Fatigue in Systemic Lupus Erythematosus: Contributions of Disease Activity, Pain, Depression, and Perceived Social Support

REBECCA L. JUMP, MICHAEL E. ROBINSON, ASHLEY E. ARMSTRONG, ELENA V. BARNES, KRISTIN M. KILBOURN, and HANNO B. RICHARDS

ABSTRACT. ***Objective.*** Pain and psychological distress are associated with fatigue, and social support may play a buffering role in the adjustment to a chronic disease. Investigations of the relationship between fatigue and disease activity in chronic diseases have provided inconclusive findings. The influence of medications on perceived fatigue remains unclear. We investigated the relationship between pain, depression, fatigue, and disease activity in patients with systemic lupus erythematosus (SLE).

Methods. Participants (n = 127) completed a psychosocial questionnaire during routine clinic visits. Hierarchical multiple regression analysis was conducted to predict the contribution of disease activity, pain, depression (Beck Depression Inventory), and perceived social support to fatigue.

Results. Disease activity as measured by SLE Disease Activity Index (SLEDAI) did not significantly predict self-reported levels of fatigue. Medication usage did not predict fatigue levels. Pain and depression were both unique positive predictors of fatigue. Controlling for pain and depression, perceived social support contributed negatively to the variance in fatigue scores, suggesting a buffering effect. This model reliably explained 42% of the variance in fatigue scores.

Conclusion. Our results emphasize the importance of depression, pain, and perceived social support in predicting reported fatigue levels in patients with SLE. In contrast, disease activity measured by SLEDAI does not appear to account for fatigue in SLE. Understanding the effect of psychosocial factors on fatigue in SLE may improve patient outcomes through psychosocial interventions aimed at reducing pain and increasing coping skills and social support. (J Rheumatol 2005;32:1699–705)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS FATIGUE DISEASE ACTIVITY
DEPRESSION PAIN SOCIAL SUPPORT

Systemic lupus erythematosus (SLE) is a prototypical autoimmune disease in which almost every organ may be affected. Diagnosis depends on multisystem involvement and the presence of autoantibodies, together forming the diagnostic criteria for SLE[1]. SLE exhibits considerable variation in disease manifestations between individual patients. The course of SLE generally involves periods of intense flares and periods of remission[2]. Fatigue is a commonly reported symptom in most chronic diseases[3] and one of the most widely reported symptoms in SLE. In a cohort of 223 SLE patients, 85.7% reported fatigue[4], and fatigue was the most disabling symptom in 53% of another cohort of 59 patients[5]. Fatigue is a primary contributor to functional disability[6] and visits to healthcare providers[7]. Several studies have found that 12% to 13% of patient visits to primary care physicians are related to a primary complaint of fatigue[7-9].

Although the etiology of fatigue in SLE is unknown, numerous physiologic and disease factors may account for fatigue in this population. Such factors include level of aerobic fitness[10], pain, clinical and laboratory features of SLE[4,11], coexistence of fibromyalgia (FM)[12], and poor sleep patterns[13]. Medications commonly used to treat autoimmune disease are also suspected to influence fatigue. However, apart from trials examining the efficacy of a particular drug, the effects of medications on subjective reports of fatigue in SLE patients remain poorly understood. In summary, a specific predictor of fatigue in SLE has not been established.

Studies investigating fatigue and disease activity have provided inconsistent findings for a possible biologic explanation for fatigue. Bruce and colleagues[14] found disease activity and damage accounted for only 4.8% and 4%,

From the Department of Medicine, Division of Rheumatology and Clinical Immunology, and Department of Clinical and Health Psychology, University of Florida, Gainesville, Florida; and AMC Cancer Research Center, Denver, Colorado, USA.

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R.L. Jump, MA; A.E. Armstrong; E.V. Barnes, MD; H.B. Richards, MD, Department of Medicine, Division of Rheumatology and Clinical Immunology; M.E. Robinson, PhD, Department of Clinical and Health Psychology, University of Florida; K.M. Kilbourn, PhD, MPH, AMC Cancer Research Center.

Address reprint requests to Dr. H.B. Richards, Division of Rheumatology and Clinical Immunology, PO Box 100221, 1600 SW Archer Road, University of Florida, Gainesville, FL 32610-0221.
E-mail: richahb@medicine.ufl.edu

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respectively, of the variance in fatigue scores in a sample of 81 lupus patients. Omdal and colleagues[15] reported no significant association between fatigue and disease activity as measured by the SLE Disease Activity Index (SLEDAI)[16] and numerous biological measures of disease or inflammation. In contrast, others[5,11,17] found significant positive associations between fatigue and disease activity. Although fatigue is commonly assumed to reflect disease activity, it often persists despite decreases in physiological markers of disease activity, suggesting that additional factors play a role in maintaining fatigue levels.

In recent years, psychosocial variables have been found to have compelling associations with fatigue levels in diseases such as SLE[4,13,15,17], rheumatoid arthritis (RA)[3,6], multiple sclerosis[18], and ovarian carcinoma[19]. In SLE the psychological aspects are poorly understood, despite estimated rates for neuropsychiatric manifestations ranging from 33% to 60% and affective disorders ranging from 50% to 80%[20]. Physical health problems, particularly those that are chronic, are considered a significant risk factor for depression[21]. Indeed, depression is the most common psychiatric problem in patients with SLE. In a review of the literature, Giang[22] found that 31%–52% of lupus patients who underwent a structured or semistructured interview were experiencing depression.

The benefits of social support on numerous aspects of physical and psychological health have been given extensive consideration in the chronic illness literature. Social support is negatively correlated with psychological distress and has been shown to influence health behaviors, such as seeking medical care[23]. McCracken and colleagues[24] found that good social support was related to perceptions of health in 46 adult SLE patients, and that seeking social support was associated with lower levels of pain, physical disability, psychological distress, and depression. Social support has been hypothesized to serve as a buffer during both acute and chronic stressors, thereby protecting the individual against immune dysregulation[25]. Several studies[4,20,26] have considered fatigue, mood, and social support variables in SLE patients; however, the direct relationship between fatigue and social support has not been determined.

Research on relationships among mood, symptom reports, and disease factors in SLE represents an underdeveloped area in the chronic illness literature. Fatigue is undoubtedly a significant source of disability and illness burden for SLE patients. The underlying etiology remains elusive, although numerous disease, lifestyle, and psychological factors have been proposed. Studies investigating the relationship between disease activity and subjective reports of fatigue have produced inconsistent results, whereas psychological factors, particularly depression, are consistently related to fatigue. Finally, factors that might predict lower levels of fatigue have not previously received attention.

We explored the relationships among pain, depression, and perceived social support in a sample of female patients with SLE. We addressed several limitations noted in other studies of fatigue in SLE. Our study includes a relatively large sample of female SLE patients, which eliminates the possible confounding effects of sex. It examines the concurrent relationships of pain and mood to fatigue, allowing investigation of the differential effects of these factors. By assessing social support and including it in the model, this study simultaneously considers factors that may exacerbate or buffer the negative influence of psychological and disease factors on fatigue.

MATERIALS AND METHODS

Participants consisted of 127 female patients with a diagnosis of SLE; i.e., ≥ 4 of the American College of Rheumatology (ACR) criteria for SLE[1]. They were consecutively recruited during visits to the University of Florida Autoimmune Disease Center clinic. The mean age was 40.6 years (SD 12.2). The ethnic composition was 48.8% (n = 62) Caucasian, 36.2% (n = 46) African American, and 15.0% other groups (n = 19). The mean years of education was 13.4 (SD 2.2). Duration of illness ranged from < 1 to 38 years (mean 9.0, SD 7.7). Tender point data were available for 109 participants. Twenty percent (n = 21) of participants were positive for at least 2 tender points and 9.2% (n = 10) had > 11 tender points and widespread pain, thereby meeting ACR criteria for FM syndrome[27].

Inclusion criteria were female sex, age ≥ 18 years, good command of English language, literacy, and a minimum education level of 8th grade. Due to the small number of men in the cohort (n = 8), they were eliminated from study in order to prevent possible confounding effects of sex on the variables of interest. Exclusion criteria included cognitive, emotional, or physical problems interfering with the patient's ability to provide informed consent. All study procedures were reviewed and approved by the University of Florida Health Science Center Institutional Review Board.

Information was also obtained for the use of the following nonpsychiatric medications: corticosteroids, antimalarials, nonsteroidal antiinflammatory (NSAID) medications and cytotoxic agents. In this cohort, 65.2% of participants reported current use of corticosteroids, 53% antimalarials, 44.3% NSAID, and 23.5% cytotoxic agents. Information was also collected on the use of antidepressants and benzodiazepines. Data were available on 104 out of 127 (82%) participants. Thirty-two percent (n = 33) of participants were using an antidepressant (67%), benzodiazepine (24%), or both (9%).

Measures. Detailed demographic data were collected during the initial assessment. Information related to medical diagnosis and disease duration was recorded. Participants completed a battery of psychosocial measures, including a series of visual analog scales (VAS) and measures of perceived social support and depression described below.

Fatigue. Fatigue was measured using a 100 mm VAS anchored with "No fatigue" and "Worst fatigue imaginable." The fatigue VAS has been compared to multiple-item fatigue measures and shown to be a valid measurement tool[17]. There is good correlation between the fatigue VAS and 2 multiple-item measures of fatigue, the Chalder Fatigue Scale[28] and the Fatigue Severity Scale[5], in SLE patients.

Pain. The pain VAS is a 100 mm line anchored by the descriptors "No pain" and "Worst pain imaginable." Adequate reliability and validity have been reported[29].

Depression. The Beck Depression Inventory (BDI)[30], a 21 item self-report measure, was used to assess the presence of cognitive, affective, and physiological symptoms of depression, yielding a total score. The BDI is well validated and widely used in medical populations. Cronbach's coefficient alpha in this sample was 0.90. The mean BDI score in this sample was 12.43 (SD 9.14).

Perceived social support. Social support was measured using the Perceived Social Support Scale[31], a 12 item measure employing a 7 point Likert response scale ranging from 1 (Very strongly disagree) to 7 (Very strongly agree). This scale addresses perceived support from family, friends, and significant others. Test-retest reliability was reported as 0.85 and Cronbach's coefficient alpha was 0.88[31]. Cronbach's alpha in this sample was 0.95. Scores ranged from 12 to 84 (mean 66.4, SD 17.2).

Disease activity. The SLEDAI[16] is a physician rating scale consisting of 24 descriptors associated with 9 organ systems. Clinical and laboratory measures of SLE activity are included. Items are weighted according to severity and life-threatening items receive greater weights. The weighted items are summed to obtain an overall score. The range for possible scores is 0–105. The SLEDAI has been validated and shown to be sensitive to changes over time[16,32,33].

Procedures. Following each participant's clinic visit, participants completed the psychosocial questionnaire packet, consisting of a battery of self-report written questionnaires. Instructions for the questionnaire were provided by a trained research assistant. Demographic and medication information was obtained from data collected during clinic visits.

RESULTS

Table 1 provides an overview of descriptive statistics for the variables analyzed in this study. Univariate descriptive statistics were used to examine mean fatigue ratings in comparison with other common symptoms across the sample. VAS ratings for fatigue, pain intensity, depression, anxiety, anger, and confusion revealed that fatigue was the highest rated symptom. As shown in Table 1, the mean rating for fatigue was 48.23 (SD 32.07), with scores ranging from 0 to 99. The next highest ratings were anxiety (31.87; SD 30.81) and pain (30.85; SD 28.72). Fatigue was rated significantly higher than all other symptoms assessed, including anxiety ($t\ (123) = 5.50$, $p < 0.001$).

To test for potentially confounding effects of medication usage on levels of fatigue, a binary variable was created to identify participants who were taking versus not taking a medication within the following categories: corticosteroids, antimalarials, NSAID, and cytotoxic agents. Groups (taking versus not taking) were then compared across medication categories using independent samples t tests. No significant differences were found for fatigue scores between participants who were taking versus those not taking corticosteroids, antimalarials, or cytotoxic agents. Participants using NSAID reported significantly higher levels of fatigue ($t = (110)\ -2.18$, $p = 0.032$) than those not using NSAID (mean 53.9 vs 40.1). An additional t test was conducted to examine pain levels in participants taking versus not taking NSAID. Participants using NSAID reported significantly higher levels of pain ($t = (109)\ -2.46$, $p = 0.015$) than nonusers (mean 35.6 vs 23.0). Analysis of covariance (ANCOVA) was conducted to determine whether the correlation between pain and fatigue accounted for the discrepancy between users and nonusers of NSAID on fatigue. When pain was entered in the model as a covariate, users and nonusers of NSAID did not differ significantly on fatigue scores ($F\ (1, 110) = 1.40$, $p = 0.239$, $\eta_p^2 = 0.013$). There were no group differences on pain scores for participants taking corticosteroids, antimalarials, or cytotoxic agents.

Use of antidepressant medications and benzodiazepines was also analyzed as a potential confounding factor contributing to fatigue scores. For the following analyses, a binary variable was created to identify participants who were taking versus not taking a psychotropic medication. Groups (taking vs not taking) were compared using independent samples t tests. No significant differences were found for fatigue, pain, SLEDAI, or perceived social support scores between participants who were taking versus those not taking antidepressants and/or benzodiazepines. Participants taking psychotropic medication reported significantly higher levels of depression ($t = (97)\ 3.78$, $p = 0.00$) than nonusers (mean 17.6 vs 10.2).

We conducted a correlational analysis to determine the associations among the study variables. Fatigue was moderately associated with pain intensity ($r = 0.43$, $p < 0.001$) and depression ($r = 0.48$, $p < 0.001$). Perceived social support was inversely correlated with fatigue ($r = -0.26$, $p < 0.01$). Perceived social support was also negatively correlated with depression ($r = -0.31$, $p < 0.01$), but not pain intensity. Neither fatigue nor mood symptoms were significantly associated with disease activity; however, pain was weakly positively correlated with disease activity ($r = 0.23$, $p < 0.05$).

Table 1. Study variables for the overall sample.

Variable	Range	Minimum	Maximum	Mean	SD
Fatigue VAS	0–100	0	99	48.23	32.07
Pain Intensity VAS	0–100	0	99	30.85	28.72
Anxiety VAS	0–100	0	100	31.87	30.81
Depression VAS	0–100	0	99	26.12	28.24
Anger VAS	0–100	0	68	8.72	14.23
Confusion VAS	0–100	0	96	18.0	24.02
SLEDAI Total	0–105	0	22	3.23	4.21
BDI	0–63	0	41	12.43	9.14
PSSS	12–84	12	84	66.4	17.19

VAS: visual analog scale, SLEDAI: SLE Disease Activity Index, BDI: Beck Depression Inventory, PSSS: Perceived Social Support Scale.

Results are summarized in Table 2. A second correlational analysis examined the relationship between duration of illness and the study variables. No significant associations were found, suggesting that illness duration is not related to pain and fatigue levels, perceived social support, or negative mood ratings in SLE.

Hierarchical regression analysis was used to examine the differential contributions of disease activity, pain, depression, and perceived social support to the prediction of fatigue. Results of the analysis are presented in Table 3. The overall model accounted for 42% of the variance in fatigue scores. Disease activity, entered in the first block, was not a significant predictor of fatigue scores, which was expected based on the nonsignificant correlation with fatigue. Pain intensity accounted for 21% of the variance ($F(2, 90) = 13.6$, $p = 0.00$). Controlling for disease activity and pain intensity, depression contributed an additional 15% of the variance in fatigue scores ($F(3, 89) = 18.4$, $p = 0.00$). Finally, controlling for disease activity, pain, and depression, perceived social support accounted significantly for an additional 4% of the variance in fatigue scores ($F(4, 88) = 15.8$, $p = 0.00$).

In the final model, standardized coefficients revealed that pain, depression (ps < 0.001), and perceived social support ($p < 0.05$) remained significant predictors of fatigue. Standardized beta coefficients for pain (0.374), depression (0.358), and perceived social support (–0.171) suggested that pain and depression are stronger independent predictors of fatigue than perceived social support. In sum, greater pain and depression and less social support explained close to half of the variance in perceived levels of fatigue in this cohort of patients with SLE.

In an attempt to account for the potentially confounding effects of FM on fatigue ratings, tender point scores were included in the analysis. Ratings for fatigue were missing for 3 of the 10 participants with tender point counts > 11, reducing the number of participants meeting FM criteria for tender point count to 7. The mean fatigue VAS rating for this group was 80.71 (SD 13.24) versus 45.36 (SD 32.06) for the 99 participants who did not meet the FM criteria for tender point count. These results suggest that the presence of FM does influence perceived fatigue scores; however, a larger sample would be necessary to determine the properties of this relationship. Given the low frequency of tender point counts above zero and the even smaller number of participants with > 11 tender points, it is unlikely that presence of FM would influence the overall results in this cohort of 127 participants. In order to substantiate this claim, the hierarchical regression analysis was repeated, excluding the 10 participants meeting FM criteria for tender point count. The results of the regression analysis remained unchanged, demonstrating that the presence of FM was not a significant confounder. Future studies with larger sample sizes would be helpful in clarifying the role of comorbid FM on fatigue scores in SLE patients.

Table 2. Inter-correlations among fatigue, disease activity, pain, depression, and perceived social support.

	Fatigue	SLEDAI	Pain	BDI	PSSS
Fatigue	—				
SLEDAI	0.129	—			
Pain	0.427^	0.229*	—		
BDI	0.484^	0.116	0.265**	—	
PSSS	–0.260**	0.061	0.052	–0.308^	—

* $p < 0.05$, ** $p < 0.01$, ^ $p < 0.001$ (2-tailed).

Table 3. Results of regression analysis: final model predicting fatigue with disease activity, pain intensity, depression, and perceived social support.

Block	Variables	R^2 Change	F Change	p
1	SLEDAI	0.025	2.37	0.127
2	SLEDAI Pain	0.206	24.17	0.000
3	SLEDAI Pain BDI	0.151	21.73	0.000
4	SLEDAI Pain BDI PSSS	0.035	5.37	0.023

DISCUSSION

We investigated the relationships of disease activity, pain, and psychosocial variables to fatigue in women with SLE. Our findings confirm that fatigue is an important feature in SLE: fatigue was the most highly rated symptom compared to other commonly reported complaints. Fatigue scores were significantly higher than the scores of all other assessed symptoms. These results are consistent with previous reports highlighting the prevalence and importance of this debilitating symptom in SLE. Our findings extend the existing knowledge by defining the differential contributions of disease activity, pain, and depression to fatigue, and by simultaneously considering the potential buffering effects of perceived social support.

The inclusion/exclusion criteria served to enhance reliability of the results by reducing factors that have the potential to distort the findings. However, such strategies can create bias that must be considered in the interpretation of results. Men were not included in the study due to the small number of male participants available. Given the paucity of research on men with SLE, we decided to eliminate the potential confounding effects of sex. It cannot be assumed that these results could be applied to a sample of male SLE patients, and future research is needed to elucidate sex differences among adjustment and symptom reporting in SLE patients. Further, the English fluency requirement precludes

the possibility of extending these results to groups of individuals whose English is not fluent. It is possible that poor communication due to insufficient language abilities is a risk factor for poorer outcomes and this needs to be addressed in future studies.

Symptom ratings within the study sample were quite variable, as indicated by the large standard deviations for mean symptom ratings. This suggests considerable heterogeneity within the cohort with regard to the perceived intensity of common physical and mood symptoms. Self-reported symptom ratings of fatigue and mood were not associated with disease activity, suggesting that mood and fatigue function independently of disease activity levels. The degree of variability found in this sample may reduce the extent to which interpretations of the results are likely to accurately reflect the cohort as a whole. Further research is required to determine whether these relationships differ within subgroups of the overall sample.

To control for potential effects of medications on fatigue levels, we tested for differences in fatigue scores between patients taking or not taking a number of common categories of medications used in SLE. We were particularly interested in the effects of corticosteroids on fatigue levels. Our results showed that individuals taking corticosteroids did not differ significantly from nonusers on subjective fatigue scores. In contrast, users of NSAID reported significantly higher fatigue levels than nonusers. Given that there is no basis to assume that increased fatigue is directly related to the effects of NSAID, we compared pain scores between NSAID users and nonusers. Similar to the results for fatigue, users of NSAID reported significantly higher levels of pain than nonusers. When controlling for pain scores, group differences between users and nonusers of NSAID were not found. Thus, we conclude that the discrepancy in fatigue scores between users and nonusers of NSAID can be explained by the high correlation between pain and fatigue, rather than a direct relationship between fatigue and NSAID use. Participants' use of antidepressants and benzodiazepines was also considered to control for effects of medications on fatigue. Results showed that individuals taking psychotropic medications did not differ significantly from nonusers on subjective fatigue scores.

Studies investigating the relationship between disease factors in SLE and fatigue have provided inconsistent results and are complicated by measurement issues. Numerous measures have been employed as a reflection of disease activity, ranging from more traditional physician-rated measures, such as the SLEDAI, to clinical and laboratory features, such as hair loss, lower lymphocyte count[34], and the presence of specific autoantibodies[35]. Further, 2 of the commonly used disease activity measures, the Systemic Lupus Activity Measure[36] and the European Consensus Lupus Activity Measure[37], include fatigue as a component score, which could result in an artificial relationship in analyses investigating the association between fatigue and disease activity. In contrast, the SLEDAI does not include a fatigue component.

The results of this study support the findings of Wang and colleagues[12] and Bruce and colleagues[14], who did not find a significant association between physician-rated disease activity and fatigue. This may be because fatigue is not directly associated with disease activity, and more accurately represents a manifestation of the individual's pain level, lifestyle (e.g., fitness level, sleep hygiene), and/or psychosocial factors. The strong association of psychosocial factors, including pain, to fatigue in this study lends credence to this possibility. Alternatively, it is possible that the SLEDAI is not an accurate measure of disease activity or that it is not comprehensive and does not adequately capture the component of disease activity that is associated with fatigue. Reports of significant fatigue persisting during periods of remission, or inactive disease, further obscure the disease-fatigue relationship. It is possible that underlying disease activity provides a pathophysiological basis for fatigue, and that pain and psychosocial factors serve to maintain fatigue independent of fluctuating disease status.

Results from our study showed that fatigue was positively associated with both pain and depression. Pain is among the most common reasons individuals seek medical care. Pain related to arthritis and arthralgias occurs in 95% of lupus patients at some point in the course of their illness[38]. The relationship between pain and fatigue in RA has been firmly established[3,6]. In debilitating diseases such as RA and SLE, reduced levels of physical activity could result in muscle deconditioning, which in turn may enhance levels of perceived fatigue[3,39,40] and pain.

Across a variety of medical and psychiatric conditions, depression is also strongly related to fatigue[41]. Several investigations have provided support for the role of psychological distress in the experience of fatigue in SLE. McKinley, *et al*[13] demonstrated that while disease activity did not exert a direct effect on fatigue, it did influence depression and sleep disruption, which in turn may wield a more direct effect on fatigue. In a cohort of 57 SLE patients, Omdal and colleagues[15] found that depression, personality states, and mental health status were significant predictors of fatigue. As with pain, fatigue appears to be a multidimensional construct with a significant psychological component.

Fatigue is a frequent complaint in many conditions involving chronic pain and is a common symptom of depression. Pain has also been consistently linked with negative mood states[42]. Thus, the potential for this symptom triad to emerge in SLE is significant. Despite the wide acceptance of the associations among pain, fatigue, and depression, the causal relationships within this symptom triad in chronic pain conditions and populations with chronic medical diseases remain poorly understood. It is possible

that the pattern of these relationships is highly variable across medical populations where different physiological mechanisms and psychosocial challenges exist. Although the cross-sectional design of our study did not allow elucidation of the causal relationships among these variables, our results offer insight into the differential contributions of pain and depression in predicting fatigue in SLE patients. The findings showed that pain and depression each contributed uniquely to the prediction of fatigue in this cohort.

Fatigue associated with a loss of energy, sluggishness, and lethargy that interfere with daily activities can be exacerbated by pain. Fatigue can also occur as a secondary symptom brought about by depression and sleep disturbances. Both pain and depression represent therapeutic targets for treatment that could result in reductions in fatigue. Nonpharmacologic and pharmacologic interventions can be integrated into a comprehensive treatment plan to reduce SLE related fatigue by reducing symptoms of depression and decreasing pain levels. While pain is often addressed through pharmacologic intervention, nonpharmacologic interventions, such as cognitive-behavioral pain management therapy, offer an adjunct to standard medical treatment. This treatment provides patients with increased understanding of the pain-mood relationship as well as skills to effectively manage their pain and enhance their activity levels. Further, the rates of depression in SLE are believed to be underestimated. Pharmacological and psychological treatments of depression offer the possibility of reducing secondary fatigue levels and improving quality of life in SLE patients.

Perceived social support has been linked with perceived pain[43] in patients with RA. However, few studies have considered the direct relationship between fatigue and perceived social support in SLE. We found a significant inverse relationship between fatigue and levels of perceived social support. In other words, lower ratings of perceived support were modestly associated with higher levels of perceived fatigue. This association has been previously reported with cancer patients. Patients with ovarian carcinoma and fatigue reported significantly lower social support as well as higher levels of depression and anxiety[19].

Taking into consideration the predominant levels of fatigue consistently reported by patients with lupus, additional understanding of the properties of their fatigue may help in identifying therapeutic targets for the treatment of this elusive source of debilitation. In particular, the biopsychosocial factors that exacerbate and maintain fatigue and the causal relationships within the pain-fatigue-distress triad deserve further investigation. The role of perceived social support and its buffering potential on the debilitating effects of pain, depression, and fatigue in SLE warrants additional study. Finally, in light of the detrimental impact of pain, depression, and fatigue on quality of life, the development of biopsychosocial interventions might offer meaningful advances and become part of a multidisciplinary approach to the treatment of SLE.

REFERENCES

1. Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271-7.
2. Parham P. The immune system. New York: Garland Publishing; 2002.
3. Belza BL, Henke CJ, Yelin EH, Epstein WV, Gilliss CL. Correlates of fatigue in older adults with rheumatoid arthritis. Nurs Res 1993;42:93-9.
4. Zonana-Nacach A, Roseman JM, McGwin G Jr, et al. Systemic lupus erythematosus in three ethnic groups. VI: Factors associated with fatigue within 5 years of criteria diagnosis. LUMINA Study Group. LUpus in MInority populations: NAture vs Nurture. Lupus 2000;9:101-9.
5. Krupp LB, LaRocca NG, Muir J, Steinberg AD. A study of fatigue in systemic lupus erythematosus. J Rheumatol 1990;17:1450-2.
6. Wolfe F, Hawley DJ, Wilson K. The prevalence and meaning of fatigue in rheumatic disease. J Rheumatol 1996;23:1407-17.
7. Andrea H, Kant IJ, Beurskens AJ, Metsemakers JF, Van Schayck CP. Associations between fatigue attributions and fatigue, health, and psychosocial work characteristics: a study among employees visiting a physician with fatigue. Occup Environ Med 2003;60:i99-104.
8. Wittchen HU, Lieb R, Wunderlich U, Schuster P. Comorbidity in primary care: presentation and consequences. J Clin Psychiatry 1999;60:29-36; discussion 7-8.
9. Cathebras PJ, Robbins JM, Kirmayer LJ, Hayton BC. Fatigue in primary care: prevalence, psychiatric comorbidity, illness behavior, and outcome. J Gen Intern Med 1992;7:276-86.
10. Tench C, Bentley D, Vleck V, McCurdie I, White P, D'Cruz D. Aerobic fitness, fatigue, and physical disability in systemic lupus erythematosus. J Rheumatol 2002;29:474-81.
11. Tayer WG, Nicassio PM, Weisman MH, Schuman C, Daly J. Disease status predicts fatigue in systemic lupus erythematosus. J Rheumatol 2001;28:1999-2007.
12. Wang B, Gladman DD, Urowitz MB. Fatigue in lupus is not correlated with disease activity. J Rheumatol 1998;25:892-5.
13. McKinley PS, Ouellette SC, Winkel GH. The contributions of disease activity, sleep patterns, and depression to fatigue in systemic lupus erythematosus. A proposed model. Arthritis Rheum 1995;38:826-34.
14. Bruce IN, Mak VC, Hallett DC, Gladman DD, Urowitz MB. Factors associated with fatigue in patients with systemic lupus erythematosus. Ann Rheum Dis 1999;58:379-81.
15. Omdal R, Waterloo K, Koldingsnes W, Husby G, Mellgren SI. Fatigue in patients with systemic lupus erythematosus: the psychosocial aspects. J Rheumatol 2003;30:283-7.
16. Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH. Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. Arthritis Rheum 1992;35:630-40.
17. Tench CM, McCurdie I, White PD, D'Cruz DP. The prevalence and associations of fatigue in systemic lupus erythematosus. Rheumatology Oxford 2000;39:1249-54.
18. Voss WD, Arnett PA, Higginson CI, Randolph JJ, Campos MD, Dyck DG. Contributing factors to depressed mood in multiple sclerosis. Arch Clin Neuropsychol 2002;17:103-15.
19. Holzner B, Kemmler G, Meraner V, et al. Fatigue in ovarian carcinoma patients: a neglected issue? Cancer 2003;97:1564-72.
20. Dobkin PL, Da Costa D, Fortin PR, et al. Living with lupus: a prospective pan-Canadian study. J Rheumatol 2001;28:2442-8.

21. Zeiss AM, Lewinsohn PM, Rohde P, Seeley JR. Relationship of physical disease and functional impairment to depression in older people. Psychol Aging 1996;11:572-81.
22. Giang DW. Systemic lupus erythematosus and depression. Neuropsychiatry Neuropsychol Behav Neurol 1991;4:78-82.
23. Cohen S. Psychosocial models of the role of social support in the etiology of physical disease. Health Psychol 1988;7:269-97.
24. McCracken LM, Semenchuk EM, Goetsch VL. Cross-sectional and longitudinal analyses of coping responses and health status in persons with systemic lupus erythematosus. Behav Med 1995;20:179-87.
25. Kiecolt-Glaser JK, McGuire L, Robles TF, Glaser R. Psychoneuroimmunology and psychosomatic medicine: back to the future. Psychosom Med 2002;64:15-28.
26. Austin JS, Maisiak RS, Macrina DM, Heck LW. Health outcome improvements in patients with systemic lupus erythematosus using two telephone counseling interventions. Arthritis Care Res 1996;9:391-9.
27. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33:160-72.
28. Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. J Psychosom Res 1993;37:147-53.
29. Price DD, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 1983;17:45-56.
30. Beck AT. Depression: Clinical, experimental and theoretical aspects. New York: Harper & Row; 1967.
31. Blumenthal JA, Burg MM, Barefoot J, Williams RB, Haney T, Zimet G. Social support, type A behavior, and coronary artery disease. Psychosom Med 1987;49:331-40.
32. Fortin PR, Abrahamowicz M, Clarke AE, et al. Do lupus disease activity measures detect clinically important change? J Rheumatol 2000;27:1421-8.
33. Petri M, Hellmann D, Hochberg M. Validity and reliability of lupus activity measures in the routine clinic setting. J Rheumatol 1992;19:53-9.
34. Wysenbeek AJ, Leibovici L, Weinberger A, Guedj D. Fatigue in systemic lupus erythematosus. Prevalence and relation to disease expression. Br J Rheumatol 1993;32:633-5.
35. Friedman AW, Alarcon GS, McGwin G Jr, et al. Systemic lupus erythematosus in three ethnic groups. IV. Factors associated with self-reported functional outcome in a large cohort study. LUMINA Study Group. Lupus in Minority Populations, Nature versus Nurture. Arthritis Care Res 1999;12:256-66.
36. Liang MH, Socher SA, Larson MG, Schur PH. Reliability and validity of six systems for the clinical assessment of disease activity in systemic lupus erythematosus. Arthritis Rheum 1989;32:1107-18.
37. Vitali C, Bencivelli W, Isenberg DA, et al. Disease activity in systemic lupus erythematosus: report of the Consensus Study Group of the European Workshop for Rheumatology Research. II. Identification of the variables indicative of disease activity and their use in the development of an activity score. The European Consensus Study Group for Disease Activity in SLE. Clin Exp Rheumatol 1992;10:541-7.
38. Schur P. General symptomology. In: Schur P, editor. The clinical management of systemic lupus erythematosus. 2nd ed. Philadelphia: Lippincott-Raven; 1996:10.
39. Robb-Nicholson LC, Daltroy L, Eaton H, et al. Effects of aerobic conditioning in lupus fatigue: a pilot study. Br J Rheumatol 1989;28:500-5.
40. Tench CM, McCarthy J, McCurdie I, White PD, D'Cruz DP. Fatigue in systemic lupus erythematosus: a randomized controlled trial of exercise. Rheumatology Oxford 2003;42:1050-4.
41. de Rijk AE, Schreurs KM, Bensing JM. Complaints of fatigue: related to too much as well as too little external stimulation? J Behav Med 1999;22:549-73.
42. Robinson ME, Riley JL. The role of emotions in pain. In: Gatchel RJ, Turk DC, editors. Psychosocial factors in pain: critical perspectives. New York: Guilford Press; 1999:74-87.
43. Parker J, Frank R, Beck N, et al. Pain in rheumatoid arthritis: relationship to demographic, medical, and psychological factors. J Rheumatol 1988;15:433-7.