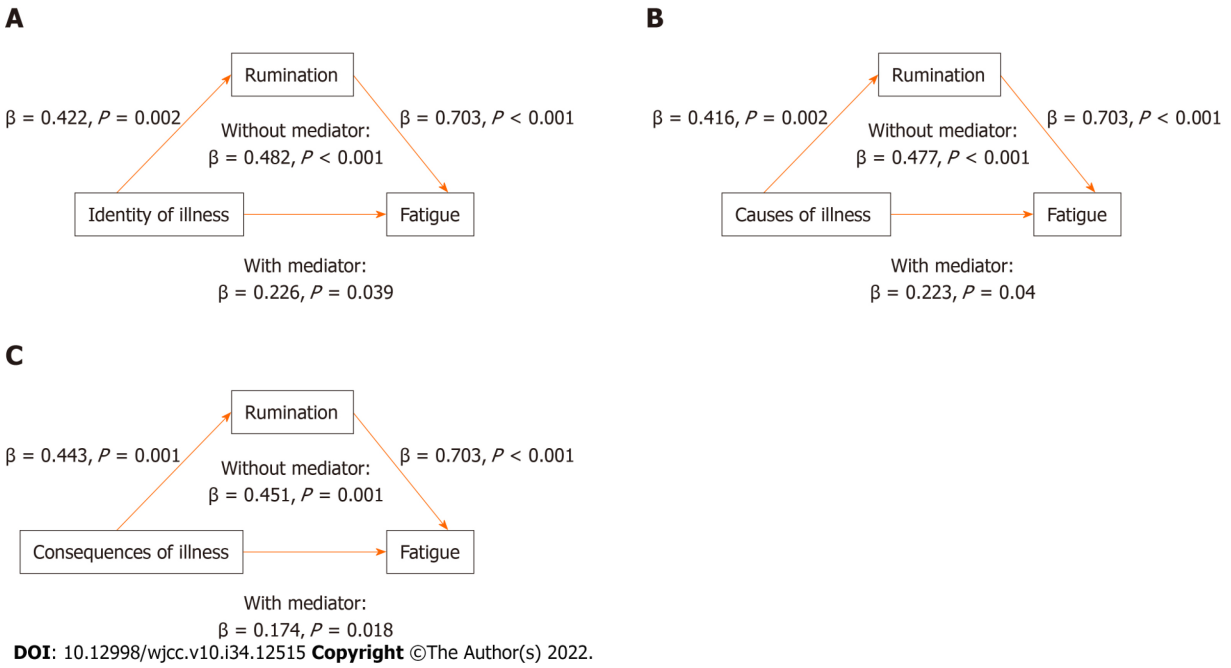

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Figure 2 Mediation models of the effect of rumination on the relationship between illness perception and fatigue. A: Identity of illness; B: Cyclical nature of illness; C: Consequences of illness.

nents of illness perception on negative emotions were reduced but remained statistically significant (identity of illness, cyclical nature of illness, consequences of illness). The Sobel test demonstrated that there was a statistically significant mediating effect of rumination on the relationship between the three components of illness perception and negative emotions (identity of illness: $Z = 2.64$, $P = 0.008$; cyclical nature of illness: $Z = 2.61$, $P = 0.009$; consequences of illness: $Z = 2.74$, $P = 0.006$).

Mediating effect of rumination on the relationship between illness perception and fatigue and negative emotions by Sobel tests and bootstrap analysis

The above analyses demonstrated the reduction in the effect of independent variables (*i.e.* identity, cyclical nature and consequences of illness), after including the mediator, rumination in the model, but the effect of the mediator remains significant. In Table 4, the Sobel test (the two-tailed z-test) shows that the mediation effects of rumination on identity, cyclical nature and consequences of illness and fatigue/negative emotions were significantly different from zero in RA/SLE patients ($P < 0.05$). These effects were further validated with bootstrap analysis which showed a significant indirect effect of illness identity on fatigue through rumination (point estimate = 0.457, 95%CI: 0.081-1.116). Likewise, rumination was a significant mediator for the relationship between illness identity and negative emotions. The bootstrap estimated indirect effect was 0.714 (95%CI: 0.102-2.029). Rumination was not a significant mediator for the relationship between causes or consequences of illness and fatigue and negative emotions (Table 5).

Table 4 Mediation effect of rumination on the relationship between illness perception and fatigue/negative emotions using the sobel test

	Fatigue		Negative emotions	
	Sobel z value	*P* value	Sobel z value	*P* value
Identity of illness	2.96	0.003	2.64	0.008
Chronicity of illness	1.71	0.086	1.67	0.096
Cyclical nature of illness	2.92	0.003	2.61	0.009
Consequences of illness	3.10	0.002	2.74	0.006
Coherence of illness	-1.50	0.135	-1.46	0.143

Table 5 Summary of bootstrap analysis showing the indirect effects of rumination on the three components of illness perception and fatigue and negative emotions

Independent variables	Mediator	Dependent variable	a path coefficient	b path coefficient	c path coefficient	c' path coefficient	Bootstrap biased correct indirect effects		
							Point estimate	Lower	Upper
Identity of illness	Rumination	Fatigue	0.422[b]	0.703[b]	0.482[b]	0.226[a]	0.457[a]	0.081	1.116
Cyclical nature of illness	Rumination	Fatigue	0.416[b]	0.703[b]	0.477[b]	0.223[a]	0.288	-0.097	0.984
Consequences of illness	Rumination	Fatigue	0.443[b]	0.703[b]	0.451[b]	0.174[a]	0.056	-0.251	0.465
Identity of illness	Rumination	Negative emotions	0.422[b]	0.626[b]	0.507[b]	0.295[a]	0.714[a]	0.102	2.029
Cyclical nature of illness	Rumination	Negative emotions	0.416[b]	0.626[b]	0.480[b]	0.266[a]	0.450	-0.134	1.826
Consequences of illness	Rumination	Negative emotions	0.443[b]	0.626[b]	0.489[b]	0.264[a]	0.088	-0.370	0.836

[a]$P < 0.05$.
[b]$P < 0.01$.

DISCUSSION

Discussion of primary findings

Although it is understudied, rumination is a common concept in mental health among adult patients with rheumatic diseases. A unique contribution of this study is the investigation of the potential mediating effects of rumination on the relationship between the specific components of illness perception and negative emotions/fatigue in patients with RA and SLE. The results are summarized as follows: Although patients with SLE were significantly younger, highly educated and more likely to be employed, they reported higher levels of perceived chronicity of illness, rumination and anxiety than patients with RA. In examining the association between individual components of illness perception and negative emotions/fatigue, all five components, including the identity, chronicity, cyclical nature, consequences and coherence of illness, were associated with a greater severity of negative emotions and fatigue in patients with RA and SLE. Rumination was associated with a greater severity of negative emotions and fatigue and was found to contribute a unique variance to fatigue and negative emotions. With respect to the mediational analysis, rumination mediated the relationship between specific components of illness perception (*i.e.*, identity, cyclical nature and consequences of illness) and negative emotions/fatigue; this finding is consistent with our hypothesis.

Interpretation of findings in the current literature

Based on the CSM[18,19], the direct and indirect effects of the five illness perception dimensions on the two psychological outcomes through total rumination were examined in this study. Overall, the results supported the general notion that illness perceptions play important roles in affecting psychological outcomes in the chronically ill population. These patterns of results are in line with results from a meta-

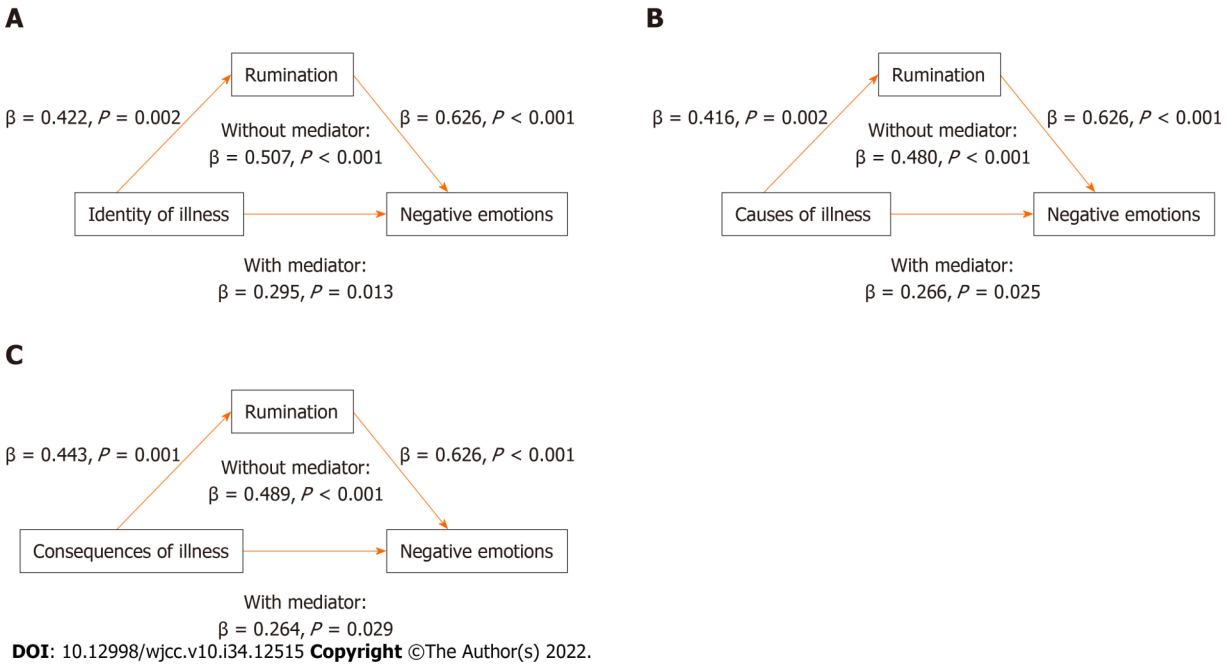

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Figure 3 Mediation models of the effect of rumination on the relationship between illness perception and negative emotions. A: Identity of illness; B: Cyclical nature of illness; C: Consequences of illness.

analytic review of illness representations and perceptions across disease groups[79] and suggest the important role that cognitions play in affecting disease outcome. It is notable that among the dimensions of illness perceptions, illness identity had the highest correlations with fatigue and negative emotions and was consistently significant in multiple mediational analyses performed in this study including regressions, Sobel tests, and bootstrap analysis. This concurs with some studies conducted on other disease groups that found perceived identity to play the most important role, among other dimensions, in predicting illness outcomes[80,81]. In the current study, both RA and SLE are autoimmune diseases that are systemic in nature, with the possibility that the immune system may attack many different cells, tissues, organs and systems of the body. Perceived identity could play a more salient role in affecting psychological outcomes in this case as patients may be monitoring certain signs and symptoms, which they ascribed to be part of their illness, as indicators of disease course and progression.

The results from our mediating analyses on rumination are, for the most part, similar to the findings from previous research in patients with chronic medical diseases[33,54]. The ruminative response to the identity, cyclical nature and consequences of RA or SLE contributes significantly to the mediational process. Rumination may likely cultivate negative emotions or fatigue by providing a reminder of the negative aspects of the identity, cyclical nature and consequences of RA and SLE. Importantly, rumination did not mediate the relationship between illness chronicity/coherence and negative emotions/fatigue, indicating that patients with RA and SLE may have accepted the chronic nature inherent to RA or SLE. In terms of the direct associations between rumination and negative emotions, other studies have found similar results [38,82]. Furthermore, rumination may affect immune function because a greater frequency of rumination was positively associated with higher total leucocyte and lymphocyte counts in older people[76]. Rumination may likely lead to inflammatory responses in patients with RA and SLE and may increase the levels of fatigue, although such postulation requires additional studies to confirm this hypothesis.

Clinical implications of this study

Illness perceptions are largely a subjective experience, and they may change according to new experiences or the course of the illness [83], suggesting that such cognitions are modifiable. The identification of rumination as the mediation factor has relevance for understanding the psychological mechanisms underlying negative emotions and fatigue and guiding psychological interventions for patients with RA and SLE. The results of the current study have several clinical implications. For example, the treatment of negative emotions and fatigue in patients with RA and SLE may focus on strategies specifically designed to modify ruminative responses to the identity, cyclical nature and consequences of the illness. Strategies for reducing rumination include functional analyses to help patients with RA and SLE realize that their rumination is unlikely to be helpful. The patients are advised to develop a more adaptive style of thinking and emotional processing[84] that may be beneficial as a buffer against negative emotions and fatigue for patients who are dealing with their illness perception. Other strategies include rumination-cued distraction, which involves training

patients with RA and SLE to use rumination as a cue to engage in other adaptive activities to distract themselves[85], to use problem solving[84] and to provide attention-training treatment with the purpose of enhancing cognitive control over rumination[86]. These strategies can be incorporated into cognitive behavior therapy (CBT), in which nonadaptive illness representations and ruminative thoughts can be challenged. The compatibility between the CSM and CBT has been highlighted by McAndrew *et al*[87]. In CBT, the clinician is interested in what is sustaining a problem. The SRM helps by identifying the nonadaptive illness representations so that treatment focusing on altering maladaptive behaviors and thoughts can proceed *via* CBT. There is currently evidence that patients' perceptions of their illness can be successfully altered by cognitive-based interventions, leading to improved outcomes. In a randomized control trial conducted by Petrie *et al* [88] for patients with myocardial infarction, it was found that after bringing forth significant positive changes in patients' views of their condition, there were improvements in functional outcomes as well. Patients in the intervention group felt that they were better prepared to be discharged from the hospital than those in the control group. They also returned to work at a significantly faster rate and reported fewer angina symptoms at the three-month follow-up. Thus, it is proposed that structured programs in the form of therapies be established in hospital chronic illness units. Such programmes could have a focus on cognitive restructuring or cognitive-behavioral therapies, seeking to modify patients' cognitions in adaptive ways. Patients could be trained to cope with their condition using helpful coping strategies so that the ill effects of ruminative coping could be avoided. Liaison psychiatrists and rheumatologists may also offer education and provide patients with information regarding the cause, prognosis and complications of RA and SLE to increase their understanding. Furthermore, mindfulness mediation-based intervention (MBIs) is suggested to prevent excessive rumination and facilitate acceptance and thus improve psychological outcomes in patients with RA and SLE[47-49]. Standard MBIs for patients with chronic disease include mindfulness-based stress reduction and mindfulness-based cognitive therapy which are usually led by certified instructors with a mental health background[89,90]. Several interventional studies also examined the efficacy of other adapted MBIs in RA patients, including the vitality training program [91], internal family systems[92], and mindful awareness and acceptance therapy[93]. A meta-analysis evaluated the efficacy of these MBIs on psychological outcomes in patients with rheumatic diseases and found that MBIs effectively improved depressive symptoms, psychological distress, and self-efficacy in these patients[47].

Limitations of this study

There are a number of limitations to this study. First, female and Asian patients were overrepresented in the sample. Therefore, our findings are preliminary and warrant replication in future studies, especially in other ethnic groups. A second limitation of this study was the sample selection because the current sample was limited to RA and SLE outpatients. Although the patients with RA and SLE reported similar scores on most subscales of illness perception, global fatigue index, and depression and stress, it is arguable whether the RA and SLE groups should be combined as one group for the analysis, as the SLE patients were younger, more educated, and more likely to be employed than the RA patients recruited in this study. The results generated from this study may thus not be identical to a group of patients with only RA or those with only SLE. Third, the sample size was small. Additional studies with larger sample sizes will be needed to confirm our results and analyze RA and SLE separately. Additionally, the relatively small sample size for this study could have led to less power. This has potential implications for mediational analyses[94,95]. Rumination may have played a greater mediating role in the relationship between illness perception and negative emotions/fatigue in patients with SLE if a larger sample size was available, as evidenced by their higher rumination scores. Fourth, we examined self-reported symptoms of negative emotions rather than DSM-IV-TR diagnoses based on a structured clinical interview. Our results therefore apply only to the role of rumination in the symptoms of depression and anxiety, not to the actual comorbidity of anxiety and depressive disorders. Fifth, the problems inherent to self-administered questionnaires could have affected the results in this study[88]. These problems may include the respondents' exaggeration, their reluctance to reveal private details, social desirability bias and recall bias. Finally, the cross-sectional findings suggest that rumination is a mediator explaining illness perception and negative emotions/fatigue; however, they provide no information concerning whether rumination is involved in the temporal progression of negative emotions or fatigue. Despite these limitations, we believe we have provided implicative data for future studies regarding the role of rumination in the well-being of patients with RA and SLE.

CONCLUSION

In conclusion, we found that illness perceptions played important roles in affecting psychological health in patients with RA or SLE, and rumination was a unique mediator between three components of illness perception, specifically the identity, cyclical nature and consequences of illness, and negative emotions/fatigue, further expanding the theories of CSM to rheumatic diseases and highlighting the important role of cognitions, which are fortunately modifiable, in affecting disease outcomes regulating

probably by inflammatory responses. Our results underscore the importance of incorporating interventions targeting rumination into psychological treatment for negative emotions and fatigue in patients with RA and SLE. Structured programs such as CBT and MBIs may be established by liaison psychiatrists and rheumatologists in hospital chronic illness units to modify patients' cognitions in adaptive ways and improve psychological well-being, functional and clinical-related outcomes, and working environmental adaptation after discharge.

ARTICLE HIGHLIGHTS

Research background

Although illness perception is proposed to be associated with psychological health in patients with rheumatic diseases, empirical evidence is lacking to support this hypothesis. Furthermore, the contribution of ruminative coping style to this relationship is unclear yet.

Research motivation

Psychological symptoms observed in patients with rheumatic diseases in clinical practice.

Research objectives

This study aimed to investigate the association of illness perception and fatigue and negative emotions in patients with chronic rheumatic diseases and the potential mediating effects of rumination.

Research methods

Illness perception, rumination, fatigue and negative emotions were assessed by the Illness Perception Questionnaire-Revised, Stress Reactive Rumination Scale, Multidimensional Assessment of Fatigue, and the Depression, Anxiety and Stress Scale respectively. Multivariate regression analysis, the Sobel test, and the bootstrap were used to identify the mediating effect of rumination.

Research results

All the subscales of illness perception were found significantly associated with fatigue and negative emotions. In mediational analysis, rumination mediated three components of illness perception (the identity, cyclical nature, and consequences of illness) and negative emotions/fatigue.

Research conclusions

Perceived identity, cyclical nature, and consequences of illness are significantly associated with fatigue and negative emotions in patients with chronic rheumatic diseases and these associations are mediated by rumination. Psychological intervention should target rumination to improve physical and emotional well-being of patients with chronic rheumatic diseases.

Research perspectives

Identification of the mediating role of rumination in the relationship between illness perception and negative emotions and fatigue has important implications clinically for developing cognitive interventions for patients with rheumatoid arthritis and systemic lupus erythematosus.

FOOTNOTES

Author contributions: Lu Y acquired the funding, performed data analysis and wrote the manuscript; Ho RC and Tang C designed the study and corrected the manuscript; Neo M performed the majority of experiments; and all authors reviewed and approved the final version of the manuscript.

Institutional review board statement: The study was approved by the National Healthcare Group Ethics Committee (reference number: DSRB E/10/228) and written informed consent was obtained from all participants.

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